Asthma and Reflux: A common association

DR JOHN WYETH
Aims

- Refresh understanding of reflux
- Know atypical presentations of reflux
- Understand investigation and management options for reflux
Clinical Spectrum of Reflux

GERD is a condition that develops when the reflux of stomach content causes troublesome symptoms and/or complications.

Esophageal Syndromes
- Symptomatic Syndromes
  - Typical reflex syndrome
  - Reflux chest pain syndrome
- Syndromes With Esophageal Injury
  - Reflux esophagitis
  - Reflux stricture
  - Barrett’s esophagus
  - Adenocarcinoma

Extraesophageal Syndromes
- Established Association
  - Reflux cough
  - Reflux laryngitis
  - Reflux asthma
  - Reflux dental erosions
- Proposed Association
  - Sinusitis
  - Pulmonary fibrosis
  - Pharyngitis
  - Recurrent otitis media
Asthma, Cough and Reflux

- Pathological reflux common
  - 30-80% of patients with asthma
  - Reflux third most common cause of cough (20%)
- Postulated mechanisms
  - Intra-oesophageal reflux
  - Extra-oesophageal reflux
  - Micro-aspiration
- Exacerbation of cough
  - Asthma
  - CORD
Case One: Reflux

- 55 year old male presents with typical acid reflux symptoms
- Long history and use of antacids for symptom control
- Started on omeprazole by GP and referred for endoscopy
Diagnosis of Reflux

- **Typical History**
  - Heartburn
  - Reflux

- **Endoscopic Features**
  - Erosions or ulcers at oesophago-gastric junction
  - 40% patients will have normal endoscopy
Drug management of acid reflux

<table>
<thead>
<tr>
<th>Drug Type</th>
<th>Mechanism of Action</th>
<th>Onset of Action</th>
<th>Duration of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antacids / Alginates</td>
<td>Local effect: acid neutralization ('sponge')</td>
<td>5-10 mins</td>
<td>Up to 90 mins</td>
</tr>
<tr>
<td>H2 antagonist</td>
<td>Systemic effect: Inhibition of certain histamine receptors</td>
<td>~60 mins</td>
<td>Up to 12 hours</td>
</tr>
<tr>
<td>Proton Pump Inhibitor</td>
<td>Systemic effect: enzyme blocking</td>
<td>~2-4 hours</td>
<td>17-24 hours</td>
</tr>
</tbody>
</table>
Individual Variation in Response to PPI

Time Gastric pH Above 3

Mean duration of effect was:
10 mg = 13 hrs (30% lasted < 6 hours)
20 mg = 19 hrs
40 mg = 21 hrs

Omeprazole not always effective

Omeprazole efficacy in treating heartburn symptoms across all 14 days

- **Omeprazole 20mg**
- **Omeprazole 10mg**
- **Placebo**

Study 1:
- Omeprazole 20mg: 60%
- Omeprazole 10mg: 58%
- Placebo: 40%

Study 2:
- Omeprazole 20mg: 65%
- Omeprazole 10mg: 62%
- Placebo: 50%

Statistical significance:
- Omeprazole 20mg vs. Placebo: $P \leq 0.001$
- Omeprazole 10mg vs. Placebo: $P \leq 0.001$
Case Two: Sensitive Oesophagus?

- A 42 year old female presents with chest pain. She denies reflux and has had a normal cardiac work up.
- Endoscopy, without prior treatment with proton pump inhibitor therapy, reveals no changes of oesophagitis (NERD)
- What are the options?
Spectrum of Reflux

Symptoms

Acid Reflux

Oesophageal Damage
The frequency of acid reflux symptoms is directly related to the degree of oesophageal acid exposure.
Oesophageal pH Monitoring

- Measures change in oesophageal pH
- Definition of acid reflux is a drop to pH < 4
- Ambulatory system and 24 hour recording
- Analysis by activity
  - Supine
  - Meals
- Analysis by composite scores
  - De Meester
- Analysis by symptoms
  - Symptom index
Diagnosis of Reflux by pH

### Reflux event

![Reflux event diagram](image)

### Summary calculation

#### Acid Reflux Composite Score Analysis (DeMeester) (pH)

<table>
<thead>
<tr>
<th>Metric</th>
<th>Patient Value</th>
<th>Patient Score</th>
<th>Normal Threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upright Time In Reflux</td>
<td>20.0%</td>
<td>8.5</td>
<td>&lt; 8.4</td>
</tr>
<tr>
<td>Recumbent Time In Reflux</td>
<td>0.0%</td>
<td>0.4</td>
<td>&lt; 3.5</td>
</tr>
<tr>
<td>Total Time In Reflux</td>
<td>11.2%</td>
<td>8.1</td>
<td>&lt; 4.5</td>
</tr>
<tr>
<td>Episodes Over 5 min.</td>
<td>8.4</td>
<td>7.4</td>
<td>&lt; 3.5</td>
</tr>
<tr>
<td>Longest Episode</td>
<td>49.9 min</td>
<td>6.5</td>
<td>&lt; 19.8</td>
</tr>
<tr>
<td>Total Episodes</td>
<td>43.2</td>
<td>2.9</td>
<td>&lt; 46.9</td>
</tr>
<tr>
<td><strong>Composite Score</strong></td>
<td><strong>33.9</strong></td>
<td><strong>&lt; 14.7</strong></td>
<td></td>
</tr>
</tbody>
</table>
Symptom Index

