

## Technical note

# Simultaneous tracheal and oesophageal pH measurements in asthmatic patients with gastro-oesophageal reflux

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### Summary

**Background** - An association between asthma and gastro-oesophageal reflux is well recognised but the underlying mechanism is unclear. One suggestion is that gastric juice is aspirated into the tracheal and upper airways but detection of these events is difficult and involves radioisotopic studies. A new method of making direct measurements of tracheal and oesophageal pH over a 24 hour period is described, together with its application to patients with asthma.

**Methods** - The technique involves insertion of simultaneous tracheal and oesophageal pH probes under general anaesthesia. Continuous monitoring of pH over a 24 hour period is possible, permitting comparison with peak flow readings during wakefulness and at night should the patient be disturbed. Representative data from four patients with asthma (mean FEV<sub>1</sub> 62% predicted) and symptomatic gastro-oesophageal reflux, together with data from three non-asthmatics, is presented.

**Results** - Thirty seven episodes of gastro-oesophageal reflux lasting more than five minutes were recorded. Of these, five were closely followed by a fall in tracheal pH from a mean (SE) of 7.1 (0.2) to 4.1 (0.4) and a fall in peak expiratory flow (PEFR) of 84 (16) l/min. When gastro-oesophageal reflux occurred without tracheal aspiration the fall in PEFR was 8 (4) l/min.

**Conclusions** - This new technique was well tolerated and allowed quantitation of the number, duration, and timing of episodes of tracheal micro-aspiration. Unlike acid reflux without aspiration, these events appear to be related to significant acute changes in lung function in asthmatic patients. Further studies with this new method may elucidate the role of gastro-oesophageal reflux in asthma.

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A number of reports have suggested an association between abnormal pulmonary function and gastro-oesophageal reflux.<sup>1,2</sup> Several authors have documented an improvement in asthmatic symptoms in patients where gastro-oesophageal reflux has been successfully treated either by surgical or medical means.<sup>2,3</sup> Two different mechanisms for gastro-oesophageal reflux-associated asthma have been proposed. The "reflex" theory proposes that gastro-oesophageal reflux stimulates oesophageal mucosal receptors and induces a vagally mediated reflex bronchoconstriction. This theory has been supported by some (but not all) studies of acid perfusion in the oesophagus.<sup>4-6</sup> Alternatively, micro-aspiration of gastric contents into the upper airway may cause bronchospasm and mucosal oedema. This view is supported by the finding of posterior laryngitis in patients with gastro-oesophageal reflux<sup>7</sup> and animal studies in which acid inhaled into the airways produced significant bronchoconstriction.<sup>8</sup> However, this direct chemical effect has not been consistently found in asthmatic patients studied by radioisotopic techniques.<sup>9</sup> These involve the use of a gamma camera, are hard to relate to individual episodes of micro-aspiration, and will be influenced by the rate at which the radioisotope and aspirated material are cleared from the oesophagus.

Prolonged oesophageal pH monitoring is known to be a sensitive and specific measure of gastro-oesophageal reflux.<sup>10</sup> Until recently prolonged tracheal pH monitoring has not been feasible. However, the development of a 1 mm diameter pH probe (Synectics Medical Ltd, Middlesex, UK) has allowed the transtracheal placement of this probe via a narrow gauge flexible cannula for prolonged tracheal pH monitoring. We have used this probe to perform continuous ambulatory oesophageal and tracheal pH monitoring in four asthmatic patients complaining of gastro-oesophageal reflux and nocturnal falls in peak flow and in three non-asthmatic individuals without reflux who acted as control subjects.

### Methods

Both tracheal and oesophageal probes were inserted via a rigid bronchoscope and fibreoptic

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Figure 1 Bronchoscopic view of transtracheal cannula through which the pH probe is inserted. The probe can be positioned under direct vision to ensure its stability and contact with the tracheal wall.

duodenoscope, respectively, under general anaesthesia using intravenous suxamethonium and propofol. Local anaesthetic agents were avoided as these are known to be acidic and might influence the results.<sup>11</sup> The 1 mm tracheal pH probe was passed through the cricothyroid membrane via a 14 gauge cannula (Wallace, Colchester, Essex, UK) (fig 1) and placed in the trachea 2 cm above the carina. The position of the pH probe was confirmed using a flexible Olympus BF3 fiberoptic bronchoscope and its stability confirmed by subsequent radiography. The oesophageal pH probe (1.5 mm) was positioned 5 cm above the lower oesophageal sphincter, a position previously determined by oesophageal manometry and verified by endoscopy.

Simultaneous oesophageal and tracheal pH measurements were recorded using the Synectics ambulatory system with semi-disposable antimony monocrystal pH electrodes. The technique has a detection sensitivity of 0.1 pH units with a system drift over 100 hours of <0.1 units. A reference electrode was secured on the sternum of the patients. The pH was recorded every five seconds in a dual channel digitrapper MK (Synectics) and transferred at the end of the 24 hour study to an Amstrad PC. Data analysis was performed using dedicated software (Synectics Liberty System and "Eosophagram" software).

