Are the Concepts of Asthma and COPD Outmoded?

AProf Jeff Garrett
Respiratory Physician
Airway inflammation

- Underlying pathology in asthma
- No good test to measure degree of airway inflammation
- New “tests of airway inflammation”
  - bronchoscopy: BAL/bronchial biopsy
  - induced sputum (monoclonal Antibody, ELISA technique)
  - exhaled nitric oxide (eNO)
- Not widely available outside clinical trials but changing
Sputum: causes of increase in cell type

Eosinophilic:  uncontrolled asthma
              non compliance with medications
              occupational asthma
              Steroid responsive COPD

Neutrophilic:  irritants - cigarettes, occupational
                infections – bacterial, viral
Inflammatory subtypes in asthma: Assessment and identification using induced sputum


- **Eosinophilic**
  - Eosinophils > 1.01%
  - Neutrophils > 61%

- **Neutrophilic**
  - Neutrophils > 61%

- **Paucigranulocytic**
  - Eosinophils 31%

- **Mixed**
  - Neutrophils 8%

20%
Inflammatory Phenotypes of airflow obstruction

Eosinophilic

- Atopic Asthma
- Extrinsic Asthma
- Eosinophilic Bronchitis
- Occupational Asthma

Neutrophilic

- Allergens
- LMW chemicals
- Viral infections
- Smoking
- ??

Post viral wheeze

COPD

Intrinsic asthma

Bacterial Infections

Bronchiectasis

Allergens

??

??

??

??

??

??

??

 LMW chemicals

Viral infections

Smoking

Bacterial Infections

Extrinsic Bronchitis

Eosinophilic Bronchitis

Occupational Asthma

COPD

Intrinsic asthma

Bronchiectasis

Clinical Science 2002

Bronchial Inflammation

Asthma Like
(wheeze)

Bronchitis Like
(Cough and Sputum)
Results of Bacci Study: 1000mcg beclomethasone/day for 4 weeks

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>After 4 wks</th>
<th>Baseline</th>
<th>After 4 wks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High Sputum Eosinophils</td>
<td></td>
<td>Low Sputum Eosinophils</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(n=50 or 74% of sample)</td>
<td></td>
<td>(n= 17 or 26% of sample)</td>
<td></td>
</tr>
<tr>
<td>Eosinophils (%)</td>
<td>18.2</td>
<td>1.8 *</td>
<td>1</td>
<td>0.6</td>
</tr>
<tr>
<td></td>
<td>(3.1-80.1)</td>
<td>(0 – 14.5)</td>
<td>(0 – 2.7)</td>
<td>(0 – 11.9)</td>
</tr>
<tr>
<td>Neutrophils (%)</td>
<td>41</td>
<td>51.5</td>
<td>60.6</td>
<td>62.5</td>
</tr>
<tr>
<td></td>
<td>(8.2 – 86.2)</td>
<td>(5.6 – 92.2)</td>
<td>(26.4 – 94.7)</td>
<td>(0 – 82.8)</td>
</tr>
<tr>
<td>ECP (μg/L)</td>
<td>420</td>
<td>122 *</td>
<td>24</td>
<td>68</td>
</tr>
<tr>
<td></td>
<td>(1 – 1,920)</td>
<td>(4 – 1,010)</td>
<td>(2 – 380)</td>
<td>(4 – 1,432)</td>
</tr>
</tbody>
</table>

Data presented as median (range)
ECP = Eosinophil Cationic Protein
*Significant difference between groups for eosinophils & ECP at baseline  p< 0.01
## Lung function before and after corticosteroid treatment

<table>
<thead>
<tr>
<th>Variables</th>
<th>High Sputum Eosinophils</th>
<th>Low Sputum Eosinophils</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>After 2 wk</td>
</tr>
<tr>
<td>FEV1, % predicted</td>
<td>87.9 ± 15.4</td>
<td>97.3 ± 14.5§</td>
</tr>
</tbody>
</table>
‘Inflammometry’

- The use of information gathered from measures of airway inflammation to guide assessment and treatment.

