PCRS National Respiratory Conference
Building confidence in a changing world

Is FeNO feasible?
Carol Stonham
Co-facilitator Carla Astles
Understanding FeNO

- What is FeNO?
- What does it measure?
- Where does FeNO testing sit in asthma guidelines?
- What is the practical application?
- What service deliver model might work?
- Who pays?
What is FeNO?

Inflammatory cascade

- Plasma cells
- Mast cells: release cytokines, prostaglandins, leukotrienes and histamine
- Epithelial cells: become APCs: release cytokines
- Basophils and neutrophils: release cytokines
- B cells: become APCs
- Cytotoxic T cells and T helper cells
- Cytokines
- Eosinophils: release cytokines, toxic oxygen radicals and chemotactic factors
- Macrophages: release cytokines
- Acute, Sub-acute, Chronic

Antigens

Macrophages: become APCs: release cytokines and histamine

Release antibodies

Bronchoconstriction
FeNO is a biomarker of allergic airway inflammation

- NO produced is generally higher in individuals with asthma than in those without asthma
- Often correlates with eosinophilic inflammation

Adapted from 1
What does it measure?

- Increasing eosinophilic inflammation in the airways increases the NO exhaled
Raised FeNO predicts steroid responsiveness

Where does FeNO testing sit in asthma guidelines?

Where does FeNO testing sit in asthma guidelines?


1 In children under 5 years and others unable to undertake spirometry in whom there is a high or intermediate probability of asthma, the options are monitored initiation of treatment or watchful waiting according to the assessed probability of asthma.
Algorithm A Initial clinical assessment for adults, young people and children with suspected asthma

1. Adults, young people and children with symptoms of asthma
   - Take a structured clinical history. Specifically check for:
     - wheeze, cough or breathlessness, and any daily or seasonal variation in these symptoms
     - any triggers that make symptoms worse
     - a personal or family history of atopic disorders

2. Examine people with suspected asthma to identify expiratory polyphonic wheeze and signs of other causes of respiratory symptoms, but be aware that even if examination results are normal the person may still have asthma

3. Do not use symptoms alone without an objective test to diagnose asthma
   - Do not use a history of atopic disorders alone to diagnose asthma

4. Acute symptoms at presentation
   - Treat people immediately and perform objective tests if the equipment is available and testing will not compromise treatment
     - If objective tests cannot be done immediately, carry them out when acute symptoms have been controlled and advise patients to contact their healthcare professional immediately if they become unwell while waiting to have objective tests
   - Be aware that the results of spirometry and FeNO tests may be affected by treatment with inhaled corticosteroids

5. Children under 5
   - Treat symptoms based on observation and clinical judgement, and review the child on a regular basis. If they still have symptoms when they reach 5 years, see algorithm B for objective tests
   - Do not offer the following as diagnostic tests for asthma:
     - skin prick tests to aeroallergens
     - serum total and specific IgE
     - peripheral blood eosinophil count
     - exercise challenge (to adults aged 17 and over)

6. Children and young people aged 5 to 16
   - See algorithm B for objective tests
   - Use skin prick tests to aeroallergens or specific IgE tests to identify triggers after a formal diagnosis of asthma has been made

7. Adults aged 17 and over
   - Check for possible occupational asthma by asking employed people:
     - Are symptoms better on days away from work?
     - Are symptoms better when on holiday?
     - Make sure answers are recorded for later review
   - See algorithm C for objective tests
     - Refer people with suspected occupational asthma to an occupational asthma specialist

This algorithm is based on recommendations from NICE’s guideline on asthma, diagnosis, monitoring and chronic asthma management (2017)
Algorithm B: Objective tests for asthma in children and young people aged 5 to 16

**Order of tests**
- Perform spirometry in children and young people with symptoms of asthma
- Consider BDR test if spirometry shows an obstruction

**Interpretation of test results for children and young people aged 5 to 16 with symptoms suggestive of asthma**

- Does spirometry show an obstruction?
  - Yes: Is there reversible airflow obstruction?
    - Yes: Are FeNO levels 35 ppb or more?
      - Yes: Is there variability in peak flow readings?
        - Yes: Suspect asthma and review diagnosis after treatment
        - No: Consider alternative diagnosis and referral for specialist assessment
      - No: Diagnose with asthma
  - No: Is there variability in peak flow readings?
    - Yes: Suspect asthma and review diagnosis after treatment
    - No: Consider alternative diagnosis and referral for specialist assessment

