BRONCHIAL ASTHMA DIAGNOSIS AND CLASSIFICATION

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Importance of Asthma Diagnosis

- A correct diagnosis of asthma is essential for initiation of appropriate management.
- Asthma symptoms may be intermittent and they are nonspecific, and may result in misdiagnosis, like with wheezy bronchitis, COPD, or the breathlessness of old age.
- Among children, misdiagnoses include various forms of bronchitis or croup, and may lead to inappropriate treatment.

Diagnosis of Asthma

The diagnosis of asthma can be made with the help of

History

Physical Examination

Laboratory Studies

HISTORY

- The history of symptoms, their pattern of occurrence, precipitating or aggravating factors, and the profile of a typical exacerbation are helpful in the clinical evaluation.
- A clinical diagnosis of asthma is often made by symptoms such as :
- Episodic breathlessness,
- Wheezing,
- Cough and Chest tightness.

Questions to Consider in the Diagnosis of Asthma

- Has the patient had an attack or recurrent attacks of wheezing?
- Does the patient have a troublesome cough at night?
- Does the patient wheeze or cough after exercise?
- Does the patient experience wheezing, chest tightness, or cough after exposure to airborne allergens or pollutants?
- Do the patient's cold "go to the chest" or take more than 10 days to clear up?
- Are symptoms improved by appropriate asthma treatment?

Other factors in history that support the diagnosis are

- Episodic nature of symptoms
- Seasonal variability of symptoms
- Early-morning symptoms or nocturnal episodes
- A positive family history of asthma and atopic disease
- Relief in the symptoms with appropriate asthma therapy

PHYSICAL EXAMINATION

- The most usual abnormal physical finding is wheezing on auscultation, a finding that confirms the presence of airflow limitation.
- Wheezing is caused by turbulent airflow through narrowed airways.
- Wheezing may be absent in some people with severe asthma exacerbation or only detected when the person exhales forcibly due to severely reduced airflow and ventilation

Other physical findings which may be present in severe asthma exacerbation are:

- Cyanosis
- Drowsiness
- Difficulty in speaking
- Tachycardia
- Hyperinflated chest
- Use of accessory muscles of respiration
- Intercostal recession

LABORATORY STUDIES

• The laboratory studies in the diagnosis of asthma include those that help in the conformation of the diagnosis of asthma and those that exclude other conditions that may mimic asthma or complicate its clinical presentation

- Various Laboratory studies for the diagnosis of Asthma and its exclusion are:
- Pulmonary Function Tests-
 - Spirometry
 - Peak Expiratory Flow Rate measurement
- Measurement of Airway responsiveness
- Measurement of Allergic status
- Blood Tests
- Sputum Examination
- Radiography

Pulmonary Function Tests

- Pulmonary function tests are important for confirming the diagnosis of asthma, assessment of the severity of airflow limitation, its reversibility and its variability and monitoring the response to therapy.
- Various methods are available to assess airflow limitation, but two methods have gained widespread acceptance for use in patients over 5 years of age. These are spirometry, particularly the measurement of forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC), and peak expiratory flow (PEF) measurement.

Spirometry

Spirometry is the recommended method of measuring

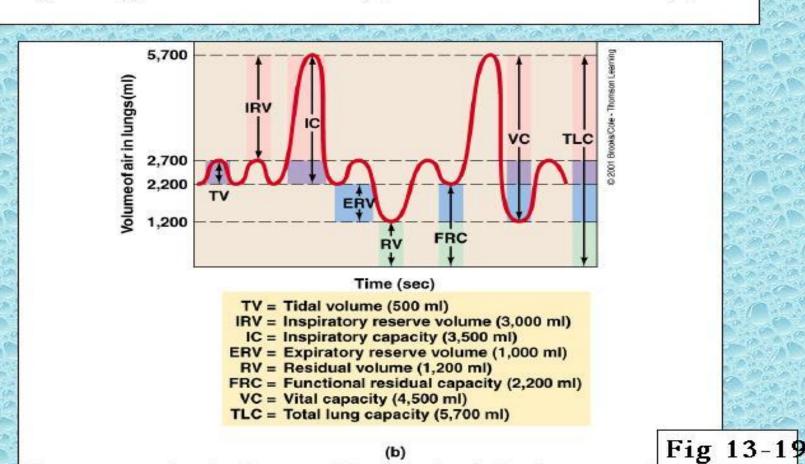
airflow limitation and reversibility to establish a

diagnosis of asthma. Measurements of FEV1 and FVC

are undertaken during a forced expiratory manoeuvre

using a spirometer.

