

# Asthma review

- Khalil Ansarin, MD, FCCP
- Division of Pulmonary, Critical Care, Sleep Medicine  
Tabriz University of Medical Sciences,  
Tabriz , Iran

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# Differential diagnosis of asthma

Vocal cord dysfunction

Congestive heart failure

Foreign body aspiration

COPD

Rhinosinusitis

Gastroesophageal reflux disease

Post-viral coughing

Eosinophilic bronchitis

Pertussis

ACE-inhibitor cough

Chronic bronchitis

Pulmonary embolism

Sarcoidosis

Bronchiectasis

Constrictive bronchiolitis

Tracheal stenosis

Laryngeal stenosis

Bronchiolitis obliterans

Postnasal drip

Tracheomalacia

Mediastinal mass

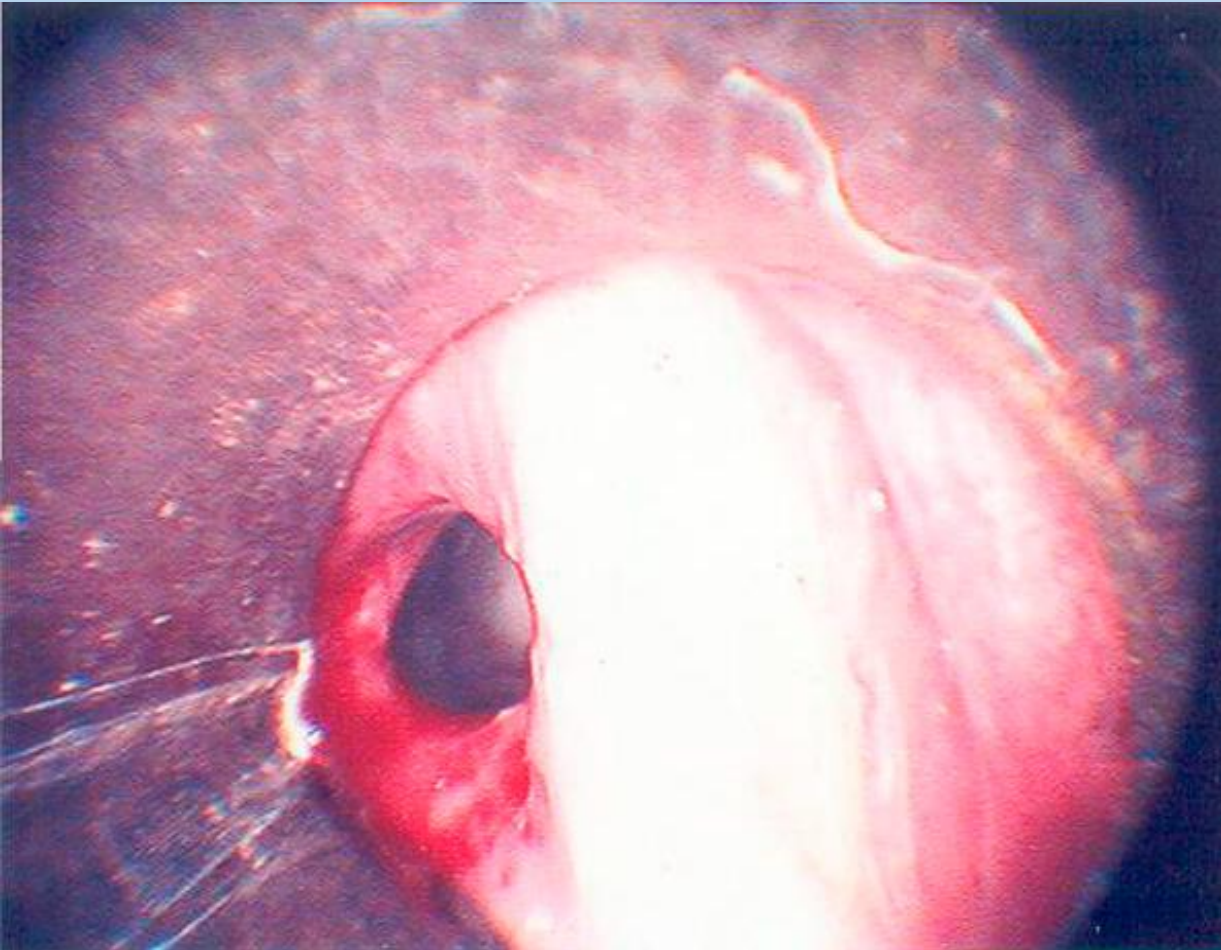
Carcinoid tumor

Goiter (huge)

