CURRENT TOPIC

Reflux vomiting

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It is generally accepted that vomiting may occur by regurgitation of stomach contents as a result of gastro-oesophageal reflux or by evoking the emetic reflex causing contraction of the diaphragm, intercostal and anterior abdominal muscles, and forcible expulsions of gastric contents. Regurgitation of feeds because of gastro-oesophageal reflux is common in the young infant and in most, is little more than an inconvenience, with the affected infant healthy and thriving. In a few, however, regurgitation is symptomatic and is an important clinical problem resulting in failure to thrive, haematemesis, iron deficiency anaemia, oesophagitis, stricture formation, apnoea, obstructive airways disease, and aspiration pneumonia. In an important study Carré showed that 60% of infants who regurgitated stopped by 18 months of age with most symptoms settling by the age of 9 months.¹ Thirty percent of the infants he studied continued to have symptoms until at least 4 years of age and 10% developed one or more of the above complications. The prevalence of gastro-oesophageal reflux, and the frequency of the above complications is, however, difficult to ascertain as most infants who regurgitate do not come to medical attention and in nearly all, spontaneous resolution of their symptoms occurs. In a further study by Carré he suggested that one in 500 infants who attended a paediatric outpatient clinic had gastro-oesophageal reflux.² While the prevalence and incidence of complications of gastro-oesophageal reflux in infants might not be clear, a consideration of the anatomy and physiology of the motor activity of the oesophagus and stomach provides a framework within which the nature of reflux vomiting can be understood.

The anatomy and physiology of the oesophagus and lower oesophageal sphincter

The anatomy of the oesophagus is different to any other part of the gastrointestinal tract. The mucosa is composed of stratified squamous epithelium that is not resistant to gastric acid. The muscularis propria of the upper third is composed of striated muscle and it is only in the lower third that there is smooth muscle arranged into an outer longitudinal and inner circular layer with a nerve plexus between them. At the lower end of the oesophagus the muscle layer is modified into an area resistant to stretch, the lower oesophageal sphincter, which exhibits tonic high pressure. A number of fea-

tures account for this activity. The smooth muscle of the high pressure zone is different from that of the body of the oesophagus in terms of its compliance³ and sensitivity to polypeptide hormones.⁴ The length of the intra-abdominal segment of the oesophagus, the gastro-oesophageal angle, diaphragmatic crura, and mucosal flap valve, all form important accessory features for the maintenance of the effective function of the lower oesophageal sphincter.^{5 6}

Boluses of food are propelled to the stomach in 5-15 seconds by a series of events resulting in contraction of pharyngeal muscles, peristalsis of the body of the oesophagus and relaxation of the lower oesophageal sphincter. These events are controlled by two major elements. The brain stem, particularly the ninth, 10th, and 12th nerve nuclei control contraction of the striated muscle of the mouth, pharynx, and upper oesophagus, and the smooth muscle of the remainder of the body of the oesophagus. The nature of the lower oesophageal sphincter itself is important in maintaining the high pressure zone in addition to the effects of intrinsic and extrinsic innervation. In addition to the lower oesophageal sphincter relaxing in response to swallowing, the proximal stomach also relaxes to accommodate the ingested food. Coordinated contraction of the gastric antrum, pylorus, and duodenum results in the stomach emptying the ingested food into the small intestine.

Mechanisms of gastro-oesophageal reflux

Gastro-oesophageal reflux may occur because of a variety of defects of function and structure of the components described above. A difference in pressure between the stomach and oesophagus is clearly important as is failure of the mechanisms present that prevent the flow of gastric contents down such a pressure gradient. Recent studies suggest that a fall in lower oesophageal sphincter pressure to 0.4 kPa (3 mm Hg) or less must occur for gastric contents to be refluxed into the oesophagus.⁷

Episodes of reflux are associated with three groups of disorder of the lower oesophageal sphincter: (i) a low basal sphincter pressure, (ii) inappropriate sphincter relaxation, which is either synchronous or asynchronous with swallowing, or (iii) transient increases in intra-abdominal or gastric pressure alone or in combination with any of the above. In most normal individuals some gastro-oesophageal reflux occurs postprandially due to rises in intragastric

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pressure with reflux occurring when there is complete relaxation of the lower oesophageal sphincter as occurs with swallowing. Such refluxed material in the normal individual is rapidly cleared from the oesophagus by secondary peristalsis.

