Gut, 1990, 31, 370-373

ALIMENTARY TRACT

# Predictive value of oesophageal pH variables in children with gastro-oesophageal reflux

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## Abstract

**Sixty three 24 hour oesophageal pH studies were performed in children with known or suspected gastro-oesophageal reflux and their progress was followed for at least a year. Forty two studies were of children who were well at follow up who were not receiving medical treatment for gastro-oesophageal reflux, and had not required antireflux surgery. Twenty one studies were from children who were still on treatment for gastro-oesophageal reflux or had undergone antireflux surgery. The results were analysed using non-parametric statistics to assess the value of pH recordings in predicting which children were likely to have continuing problems. Sleep reflux (minutes/hour) and acid clearing time were the most highly significant variables ($p<0.0005$ and $p<0.0001$ respectively). The results suggest that either sleep gastro-oesophageal reflux of more than 6·4 minutes/hour or an acid clearing time of seven minutes or more are good predictors of the clinical outcome (specificity 88·1%, sensitivity 81·0%). Three of the five children with false positive results were under 10 months of age. Positive results in this age group should therefore be interpreted with caution.**


Monitoring pH in the lower oesophagus is generally considered to be the most sensitive test for detecting gastro-oesophageal reflux.[1 2 3] The significance of reflux so discovered is more difficult to assess. Currently the index devised by Johnson and DeMeester[4] is the most commonly applied for assessing the severity of gastro-oesophageal reflux in adults. This index differentiates between reflux occurring in the upright and supine positions.[4 5] Unfortunately, monitoring body position in young children in a hospital ward presents considerable practical difficulties as few children maintain any position for very long.

The aim of this study is to devise a simple, predictive scoring system for gastro-oesophageal reflux applicable to infants and children and independent of body position. Twenty four hour oesophageal pH studies were conducted in a group of 59 children. The recordings were analysed in terms of gastro-oesophageal reflux occuring during sleep or while awake.

All children had a clinical assessment at least one year after their oesophageal pH study. The pH recording variables were then analysed to establish which if any features in the original pH recordings could be regarded as predictive of continuing symptoms of gastro-oesophageal reflux.

## Methods

### PATIENTS

Fifty nine children were referred for further evaluation of known or suspected gastro-oesophageal reflux. Four children had a second pH study done after Nissen fundoplication, giving a total of 63 pH studies. The primary indications for the pH studies are shown in Table I.

### PH TEST PROCEDURE

Oesophageal pH was monitored over 24 hours using the Microelectrodes M1506 pH electrode (UK distributors V A Howe, London). Both the pH meter (model 3050, Kent EIL, Chertsey) and the Minigor chart recorder (Labdata, London) were battery operated for electrical safety. During a pH study the equipment was placed on a small trolley, affording a degree of patient mobility, but not the complete freedom of movement of a fully ambulatory system.

The pH probe was calibrated before and after each study in buffers of pH 4, 7 and 9 at 37°C. The pH probe was positioned above the lower oesophageal sphincter, at a distance of 87% of the total oesophageal length measured from the external nares. This was estimated using the child's height[6] and checked by *x* ray screening.

The pH recordings were annotated by the nursing staff, giving details of food, drinks, sleep periods, etc. Oesophageal acid clearing time was measured by giving a drink of fruit juice of pH

TABLE I *Primary indications for 63 oesophageal pH studies in 59 children*

| *Primary indication* | *Age range (yr/mo)* | *Studies (n)* |
|---|---|---|
| Vomiting | 2m–6y0m | 20 |
| Respiratory symptoms | 1m–6y3m | 12 |
| Epigastric/chest pain | 1y9m–10y9m | 7 |
| Cerebral palsy/spina bifida | 1y5m–14y0m | 6 |
| Repaired oesophageal atresia | 8m–16y0m | 6 |
| Post-Nissen fundoplication | 6m–14y0m | 12 |
| Total | | 63 |

Four children had repeat pH studies after Nissen fundoplication and therefore appear in two categories.

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Accepted for publication
10 July 1989

3·2. A bolus of 20 ml was given to children less than one year old; 50 ml to children from one to three years old; and 100 ml to children over three years old.

## Results

### FOLLOW UP

All 59 children were followed up clinically between 12 and 30 months after their original pH study. Forty two children had discontinued all treatment for gastro-oesophageal reflux (group A). The other 17 children (group B) comprised 14 who were still on medical treatment for gastro-oesophageal reflux and three who had undergone antireflux surgery. Of the 25 children under 10 months of age at the time of their pH study, 21 were well at follow up.

Four children were referred for a second pH study after surgery for gastro-oesophageal reflux, and their first pH study was classified as from a child who underwent subsequent surgery and the second was classified according to follow up. There were therefore 21 pH recordings in group B.