- Success with induced sputum eosinophil counts. (Gold standard)

- Predicts steroid responsive disease
  - Pavord 1999
  - Pizzichini 1999
  - Brightling 2000
  - Green 2002

- A rise in counts measured longitudinally predicts subsequent loss of asthma control
  - Jatakanon 2000
  - Deykin 2004

- Management protocols aimed at titrating steroid therapy to maintain normal counts lead to superior asthma control
  - Green 2002
  - Jayaram 2005
  - Chlumsky 2006
ROC curve of eNO predicting positive eosinophilia

Sputum eosinophils

<table>
<thead>
<tr>
<th></th>
<th>&lt;3%</th>
<th>≥ 3%</th>
</tr>
</thead>
<tbody>
<tr>
<td>FeNO &lt; 0.20</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>FeNO ≥ 0.20</td>
<td>6</td>
<td>31</td>
</tr>
</tbody>
</table>

Cut point of 20 has sensitivity (31/39) 79%, specificity (7/13) 54%
ROC curve of serum eosinophils predicting positive eosinophilia

Sputum eosinophils

<table>
<thead>
<tr>
<th>&lt;3%</th>
<th>≥ 3%</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>6</td>
</tr>
</tbody>
</table>

Serum eosinophils

<table>
<thead>
<tr>
<th>&lt; 0.35</th>
<th>≥ 0.35</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>14</td>
</tr>
</tbody>
</table>

Cut point of 0.35 has sensitivity 14/20=70%, specificity 21/33=64%

Diagonal segments are produced by ties.
ROC curve of serum eosinophils at predicting +ve sputum neutrophils (>76%) 

Cut point of 0.23 has sensitivity 65%, specificity 53% (p=0.03, n=508) Scleich et al. Personal communication
Inhaled Steroids

- Flat dose response (greatest benefit with low-medium dose)
- Outcome measures downstream from direct (anti-inflammatory effects):
  - Lung Fn
  - BHR
  - Symptom Control
  - Exacerbations
  - Sputum Eosinophils
  - FeNo
# Stepwise medication therapy for asthma

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3</th>
<th>Step 4</th>
<th>Step 5</th>
<th>Step 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>No daily controller medication</td>
<td>Low-dose ICS Alternatives: cromolyn, LRA nedocromyl, or theophylline OR Low-dose ICS + LABA Alternatives: low-dose ICS + either LRA, theophylline, or zileuton</td>
<td>Either medium-dose ICS + LABA Alternative: Medium-dose ICS + either LRA, theophylline, or zileuton</td>
<td>Consult with asthma specialist for step 4 and above</td>
<td>High-dose ICS + LABA + oral systemic steroids + Consider omalizumab for patients with allergies</td>
<td>Consult with asthma specialist at step 3</td>
</tr>
</tbody>
</table>

- SABA prn for quick-relief
- SABA prn for quick-relief
- SABA prn for quick-relief
- SABA prn for quick-relief
- SABA prn for quick-relief
- SABA prn for quick-relief
Mr A.N – 48yr old Maori. $\frac{\text{FEV}_1}{\text{FVC}} = 1.7/3.5$ (FEV$_1$ 70% predicted)

- **Seretide 125/25**
  - II b.d
  - $(S_x + +)$

- **Seretide 125/25**
  - II b.d
  - **Flixotide 250**
  - II b.d
  - (FEV$_1$ 2.1)

- **Seretide 125/25**
  - II b.d
  - (II $S_x$)

**Graph:**
- **Y-axis:** Serum eosinophil count
- **X-axis:** Time (Jan 2013 to Mar 2014)
- **Data points:**
  - January 2013: 0.5
  - February 2013: 0.35
  - March 2013: 0.5
  - April 2013: 0.35
  - May 2013: 0.5
  - June 2013: 0.35
  - July 2013: 0.5
  - August 2013: 0.35
  - September 2013: 0.5
  - October 2013: 0.35
  - November 2013: 0.5
  - December 2013: 0.35
  - January 2014: 0.5
  - February 2014: 0.35
  - March 2014: 0.5