Vascular rings / aneurysms

*\* not a complete list*

# TRACHEAL STENOSIS



Flow

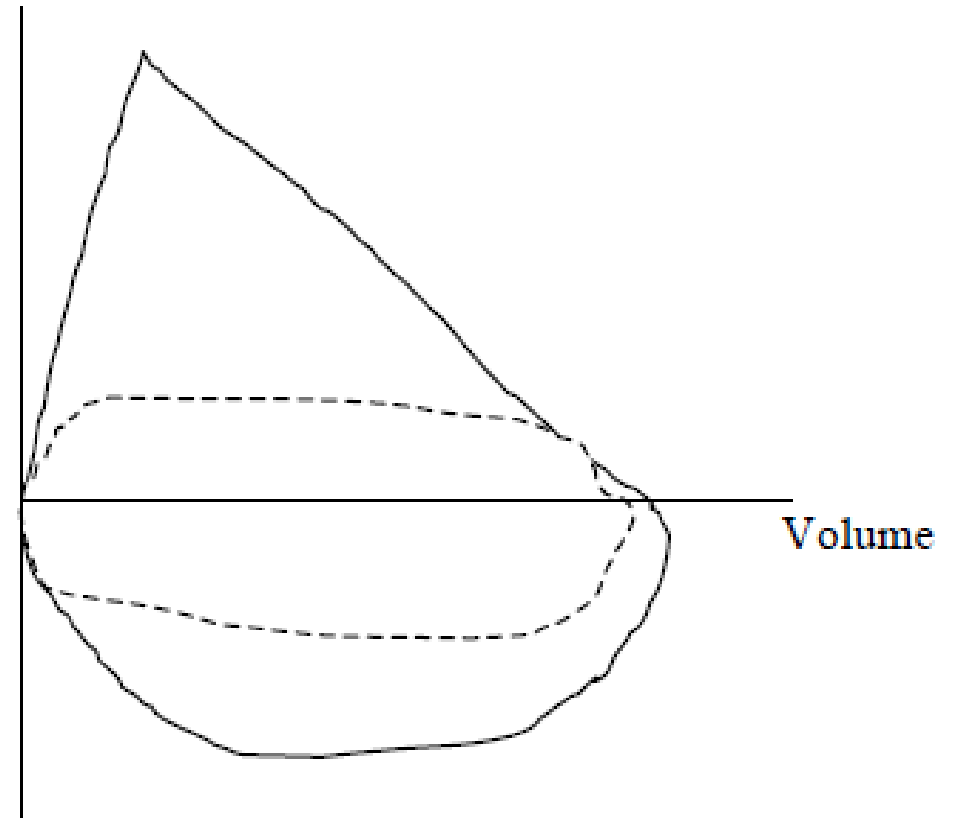
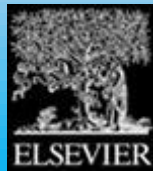
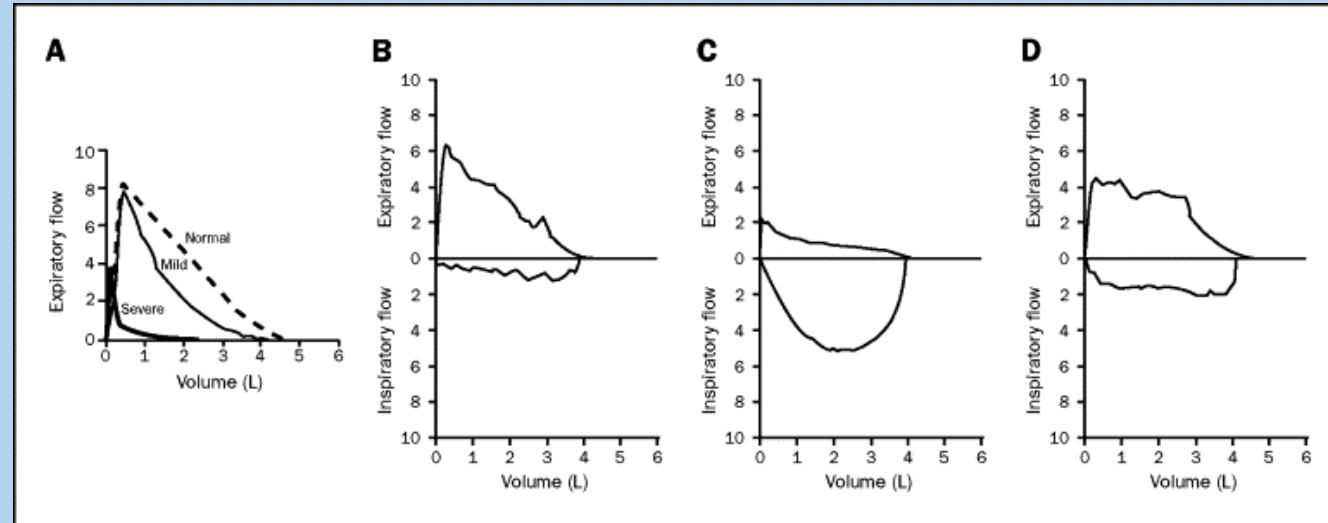


Figure 1



# **Asthma: diagnosis and monitoring of asthma in adults, children and young people**

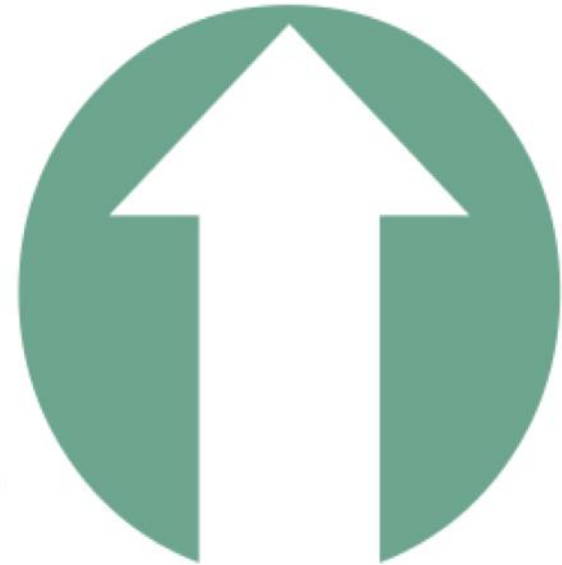
**NICE guideline**

**Draft for consultation, January 2015**

If you wish to comment on this version of the guideline, please be aware that all the supporting information and evidence is contained in the full version.