### ANALYSIS OF PH RECORDINGS

Sixty three oesophageal pH recordings were obtained from the 59 children. Total sleep time varied from nine hours to 17 hours. A reflux episode was defined as a drop in oesophageal pH to 4 or less. Acid clearing time was defined as the time between the end of ingestion of the bolus of fruit juice and the return of the oesophageal pH to greater than 4. The recordings were analysed to provide the following information.: (i) Gastro-oesophageal reflux whilst awake (minutes/hour); (ii) Number of reflux episodes whilst awake lasting ≥five minutes; (iii) Duration of longest reflux episode whilst awake (minutes); (iv) Acid clearing time (minutes); (v) Gastro-oesophageal reflux during sleep (minutes/hour); (vi) Number of reflux episodes during sleep lasting ≥five minutes; (vii) Duration of longest reflux episode during sleep (minutes).

Most of these variables were not normally distributed and therefore non-parametric statistics were used for the analysis.

### POPULATION ANALYSIS

The Kruskal-Wallis one way analysis of variance by ranks test was used to determine whether the children in the different diagnostic categories (Table I) could be considered as taken from the same overall population. The diagnostic groups were not from the same overall population for: age; acid clearing time; number of reflux episodes lasting five minutes or more whilst awake; and the longest reflux episode whilst awake. Children presenting with vomiting were generally much younger than children in the other categories, as might be expected ($p<0·001$). Age was not, however, significantly correlated with any of the seven variables. Acid clearing time was longer in children with repaired oesophageal atresia and children with neurological problems ($p<0·01$), and the other two variables were greater in children with neurological problems (number of reflux episodes lasting five minutes or more whilst awake: $p<0·01$; and longest episode whilst awake: $p<0·05$).

### DIFFERENCES BETWEEN GROUP A AND GROUP B

The children who were well at follow up (group A) were compared with those who were still on medical treatment or had required surgery for gastro-oesophageal reflux at follow up (group B) using the Mann-Whitney U test. Initially, the comparison was made for age and the four variables for which all the children could be considered as from the same population. The results are shown in Table II. Group B were significantly older than group A. All the sleep variables and awake reflux (minutes per hour) were also significantly different. The most significant was sleep reflux (minutes per hour) with a median in group A of 0·0 minutes and in group B of 6·7 minutes ($p<0·0005$).

To check the significance of the other variables the Mann-Whitney U test was repeated for all children excluding those presenting with repaired oesophageal atresia or neurological problems. These 51 children could be considered as from the same overall population for all seven variables. The results are shown in Table III. The only significant variables were the same as for the total group above, and sleep reflux (minutes/hour) was again found to be the most significant variable. Using the values of sleep reflux obtained from Table II, the point estimate of the difference between the medians (6·4 minutes) was taken as a suitable predictive value. Twelve of the 21 children in group B had shown sleep reflux of greater than 6·4 minutes/hour, compared with only three of the 42 children in group A.

Nine children had sleep reflux of less than 6·4 minutes/hour, but were still on medical treatment for gastro-oesophageal reflux or had required surgery at follow up. The Kruskal-Wallis one way analysis of ranks test indicated that these children could be considered as coming from the same overall population for all seven variables. The Mann-Whitney U test was used to compare this group with the 42 children who were well at follow up (Table IV). The only three variables which were significantly different between the treated and untreated children were acid clearing time; awake reflux (minutes/hour); and the number of reflux episodes lasting five

TABLE II *Results of 63 oesophageal pH studies, obtained using the Mann-Whitney 'U' test.*

| | *Median value* | | | |
|---|---|---|---|---|
| | *Group A* | *Group B* | *Δ(95% CI)* | *p* |
| Age (mo) | 8·0 | 30·0 | 12·0 (0·9, 28·9) | p<0·05 |
| Awake reflux (min/h) | 3·7 | 8·4 | 4·3 (1·8, 6·5) | p<0·005 |
| Sleep reflux (min/h) | 0·0 | 6·7 | 6·4 (0·2, 8·5) | p<0·0005 |
| Reflux episodes lasting ≥5 minutes during sleep (n) | 0 | 2 | 1 (0, 3) | p<0·005 |
| Longest reflux episode during sleep (mins) | 0 | 15 | 10 (0, 20) | p<0·005 |

Group A: 42 studies from children no longer on treatment for gastro-oesophageal reflux at follow-up. Group B: 21 studies from children still on treatment for gastro-oesophageal reflux at follow-up, or who had undergone anti-reflux surgery. Δ denotes the point estimate of the difference between the medians, given with a 95% confidence interval. p is the probability that there is no difference between group A and group B.