During the 24 hour study period each patient was requested to keep an hourly chart recording the peak expiratory flow rate (PEFR) when awake and a detailed diary of all events including mealtimes, sleeptime, and any symptoms. The patients were freely ambulatory throughout the test period. After insertion of the probes and at the end of the 24 hour study period posteroanterior and lateral chest radiographs were taken to confirm the positions of the pH probes. The PEFR was omitted for the first two hours after the operation to allow recovery from the general anaesthetic.

In this study an episode of gastro-oesophageal reflux was taken to be significant if the

oesophageal pH was less than four. Evidence of tracheal aspiration was defined arbitrarily as tracheal pH less than 5.5. To facilitate comparisons between the acute changes in pH and less frequent measurements of PEFR, data are expressed as mean (SE). Statistical analysis was by the unpaired *t* test.

The study was performed in four asthmatic patients (two men) and three controls (two men). The controls were undergoing rigid bronchoscopy for suspected bronchial carcinoma, although no endobronchial lesions were seen. The four patients with both gastro-oesophageal reflux and asthma had a mean FEV<sub>1</sub> of 1.92 (0.37) litres. All showed daily fluctuations of more than 20% in PEFR, increased their FEV<sub>1</sub> by 21.2 (0.7)% after salbutamol, and had suffered from asthma for a mean of 38 years (range 30–50). All were treated with inhaled  $\beta$  agonists (one via nebulisation) and received a mean of 1.2 mg beclomethasone dipropionate per day. One patient was also taking 10 mg prednisolone orally. All four patients complained of significant reflux, three requiring oral omeprazole 20 mg once daily and one ranitidine 300 mg twice daily. All antireflux treatment as well as oral theophyllines and oral  $\beta$  agonists were discontinued at least 72 hours before study, but inhaled bronchodilator therapy was continued as prescribed.

Approval for this study was granted by the hospital ethics committee and all patients gave written, informed consent.

## Results

The procedure was well tolerated and without significant side effects although some patients complained of local discomfort at the site of the tracheal pH electrode. Representative data from a control subject and the asthmatic patients are shown in figs 2 and 3. No control subject had evidence of gastro-oesophageal reflux or tracheal micro-aspiration and none showed more than 20% variability in PEFR. Among the asthmatic patients there were 37

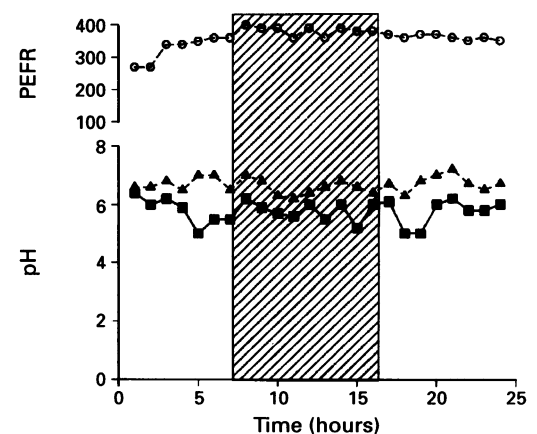


Figure 2 Simultaneous tracheal and oesophageal pH recordings compared with serial peak flow recordings over a 24 hour period in a non-asthmatic control subject. ■ = oesophageal pH, ▲ = tracheal pH, ○ = PEFR. The hatched area indicates the period during which the patient was supine.