**Abbreviations:**
FeNO, fractional exhaled nitric oxide
BDR, bronchodilator reversibility

This algorithm is based on recommendations from NICE’s guideline on asthma diagnoses, monitoring, and chronic asthma management (2017)

**Positive test thresholds**
- Obstructive spirometry: FEV1/FVC ratio less than 70% (or below the lower limit of normal if available)
- FeNO: 35 ppb or more
- BDR: Improvement in FEV1 of 12% or more
- Peak flow variability: variability over 20%
Algorithm C Objective tests for asthma in adults aged 17 and over

Order of tests

- Measure FeNO first followed by spirometry in adults with symptoms of asthma
- Carry out BDR test if spirometry shows an obstruction
- If diagnostic uncertainty remains after FeNO, spirometry and BDR, monitor peak flow variability for 2 to 4 weeks
- If diagnostic uncertainty remains after measuring peak flow variability, refer for a histamine or methacholine direct bronchial challenge test
- If histamine or methacholine direct bronchial challenge test is unavailable:
  - suspect asthma and review diagnosis after treatment or
  - refer to a centre with access to histamine or methacholine challenge testing

Interpretation of test results for adults aged 17 and over with symptoms suggestive of asthma

Does spirometry show an obstruction?

- Yes
  - Are FeNO levels 40 ppb or more?
    - Yes
      - Is there variability in peak flow readings?
        - Yes
          - Are FeNO levels between 25 and 30 ppb?
            - Yes
              - Diagnose with asthma
            - No
              - Suspect asthma and review diagnosis after treatment
        - No
          - Are FeNO levels between 25 and 30 ppb?
            - Yes
              - Diagnose with asthma
            - No
              - Consider alternative diagnoses or referral for a second opinion
    - No
      - Diagnose with asthma
  - No
    - Is there variability in peak flow readings?
      - Yes
        - Are FeNO levels between 25 and 30 ppb?
          - Yes
            - Diagnose with asthma
          - No
            - Suspect asthma and review diagnosis after treatment
        - No
          - Are FeNO levels between 25 and 30 ppb?
            - Yes
              - Diagnose with asthma
            - No
              - Consider alternative diagnoses or referral for a second opinion
      - No
        - Are FeNO levels between 25 and 30 ppb?
          - Yes
            - Diagnose with asthma
          - No
            - Consider alternative diagnoses or referral for a second opinion

Is there airway hyperreactivity?

- No
  - Diagnose with asthma
- Yes
  - Consider alternative diagnoses or referral for a second opinion

Abbreviations:
FeNO, fractional exhaled nitric oxide
BDR, bronchodilator reversibility

This algorithm is based on recommendations from NICE’s guideline on asthma: diagnosis, monitoring and chronic asthma management (2017)

Positive test thresholds:
Obstructive spirometry: FEV1/FVC ratio less than 70% (or below the lower limit of normal if available)
FeNO: 40 ppb or more
BDR: improvement in FEV1 of 12% or more and increase in volumes of 200 ml or more
Peak flow variability: variability over 20%
Direct bronchial challenge test with histamine or methacholine: PC20 of 5 mg/ml or less

© NICE 2017. All rights reserved. Subject to NICE’s terms of use.
What is the practical application?
The significance of inflammation

Airway inflammation

Environmental and genetic factors

How assessed?

Airway hyper-responsiveness

Airway obstruction

Clinical symptoms

Airway obstruction (spirometry)

Airway hyper-responsiveness (PC_{20}, BD response)

Clinical symptoms (questionnaires)

Environmental and genetic factors

http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf
Assessment of airway inflammation

- **Invasive**
  - Bronchoscopy
  - Bronchial wash
  - BAL
  - Biopsy

- **Non-invasive**
  - Sputum investigation
  - Breath condensates
  - NO in exhaled air (FeNO)
What about blood eosinophils?

- What is the threshold?
- Time period to consider
- Systemic factors affecting results
- Systemic marker for localized inflammation?
Consider a patient

- 17yr old boy with asthma, plays a lot of football
- Stopped ICS as ‘felt no longer needed it’
- Little symptom breakthrough recognised but once pressed realised he had "normalised" and tolerated some symptoms.
Where might extra info be useful?
Useful additional information

- FeNO was in 70’s
- Education re action of ICS and developing lung health
- Dad "upset" they hadn't recognised symptoms - all went away with intention to stick to ICS
- Failed follow up appointment
Another person to consider........