**SLTA:**
Management of COPD

I: Mild
- FEV₁/FVC < 0.70
- FEV₁ ≥ 80% predicted

II: Moderate
- FEV₁/FVC < 0.70
- 50% ≤ FEV₁ < 80% predicted

III: Severe
- FEV₁/FVC < 0.70
- 30% ≤ FEV₁ < 50% predicted

IV: Very Severe
- FEV₁/FVC < 0.70
- FEV₁ < 30% predicted or FEV₁ < 50% predicted plus chronic respiratory failure

Active reduction of risk factor(s); influenza vaccination
Add short-acting bronchodilator (when needed)
Add regular treatment with one or more long-acting bronchodilators (when needed); Add rehabilitation
Add inhaled glucocorticosteroids if repeated exacerbations
Add long term oxygen if chronic respiratory failure.
Consider surgical treatments
Survival Curves for Pneumonia and COPD exacerbation in TORCH: fluticasone/salmeterol versus salmeterol (using Poisson/exponential model)

- **Pneumonia**
  - NNT(H) = 95 (6 months)
  - NNT(H) = 50 (1 year)
  - NNT(H) = 27 (2 years)
  - NNT(H) = 19 (3 years)

- **Exacerbation**
  - NNT(B) = 26 (6 months)
  - NNT(B) = 21 (1 year)
  - NNT(B) = 26 (2 years)
  - NNT(B) = 43 (3 years)

NNT is the inverse of the vertical distance between the survival curves (shown as vertical arrows).

- **6 months**
- **One year**
- **Two years**
- **Three years**
# Overlap between COPD and Pneumonia in CMDHB

<table>
<thead>
<tr>
<th>Year</th>
<th>Primary diagnosis of COPD without pneumonia</th>
<th>COPD with Pneumonia as secondary diagnosis</th>
<th>Pneumonia as primary diagnosis with COPD as secondary diagnosis</th>
<th>Percentage of COPD patients with pneumonia</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000/2001</td>
<td>580</td>
<td>23</td>
<td>220</td>
<td>30%</td>
</tr>
<tr>
<td>2001/2002</td>
<td>644</td>
<td>102</td>
<td>202</td>
<td>32%</td>
</tr>
<tr>
<td>2002/2003</td>
<td>647</td>
<td>94</td>
<td>133</td>
<td>26%</td>
</tr>
<tr>
<td>2003/2004</td>
<td>749</td>
<td>120</td>
<td>121</td>
<td>24%</td>
</tr>
<tr>
<td>2004/2005</td>
<td>786</td>
<td>135</td>
<td>102</td>
<td>23%</td>
</tr>
<tr>
<td>2005/2006</td>
<td>761</td>
<td>147</td>
<td>61</td>
<td>21%</td>
</tr>
<tr>
<td>2006/2007</td>
<td>837</td>
<td>115</td>
<td>75</td>
<td>19%</td>
</tr>
<tr>
<td>2007/2008</td>
<td>867</td>
<td>82</td>
<td>83</td>
<td>16%</td>
</tr>
<tr>
<td>2008/2009</td>
<td>905</td>
<td>70</td>
<td>86</td>
<td>15%</td>
</tr>
<tr>
<td>2009/2010</td>
<td>801</td>
<td>97</td>
<td>82</td>
<td>18%</td>
</tr>
<tr>
<td>2010/2011</td>
<td>937</td>
<td>100</td>
<td>85</td>
<td>16%</td>
</tr>
<tr>
<td>2011/2012</td>
<td>962</td>
<td>138</td>
<td>85</td>
<td>19%</td>
</tr>
<tr>
<td>2012/2013</td>
<td>1,070</td>
<td>127</td>
<td>113</td>
<td>18%</td>
</tr>
</tbody>
</table>
‘Accepted’ facts:

- Eosinophilic airway inflammation is important in pathogenesis of severe COPD exacerbations

  - ‘Eosinophilic airway inflammation and exacerbations of COPD: a randomized controlled trial’ – European Respiratory Journal 2007; 29: 906-913

- Airway eosinophilia is associated with steroid responsiveness in COPD

Peripheral eosinophilia is a sensitive and specific biomarker for airway eosinophilia during COPD exacerbations.