In children with symptomatic gastro-oesophageal reflux most reflux episodes are due to transient relaxation of the lower oesophageal sphincter, which is asynchronous with swallowing.^{8,9} However, in those that do not have symptomatic or complicated gastro-oesophageal reflux—that is, those who are healthy, thriving infants who usually regurgitate postprandially—the mechanism is different. In such infants reflux occurs most usually synchronously with swallowing but the lower oesophageal sphincter relaxation occurs for a longer period of time than in infants who do not have lower gastro-oesophageal reflux.⁹ Thus it would seem that their reflux is an exaggeration of the physiological reflux that occurs in normal individuals during and after eating. Low basal lower oesophageal sphincter pressures are an unusual association with gastro-oesophageal reflux and in two studies were only found in those with severe oesophagitis or neurological disorders.^{8,9} Thus the idea of a 'lax cardio-oesophageal sphincter' commonly being responsible for gastro-oesophageal reflux is not borne out by scientific study.

Whether oesophagitis occurs is dependent on the ability of the infant to clear the oesophagus of refluxed gastric acid. In infants who only 'spit up', peristalsis of the oesophageal body is the same as in control infants and refluxed acid is cleared promptly. In those who have symptomatic gastro-oesophageal reflux and transient inappropriate or asynchronous lower oesophageal sphincter relaxation the amplitude of both primary and secondary peristaltic waves are reduced and acid clearance times prolonged.⁹ These findings are most pronounced in infants with severe oesophagitis where in addition, low amplitude bizarre multi-peaked waveforms are seen, which are reminiscent of those occurring in neuropathic forms of intestinal pseudo-obstruction. Measurement of oesophageal transit shows that delayed oesophageal acid clearance in patients with oesophagitis is due to a disorder of oesophageal propulsion.¹⁰ In simultaneous motility-barium clearance studies low amplitude and bizarre peristaltic waves result in retrograde flux of barium back through the advancing peristaltic contraction.¹¹ The retrograde flow causes incomplete clearance of the barium. Whether the disturbed motor activity is simply as a consequence of the smooth muscle and oesophageal innervation operating in the environment of the inflammatory response to the prolonged acid exposure or whether it is caused by an underlying disorder of the motor control mechanisms is not entirely clear but at least two studies in adults suggest the latter.^{11,12}

It seems clear that mechanisms of gastro-oesophageal reflux involve the interplay of oesophageal motility and lower oesophageal sphincter pressure. In both preterm¹³ and term infants¹⁴ the development of increasing tonic

lower oesophageal sphincter pressure shows a close correlation with gestational and postnatal age. No such studies of oesophageal motility are however available. Carré's studies clearly indicate that in most infants with gastro-oesophageal reflux a developmental profile is followed that is different to infants who do not have reflux and would seem to most commonly be associated with delay of development of the mechanisms controlling lower oesophageal sphincter relaxation during swallowing.¹ In a few infants who have symptomatic gastro-oesophageal reflux the developmental delay is not confined to the lower oesophageal sphincter but also involves oesophageal peristalsis and may be very much more profound. As with other areas of the intestine the developmental processes concern both smooth muscle and innervation.¹⁵ In a small proportion of the symptomatic infants reflux will occur as a result of disease. This is most obvious in pseudo-obstructive disorders where smooth muscle or the myenteric plexus is diseased or in cerebral palsy or tumour where defective extrinsic innervation results in a lax incompetent lower oesophageal sphincter. It is commonly held that a hiatus hernia is an anatomical abnormality, which results in more severe forms of gastro-oesophageal reflux. A hiatus hernia is a radiological description of the intra-abdominal segment of the oesophagus moving into the thorax, however, and is seen equally in infants with trivial or serious symptomatic reflux. Whether gastro-oesophageal reflux is trivial or serious is dependent upon the nature of the underlying disorder of oesophageal motor activity rather than the presence or absence of a hiatus hernia.