- Female never smoker
- Diagnosed with asthma age 22 now age 63
- 2-3 infections/year treated with oral abs, rarely steroids due to purulence of sputum & lack of wheeze.
- MRC2
- Relevant other Sx or Hx incl. nasal polyps, indigestion
- Rx Symbicort 400/12 BD
- C/O “tight chest” on occasion
- Her concern = Chest infections
- FeNO 63ppb
- Observation = ?element of dysfunctional breathing

- Discuss Spirometry, relevance of FeNO, consideration of further Ix and and any next steps.
- Did FeNO add value or change your plan?
Where might extra info be useful?

- Diagnosis
- Symptom management – stepping up
- Confidence in stepping down
- Demonstrating inflammation
- Compliance/concordance/adherence
- Asthma or COPD?
What service deliver model might work?

- Practice based delivery (cost, training, care close to home)
- Cluster delivery (share costs)
- Locality delivery
- Specialist service
- Secondary care service
- Private investors
PC Locality based service model
Outcomes

14 patients confirmed with Respiratory Diagnosis, 14 confirmed Not Respiratory Diagnosis (see Chart 6)

For the 14 patients confirmed Not Respiratory, these patients would otherwise have been prescribed Clenil 100mcg 2 puffs twice daily and Salbutamol (as needed) for life, with an estimated cost per patient per year of £35.41

• Extrapolated 1 year saving (52 Non Respiratory patients over 1 year of clinics) = 52 x £35.41 = £1841
  Total avoided cost per patient would vary greatly down to age

• For these 14 patients, based on the assumption they would have been prescribed the above medications for life (calculated using local life expectancy of 82 years in 2012), there is an extrapolated total cost avoidance of £19,263 over their lifetimes

12 prescriptions were stopped and 3 doses reduced; 10 new prescriptions were started (Chart 7)

FeNO test changed diagnosis for 10 patients, and assisted with diagnosis for 33 patients (Chart 9)

We would also look to analyse impact on hospital admissions for respiratory related conditions, when we have sufficient amount of data.
FeNO Pilot Phase 2 – Patient Feedback

How satisfied are you with your appointment at today's respiratory service?

How helpful was your appointment today in better understanding your…

Do you feel better prepared to manage your condition following today's Respiratory appointment?

Would you recommend the Respiratory Service to a friend or family…
FeNO Pilot Phase 2 - Practice Feedback

Appointment booking was quick and easy

The referral form was quick and easy to complete and send.

The referral form was quick and easy to complete and send.

Overall I am happy with the service.

Waiting time for an appointment was reasonable.

The information was relevant to the reason for referral/answered the question I had asked.

Overall I am happy with the service.
FeNO Pilot Phase 2 - Practice Feedback

"Excellent service, hugely beneficial to some difficult patients. This saved a referral to a secondary care respiratory team."

"Support with sometimes tricky diagnosis has been invaluable."

The quality of information back to the practice was good.

The timeliness of the information back to the practice was good.

Excellent service, hugely beneficial to some difficult patients. This saved a referral to a secondary care respiratory team."
Where are we now?

Primary care provision for FeNO?

‘Specialist’ provision?
Enablers for FeNO

- Inclusion in guidelines
- Demonstration of cost savings
- Better care
- Federations, clusters, CCGs, ICOs, ICSs
- Broadening health care teams – clinical pharmacists, Physicians Assistants
- Campaign groups – Asthma UK.
Barriers for using FeNO

- Conflicting guidelines
- Confusion amongst clinicians
- Cost
- Independent budgets
- Unfamiliarity
Who pays?

- Individual practices
- Clusters or federations
- Localities
- CCGs
- Hospital trusts
- Private investors
- Manufacturers
Is FeNO Feasible?

- What is FeNO?
- What does it measure?
- Where does FeNO testing sit in asthma guidelines?
- What is the practical application?
- What service deliver model might work?
- Who pays?
Hands on practice

- Bedfont
- Bosch
- Circassia
We need your feedback!

Rate each session:

Please check into each session you attend on the app and give it a star rating from 1 (poor) to 5 (excellent)