Patient #1

Mr KM 30yr Samoan diagnosed with asthma at the age of 3. History of seasonal allergic rhinitis and eczema. Lifelong non-smoker, has no family history of asthma and no history of Aspirin or NSAID intolerance. He has had 5 exacerbations of asthma over the last 12 mths, requiring systemic corticosteroids. His asthma symptoms are predominantly wheeze, chest tightness and breathlessness. He occasionally coughs and brings up small plugs of yellow sputum. He currently uses his Salbutamol inhaler up to 20x a day and experiences nocturnal awakening. Trigger factors include exercise, changes in weather and anxiety.

Current treatment:
Fluticasone 125mcg 2 puffs bid, Salmeterol 25mcg 2 puffs bid, Salbutamol 100mcg 2 puffs PRN

Spirometry:
FEV1  FEV1%  FVC  FVC%
2.19   56   4.46   91

Additional investigations:
1. Serum eosinophils: 0.7
2. Total IgE: 15000iu
3. Aspergillus RAST: 1 band
4. Exhaled Nitrous Oxide (eNO): 6 ppb
Questions

1. Which sputum subtype do you think he is?
   A. Predominantly eosinophilic (>1%)
   B. Predominantly neutrophilic (>61%)
   C. Mixed eosinophilic/neutrophilic (>1% eos, >61% neut)
   D. Paucigranulocytic (<1% eos, <1% neuts)
Questions

2. Which of the following changes to treatment would you make, if any?
   A. Commence or increase dose of inhaled corticosteroids
   B. Add or increase dose of LABA
   C. Change to combination therapy (Symbicort/Seretide)
   D. Commence a course of or increase dose of oral steroids (if already on oral steroids)
   E. Add leukotriene antagonist
   F. Commence a course of oral macrolide
   G. Do not alter or commence asthma therapy
Patient #2
Ms JT is a 29yr old Maori home-maker. She was diagnosed with asthma at age 5 and has a history of allergic rhinitis and eczema. Both her sister and her children have asthma. She is an ex-smoker with a 10pack year history and admits to occasional recreational cannabis use. She has not documented history of Aspirin or NSAID intolerance. She was previously hospitalised with pneumonia 2 years ago.
Over the past year, she has had 2 moderately severe exacerbations of asthma requiring antibiotics on both occasions and hospital admission once.
Her symptoms are daily wheeze, shortness of breath and sputum production (approx 1-2 tbs per day). She notices no diurnal variation in symptoms but comments that they are worse when she forgets to take her preventer inhalers. Her triggers include dairy food intake and dusty environments. She uses Salbutamol MDI 1-3 times per week.

Medications:
Salmeterol (25mcg); Fluticasone (125mcg) 2 puffs bid; Salbutamol 2 puffs PRN

Spirometry:
FEV1  FEV1%  FVC  FVC%
1.49  45  2.5  60

Additional Investigations:
1. Serum eosinophils 0.92
2. Total IgE: 5250
3. Aspergillus RAST: negative
4. Exhaled Nitrous Oxide (eNO): 36 ppb
Questions

1. Which sputum subtype do you think would predominate?
   A. Predominantly eosinophilic (>1%)
   B. Predominantly neutrophilic (>61%)
   C. Mixed eosinophilic/neutrophilic (>1% eos, >61% neut)
   D. Paucigranulocytic (<1% eos, <1% neuts)
Questions