## CLINICAL FEATURES THAT INCREASE THE PROBABILITY OF ASTHMA

- More than one of the following symptoms: wheeze, breathlessness, chest tightness and cough, particularly if:
  - ~ symptoms worse at night and in the early morning
  - ~ symptoms in response to exercise, allergen exposure and cold air
  - ~ symptoms after taking aspirin or beta blockers
- History of atopic disorder
- Family history of asthma and/or atopic disorder
- Widespread wheeze heard on auscultation of the chest
- Otherwise unexplained low FEV<sub>1</sub> or PEF (historical or serial readings)
- Otherwise unexplained peripheral blood eosinophilia



## CLINICAL FEATURES THAT LOWER THE PROBABILITY OF ASTHMA

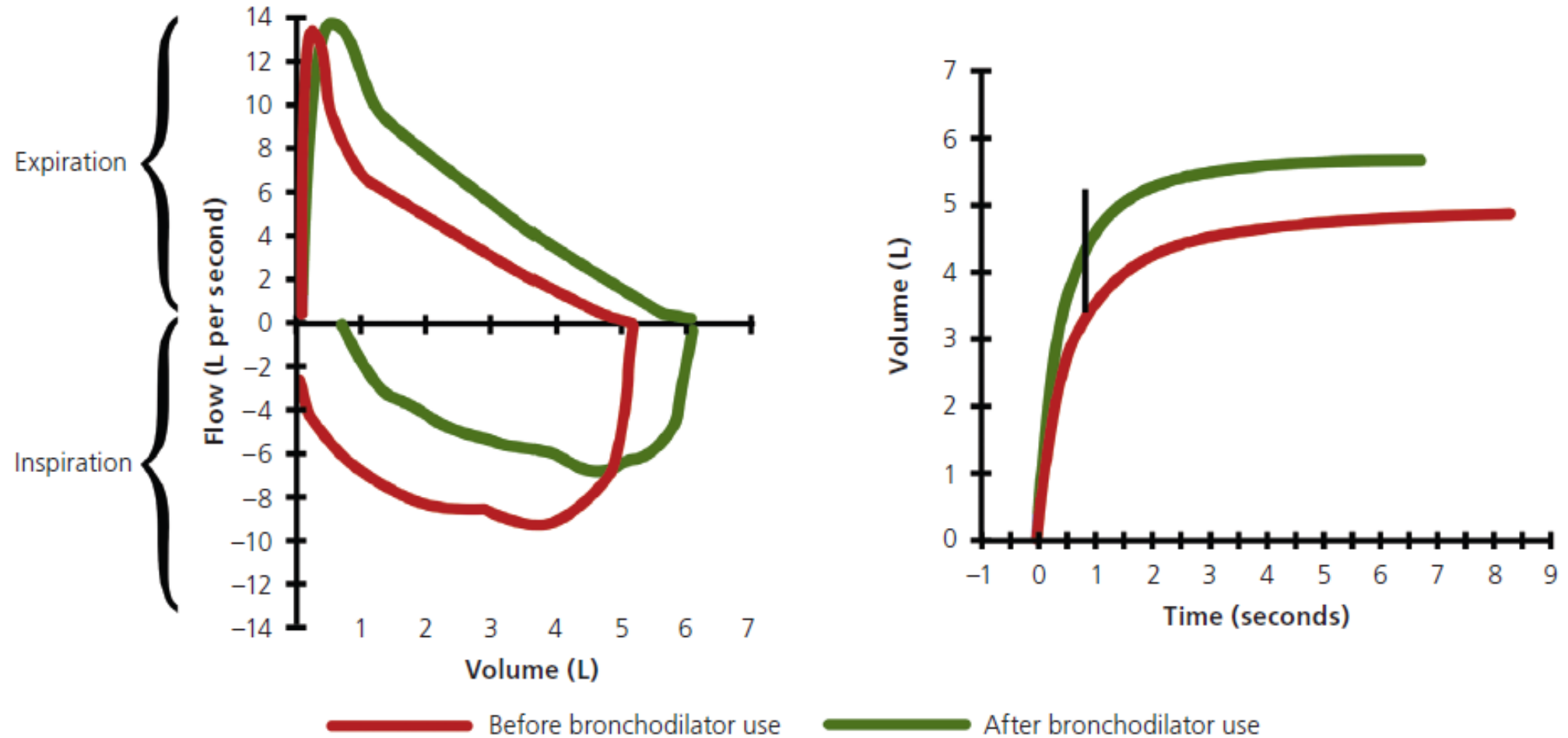
- Prominent dizziness, light-headedness, peripheral tingling
- Chronic productive cough in the absence of wheeze or breathlessness
- Repeatedly normal physical examination of chest when symptomatic
- Voice disturbance
- Symptoms with colds only
- Significant smoking history (ie > 20 pack-years)
- Cardiac disease
- Normal PEF or spirometry when symptomatic\*



# Investigations

- Peak flow recording/simple spirometry
- 20% diurnal PEF variation on >3 days per week, in a week of peak flow diary measures
- FEV<sub>1</sub> > 15% decrease after 6 minutes exercise
- FEV<sub>1</sub> > 15% (and 200 ml) increase after 2 week trial of oral steroid (30 mg prednisolone od)
- Bronchodilator reversibility testing FEV<sub>1</sub> > 12% (or 200 ml) increase after short-acting  $\hat{I}_2^2$  agonist

