

From Insight to Action

Transforming Diagnosis & Management in Asthma Care



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Disclaimer

I recognize that I must follow all guidelines and criteria regarding vested interest. I have the following real or perceived conflicts of interest that relate to this presentation:

I am an employee of Methapharm, Inc.

- **Manufacturer and distributor of Provocholine®**
- **Distributor of Vivatmo pro FeNO**



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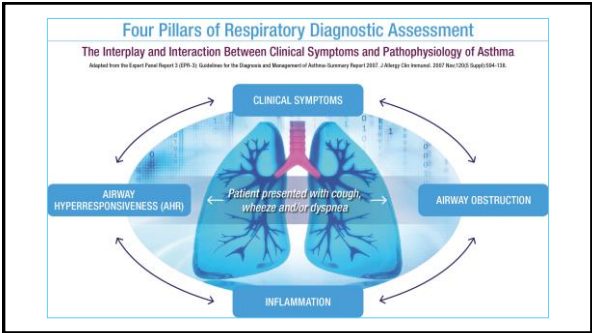
Objectives

Following this presentation the learner shall:

- Recognize guideline recommendations for asthma diagnosis
- Identify the tests available for proper asthma diagnosis and the importance of utilizing objective testing
- Identify the proper steps in asthma diagnosis by following 4 patient case studies pertaining to the patient journey



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Global Initiative for Asthma (GINA) 2025 Guidelines for Diagnosing Asthma

- History of symptom patterns and variable expiratory airflow
- Documented bronchodilator responsiveness testing or other function tests *may need more than 1 test to confirm/exclude asthma
- Use Peak Flow (PF) rather than relying on symptoms alone
- If lung function testing is not available or results are normal, FeNO can support the dx of T2 asthma - but be cautious, not always elevated and low levels do not rule asthma out, can also be high in non-asthmatic patients
- **TEST BEFORE TREATING, wherever possible (confirm before initiating ICS)**

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Expert Panel Report 3
(EPR 3)
Guidelines for
Diagnosing Asthma

National Heart, Lung, and Blood Institute
National Asthma Education and Prevention Program

Expert Panel Report 3:
Guidelines for the Diagnosis and
Management of Asthma

Full Report 2007

Recommended methods to establish the diagnosis are:

- Detailed medical history
- Physical exam
- Spirometry to demonstrate obstruction and assess reversibility
- Additional studies as necessary to exclude alternate diagnoses

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EPR 3
Guidelines for
Diagnosing
Asthma

National Heart, Lung, and Blood Institute
National Asthma Education and Prevention Program

Expert Panel Report 3:
Guidelines for the Diagnosis and
Management of Asthma

Full Report 2007

- Indicators (symptoms) are not diagnostic by themselves, but the presence of multiple key indicators increases the probability of a diagnosis of asthma.
- Spirometry is needed to establish a diagnosis of asthma.

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EPR 3
Guidelines for
Diagnosing
Asthma

National Heart, Lung, and Blood Institute
National Asthma Education and Prevention Program

Expert Panel Report 3:
Guidelines for the Diagnosis and
Management of Asthma

Full Report 2007

Differential Diagnosis of Asthma, consider:

- Additional PFT
 - lung volumes, evaluate inspiratory loops, DLCO,
- Bronchoprovocation
 - Methacholine, histamine, cold air, exercise challenge
- Chest imaging
- Allergy testing
- Biomarkers of inflammation
 - FeNO
 - Eosinophils

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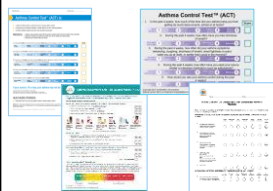
Objective Tests

From Insight to Action



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Asthma Questionnaires



Asthma Impairment and Risk Questionnaire (AIRQ)

- 10 questions
- Yes/no
- ≥ 12 y/o

Asthma Control Test™

- 5 questions
- 1-5 range
- ≥ 12 y/o

Asthma Quality of Life Questionnaire (AQLQ)

- 32 questions, covering 4 domains
- 0-7 range, 0 severe, 7 not impaired at all
- 17-70 y/o

Asthma Control Questionnaire (ACQ)

- 7 questions
- 0-6 range, 0 = no impairment, 6 = severe impairment
- Adult and pediatric versions

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QUESTION 1

Which, if any questionnaires are you familiar with?