TABLE III *Results of oesophageal pH studies excluding the 12 children with neurological problems or repaired oesophageal atresia. Results were obtained using the Mann-Whitney 'U' test.*

| | Median value | | | |
|---|---|---|---|---|
| | Group C | Group D | Δ(95% CI) | p |
| Age (mo) | 7·0 | 53·5 | 15·0 (1·2, 53·9) | p<0·05 |
| Awake reflux (min/h) | 3·5 | 7·9 | 3·6 (0·2, 6·5) | p<0·05 |
| Reflux episodes lasting ≥5 minutes whilst awake (n) | 1 | 1 | 0 (−1, 1) | ns |
| Longest reflux episode whilst awake (min) | 6 | 6 | 0 (−3, 3) | ns |
| Acid clearing time (min) | 2·5 | 2·75 | 0·0 (−0·5, 3·5) | ns |
| Sleep reflux (min/h) | 0·0 | 10·2 | 6·7 (3·0, 15·3) | p<0·0005 |
| Reflux episodes lasting ≥5 minutes during sleep (n) | 0 | 2 | 2 (0, 3) | p<0·005 |
| Longest reflux episode during sleep (min) | 0 | 18 | 15 (4, 23) | p<0·005 |

Group C: 39 studies from children no longer on treatment for gastro-oesophageal reflux at follow up. Group D: 12 studies from children still on treatment for gastro-oesophageal reflux at follow-up, or who had undergone antireflux surgery. Δ denotes the point estimate of the difference between the medians, given with a 95% confidence interval. p is the probability that there is no difference between group C and group D. ns means not significant.

minutes or more whilst awake. Acid clearing time was the most significant (p<0·0001) and was therefore chosen as a second predictive test. The point estimate of the difference between the medians in the treated and untreated groups was 4·5 minutes. The median acid clearing time in the untreated group was 2·5 minutes, so 7 minutes was chosen as the predictive value. Applying this to the nine children there were five true positives. Of the 42 children who were well at follow up, there were only two false positives using this predictor.

### PREDICTIVE VALUE OF SLEEP REFLUX AND ACID CLEARING TIME

Sleep reflux of 6·4 minutes per hour or more, or an acid clearing time of 7 minutes or more were applied as predictors of the likelihood of continuing symptoms of gastro-oesophageal reflux. Of 63 pH studies, there were four false negatives and five false positives. This gives a specificity of 88·1% (95% confidence interval (9·8%)) and a sensitivity of 81·0% (95% confidence interval (16·8%)).

### FALSE POSITIVES AND FALSE NEGATIVES

Three of the children with false positive results – that is, they may have still been refluxing but had no symptoms or problems at follow up, were below 10 months of age at the time of their pH study. Another child had repaired oesophageal atresia, and showed an acid clearing time of 12·5 minutes. The fifth child was studied six months after fundoplication, and had an acid clearing time of nine minutes.

Of the four false negatives, one child presented with vomiting and the other three with neurological problems. None had any sleep reflux. All four showed reflux whilst awake of greater than seven minutes and acid clearing times of greater than 3·5 minutes. One child with spina bifida had awake reflux of 20·2 minutes per hour and an acid clearing time of 5·5 minutes.

TABLE IV *Results of oesophageal pH studies excluding the 12 children from Group B with sleep reflux of 6·4 minutes per hour or greater. Results were obtained using the Mann-Whitney U test.*

| | Median value | | | |
|---|---|---|---|---|
| | Group A | Group B | Δ(95% CI) | p |
| Age (mo) | 8·0 | 17·0 | 9·5 (−19·1, 21·8) | ns |
| Awake reflux (min/h) | 3·6 | 8·3 | 4·1 (0·9, 6·6) | p<0·05 |
| Reflux episodes lasting ≥5 minutes whilst awake (n) | 1 | 3 | 1 (0, 3) | p<0·05 |
| Longest reflux episode whilst awake (min) | 6 | 7 | 4 (0, 8) | ns |
| Acid clearing time (min) | 2·5 | 8·0 | 4·5 (2·5, 8·0) | p<0·0001 |
| Sleep reflux (min/h) | 0·0 | 0·0 | – | ns |
| Reflux episodes lasting ≥5 minutes during sleep (n) | 0 | 0 | – | ns |
| Longest reflux episode during sleep (min) | 0 | 0 | – | ns |

Group A: 42 studies from children no longer on treatment for gastro-oesophageal reflux at follow up. Group B': New group B – nine studies from children still on treatment for gastro-oesophageal reflux at follow-up, or who had undergone antireflux surgery. These nine had sleep reflux of less than 6·4 minutes per hour. Δ denotes the point estimate of the difference between the medians, given with a 95% confidence interval. p is the probability that there is no difference between group A and group B'. ns means not significant.

## Discussion

The occurrence of gastro-oesophageal reflux is not in itself an abnormality[5 7] The value of oesophageal pH monitoring must therefore lie in its ability to help identify patients who will require continuing medical treatment or surgical intervention to control their symptoms of gastro-oesophageal reflux.