# Bronchodilator testing



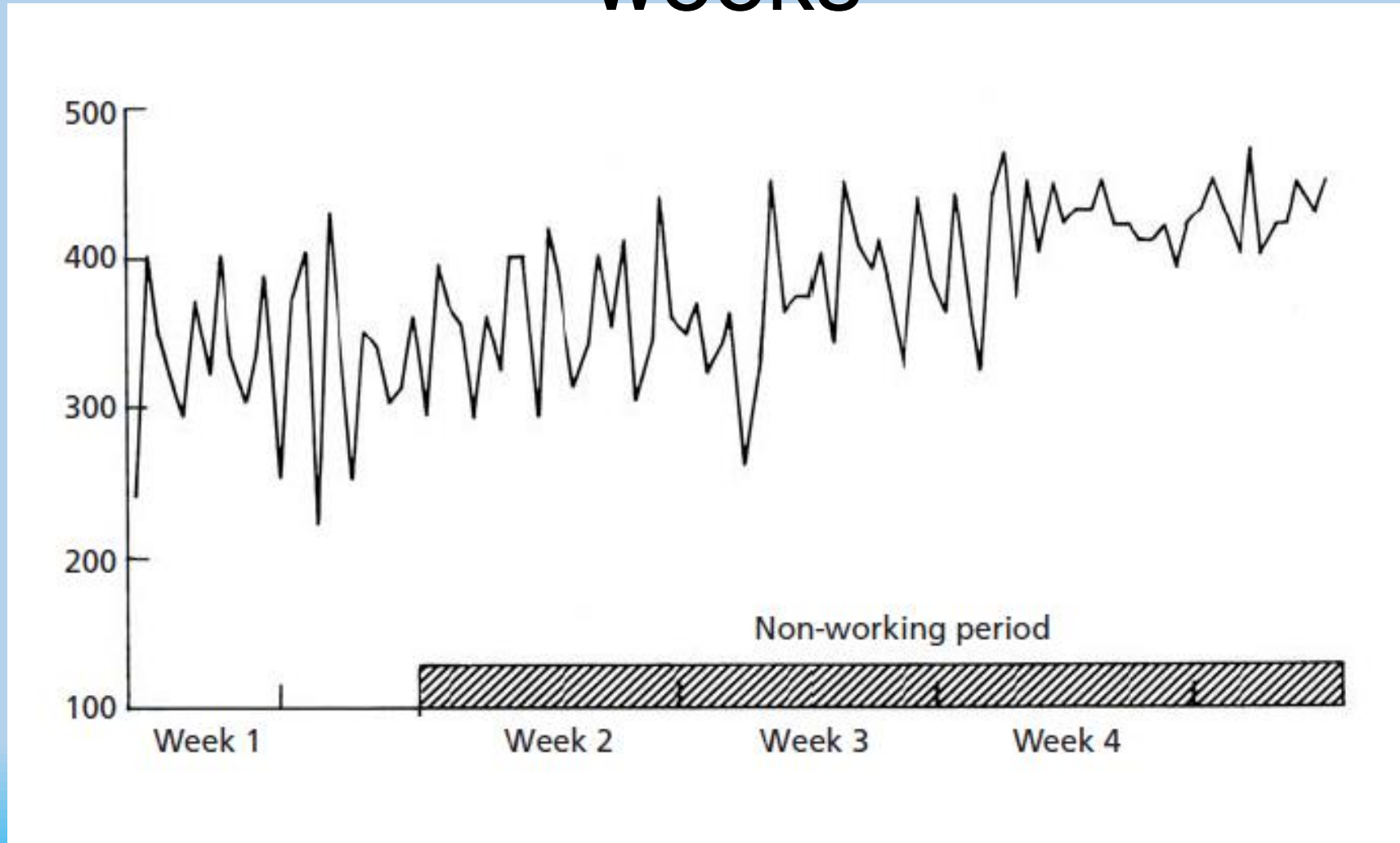


**TABLE 2****Factors that decrease bronchial responsiveness**

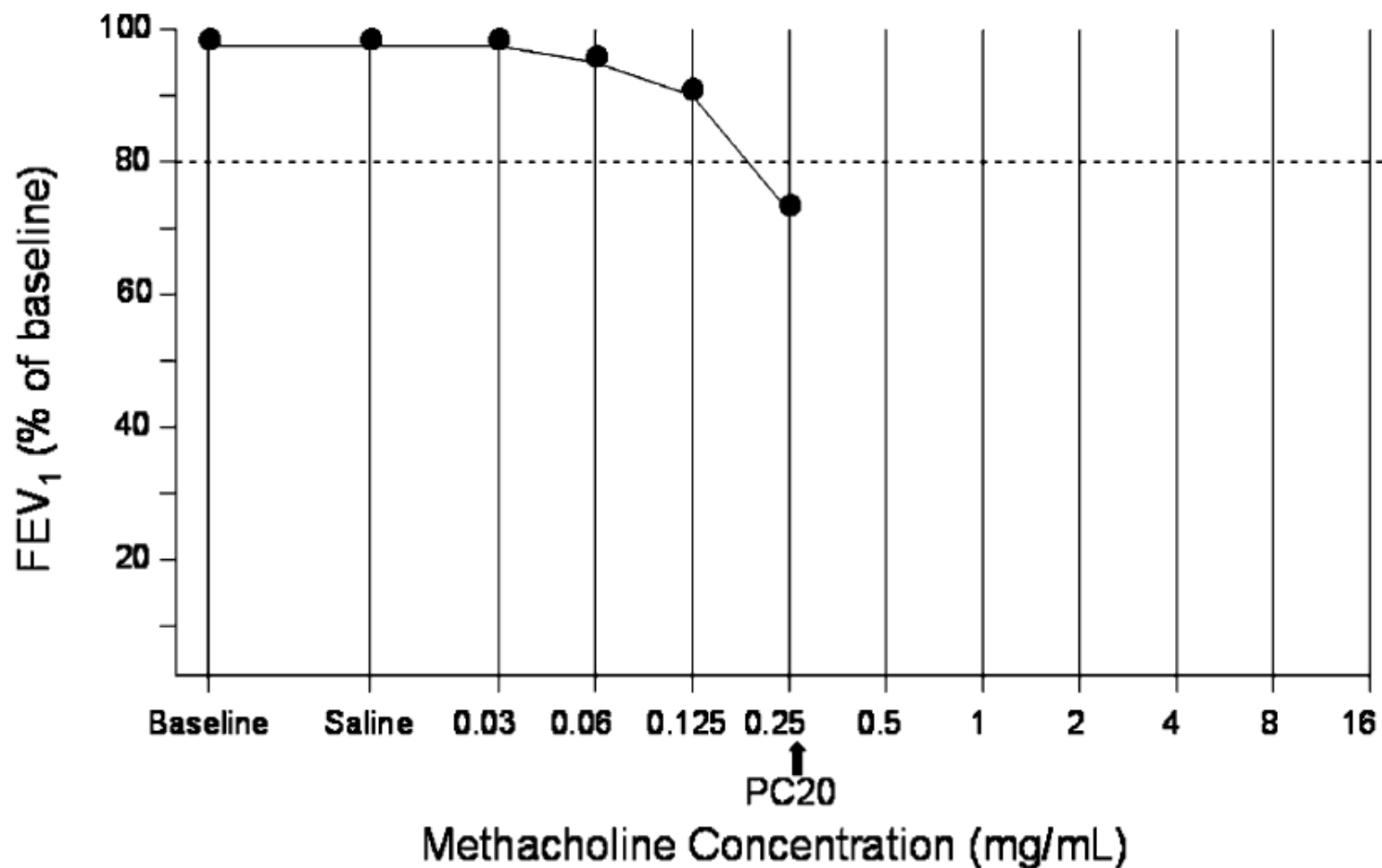
FACTOR	MINIMUM TIME INTERVAL FROM LAST DOSE TO STUDY
Short-acting inhaled bronchodilators, eg, isoproterenol, isoetharine, metaproterenol (Alupent), albuterol (Proventil), terbutaline (Brethine)	8 hours <sup>11</sup>
Medium-acting bronchodilators, eg, ipratropium	24 hours <sup>12</sup>
Long-acting inhaled bronchodilators, eg, salmeterol (Serevent), formoterol (Foradil), tiotropium (Spiriva)	48 hours <sup>13</sup> (perhaps 1 week for tiotropium)
<b>Oral bronchodilators</b>	
Liquid theophylline	12 hours
Intermediate-acting theophyllines	24 hours
Long-acting theophyllines	48 hours
Standard beta-2 agonist tablets	12 hours
Long-acting beta-2 agonist tablets	24 hours
Cromolyn sodium (Intal)	8 hours
Nedocromil (Tilade)	48 hours
Hydroxazine, cetirizine	3 days
Leukotriene modifiers	24 hours <sup>1</sup>
Coffee, tea, cola drinks, chocolate	Day of study

Note: The American Thoracic Society does not recommend routinely withholding oral or inhaled corticosteroids, but their anti-inflammatory effect may decrease bronchial responsiveness.<sup>14,15</sup> Inhaled corticosteroids may need to be withheld depending on the question being asked.

