

# ARCHIVES OF DISEASE IN CHILDHOOD

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## ANNOTATIONS

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### Gastro-oesophageal reflux and the lung

Numerous reports in recent years have described the association of gastro-oesophageal reflux with respiratory symptoms, both among children being treated for gastro-oesophageal reflux and in those presenting with lower respiratory tract symptoms or apnoea. These studies, recently reviewed by Orenstein and Orenstein, have tended to focus on small, highly selected groups of children, and raise important questions concerning the nature, scale, and clinical implications of the associations observed, particularly during infancy.<sup>1</sup>

Despite intensive research interest in the pathophysiology of gastro-oesophageal reflux,<sup>2</sup> the development of methods for its detection,<sup>2,3</sup> and the elucidation of mechanisms of pulmonary dysfunction resulting from it,<sup>1,4</sup> the answers to many of the questions remain incomplete. This annotation highlights certain controversial areas and outlines an approach to the evaluation of children with respiratory symptoms and suspected gastro-oesophageal reflux.

#### Gastro-oesophageal reflux in 'normal' infants and children

It is well known that possetting occurs in otherwise healthy infants without respiratory or other alimentary symptoms. The development of sophisticated techniques for the investigation of gastro-oesophageal reflux, particularly 24 hour oesophageal pH monitoring, has led to its detection in completely asymptomatic infants.<sup>2,5,6</sup> As some gastro-oesophageal reflux is a normal occurrence, attempts have been made to define 'abnormality' in terms of the amount (volume or duration) of reflux and its pattern in relation to feeding and behavioural state.<sup>7,8</sup> Unfortunately, because of ethical constraints, the 'normal' populations studied have often been small with a wide age range and may not have been completely healthy. The 285 infants studied by Vandenas and Sacre-Smits provide the largest available collection of 'normal' results for 24 hour oesophageal pH studies.<sup>5</sup> The upper limits of normal derived from these are higher than other published values,<sup>6</sup> however, and overlap with the results of symptomatic patients studied by other groups.<sup>2,9</sup>

The difficulty in defining 'abnormal' gastro-oesophageal reflux is a major problem when considering its relation to respiratory symptoms.<sup>1</sup> Although some studies suggest that nocturnal reflux may be important in determining respiratory symptoms<sup>8</sup> or apnoea,<sup>10</sup> it has not been possible to define patterns of gastro-oesophageal reflux which occur only in children with these symptoms. An excess of gastro-

oesophageal reflux during sleep may also be found in infants and children without symptoms of lung disease or apnoea or objective evidence of pulmonary dysfunction.<sup>7,11</sup> Conversely, subjects with pulmonary symptoms may not have demonstrably 'abnormal' gastro-oesophageal reflux,<sup>1,12</sup> even when antireflux treatment improves these symptoms.<sup>9</sup> In certain children the response to gastro-oesophageal reflux, even when 'normal' in amount, may be the key event. In this situation any reflux might be potentially harmful.

#### The coexistence of gastro-oesophageal reflux and respiratory symptoms

The finding of 'significant' gastro-oesophageal reflux in a child with respiratory symptoms, or conversely respiratory symptoms in a child shown to have gastro-oesophageal reflux, may occur by chance, as a manifestation of a disorder affecting both gastrointestinal and respiratory systems, or as a cause and effect relationship. Gastro-oesophageal reflux might be responsible for pulmonary dysfunction or vice versa, or both might apply.

One way to support the contention that gastro-oesophageal reflux causes respiratory disorders is to demonstrate that its successful treatment alleviates respiratory symptoms. The natural history of gastro-oesophageal reflux, respiratory symptoms, and apnoea is to improve, particularly in infancy,<sup>13,14</sup> so that ideally the response to active treatment should be documented objectively and be followed by the recurrence of both gastro-oesophageal reflux and the original symptoms after withdrawal of treatment. The latter is impossible after surgery and has only rarely been reported with medical treatment, usually because parents had discontinued medication against advice rather than as part of a controlled study.<sup>11,12</sup> Although improvement in gastro-oesophageal reflux on treatment has usually been documented, pulmonary function has seldom been assessed, reliance being placed on symptomatic improvement as evidence of success.

There is, nevertheless, considerable circumstantial evidence that treatment of gastro-oesophageal reflux reduces respiratory symptoms in selected groups of patients, particularly those with recurrent pneumonia.<sup>1,9,11,12,15</sup> The evidence is less convincing in asthma where improvement, if it occurs, has tended to be measured by a reduction in the use of asthma medication rather than by abolition of symptoms.<sup>9,15</sup> When infants have suffered multiple, fre-

quent apnoeic episodes that cease after adequate medical treatment or surgery it is difficult to remain sceptical about the underlying importance of gastro-oesophageal reflux.<sup>14 16</sup> This pattern is only observed, however, in a small proportion of infants who present with recurrent apnoea.