2. Which of the following changes to treatment would you make, if any?
   
   A. Commence or increase dose of inhaled corticosteroids
   
   B. Add or increase dose of LABA
   
   C. Change to combination therapy (Symbicort/Seretide)
   
   D. Commence a course of or increase dose of oral corticosteroids (if already on oral steroids)
   
   E. Add leukotriene antagonist
   
   F. Commence a course of oral macrolide
   
   G. Do not alter or commence asthma therapy
Patient #3

Ms EH is a 56yr old Caucasian school teacher. She was diagnosed with asthma at the age of 30. She also suffers from allergic rhinitis and mild symptoms of gastro-oesophageal reflux and does not have a history of Aspirin sensitivity. She is a non-smoker. Both her mother and uncle have asthma. By her own admission, Ms EH is a poor perceiver of asthma symptoms. On multiple occasions her friends notice her wheeze and breathlessness before she does. She has not recognised any specific triggers for asthma, except chest infections, which she experiences up to five times a year, each requiring a course of antibiotic.

Her medications include:
Salbutamol MDI 2bd via spacer; Symbicort 200/6 2 bd; Cetirizine 1 tablet od

Her spirometry reveals:
FEV1  FEV1%  FVC  FVC%
1.38   61     2.1   69

Additional Investigations:
1. Serum eosinophils 0.23
2. Total IgE: 140
3. Aspergillus RAST: negative
4. Exhaled Nitrous Oxide (eNO): 15 ppb
Questions

1. Which sputum subtype do you think would predominate?
   A. Predominantly eosinophilic (>1%)
   B. Predominantly neutrophilic (>61%)
   C. Mixed eosinophilic/neutrophilic (>1% eos, >61% neut)
   D. Paucigranulocytic (<1% eos, <1% neuts)
Questions

2. Which of the following changes to treatment would you make, if any?
   
   A. Commence or increase dose of inhaled corticosteroids
   
   B. Add or increase dose of LABA
   
   C. Change to combination therapy (Symbicort/Seretide)
   
   D. Commence a course of or increase dose of oral corticosteroids (if already on oral steroids)
   
   E. Add leukotriene antagonist
   
   F. Commence a course of oral macrolide
   
   G. Do not alter or commence asthma therapy
Asthma Admissions (Adults) in NZ

- 3000/yr (4th OECD)
- 2-3 fold variation between DHBs
- Significantly higher Maori/Pacific, lower SED
Asthma Therapy

- Reliever inhaler medications – Maori/PI > European
- Inhaled steroids – PI < others
- <30% of asthma admissions receive and utilise inhaled steroids appropriately
- 50% of outpatients are poorly adherent with inhaled steroids and 70% on suboptimal doses
- 36% of asthma admissions - Influenza vaccine
Hospital Admission data

- Majority COPD pts discharged from MMH prescribed Inhaled steroids (ICS) and are fully compliant, 80% COPD pts in East Health (65% UK) on ICS (vs 10-15% who benefit)

- All asthmatics discharged from MMH prescribed ICS but only 30% fully compliant
Spirometry in General Practice

- 50% GPs own spirometer (25% Piko6, 25% Flow/Volume)
- Upskill GP/practice nurses with 2 hour workshop
  - 40% ATS standards (DVD)
  - 60% ATS standards (2 hr workshop)
  - 80% ATS Standards (primary care service/resp physicians)
  - 88% ATS Standards (Lung Fn lab)
- QIP overseen by physiologist
Why should I check inhaler technique & adherence?

**Cons**
- I don’t have time
- All of my patients know how to use their inhalers
- I don’t have time
- It’s just a bureaucratic nit-picking requirement to reduce Xolair costs
- I don’t have time
- Patients don’t tell the truth about adherence anyway
- Ummm, can you just remind me how to use this inhaler?