- A. Asthma Impairment and Risk Questionnaire (AIRQ)
- B. Asthma Control Questionnaire (ACQ)
- C. Asthma Control Test
- D. Other

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Lab Work



Blood Draw ~
White blood cells –
Normal 4,500-10,000 cells/mcL

Blood eosinophils ~
Mild, 500-1000µL
Moderate 1000-5000 µL
Severe ≥ 5000 µL

Sputum Culture ~
Eosinophils 2-3%

Blood Tests - Blood Tests | NHLBI, NIH

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Lab Work Limitations

- Elevated eosinophils are seen in other conditions
- Not all asthmatics experience eosinophil
- Have to wait on results
- Blood draw required
- Sputum can be challenging to collect

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Spirometry, Pre/Post Bronchodilator Responsiveness

- Valuable tool to be used with other physical findings, symptoms, and history to reach a diagnosis
- Included in all the guidelines as part of the diagnostic process



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QUESTION 2

How do you evaluate bronchodilator responsiveness?

A. 12% and 200 ml increase

B. 10% increase

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Spirometry Indications

Diagnosis

- To evaluate symptoms, signs, or abnormal laboratory test results
- To measure the physiologic effect of disease or disorder
- To screen individuals at risk of having pulmonary disease
- To assess preoperative risk
- To assess prognosis

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Spirometry

Monitoring

- To assess response to therapeutic intervention
- To monitor disease progression
- To monitor patients for exacerbations of disease and recovery from exacerbations
- To monitor people for adverse effects of exposure to injurious agents
- To watch for adverse reactions to drugs with known pulmonary toxicity
- Disability/impairment evaluations
- To assess patients as part of a rehabilitation program
- To assess risks as part of an insurance evaluation
- To assess individuals for legal reasons

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Bronchodilator Responsiveness

- Previously "reversibility testing" now "bronchodilator responsiveness testing" is used to avoid the inference that "reversibility" implies the complete elimination of airway obstruction
- Normal baseline spirometry does not rule out a bronchodilator response, all initial spirometry done for diagnostic reasons should be performed before and after bronchodilator administration
- ERS/ATS recommendation from 2005 (increase in FEV1 or FVC > 200 ml and >12% from baseline) now the 2022 recommendation (increase in FEV1>10% predicted)

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Spirometry Limitations

- Age limitations
- Cognitive limitations
- Physical limitations
- May be normal if not symptomatic
- Does not reflect airway inflammation
- Operator skill is important

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CT SCAN

- Provide more detailed images of the lungs.
- Identify structural changes
- Identify comorbid or mimics
- Provides measurement of airway and density to determine severity



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Fractional Exhaled Nitric Oxide (FeNO)

- Point of care test
- Assess current level of airway inflammation
- Identify patient's likelihood of corticosteroids responsiveness
- Optimize adherence to corticosteroids treatment to aid in reducing exacerbations
- Determine biological therapy as indicated

	FeNO		
	Normal	Elevated	High
Symptoms present at 2 weeks	Adults < 25 ppb Children < 20 ppb	Adults 25-50 ppb Children 20-30 ppb	Adults > 50 ppb Children > 30 ppb
	Diagnosis ▶ Eosinophilic airway inflammation unlikely ▶ Alternative diagnoses ▶ Unlikely to benefit from ICS	Diagnosis ▶ Be cautious ▶ Evaluate clinical context ▶ Monitor change in FeNO over time	Diagnosis ▶ Eosinophilic airway inflammation present ▶ Likely to benefit from ICS
Symptoms present at 2 weeks	Monitoring (in patients with diagnosed asthma) ▶ Possible alternative diagnosis ▶ Unlikely to benefit from increase in ICS	Monitoring (in patients with diagnosed asthma) ▶ Persistent allergen exposure ▶ Inadequate ICS dose ▶ Poor adherence ▶ Steroid resistance	Monitoring (in patients with diagnosed asthma) ▶ Persistent allergen exposure ▶ Inadequate ICS dose ▶ Poor adherence or inhaler technique ▶ Steroid resistance ▶ Risk of exacerbation
	Management ▶ Adequate ICS therapy ▶ Good adherence ▶ ICS spacer	Management ▶ Adequate ICS therapy ▶ Good adherence ▶ Monitor change in FeNO	Management ▶ ICS withdrawal or dose reduction may result in relapse ▶ Poor adherence or inhaler technique

