EOSINOPHILIC (AND NON-EOSINOPHILIC) ASTHMA
WHO AM I AND COI

• Respiratory SMO at Wellington Hospital
• Deputy Director of the Medical Research Institute of New Zealand
• Specialist interest in asthma and obstructive airways disease
WHO AM I AND COI

• I have received support to attend educational meetings from AstraZeneca, Boehringer-Ingelheim, GSK and Novartis and presented independent medical education at symposia funded by AstraZeneca, Boehringer-Ingelheim, and Novartis

Research funders:
Health Research Council  AstraZeneca
Wellington Medical Research  GSK
Foundation  Fisher & Paykel
Asthma Foundation New Zealand  Genentech / Roche
WHAT I’M NOT GOING TO ATTEMPT
AIMS

• What is eosinophilic asthma?
• How is it diagnosed?
• Why should we care?
• What about non-eosinophilic / treatable traits?
ISN’T ALL ASTHMA THE SAME?
HOW IS EOSINOPHILIC ASTHMA DIAGNOSED?

- Induced sputum
- Blood eosinophils
- Exhaled nitric oxide
Induced sputum samples

Zsoka Weiszhar, and Ildiko Horvath Breathe 2013;9:300-306
HOW IS IT DIAGNOSED?

- Induced sputum
- Blood eosinophils
- Exhaled nitric oxide
WHAT CAUSES IT?
Two different pathways lead to eosinophilic airway inflammation in asthma.
WHY SHOULD I CARE?

- Diagnosis of asthma
- Management of asthma
DIAGNOSIS OF ASTHMA

PRESENTATION WITH SUSPECTED ASTHMA

CLINICAL ASSESSMENT
- History and examination
- Measurement of PEF or FEV₁ including bronchodilator responsiveness

ASTHMA LIKELY

START ASTHMA TREATMENT AND REVIEW RESPONSE
- Good response
  - Continue to monitor and treat
- Poor response
  - Consider further investigations and/or specialist referral

Consider alternative diagnoses
- Alternative diagnoses confirmed
  - YES Treat accordingly
Asthma exacerbations and sputum eosinophil counts: a randomised controlled trial

Ruth H Green, Christopher E Brightling, Susan McKenna, Beverley Hargadon, Debbie Parker, Peter Bradding, Andrew J Wardlaw, Ian D Padvord
Mepolizumab and Exacerbations of Refractory Eosinophilic Asthma

Severe eosinophilic asthma treated with mepolizumab stratified by baseline eosinophil thresholds: a secondary analysis of the DREAM and MENSA studies

Hector G Ortega, Steven W Yancy, Rhonda Mayer, Necdet R Gunay, Oliver N Keene, Eugene R Bleeker, Christopher F Brightling, Ian D Pavord
ASTHMA MANAGEMENT

• Blood eosinophils >0.4 is a marker of increased risk of exacerbations
• Presence of eosinophilia predicts response to inhaled steroids
• Adjusting steroid dosing based on sputum eosinophils can improve outcomes
• Persistent eosinophilia despite treatment may indicate steroid insensitive disease OR poor adherence / technique
• Eosinophilia predicts response to anti-IL5 therapies
WHAT ABOUT NON-EOSINOPHILIC ASTHMA?

• Look for other treatable traits
• Try to avoid excessive steroids
• If frequent infective exacerbations and nothing else to optimise consider azithromycin
TREATABLE TRAITS

Treatable traits: toward precision medicine of chronic airway diseases

Alvar Agustí¹, Elisabeth Bel², Mike Thomas³, Claus Vogelmeier⁴, Guy Brusselle⁵, Stephen Holgate⁷, Marc Humbert⁸, Paul Jones⁹, Peter G. Gibson¹⁰, Jørgen Vestbo¹¹, Richard Beasley¹² and Ian D. Pavord¹³
TREATABLE TRAITS

Specific characteristics of patients including phenotypes of airways disease, overlapping disorders, comorbidities, environmental and lifestyle factors, that potentially contribute to respiratory health, that are potentially amenable to specific treatments.
**Table 5: Treatable traits in asthma.**

**Overlapping disorders:**
- COPD
- Bronchiectasis
- Allergic bronchopulmonary aspergillosis
- Dysfunctional breathing including vocal cord dysfunction.

**Comorbidities:**
- Obesity
- Gastro-oesophageal reflux disease
- Rhinitis
- Sinusitis
- Depression/anxiety.

**Environmental:**
- Smoking
- Occupational exposures
- Provoking factors including aspirin, other NSAIDs and beta blockers.