No studies in childhood have tested the proposition that treatment of respiratory symptoms might relieve gastro-oesophageal reflux, although theophyllines and  $\beta$  sympathomimetics may exacerbate it.<sup>1</sup> In adults there are conflicting reports of the effect on gastro-oesophageal reflux of asthma induced by bronchial challenge. Both a reduction<sup>17</sup> and an increase<sup>18</sup> in gastro-oesophageal reflux have been reported. Although large swings in intrapleural pressure induced by respiratory efforts have been thought to favour increased gastro-oesophageal reflux,<sup>4</sup> there is little evidence that this actually occurs and increased diaphragmatic work has also been thought to improve lower oesophageal sphincter competence.<sup>19</sup>

A cause and effect relationship can also be inferred from a temporal relationship between respiratory changes and gastro-oesophageal reflux. Clinically this has been demonstrated in individual children with stridor, wheeze, and apnoea both with natural and simulated gastro-oesophageal reflux,<sup>1 8 16 20</sup> although no temporal relationship has been found in larger groups of infants with apnoea.<sup>1 20</sup> In many studies in adult asthmatics, and some in children,<sup>21</sup> gastro-oesophageal reflux has been simulated (by introducing acid into the oesophagus) while monitoring respiratory function. Increased bronchial reactivity has been found in a proportion of such cases, usually those who also have heartburn.<sup>1 21</sup>

#### **Mechanisms by which respiratory symptoms may result from gastro-oesophageal reflux**

Respiratory symptoms resulting from gastro-oesophageal reflux could be caused by aspiration or by the stimulation of vagal nerve endings in the oesophageal mucosa.<sup>1 4</sup> In animal studies a stronger vagal response has been elicited with small amounts of acid in the trachea than by large amounts in the oesophagus. Microaspiration has therefore been postulated to explain the clinical association.<sup>4</sup>

The presence of a vagal response inducing bronchoconstriction has been inferred from the studies with simulated gastro-oesophageal reflux described above. There is, as yet, no satisfactory explanation for the difference in reaction between individuals or the occurrence of symptoms after some but not all episodes of reflux. This unpredictability is also true when aspiration is suspected though sometimes the link between reflux and respiratory symptoms is clearly demonstrated, for example, in infants or children with tracheo-oesophageal fistula, neurological damage, or coma.

Even when aspiration is suspected clinically as the cause of recurrent pneumonia it has been demonstrated in at most 25% of such cases by radioisotope scan.<sup>1 3 22</sup> It has also been detected in 20% of 'near-miss SIDS' cases in the absence of lower respiratory tract signs,<sup>22</sup> but not yet in children with recurrent wheeziness. This low incidence of detected aspiration could mean that its contribution to the causation of respiratory problems is small, or that aspiration is infrequent even when it is the cause, or that the sensitivity of the technique for detecting aspiration is poor. Other methods of detecting aspiration, such as the presence of fat laden macrophages in tracheal aspirates, are available but may not be sufficiently specific to be useful.<sup>23</sup>

#### **Clinical evaluation of the child with respiratory symptoms and suspected gastro-oesophageal reflux**

Clearly, infants and children with symptoms suggestive of

gastro-oesophageal reflux should be investigated and treated irrespective of coincidental respiratory symptoms. In those with respiratory symptoms, a careful history and clinical examination is the starting point for assessment. Gastro-oesophageal reflux should be considered when symptoms are persistent, especially in children with recurrent pneumonia and those in whom choking has been troublesome. It should also be considered in children with poorly controlled asthma who have appreciable nocturnal symptoms, recurrent changes on radiography, or unexplained severe exacerbations.

A barium swallow may be helpful in demonstrating swallowing incoordination or a structural lesion but it is not a good method for diagnosing gastro-oesophageal reflux.<sup>1 2</sup> The search for gastro-oesophageal reflux should include a 24 hour oesophageal pH study and, if negative, a radioisotope scan, during which evidence of aspiration should also be sought. Although, as discussed above, a negative scan does not exclude aspiration, a positive result from a careful study is reliable evidence of aspiration.

'Significant' gastro-oesophageal reflux should be diagnosed if the pH study result, as a whole or in particular time periods, exceeds the published normal results collected from a relevant age group with the technique most closely resembling that used, if sufficient local normal results are not available. Radioisotope studies are usually considered positive if any reflux is seen, although this may be too non-specific an approach, particularly in infants.<sup>2 3</sup> Children with positive results should be treated in the hope that respiratory symptoms will subside but in particularly severe cases, especially with a suggestive history, it may be worth trying antireflux treatment even for 'normal' amounts of gastro-oesophageal reflux.

In young infants the thickening of feeds and prone anti-Trendelenberg positioning may be sufficient antireflux treatment. An alginate containing antacid like Gaviscon (Reckitt and Colman) and the gastrokinetic agent cisapride may be useful but the side effects of metoclopramide limit its role and bethanecol may exacerbate bronchospasm.<sup>1</sup> As no medical treatment is totally satisfactory and the individual response is so variable, changing or combining treatments can sometimes effect improvement. At present surgery is the only uniformly reliable method for eliminating gastro-oesophageal reflux and this is justified, after failure of medical treatment, when the symptoms are severe and there is good evidence that gastro-oesophageal reflux is relevant.