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FeNO Limitations

- High FeNO levels for reasons other than asthma
- Low FeNO does not rule asthma out
- Not currently available for home use
- Not currently indicated for very young children

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QUESTION 3

Do you use FeNO in your lab/clinic?
A. Yes
B. No

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Bronchial Challenge Testing

Indications - Bronchial challenge testing is used to assess airway hyperresponsiveness (AHR) in patients who do not have clinically apparent asthma.

Direct Stimuli – methacholine chloride, histamine

Indirect Stimuli – exercise, eucapnic voluntary hyperpnea, mannitol, hypertonic saline, adenosine, cold air



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BCT Limitations

- Not as widely available as Spirometry
- Require highly skilled staff
- Not standalone diagnostic tests
- Some need capital equipment and space
- Fears of safety for patients and staff
- Misunderstanding of why and which challenge to order

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QUESTION 4

Our PFT Lab uses _____ challenge testing.

A. Methacholine

B. Exercise

C. Mannitol

D. No

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Allergy Testing

Allergy testing, also known as skin, prick or blood testing, is a method for determining to what substances a person is allergic.

Methods –

- Skin prick testing, most common, reliable and relatively painless
- Intradermal – injected into the epidermis
- Patch testing – a patch is placed for ~48 hours

Blood tests are generally used when skin tests might be unsafe or won't work



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Allergy Testing Limitations

- Skin Testing – irritation at the sight of testing, on extremely rare occasions – anaphylaxis
- Blood testing – needle stick
- False positives – 50-60%
- Not to be used alone to confirm food allergy diagnosis – need to include history & symptoms

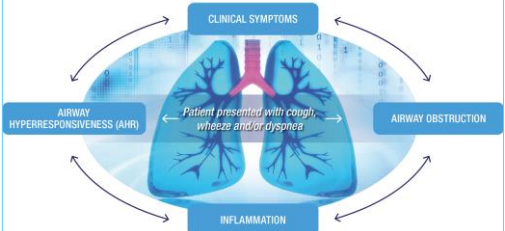
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Four Pillars of Respiratory Diagnostic Assessment

The Interplay and Interaction Between Clinical Symptoms and Pathophysiology of Asthma

Adapted from the Expert Panel Report 3 (GPR-3): Guidelines for the Diagnosis and Management of Asthma-Summary Report 2007. J Allergy Clin Immunol. 2007 Nov;120(5 Suppl):S64-S116.



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Medications



GINA 2025
Adults & adolescents
12+ years

Aspirin
Corticosteroids
Anticholinergics
Long-acting beta₂-agonists
Short-acting beta₂-agonists
Leukotriene receptor antagonists
Mast cell stabilizers
Biologics

Step 1: SABA as needed for symptom relief
Step 2: Low-dose ICS or LABA or LTRA or combination
Step 3: Medium-dose ICS or LABA or LTRA or combination
Step 4: High-dose ICS or LABA or LTRA or combination
Step 5: High-dose ICS or LABA or LTRA or combination + biologic or other add-on therapy

GINA 2025: Adults & adolescents 12+ years

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Medications

Endotype	Medication	Target
T2-High	Omalizumab	Anti-IgE
	Mepolizumab	Anti-IL 5
	Reslizumab	Anti-IL 5
	Dupilumab	Anti-IL4 and IL13
	Benralizumab	Anti-IL 5
	Tezepelumab	Not specific
	Most recent	Depemokimab

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Case Studies

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Transforming Diagnosis &
Management in Asthma Care

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Transforming Asthma Care

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Case Study 1

caleb



- 19 y/o male
- College student

Reason for Visit

- Symptoms, present for 6 months
 - Chest tightness
 - Wheeze
 - occasional, some NOC wakening
 - Cough
 - occasional, some NOC awakenings
- Worse during and after exercise
- Has tried cough syrup, no other meds trialed

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Initial Diagnostic Workup

Physical Exam –

- Normal
- Chest x-ray done - normal

Patient reported history –

- No asthma or lung disease
- Non-smoker
- Lives in apartment with 2 roommates
 - One smoker
 - One has a cat

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QUESTION 5

Next Step(s)?