Various attempts have been made to devise a useful scoring system. Most are complex and involve individual weighting of the pH variables. All have tried to distinguish between 'normal' and 'abnormal' gastro-oesophageal reflux using asymptomatic controls.[2 8 9] This approach is open to error because no absolute touchstone of normality exists. The study described here has attempted a new approach: to distinguish between gastro-oesophageal reflux likely to resolve and gastro-oesophageal reflux likely to cause continuing symptoms.

The significance of body position should perhaps be questioned. In this study the oesophageal pH pattern produced by gastro-oesophageal reflux occurring while awake was quite different from that produced during sleep. Most children spent some time awake whilst supine and it was observed that body position had very little effect on the recordings. A recent study in adults[10] has also found no evidence to support the upright, supine, or combined patterns of reflux[4 5] as being independent entities.

With these points in mind a simple index has been derived from oesophageal pH studies in children. There are two variables in the oesophageal pH recording – sleep reflux and acid clearing time – which are independent and combine to give a good indication of the probable course of gastro-oesophageal reflux in 81% of cases. Few children with delayed acid clearing time had significant sleep reflux and *vice versa*. There may be, therefore, two separate types of symptomatic gastro-oesophageal reflux in children which may lead to continuing problems.

Episodes of gastro-oesophageal reflux occurring during sleep tend to be prolonged because of the lack of swallowing in deep, non-REM sleep.[11] The importance of sleep reflux is clear, but the mechanisms responsible for it are not understood. Many symptomatic children with gross awake reflux have no reflux during sleep. Recent studies have suggested that sleep reflux can be decreased by avoiding food and drink for three hours before going to bed. It is possible that children with significant sleep reflux have

delayed gastric emptying, with relatively large food residues remaining in the stomach during sleep. This could well predispose the child to sleep reflux.

A single 24 hour value for time spent with an oesophageal pH of less than pH4 was initially considered. The results appeared to be highly significant with median values of 4·7 and 14·5 minutes per hour for groups A and B respectively ($p<0·0001$). The 24 hour score is highly correlated ($p<0·001$) with sleep reflux (minutes per hour), however, and will therefore depend on the amount of sleep during the 24 hour recording. The specificity (85·7%) and sensitivity (76·2%) of the single 24 hour score coupled with acid clearing time are inferior to the sleep reflux/acid clearing time combination. For these reasons it seemed preferable to consider sleeping and waking periods separately during the 24 hours.

Delayed acid clearing time was the other pH variable to emerge as highly significant. Perhaps abnormal peristalsis is responsible, or impaired salivary buffering. It is surprising that the longest reflux episode occurring whilst awake was not found to be significant in this group (Table IV). This may be because the longest reflux episode awake will depend on both acid clearing time and the quantity of refluxed material. It is possible that a fully ambulatory study at home, by removing the known effect on gastro-oesophageal reflux of the hospital setting, would have shown the longest reflux episode to be significant. Fully ambulatory studies in children are, however, not always practicable because of the possible damage to the recording equipment.

The results nevertheless suggest that prolonged exposure of the oesophagus to acid is an important factor in the clinical course of gastro-oesophageal reflux. This is in agreement with other groups who have suggested that one long episode of reflux is more damaging than many short episodes adding up the same exposure time.[12 13]

Three points specific to several subgroups of children can also be made: (a) Children below 10 months of age with symptoms of gastro-oesophageal reflux are likely to improve spontaneously as they grow older.[14] Caution should therefore be exercised in interpreting this test, and indeed any test for gastro-oesophageal reflux in children of less than 10 months. Three of the children with false positive results were in this group. (b) The children presenting with neurological problems had either cerebral palsy or spina bifida, both of which are associated with poor muscle tone. Lower oesophageal sphincter function and peristaltic clearance of the oesophagus are both likely to be impaired in this group. Acid clearing time, duration of the longest reflux episode awake and the number of reflux episodes lasting five minutes or more are all variables which reflect peristaltic function and/or lower oesophageal sphincter competence to some extent. It is therefore not surprising that this disgnostic category differed from the others for all of these three variables. (c) Children with repaired oespophageal atresia are predisposed to gastro-oesophageal reflux and its complications.[15] Peristalsis is usually abnormal and the function of the lower oesophageal sphincter is impaired. This group showed prolonged acid clearing times.

Acid clearing time gives an indication of peristaltic function, but gives no indication of the amount of time spent with an oesophageal pH of less than pH4. Some kind of combination of acid clearing time and number of reflux episodes occurring may prove more useful, particularly in children with repaired oesophageal atresia or neurological problems. A larger study would determine the usefulness of such a combination.

In conclusion, this study identifies two different features of oesophageal pH recordings which can be of predictive value in assessing the likely clinical outcome: sleep reflux of 6·4 minutes per hour or more, or an acid clearing time of 7 minutes or more.


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