Number of Times Symptom Occurred when pH < 4

\[
\times 100
\]

Total Number of Times Symptom Reported

Positive SI \( \geq 50\% \)

Medical Therapy

PPI efficacy for potential manifestations of GERD

Estimates based on available RCT data

- **Esophagitis healing**
  - Mild
  - Severe

- **Heartburn relief**
  - Esophagitis
  - NERD

- **Regurgitation relief**

- **Chest pain (50% relief)**
  - GERD (+pH)
  - GERD (-pH)

- **Chronic cough (improved)**
  - GERD (+pH)
  - GERD (-pH)

- **Hoarseness (improved)**
  - GERD (-)
Case Three: Non-acid reflux

- 72 year old man with long history of reflux
- Good control of reflux symptoms with omeprazole
- Endoscopy negative
- Presents with persistent cough
- 24 Hr pH impedance study performed
What Is Impedance?

Opposition to Current Flow

- Inversely related to the electrical conductivity of an organ’s wall & contents.
Why Does Impedance Change?

No bolus = few ions = high impedance

Bolus present = many ions = low impedance
Impedance Range

Low Conductivity = High Impedance

- Air
- Oesophageal Lining
- Saliva
- Food
- Refluxate

High Conductivity = Low Impedance
Intraluminal Impedance Trace

Impedance

Preswallow Impedance

Air

Liquid bolus

Contraction wave

Time

seconds

Ohms
Acid reflux

Non-acid reflux

Impedance

pH

Oesophageal

Gastric
Cough and Non-Acid Reflux Event
## Acid Reflux Composite Score

<table>
<thead>
<tr>
<th>Metric</th>
<th>Value</th>
<th>Score</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upright Time In Reflux</td>
<td>4.6%</td>
<td>2.0</td>
<td>&lt; 8.4</td>
</tr>
<tr>
<td>Recumbent Time In Reflux</td>
<td>1.0%</td>
<td>1.4</td>
<td>&lt; 3.5</td>
</tr>
<tr>
<td>Total Time In Reflux</td>
<td>3.4%</td>
<td>2.4</td>
<td>&lt; 4.5</td>
</tr>
<tr>
<td>Episodes Over 5 min.</td>
<td>2.6</td>
<td>2.5</td>
<td>&lt; 3.5</td>
</tr>
<tr>
<td>Longest Episode</td>
<td>12.2 min</td>
<td>1.7</td>
<td>&lt; 19.8</td>
</tr>
<tr>
<td>Total Episodes</td>
<td>28.1</td>
<td>1.7</td>
<td>&lt; 46.9</td>
</tr>
<tr>
<td><strong>Composite Score</strong></td>
<td>1</td>
<td>1.7</td>
<td>&lt; 14.7</td>
</tr>
</tbody>
</table>
Symptom Correlation to Reflux

Symptom = Cough

<table>
<thead>
<tr>
<th>Cough Events</th>
<th>Acid Related</th>
<th>Non-Acid Related</th>
<th>All Reflux Events</th>
<th>Symptom Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>23</td>
<td>0</td>
<td>17</td>
<td>17</td>
<td>74%</td>
</tr>
</tbody>
</table>
Is surgery effective for non-acid reflux?

- **Control of reflux**

- **Control of symptoms**
  - Case Report - Fundoplication eliminates chronic cough due to non-acid reflux identified by impedance pH monitoring. Maine et al. Thorax 2005;60:521-523
    - 6/6 patients improved with surgery
Outcome of anti-reflux surgery and respiratory symptoms

<table>
<thead>
<tr>
<th>Cough only</th>
<th>Respiratory symptoms and cough</th>
<th>Respiratory symptoms no cough</th>
</tr>
</thead>
<tbody>
<tr>
<td>80%</td>
<td>76%</td>
<td>66%</td>
</tr>
<tr>
<td>improved by 6 weeks</td>
<td>improved by 6 weeks</td>
<td>improved by 6 weeks</td>
</tr>
<tr>
<td>63%</td>
<td>60%</td>
<td>55%</td>
</tr>
<tr>
<td>improved by 6 months</td>
<td>improved by 6 months</td>
<td>improved by 6 months</td>
</tr>
</tbody>
</table>
Impedance Studies in Gastroenterology

- A new technology
- Measures physiological function of oesophagus
- Improved sensitivity in diagnosis of reflux disorders
  - Non-acid reflux
  - Atypical reflux presentations
  - Better selection of patients for anti-reflux procedures
- An adjunct in manometry
Take home messages

- Reflux and cough is common
- A trial of medical therapy in the absence of “alarm features” is recommended as first line of management.
- Non-acid reflux may be the cause and will need oesophageal pH impedance for diagnosis.
- Anti-reflux therapy has been shown to be effective in a group of patients.