- A. ICS/LABA/LAMA
- B. Spirometry Pre/Post
- C. Methacholine Challenge
- D. FeNO

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Lung Function

FENO

- 23 ppb - normal

Spirometry pre/post bronchodilator responsiveness

- No significant response, 5% reversibility

Is this asthma?

- Maybe

Next step(s)?



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QUESTION 6

Next Step(s)?

A. Trial ICS/SABA

B. Chest CT

C. Direct Bronchial Challenge Test

D. Indirect Bronchial Challenge Test

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Methacholine Challenge Test

Outcome

- PC20 = 0.125mg/mL
- PD20 = <0.03 μ mol (<6 μ g)

Interpretation –

- Marked airway hyperresponsiveness
- In conjunction with other tests, asthma is likely the correct diagnosis

PC20 (mg/mL)	PD20 μ mol(μ g)	Interpretation
> 16	>2(> 400)	Normal
4 – 16	0.5-2.0 (100 – 400)	Borderline AHR
1 - 4	0.13-0.5 (25 – 100)	Mild AHR
0.25 – 1.0	0.03-0.13 (6 – 25)	Moderate AHR
< 0.25	<0.03 (< 6)	Marked AHR

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Treatment

GINA Step 1

- Low dose ICS/LABA

Follow up in 3 months

- Patient reports using inhaler one time daily
- No reported symptoms



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Case Study 2

Virginia



- 32 y/o woman
- Works in finance

Reason for visit

- Symptoms, sudden onset, started approx. 2 months ago:
 - SOB
 - Chest tightness
 - Voice changes
- Symptom frequency
 - Random
 - Occur at work and home
 - Last for 30-60 minutes
 - During episodes experiences difficulty speaking
 - Hoarse voice
- Triggers
 - Strong smells
 - perfumes

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Initial Diagnostic Workup

Physical Exam –

- Normal
- Chest x-ray done – normal
- EKG done – normal

Patient reported history –

- No asthma or lung disease
- Non-smoker
- Denies cough or heartburn
- Continues to exercise without problems

Has an ICS/LABA from primary physician, does not make a difference

Next step(s)?

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QUESTION 7

Next Step(s)?

- A. Increase ICS/LABA
- B. Spirometry Pre/Post
- C. FeNO
- D. Methacholine Challenge

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Lung Function

FENO –

- 10 ppb
- Normal

Spirometry pre and post bronchodilator -

- No airflow obstruction
- Normal

Is this asthma?

- Maybe?

Next step(s)?



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QUESTION 8

Next Step(s)?

- A. Methacholine Challenge
- B. Mannitol Challenge
- C. Endoscopy
- D. Allergy Testing

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Methacholine Challenge Test

Outcome

- PC20 = > 16mg/L
- PD20 = > 2 μmol (>400μg)

Interpretation –

- Test is negative
- Asthma is unlikely

PC20 (mg/mL)	PD20 μmol(μg)	Interpretation
> 16	>2(> 400)	Normal
4 – 16	0.5-2.0 (100 – 400)	Borderline AHR
1 - 4	0.13-0.5 (25 – 100)	Mild AHR
0.25 – 1.0	0.03-0.13 (6 – 25)	Moderate AHR
< 0.25	<0.03 (< 6)	Marked AHR

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Treatment/Outcome

- Advised to discontinue ICS/LABA
- Referred to ENT for follow up
- ENT performed provoked laryngoscopy
- VCD confirmed
- Referred to Speech Therapy for biofeedback exercises
- Symptoms improved