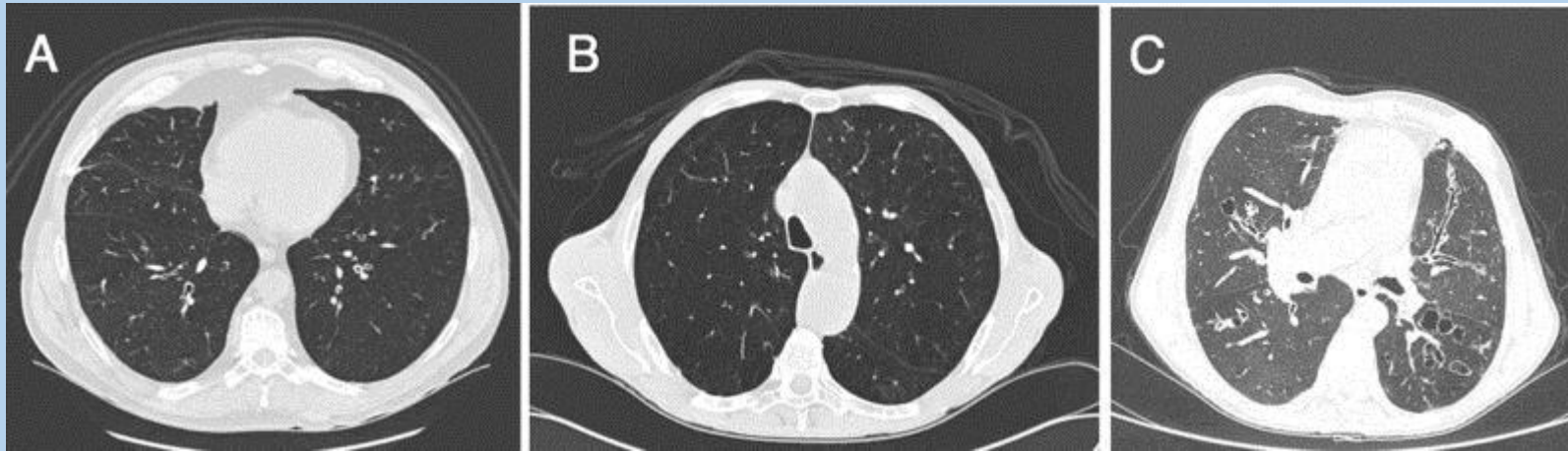
# Occupational asthma; PEF change after 2 weeks



# Provocation testing in asthma



# CT in three airway diseases



## Diagnosing Asthma In A Real Life Setting - Which Test To Use?

**V. Backer<sup>1, 2</sup>, A. Sverrild<sup>1</sup>, C. S. Ulrik<sup>3</sup>, U. Boedtger<sup>4</sup>, N. Seersholm<sup>5</sup>, C. Porsbjerg<sup>1</sup>,**

<sup>1</sup>Bispebjerg University hospital, Copenhagen, Denmark, <sup>2, 3</sup>Hvidovre Hospital and University of Copenhagen, Hvidovre, Denmark, <sup>4</sup>Naestved Hospital, Naestved, Denmark, <sup>5</sup>Gentofte University hospital, Gentofte, Denmark

**Corresponding author's email: backer@dadlnet.dk**

**Background:** Asthma is the most frequent chronic illness in adolescents and young adults and asthma is often under-diagnosed which may relate to difficulties use of testing tool in diagnosing the disease. The aim in the present study has been to evaluate the best diagnostic algorithm in unselected patients referred to an out-patients asthma clinic.