**Pros**
- Identifying and correcting problems will benefit patient, hospital, society:
  - Reduce hospitalisations/ED
  - Reduce burden of symptoms
  - Reduce need for toxic or expensive treatment (my taxes!)
- It will save time in the clinic
- It will start conversations with patients about their attitudes to asthma and treatment
- It will improve staff communication skills (including my own)
- I will get some great stories about the weird things patients do with their inhalers

Woolcock Institute of Medical Research
Why are inhaler technique and adherence important?

- What proportion of people may have severe asthma?
- Community pharmacy study (PAMS): 90 patients with poorly-controlled asthma (ACQ ≥1.5) despite taking high-dose ICS/LABA

![Pie chart showing the proportions of poor technique, poor technique and poor adherence, poor adherence, and good technique and good adherence.]

39% Poor technique
50% Poor technique and poor adherence
2% Poor adherence
9% Good technique and good adherence

Armour et al, J Asthma 2011
Inhaler technique tools

- Checking and correcting inhaler technique
  - Printed resources
  - Videos
  - Checklists
  - Customised devices

- Strategies for correcting inhaler technique

- How to fit inhaler technique education into clinic processes
Printed resources

- Tear-off pads from manufacturers for individual medications
  - Some instructions inconsistent, e.g. breath-hold
- National Asthma Council brochure (specifically mentioned by PBS)

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**Table 2. Pressurised metered dose inhaler suggested checklist and common errors**

<table>
<thead>
<tr>
<th>Suggested checklist of steps*</th>
<th>Problems and common errors</th>
<th>Tips</th>
</tr>
</thead>
</table>
| 1. Remove cap  
2. Hold inhaler upright and shake well  
3. Breathe out gently  
4. Put mouthpiece between teeth without biting and close lips to form good seal  
5. Start to breathe in slowly through mouth and press down firmly on canister  
6. Continue to breathe in slowly and deeply  
7. Hold breath for about 10 seconds or as long as comfortable  
8. While holding breath, remove inhaler from mouth  
9. Breathe out gently away from mouthpiece  
10. If on extra dose as needed, wait 1 minute and then repeat steps 2 to 9  
11. Replace cap | • Inability to coordinate activation with inhalation  
• Failure to hold breath for a sufficient time  
• Multiple activations without waiting or shaking in between doses  
• Incorrect position of inhaler  
• Difficult for people with osteoarthritis affecting hands  
• May be unsuitable for patients with severe COPD with poor inspiratory flow rates | • All patients using a pMDI for an inhaled corticosteroid medication should use a spacer  
• Patients with weak hands or osteoarthritis who have difficulty using a pMDI may benefit from a Haler device  
• Keep chin up and inhaler upright (not aimed at roof of mouth or tongue) |

*Check the package insert for any specific instructions relating to an individual prescribed inhaler. COPD, chronic obstructive pulmonary disease; pMDI, pressurised metered dose inhaler.

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Figure 2. Metered dose inhaler showing correct position of inhaler and good seal with lips around mouthpiece.

Figure 3. Metered dose inhaler plus spacer showing good seal with lips around mouthpiece.
Instructional videos

- National Asthma Council

- National Prescribing Service (search NPS website for “asthma devices”)

- YouTube
  - Beware incorrect technique!
Inhaler technique checklists

- Many different checklists
  - Different items
  - Different scores
  - Some only include “essential” steps

- National Asthma Council brochure a good resource, but impractical for clinic notes

- Single page with multiple checklists (Vicky Kritikos, RPAH Asthma Clinic)
Specialised devices for checking inhaler technique

Examples
- Turbuhaler trainer with whistle (AstraZeneca)
- Flo-Tone (Clement Clarke)
- AIM device (Vitalograph)

Limitation
- These devices only check some of the inhaler technique steps
- Not a substitute for face to face checking and personal education
- Unlike face-to-face checking and physical demonstration, there is no evidence at present that achieving correct technique on these devices is effective for improving asthma outcomes
- Some criteria may be inappropriately stringent, e.g. 3-second inhalation time
Improving inhaler technique

- Physical demonstration is essential
  - Face-to-face or video (van der Palen 1997; Basheti 2005)
  - Written instructions are ineffective (Bosnic-Anticevich 2010)