Investigation of gastro-oesophageal reflux

Investigation of the child suspected of having gastro-oesophageal reflux is in three stages: (i) demonstration of the presence and severity of gastro-oesophageal reflux, (ii) showing the presence of complications, and (iii) considering whether there are underlying disease states present that might give rise to gastro-oesophageal reflux.

(i) DEMONSTRATION OF PRESENCE AND SEVERITY
The 'gold' standard at the present time for detecting the presence and assessing the severity of gastro-oesophageal reflux is undoubtedly 24 hour ambulatory oesophageal pH monitoring with computerised data capture and analysis. Reliable microelectrodes for use in infants are now readily available and objective analysis of the pH recording using a number of variables including the number of reflux episodes of different specified durations, the time taken to clear refluxed acid, and the proportion of time during which pH is abnormally low have enabled reliable detection and assessment of the severity of gastro-oesophageal reflux.¹⁶⁻¹⁸

Other methods which are also used are barium meal and scintiscanning. Video or cine barium studies clearly illustrate disturbed oesophageal motor activity but gastro-oesophageal reflux may be missed as only inter-

mittent exposures are made of relatively short duration. Compared with pH study gastro-oesophageal reflux is missed by barium study in about 40% of patients and severity can only be crudely and subjectively assessed. Gastro-oesophageal scintiscanning has been shown to be more sensitive than barium studies in detecting gastro-oesophageal reflux and also allows accurate quantities. It requires at least one hour recording, however, and the patient needs to be still.

(ii) SHOWING PRESENCE OF COMPLICATIONS

The complication of gastro-oesophageal reflux require a number of investigations for their detection: a blood count for iron deficiency anaemia, a chest radiograph, a search for fat laden macrophages in sputum where gastro-oesophageal reflux is suspected of causing recurrent respiratory disorder, and endoscopy with biopsy to detect oesophagitis. Where an anatomical problem such as a stricture, hiatus hernia, gastric outlet obstruction, or malrotation is suspected a barium meal should be given and followed through to the jejunum. Where gastro-oesophageal reflux is associated with fits or apnoea a pH study combined with apnoea monitoring, sleep studies, or an electroencephalogram as appropriate, may be very useful.

(iii) PRESENCE OF UNDERLYING DISEASE

A number of underlying diseases may give rise to gastro-oesophageal reflux as indicated above. Suspected pseudo-obstructive conditions will require specialist gastroenterological investigation. Gastro-oesophageal reflux that presents atypically may be the first indication of a cerebral tumour,¹⁹ and thus computed tomography or nuclear magnetic resonance scanning of the brain may be required. The association of disturbed gastric emptying with gastro-oesophageal reflux is not entirely clear but it is well known that some 10–15% of infants with pyloric stenosis or malrotation will also have reflux. Thus barium examination must be continued to exclude these disorders. There is no place for a barium swallow alone to assess gastro-oesophageal reflux.

No single investigation provides all the information required for the management of gastro-oesophageal reflux. Ideally at least three are required: pH monitoring to detect the presence and assess the severity of gastro-oesophageal reflux, radiology for anatomical causes and strictures, and endoscopy to detect oesophagitis. These three factors will determine the nature and extent of the treatment required.

Management of gastro-oesophageal reflux

Gastro-oesophageal reflux may be controlled by a number of interventions, positioning, thickening of feeds, pharmacological agents, and surgery. The tendency for gastro-oesophageal reflux in infants to undergo spontaneous resolution by about the age of 18 months, however,

has led to confusion regarding the indications for treatment and their merit.