**Material and methods:** Subjects with symptoms suggestive of asthma referred to an out-patients clinic during a 12-month period had lung function, skin prick test, reversibility tests, peak flow variability (PEF), residual volume (RV), fractional exhaled nitric oxide (FENO), and airway hyperresponsiveness (AHR) to mannitol and methacholine measured. Asthma diagnosis was defined on the basis of an evaluation from three independent specialists in respiratory medicine with access to symptoms, lung function and atopy. Asthma was classified as likely if 2 or more classified the patients was having asthma. The specialists whom examined the patients clinically, were different from those defining the diagnose of asthma. Sensitivity, specificity and a receiver operating characteristics curve (ROC) (including area under the curve (AUC) measurements) for each test were assessed. Cut-off values of each of the tests used were estimated based on the ROC with the best acceptable sensitivity and the lowest 1-specificity value.

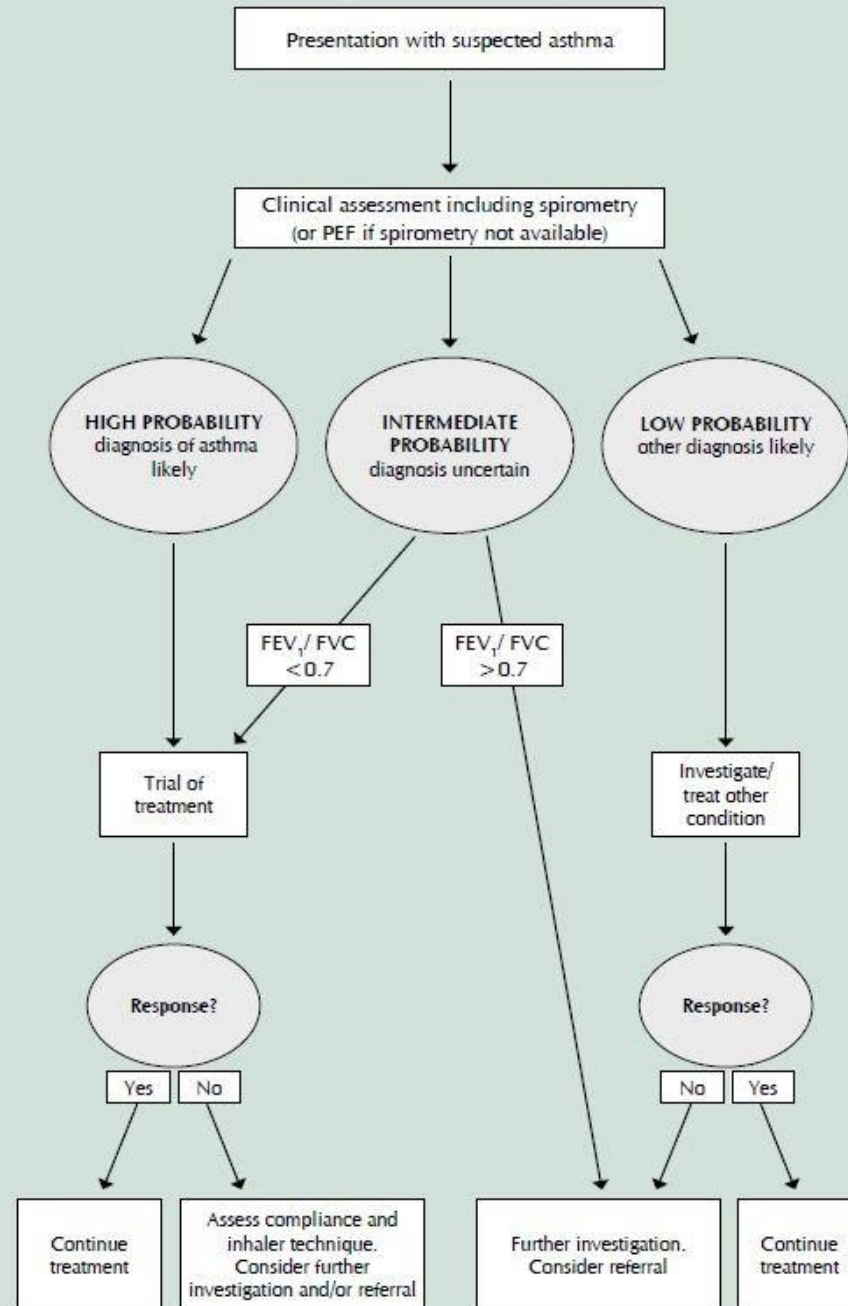
**Results:** In total of 198 patients were examined, of whom 62.6% were classified as having asthma. AHR to methacholine had the highest sensitivity of 63%, whereas reversibility to beta2-agonist had the lowest (10%) (Table 1). The highest AUC was found in the response to mannitol testing 0,654 (CI95% 0,74). Adding the results of three different tests, that being FEV1/FVC < 92% pred, AHR to methacholine or Mannitol, identified more than 90% of the patients suggested to be asthmatics.