In conclusion, there is little evidence that respiratory disease per se causes gastro-oesophageal reflux, though its treatment may. The prevalence of 'abnormal' gastro-oesophageal reflux in children with respiratory disorders and its relevance when found are not fully known. Effective treatment of gastro-oesophageal reflux in such cases may result in a decrease in respiratory symptoms. Even 'normal' amounts of reflux may be a potential problem in individuals in whom there is a close temporal association between gastro-oesophageal reflux and respiratory symptoms, meriting a trial of antireflux treatment. The development of more effective medical treatment of gastro-oesophageal reflux and the wider application of objective means of assessing respiratory outcome would allow better definition of the contribution of gastro-oesophageal reflux to the causation of recurrent or chronic respiratory symptoms in infants and children.

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## Investigation of rectal bleeding

The passage of blood through the rectum by a child often causes considerable parental anxiety. Unlike the situation in the adult,<sup>1</sup> however, the causes are often transient, almost invariably benign, and usually simply treated. Occasionally the blood indicates serious underlying pathology, and to avoid delay in detecting this possibility a positive diagnosis should be sought at initial presentation and may be found in most cases.

The age of onset clearly relates to certain diagnoses: necrotising enterocolitis and malrotation in the premature baby and neonate, anal fissures and intussusception in the young infant, and lymphoid hyperplasia and inflammatory bowel disease in the older child. Classification of aetiology of bleeding through the rectum is therefore usually based on age groups.<sup>2</sup>

A good history may lead directly to diagnosis. Passage of a firm stool, streaked with red blood (haematochezia) and accompanied by anal pain is pathognomonic of anal fissure—a common problem. The child may be aware of 'something coming down' suggesting a rectal polyp or rectal mucosal prolapse. The dietary history may suggest features of intolerance (for example, cows' milk) leading to inflammation and bleeding.<sup>3</sup> The colour and amount of blood, its relation to stool, and the presence of abdominal or anal pain all point to the anatomical location of bleeding. Though melaena suggests an upper gastrointestinal haemorrhage, brisk bleeding from oesophageal varices, duodenal ulcer, or Meckel's diverticulum may result in passage of red blood. The possibility of bleeding due to a diathesis (von Willebrand's) or systemic illness (haemolytic uraemic syndrome, connective tissue disorders, Henoch-Schönlein purpura) should be considered and a detailed family history (familial polyposis coli) and drug history (non-steroidal anti-inflammatory agents, steroids, salicylates) is important. Bleeding due to stress ulceration should be considered in association with posterior fossa tumours,<sup>4</sup> burns, and cardiac surgery. Confirmation of the presence of blood by the examination of stool or nappy is important and, if doubt exists about whether stool contains blood, a faecal occult blood test should be performed.<sup>5</sup>

Examination centres on abdominal, perianal, and rectal findings together with inspection of stools, but a complete examination is needed to pick up clues. Cutaneous haemangioma may point to gastrointestinal haemangiomas. Buccal and lip pigmentation is classical with Peutz-Jegher polyposis. Petechial rash on buttocks and legs may not have been noticed by the parents of the child with Henoch-Schönlein purpura. Relevant abdominal findings include hepatosplenomegaly (cirrhosis and portal hypertension), mass (duplication cyst or intussusception), distended or thickened bowel (Crohn's disease, ulcerative colitis), and peritonism (inflamed Meckel's diverticulum or infective causes).

Anal and rectal examination is best conducted with the child lying either supine with hips and knees fully flexed or in the left lateral position (for a right handed examiner). The reassuring presence of parent or nurse holding the child, a sympathetic explanation to the child, and a calm and gentle approach normally permits full and detailed examination provided the child has not previously been hurt or frightened by rough or rapid examination. Careful separation of the buttocks and eversion of anal mucosa may reveal a fissure in the common posterior position. An anterior fissure is sometimes found when the anus is in an anterior ectopic position and slightly stenotic: further investigation and management will be needed. Fissures may be red and painful if acute or white and indurated if more chronic and inactive. Associated skin tags raise the suspicion of Crohn's disease. If the child can be persuaded to strain (a difficult manoeuvre for most children) an anal mucosal prolapse may appear. Prolapse of the complete rectal wall (proctidentia) is usually related to significant underlying disorders (for example, cystic fibrosis or neurological disorders).

Digital rectal examination may be resisted (and also be unnecessary) if there is an anal fissure but otherwise is mandatory; its omission leads to missed diagnosis or unnecessary investigations. Rectal polyps (usually simple and solitary) may be palpated by sweeping the examining finger circumferentially round the rectal lumen until the polyp reaches the limit of mobility on its pedicle: the polyp may be prolapsed through the anus and even removed by