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Case Study 3

Andy



- 8 y/o male

Reason for visit

- Symptoms:
 - Chronic cough since age of 5
 - Nasal congestion
- Symptom frequency/triggers:
 - Increased coughing with respiratory infections
 - Coughing has increased and occurs "all the time"
- Changes:
 - Worsening in past year
 - Daily meds are not helping
 - OTC antihistamines not helping
- Triggers:
 - Respiratory infections are the only identified

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Initial
Diagnostic
Workup

Physical Exam –

- Normal vitals
- Height/weight 60% for age
- Noted allergic “shiners”
- Occluded nasal turbinates

Parent reported history –

- Infancy through first year:
 - episodic vomiting
 - Milk allergy (no milk/dairy in diet)
 - Some eczema (stable, has not worsened)

Current/Recent treatment

- Past 9 months – 2-3 course of oral antibiotics with oral steroids
- Albuterol inhaler BID
- Lab from PCP slightly elevated IgE
- Multiple low-positive IgE specific foods
 - What does IgE tell us?

Next step(s)?

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QUESTION 9

Next Step(s)?

A. Skin prick testing

B. Methacholine challenge testing

C. Spirometry pre/post

D. A & C

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Lung Function & Allergy Testing

FENO –

- 58ppb
- Elevated/high



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Lung Function & Allergy Testing

FENO -

- 58ppb
- Elevated/high

Spirometry pre and post bronchodilator -

- Prebronchodilator FEV1 = 85% predicted
- Postbronchodilator FEV1 = 94% predicted

Skin prick testing

- Small wheal/flare for dogs/mites
- Negative to pollen/foods

Is this asthma?



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QUESTION 10

What does high FeNO indicate?

- A. Possible nonadherence to medication
- B. Needs higher dose ICS
- C. Uncontrolled inflammation
- D. At risk for exacerbation
- E. All of the above

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Impressions/Further Evaluation

- Near significant bronchodilator response but not complete
 - May be due to inhaler overuse
- FeNO is significantly high at 58ppb, has uncontrolled inflammation
 - May be at risk for exacerbation if left unaddressed
- Need to assess for additional comorbidities
- Next steps



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Treatment and Follow UP

- Prescribed ICS/LABA
- Return for follow up in 12 weeks

Follow up #1:

- Physical exam – unremarkable
- FeNO – 28 ppb, markedly improved but still elevated

Discussion with parents:

- Pleased with progress and family wants to taper medications
- Advised to continue medications given multiple courses of systemic steroids recently
- Will discuss at future visit



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Treatment and Follow UP

Follow up #2 (2 months later):

- self-discontinued ICS/LABA over summer
- since school resumed has been using every other day

Physical exam –

- Normal

FeNO –

- 44 ppb
- Elevated/high

Discussion with parents:

- Inflammation is present, likely due to stopping ICS/LABA and inconsistent use
- Medication education done
- Inflammation is the cause of persistent asthma
- Follow up in 6 weeks to reassess on ICS/LABA



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Treatment and Follow UP

Follow up #3:

- Resumed ICS/LABA
- Has not missed school or required systemic steroids bursts

FeNO –

- 17 ppb
- low

Discussion with parents:

- ICS/LABA addressing inflammation and lung function
- Continue on current regime
- Follow up in 6 months to assess current level of inflammation and assess symptoms



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Case Study 4

Gwen



- 38 y/o female
- Reason for Visit
- Symptoms "constant":
 - Wheezing
 - Coughing
 - Sputum production
- Current therapy
 - ICS/LABA/LAMA
 - Oral prednisone
 - When prednisone reduced below 5mg/daily breathing gets worse
 - Started IL-5 monoclonal antibody biologic
 - 3 months, feels there has not been significant improvement

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Initial Diagnostic Workup

Physical Exam –

- Normal

Patient reported history –

- Atopic
- Never smoked

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QUESTION 11

What does atopic tell us?

- A. Tendency to develop allergic conditions
- B. Does not have allergies
- C. Describes conditions linked to strong reactions from the immune system
- D. A & C

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Initial
Diagnostic
Workup

Physical Exam –

- Normal

Patient reported history –

- Atopic
- Never smoked

Asthma Control Questionnaire is 2.8

Wants to understand why current treatment is not helping with symptoms.