**Conclusion:** In real life asthma patients, the use of diagnostic tools still remains a problem and the results of the tests are not similar to the findings in selected groups of asthma patients. The use of lung function and reversibility tests, often used in clinical setting, has very limited use, due to low sensitivity as well as low specificity. On the other hand, although the different used challenge tests also were found to have a somewhat low diagnostic value, a combination of three tests resulted in almost 100% identification of the asthma patients. In these real life asthma patients, more than one test is needed to ensure respiratory illness.

# Diagnostic values of different tests for diagnosis asthma

	<b>Sensitivity</b>	<b>Specificity</b>	<b>PPV</b>	<b>NPV</b>
FEV1/FVC <92 pred% (p=0.051)	29%	84%	75%	42%
FEV1/FVC <73 % LLN (ns)	25%	68%	57%	35%
Beta-2-revers $\geq$ 12% (min 200 mL) (ns)	14%	90%	72%	37%
Beta-2-revers min 250 mL (ns)	39%	65%	68%	37%
PEF variation ( $\geq$ 20%) (ns)	40%	58%	59%	39%
FENO $\geq$ 25 ppb (ns)	38%	68%	64%	41%
RV %pred $\geq$ 107 (p=0.07)	37%	75%	72%	41%
Mannitol	49%	70%	73%	45%
Methacholine (p<0.01)	63%	53%	72%	49%

Presentation with suspected asthma in adults



# Diagnostic algorithm B1 – objective tests for adults and young people older than 16 with obstructive spirometry

From diagnostic algorithm A: adults and young people older than 16 with obstructive spirometry (FEV<sub>1</sub>/FVC ratio less than 70%)

Do not offer as diagnostic tests:

- skin prick tests to aeroallergens
- serum total and specific IgE
- peripheral blood eosinophil count
- exercise challenge.

Offer a bronchodilator reversibility (BDR) test. Regard an improvement in FEV<sub>1</sub> of 12% or more, together with an increase in volume of 200 ml or more, as a positive test.

-ve BDR

+ve BDR

Offer a FeNO test. Regard a FeNO level of 40 ppb or more as a positive test.

Offer a FeNO test. Regard a FeNO level of 40 ppb or more as a positive test.

-ve FeNO

+ve FeNO

-ve FeNO

+ve FeNO

If the FeNO level is less than 25 ppb

If the FeNO level is between 25 and 39 ppb, consider monitoring peak flow variability for 2-4 weeks. Regard a value of more than 20% variability as a positive test.

Monitor peak flow variability for 2-4 weeks. Regard a value of more than 20% variability as a positive test.

-ve PEFv

+ve PEFv

-ve PEFv

+ve PEFv

Consider a direct bronchial challenge test with histamine or methacholine<sup>2</sup>. Regard a PC20 value of 8 mg/ml or less as a positive test.  
<sup>3</sup>see footnote in the full list of recommendations

**Suspect asthma**  
Do not rule out other diagnoses if symptom control remains poor after treatment

If the FeNO level is less than 25 ppb and there are ongoing symptoms

If the FeNO level is between 25 and 39 ppb, consider a direct bronchial challenge test with histamine or methacholine<sup>5</sup>. Regard a PC20 value of 8 mg/ml or less as a positive test.  
<sup>5</sup>see footnote in the full list of recommendations

Consider<sup>4</sup>:

- alternative diagnoses or
- referral for specialist opinion

<sup>4</sup>base the choice on clinical history (eg smoking history, age, weight, fitness level) and objective test results

Consider alternative diagnoses

Diagnose with asthma

Review<sup>3</sup> the diagnosis

<sup>3</sup>after 6-10 weeks repeat spirometry and objective measures of asthma control and review symptoms

Consider alternative diagnoses

Diagnose with asthma

-ve BCT

+ve BCT

-ve BCT

+ve BCT



Diagnose asthma in adults and young people > 16 if they have obstructive spirometry and:

- **negative BD test**, a FeNO between 25 - 39 ppb, negative PEF variability and a **positive direct bronchial challenge test** or
- **positive BD test** and a **FeNO level of 40 ppb or more** or
- **positive BD test**, a FeNO level of 39 ppb or less and **positive PEF variability** or
- **positive BD test**, a FeNO between 25 - 39 ppb, negative PEF variability & **positive direct bronchial challenge test**

Consider alternative diagnoses in adults and young people >16 Y with obstructive spirometry and:

- negative BD test and a FeNO < 25 ppb or
- positive BD test, a FeNO 25 - 39 ppb, negative PEF variability and negative direct bronchial challenge test.

# Do not offer the following as diagnostic tests for asthma:

- skin prick tests to aeroallergens
- serum total and specific IgE.
- peripheral blood eosinophil count
- Indirect bronchial challenge test with exercise*

For adults and young people older than 16

All of the following are the effects of beta2 agonists in asthma except.