**Behavioural:**
- Adherence
- Inhaler technique.
Risk assessed using biomarkers of eosinophilic airway inflammation

- Inflammation predominant disease
  - High dose ICS (oral CS)
  - Biologics

- Severe, concordant disease
  - LABA/LAMA/High dose ICS
  - Biologics

- Benign disease
  - PRN SABA
  - LABA or LAMA

- Symptom predominant disease
  - LABA/LAMA

Symptoms due to airflow limitation
SUMMARY

• Not all asthma is the same

• Around 50% of patients with asthma have evidence of eosinophilic inflammation

• Assessment of eosinophils in asthma:
  • Can help confirm the diagnosis of asthma
  • Can hint at poor adherence
  • Can help guide the use of steroids in asthma
  • In the (near) future will be essential to determine eligibility for biological therapies

• Considering treatable traits may help you personalise treatment for your patient
ANY QUESTIONS?
Effect of azithromycin on asthma exacerbations and quality of life in adults with persistent uncontrolled asthma (AMAZES): a randomised, double-blind, placebo-controlled trial

Prof Peter G Gibson, MBBS, Prof Ian A Yang, MBBS, Prof John W Upham, MBBS, Prof Paul N Reynolds, MD, Prof Sandra Hodge, PhD, Prof Alan L James, FRACP, Prof Christine Jenkins, MD, Prof Matthew J Peters, MBBS, Prof Guy B Marks, PhD, Melissa Baraket, PhD, Heather Powell, MMedSc, Steven L Taylor, BSC, Lex E X Leong, PhD, Prof Geraint B Rogers, PhD, Prof Jodie L Simpson, PhD

The Lancet
Volume 390, Issue 10095, Pages 659-668 (August 2017)
DOI: 10.1016/S0140-6736(17)31281-3
Figure 2

The number of exacerbations over weeks for Azithromycin and Placebo groups.
Incidence rate ratio: 0.59 (95% CI 0.47–0.74)

p < 0.0001
<table>
<thead>
<tr>
<th>Category</th>
<th>Number</th>
<th>Placebo</th>
<th>Azithromycin</th>
<th>Incidence rate ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-eosinophilic asthma</td>
<td>224</td>
<td>1.74</td>
<td>1.15</td>
<td>0.66 (0.47–0.93)</td>
</tr>
<tr>
<td>Eosinophilic asthma</td>
<td>196</td>
<td>1.98</td>
<td>0.96</td>
<td>0.52 (0.29–0.94)</td>
</tr>
<tr>
<td>Inhaled corticosteroid dose adjustment</td>
<td>420</td>
<td>1.86</td>
<td>1.07</td>
<td>0.58 (0.46–0.74)</td>
</tr>
<tr>
<td>Frequent exacerbators</td>
<td>140</td>
<td>2.79</td>
<td>1.47</td>
<td>0.55 (0.41–0.73)</td>
</tr>
<tr>
<td>Cough and sputum VAS</td>
<td>48</td>
<td>1.72</td>
<td>0.79</td>
<td>0.49 (0.26–0.95)</td>
</tr>
<tr>
<td>Bacteria-negative</td>
<td>188</td>
<td>1.85</td>
<td>1.18</td>
<td>0.61 (0.52–0.72)*</td>
</tr>
<tr>
<td>Bacteria-positive</td>
<td>48</td>
<td>2.64</td>
<td>1.11</td>
<td>0.39 (0.22–0.69)*</td>
</tr>
</tbody>
</table>
CASE

45 year old female factory worker with atopic asthma

On ‘Step 3’ ICS/LABA treatment, Fluticasone/salmeterol 50/25 ii BD

Repeat courses of oral steroids for exacerbations

Background of anxiety/depression.
DEFAULT OPTION

The standard stepwise approach would be to either:

• Increase the ICS dose by stepping up to a higher dose FP/SM 100/25 2 bd. On the basis that this is likely to be ICS responsive eosinophilic asthma.

• Change to budesonide/formoterol 200/6 2 bd and one as required on the basis that a change to the SMART regimen reduces the risk of severe exacerbations.
POTENTIAL TREATABLE TRAITS IN THIS CASE

• Eosinophilic asthma
• Psychogenic vocal cord dysfunction
• Allergic bronchopulmonary aspergillosis
• Chronic rhinosinusitis
• Occupational asthma
• Adherence, inhaler technique