Next step(s)?

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QUESTION
12

Next Steps?

A. Blood Eosinophils

B. FeNO

C. Spirometry pre/post

D. 6 minute walk

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Lung Function & Blood Tests

FENO –

- 56ppb
- Elevated/high

Spirometry pre and post bronchodilator -

- Prebronchodilator FEV1 = 72% predicted
- Postbronchodilator FEV1 = 78.5%
- 9% improvement

Blood Eosinophils

- 400 cells/ μ L

Is this asthma?



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QUESTION
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Next Steps?

A. Chest CT

B. Mannitol Challenge

C. Methacholine Challenge

D. Bronchoscopy

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Methacholine Challenge Test

Outcome

- PC20 = 4mg/mL
- PD20 = 05-2.0 μ mol (100-400 μ g)

Interpretation –

- Test is positive

PC20 (mg/mL)	PD20 μ mol(μ g)	Interpretation
> 16	>2(> 400)	Normal
4 – 16	0.5-2.0 (100 – 400)	Bordertine AHR
1 - 4	0.13-0.5 (25 – 100)	Mild AHR
0.25 – 1.0	0.03-0.13 (6 – 25)	Moderate AHR
< 0.25	<0.03 (< 6)	Marked AHR

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Treatment & Follow Up

Given has:

- High blood eosinophils
- High FeNO
- Positive Methacholine Challenge

Changed biologic from IL5 monoclonal antibody to TSLP monoclonal antibody

- Given has high levels of mast cell activation causing her symptoms, treated by changing biologic medication

6 week follow up:

- Decreased eosinophils
- Decreased FeNO
- Decrease ACQ



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Conclusions

There are multiple factors to consider during asthma diagnosis and management.

There is not a single "gold standard" diagnostic test.

Assessing history, symptoms, lung function, airway hyperresponsiveness, and airway inflammation throughout management, ensure proper management.

The goals of proper management are to avoid exacerbations and to minimize lung decline.

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Thank you!

Questions?

Contact Methapharm Respiratory

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Resources

- Mohan A, Lugogo NL, Hanania NA, Reddel HK, Akuthota P, O'Byrne PM, Guilbert T, Papl A, Price D, Jenkins CR, Kraft M, Bacharier LB, Boulet LP, Yawn BP, Pleschke R, Lazarus SC, Beasley R, Geuevrou G, Israel E, Schneider-Futschik EK, Yorganciglu A, Martinez F, Moore W, Sumino K; on behalf of the American Thoracic Society Assembly on Allergy, Immunology, and Inflammation. Questions in Mild Asthma: An Official American Thoracic Society Research Statement. *Am J Respir Crit Care Med.* 2023;207(11):e77-e96. DOI: 10.1164/rccm.202304-0642ST.
- N. Kang, Y. Im, K. Lee, J.-Y. Lee, D.-C. Choi, and B.-J. Lee. Development and Validation of Deep Learning Models for Diagnosing Bronchial Asthma Using Methacholine Provocation Test, Induced Sputum Analysis and Exhaled Nitric Oxide Measurement [abstract]. *Am J Respir Crit Care Med* 2023;207:A4832. <https://doi.org/10.1164/ajrccm-conference.2023.207.1.MeetingAbstracts.A4832>
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- Peribronchial cuffing. *Radiology Reference Article | Radiopaedia.org* (slide 12)
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Resources

- [Standardization of Spirometry 2019 Update An Official American Thoracic Society and European Respiratory Society Technical Statement](#) Brian L. Graham, Irene Steenbruggen, Martin R. Miller, Igor Z. Barjaktarovic, Brendan G. Cooper, Graham L. Hall, Teat S. Hallstrand, David A. Kaminsky, Kevin McCarthy, Meredith C. McCormack, Cristine E. Oropez, Margaret Rosenfield, Sanja Stanojevic, Maureen P. Swanney¹, and Bruce R. Thompson; on behalf of the American Thoracic Society and the European Respiratory Society
- <https://www.foodallergy.org/resources>
- [Allergy Blood Test vs. Skin Test: Which Is Better?](#)

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