- Relaxation airway smooth-muscle cells of all airways
- Inhibition of mast cell mediator release
- Reduction in plasma exudation
- Inhibition of sensory nerve activation
- Upregulation of  $\beta$ 2- receptors of inflammatory cells
- Decrease in airway inflammatory cells and AHR

# Please match the potential complications of asthma drugs during therapy

- Cromones
  - Leukotriene antagonists
  - SABA
  - Anticholinergics
  - LABA
  - Theophylline
  - ICS
  - Systemic steroids
  - Anti IGE
- Hoarseness
  - Increased mortality
  - Slow in action
  - Tolerance in mast cells
  - Sudden death
  - Anaphylaxis
  - Low K level
  - Glaucoma
  - Dry mouth
  - Urinaryretention
  - Adenosine A1 Receptor antagonism
  - Seizure
  - Arrhythmia
  - Osteoporosis
  - Cataracts
  - Proximal myopathy

# Aims of therapy in asthma

- Minimal (ideally no) chronic symptoms, including nocturnal
- Minimal (infrequent) exacerbations
- No emergency visits
- Minimal (ideally no) use of a required  $\beta_2$ -agonist
- No limitations on activities, including exercise
- Peak expiratory flow circadian variation <20%
- (Near) normal peak expiratory flow
- Minimal (or no) adverse effects from medicine

# Match the mechanism of action

- Beta 2 agonists
- Anticholinergics
- Cromolyn sodium
- Theophylline
- ICS
- Wider bronchodilatation
- HDAC activation
- Decrease activated T cells in Axs
- Decrease surface mast cells
- Inhibition of NF kappaB
- Reversal of histone acetylation

# Which of the following increase clearance of theophylline

- Ciprofloxacin
- Zafirleukast
- CHF
- Viral infection
- Smoking
- Barbecued meat
- Cimetidine
- Allopurinol



# Match clinical use of asthma drugs

- Theophylline
- SABA
- LABA
- Leukotriene antagonists
- ICS
- Systemic corticosteroid
- Omalizumab
- Effective in trigger induced asthma (EIA, SO<sub>2</sub> ....)
- Indicated in acute attacks
- Potentiates steroid action
- More effective in obese patients
- Decreases admission and OCS use
- Decreases nocturnal awakenings

on examination who has FEV1 of 80% predicted and FEV1/FVC of 75% beclomethazone 200mcg/d + salbutamol II puffs/q6H PRN prescribed. 3 months later the patient feels better but has to use salbutamol 3-4 times/week and occasionally wakes up at night with shortness of breath. Patient voice has changed slightly. Which of the followings is not appropriate to this patient at this time:

- Review the inhaler use technique by the patient
- Review compliance of the patient
- Switch to ICH/LABA combination
- Add theophylline
- Add monteleukast
- Add short course of OCS
- Gradually taper ICH and continue salbutamol PRN

A 40 years old man with 10 years hx of asthma comes in with sever SOB and wheezing started 12 hours earlier and gradually worsened. He is cyanotic and uses accessory muscles of respiration and cannot complete a sentence. Salbutamol 8puffs q 20'x 3 times is given with no significant change in respirator distress. Which of the followings is appropriate at this time?

- Switch to nebulizer therapy with B agonists
- Add tiotropium bromide
- Start infusion of aminophylline
- Start systemic steroids
- Intubate and ventilate the patient
- Start halothane
- Give magnesium sulfate inhalation

35 year old woman with asthma on ICS/LABA C/O worsening symptoms during premenstrual periods. Which of the following is the most appropriate line of action for this patient?

- Add salbutamol 6 hourly PRN
- Use short course of OCS
- Administer progesterone
- Change therapy to monteleukast
- Add theophylline
- Add GRFs

theophylline and prednisolone since 6 months ago  
C/O shortness of breath on daily basis with  
frequent SABA use. Weight=70 Kg and height=  
172cm. Which of the following is least advisable for  
this patient at this time.

- Evaluate technique of drug use once more
- Measure FeNO
- Evaluate ambient air exposed by the patient
- Evaluate occupational exposures
- Verify beta-blocker or COX inhibitor use
- Evaluate for hypothyroidism
- Perform bronchial biopsy

Which of the following is most effective treatment of patient with asthma who has a normal lung function and minimal symptoms but deteriorates suddenly near to death.

- Check medication use and compliance
- Administer OCS immediately after the attack
- Add salbutamol 8 puffs on attack
- Patient to carry SC epinephrine all the times
- Administer ICS/LABA high dose continuously
- Add monteleukast
- Theophylline low dose

In a severely symptomatic pt with asthma who has been on irregular treatment with ICS, LABA, and monteleukast you start ICS/LABA + SABA PRN, montelukast and oral prednison daily. 3 months later even though he had no admission, however, no significant improvement is noted in symptoms. Which of the following line of action is most appropriate at this time?

- Double the dose of oral steroid
- Add theophylline
- Switch to omalizumab
- Add cyclosporine
- start anti TNF alpha therapy

respiratory arrest after taking ibuprofen which caused respiratory distress and wheezing. Patient has long history of nasal polyps. Which of the following is correct in this patients?

- Occur in almost 30% of the asthmatics
- Usually have seasonal rhinitis
- Start mainly in childhood
- Most of the patients are atopic
- COX2 inhibitors are safe in these patients
- Usually do not respond to steroids like other asthmatics



# In a asthmatic woman who becomes pregnant which of the followings is/are true?

- There is a 30% chance of deterioration and 30% chance of improvement
- It is generally advised not to get pregnant
- It is better to avoid ICS
- LABAs are safer than SABAs
- Theophylline is contraindicated
- Prednisolone is better than Prednisone if needed
- Breast feeding is not contraindicated while using asthma drug

In a patient with asthma who is on drugs including OCS and is going to have cholecystectomy which of the following is/are true?

- FVC may drop to 45% of previous level 36-48 hours after surgery
- Systemic steroids should be given before surgery
- Surgery is relatively contraindicated in these patients
- Ketamine is a relatively safe drug in this condition

38 years old man with asthma comes with persistent shortness of breath and coughing up yellow brownish sputum in the past 6 months. He has a ill-defined 2x4 cm consolidation at LUL of the lung. Review of his CXR reveals similar consolidation in the RUL 3 months earlier. Which of the following is true regarding this patient?

- Systemic steroids are effective in these patients
- Vasculitis is most probably the cause of consolidations
- Itraconazole may prevent exacerbations
- Early treatment may prevent central bronchiectasis