- Education must be repeated
  - Skills drop off within 4-6 weeks for both patients and health professionals
  - Useful to check periodically even for highly experienced patients

- Repeated inhaler skills training is highly effective
  - Brief education in community pharmacy leads to improved asthma outcomes (Basheti JACI 2007)
  - Average 2.5 minutes (Basheti Patient Educ Couns 2008)
  - Enhanced pharmacist-patient relationship (Basheti 2008)
  - Long-term retention of health professional own skills (Basheti Am J Pharm Educ 2009)
Inhaler technique training → improved asthma control

**ACTIVE (TH)**
- Severe
- Moderate
- Mild

**CONTROL (TH)**
- Severe
- Moderate
- Mild

*Basheti et al. Pat Educ Counsel 2008*
Fitting inhaler technique checking into clinic processes

- Ensure that all staff can demonstrate correct technique
- Identify the person who is responsible for checking, and an alternate if not available
- Obtain placebo inhalers and training devices (if relevant)
- Checklist in every patient’s notes at start of clinic
- If doing pre- and post-bronchodilator spirometry, use the device that corresponds to the patient’s preventer medication
- Write the score (e.g. 8/9) in the notes, and file the checklist (dated)
Assessing adherence in severe asthma

- **Prescribing**
  - Practice software – frequency of script requests

- **Dispensing**
  - Pharmacy or managed care databases (*Andrade 2006)*

- **Consumption**
  - Physician judgement: no better than chance (*Simmons 2000)*
  - Self-report:
    - Adherence questionnaires, e.g. Morisky
    - Dose counter or canister weighing (confounded by dose dumping)
    - Electronic monitoring: date and time of every actuation
    - Serum levels, e.g. prednisone
Patient self-report

- “You’re still on 2 puffs twice a day, aren’t you?”
- “During the past week, it is estimated that you will have used 28 puffs of (each) of your study inhalers. How many puffs of your inhaler have you taken during the last week?” *(Patel et al, Respirology 2013)*
- Optimised self-report: “Lots of people don’t take their inhaler exactly as prescribed. In the last 4 weeks,
  - 1. How many days per week have you been taking your [inhaler]? 0 days, 1, 2, 3, 4, 5, 6, 7?
  - 2. How many times per day?
  - 3. How many puffs do you take each time?” *(Foster et al, Int Med J 2012)*
How accurate is self-reported adherence?
(Using optimised self-report)

Foster et al, Int Med J 2012
## Adherence questionnaires

<table>
<thead>
<tr>
<th></th>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Do you ever forget to take your medicine?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Are you careless at times about taking your medicine?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>When you feel better do you sometimes stop taking your medicine?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>Sometimes if you feel worse when you take your medicine, do you stop taking it?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Original Morisky Scale.
Electronic monitoring devices

- Asthmapolis device
- Doser device
- INCA device
- Smartinhaler Tracker device
- Smarttrack device
- Diskus Adherence Logger (DAL) device
Audiovisual inhaler reminders for missed doses

FP 250mcg bd by Smartinhaler
Final 12 wks adherence: 88% vs 66%
Improved asthma control in both groups

Charles 2007 JACI, n=110
Summary of effective adherence strategies
(few studies in severe asthma, but see Boulet & Foster, Clin Chest Med 2012)

- Unintentional poor adherence
  - Reduce cost
  - Simplify regimen
  - Reminders (location, family, phone, inhaler)

- Intentional poor adherence
  - Shared decision-making
  - SMS for individual patient barriers

- Mixed intentional/unintentional
  - Provide adherence feedback to patients
  - Motivational interviewing strategies
  - Tailored telephone calls, from health professional or computer

- Interventions that show most promise are those that
  - Can be extensively implemented at low cost
  - Allow tailoring to individual patient barriers
  - Facilitate systematic change in behaviour of health professionals and patients (Moullec, Respir Med 2012)