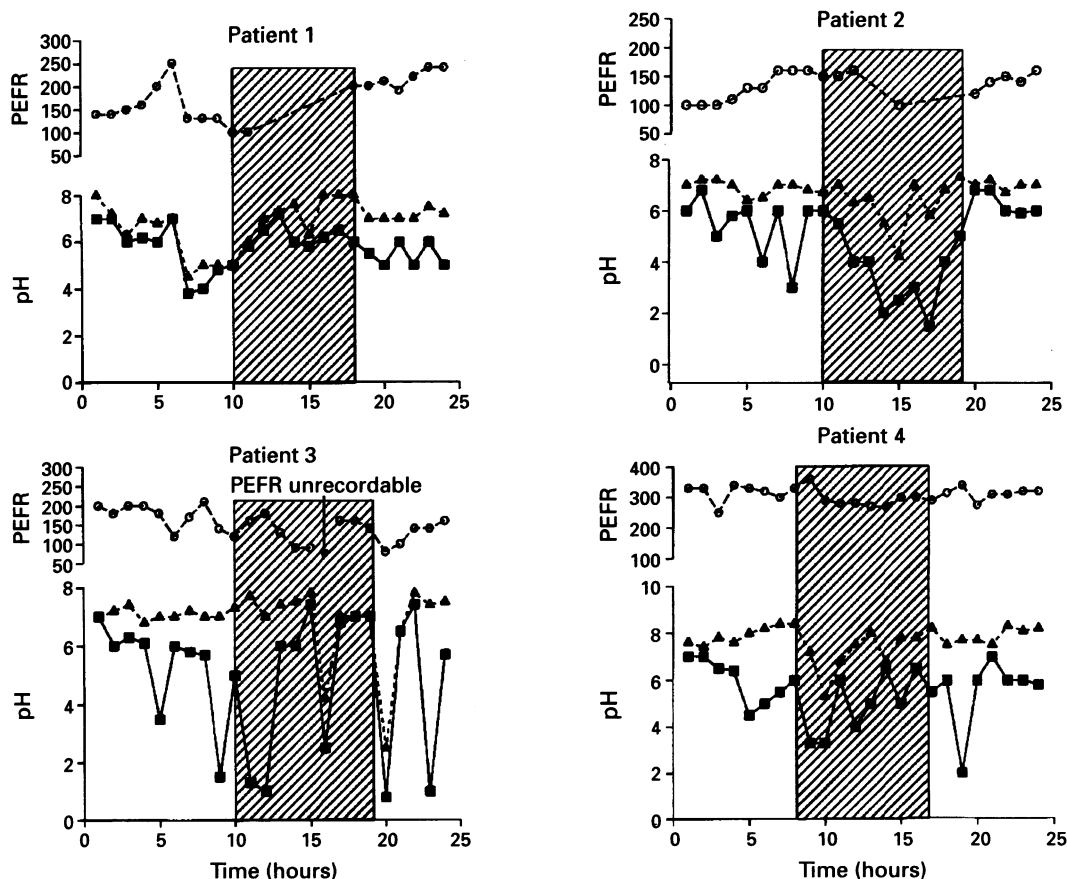


Figure 3 Data from four patients complaining of nocturnal asthma presented as in fig. 2. Note that the pH plots reflect the data recorded prior to the peak flow measurement for ease of comparison and that peak flow monitoring began at different times of the day, the lowest peak flows corresponding to night time recordings. Subject 3 showed substantial variation throughout the day although the lowest peak flow (unrecordable) did occur during the night.

significant falls in oesophageal pH suggestive of gastro-oesophageal reflux which lasted more than five minutes (mean duration 45 (13) minutes). Five of these episodes were followed by an immediate fall in tracheal pH (mean pH change 2.5 units lasting 19.4 (6.1) minutes). In only one instance was gastro-oesophageal reflux alone followed by a 20% fall in PEFR. There were five falls in PEFR of more than 20% unrelated to changes in oesophageal pH but no isolated falls in tracheal pH. The five episodes of gastro-oesophageal reflux when tracheal pH fell were associated with a dramatic reduction in PEFR (change in PEFR 84 (16) l/min) (fig 3), unlike the 32 episodes of gastro-oesophageal reflux without tracheal aspiration (change in PEFR 8 (4) l/min). There were no differences in the pre-reflux pH or PEFR between those episodes of acid reflux with or without a fall in tracheal pH. Twenty one of the 37 episodes occurred at night when the patient was semirecumbent and these included four episodes of tracheal micro-aspiration.

### Discussion

This new technique of direct tracheal pH monitoring in humans allows the study of small changes in the acidity of the trachea. Unlike previous techniques it is possible not only to confirm the presence of tracheal aspiration but to follow its time course and relate it to preceding changes in oesophageal pH as well as

independent measures of lung function such as PEFR. Monitoring was free from local complications and, unlike radioisotopic methods, was ambulatory. We introduced the catheter under general anaesthesia with a rigid bronchoscope to ensure accurate positioning of the pH probes, but have now been able to adapt this technique for use under local anaesthesia.<sup>12</sup> Local discomfort may reflect our avoidance of topical airway anaesthesia which we have shown can reduce intratracheal pH. Inhalation of nebulised saline and salbutamol will reduce the pH as this has a pH of 4.4. However, none of the episodes of micro-aspiration were preceded by nebuliser use and artefactual "contamination" of the pH signal can easily be distinguished from the pattern of pH fall and its severity.

Our patient studies were on a carefully selected group with clinically intrusive reflux symptoms sufficient to be considered for oesophageal plication. Unlike earlier studies<sup>10</sup> we have found that micro-aspiration does occur and is associated with clinically important falls in PEFR. These are unlikely to be related to coughing or to the earlier general anaesthesia as most occurred at night well after the anaesthetic and all happened after the patient had been ambulant. Since carefully conducted acid perfusion studies have failed to show an increase in airways resistance in stable asthmatics,<sup>6</sup> our data suggest that the previously reported benefits of antireflux treatment in asthmatic sub-

jects<sup>3</sup> might be due to prevention of episodes of micro-aspiration. The absence of changes in PEFr or of oesophageal or tracheal reflux in our control subjects is encouraging, but cannot exclude aspiration in non-asthmatic patients with acid reflux symptoms.

This method provides a practical means of determining whether "reflux" or "reflex" mechanisms are contributing to nocturnal asthma. If it can be combined with other physiological measurements which directly measure pulmonary resistance during sleep, a resolution of the role of differing mechanisms of acid reflux in the asthmatic subject may be possible.

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