Some indication of the type of treatment that is likely to be successful can be gained from a knowledge of the severity of the reflux. Patients in whom over 20–30% of a 24 hour period is spent with oesophageal pH below 4 almost always require surgery.²⁰ Whereas those with mild (5–10%) or moderate (10–20%) reflux will often be controlled by medical means until such time as development of the oesophageal smooth muscle and myenteric plexus has proceeded to the point where reflux is no longer a problem.

Mild gastro-oesophageal reflux or excessive 'possetting' or 'spitting up' will usually be controlled by changes in feeding practice and positioning. Giving smaller more frequent feeds is as helpful as the use of thickening agents. The two groups of agents most commonly used are carob seed preparations, Nestargel (Nestlé) and Carobel (Cow and Gate), and the alginate Infant Gaviscon (Reckitt and Colman). Infant Gaviscon also contains antacids, which give it a high sodium content and renders it unsuitable for use in infants under the age of 6 months.²¹ Positioning is a time honoured treatment for gastro-oesophageal reflux but the practice of sitting infants up at an angle of 60° has been shown by several studies to be worse than leaving them supine. The most effective position is being prone with the head raised by 30 degrees.^{18 22} Moderate gastro-oesophageal reflux is often associated with a degree of oesophagitis and antacids or H₂ blocking agents such as cimetidine or ranitidine are often helpful in controlling retrosternal chest pain. In this context Infant Gaviscon is often favoured by mothers as it is easy to give by just adding it to the infants feed. Drugs are also available that will directly reduce gastro-oesophageal reflux and improve oesophageal acid clearance. Those that are commonly used all have their effect on the myenteric plexus and include the cholinergic agonist bethanechol, and the so called prokinetic agents metaclopramide, domperidone, and cisapride. Bethanechol has unacceptable muscarinic side effects and is relatively ineffective.²³ The dopamine antagonists, metaclopramide and domperidone, both increase lower oesophageal sphincter pressure and enhance gastric emptying. Metaclopramide, however, also crosses the blood-brain barrier where it blocks dopamine D₂ receptors and may cause extrapyramidal disturbances by its effect on the basal ganglia. These effects are to some extent dose dependent and the total daily dose should not exceed 0.5 mg/kg body weight. Domperidone does not suffer from these disadvantages and is used in a dose of 0.6–1.2 mg/kg/24 hours in three divided doses. Cisapride, a new prokinetic agent, has its effect by modulating the release of acetylcholine from the myenteric plexus almost certainly by interacting with 5HT₄ receptors. A recent study suggests that it also improves oesophageal peristalsis as well as increasing lower oesophageal sphincter pressure.²⁴ A dose of 0.6 mg/kg/24 hours in three divided doses has been used.

In those with severe gastro-oesophageal reflux management is often not successful. Surgery should seriously be considered in those

infants who fail to thrive because their energy intake is reduced by recurrent vomiting, where oesophagitis is not controlled after three to four weeks of intensive medical treatment, where there is recurrent apnoea, chest infection, and haematemesis, and where a stricture has formed. The finding of a hiatus hernia with or without an associated partial thoracic stomach is not in itself an indication for surgery.²⁵ Gastro-oesophageal reflux may also be a cause of considerable morbidity in children who are severely retarded and in whom it is often misinterpreted or overlooked. Careful investigation and treatment may transform their lives. However, medical treatment is often ineffective and surgery is usually required.²⁶ The procedure most commonly used is a fundoplication with the Nissen variety being probably the most popular, which has a low mortality but some morbidity.²⁶ It is essential for adequate preoperative investigation to be done to assess whether there are associated anatomical problems such as a malrotation or disordered gastric emptying. In patients with these additional problems 'gas bloat', or more seriously acute gastric dilatation, occur more commonly postoperatively.

In the last decade the nature of gastro-oesophageal reflux and its association with the ontogeny of oesophageal motor function in the infant has been understood. More specific approaches to management are being developed but these require objective evaluation as to their indications for use and their efficacy.

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