Spirogram of Lung Volume Changes



Values are average for a healthy young adult male; values for females are somewhat lower.

FEV1 is reduced in asthma but because many lung

diseases may result in reduced FEV1, a useful

assessment of airflow limitation is the ratio of FEV1 to

FVC. The FEV1/FVC ratio is normally greater than 0.75

to 0.80, and possibly greater than 0.90 in children.

Any values less than these suggest airflow limitation.

- **FEV6** This is a more recently derived value which measures the volume of air that can forcibly be expired in 6 seconds. It approximates the FVC and in normal people the two values would be identical
- Helpful in patients with more severe airflow obstruction who make take up to 15 seconds to fully exhale, thus underestimating severity of obstruction

Reversibility testing

- Bronchodilator reversibility testing is best done as a planned procedure.
 - Assessing bronchodilator reversibility is important to determine whether fixed airway narrowing is present.
- Reversibility testing needs to be interpreted in the light of the patient's clinical history and examination.

Reversibility testing cont

- Spirometry should be undertaken when the patient is clinically stable and free from respiratory tract infection.
- Short-acting bronchodilators should be withheld for the previous 6 hours, long-acting bronchodilators for 12 hours, and sustained release theophylline for 24 hours.

FEV1/FVC should be measured **before and 15-20 minutes after bronchodilator is give**

Possible dose protocols include 400 µg salbutamol, up to 160 µg ipratropium, or the two combined.

Reversibility testing cont

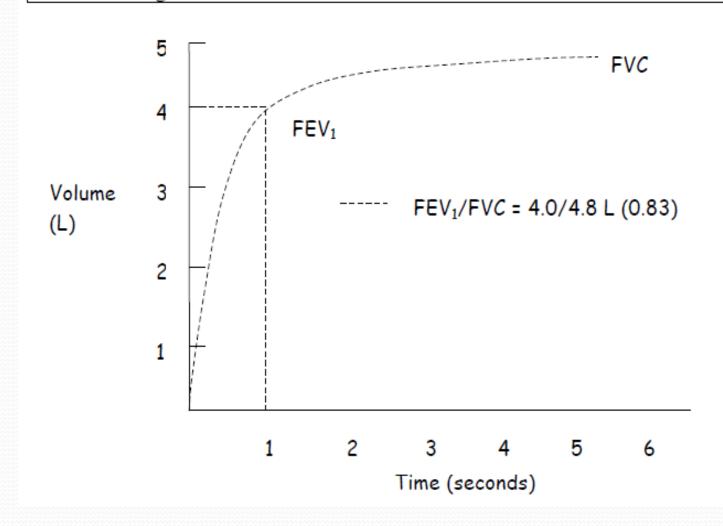
 The degree of reversibility in FEV1 which indicates the diagnosis of asthma is accepted as :-

• > or =
$$12\%$$

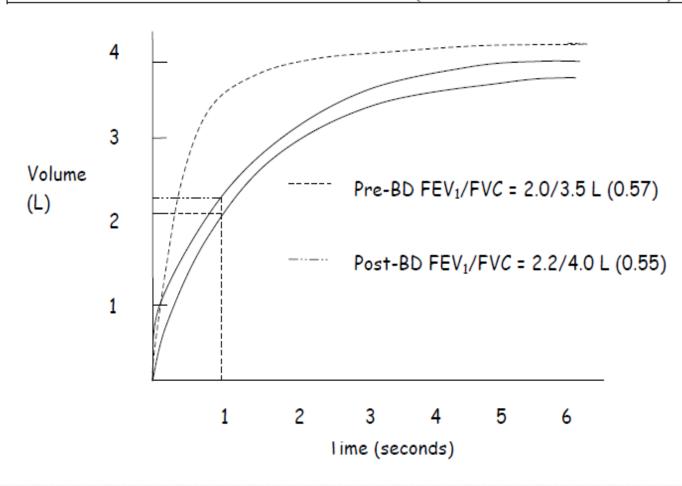
• > or = 200ml

from the pre-bronchodilator value

Figure 2. NORMAL SPIROGRAM: VOLUME-TIME CURVE







FLOW VOLUME LOOPS

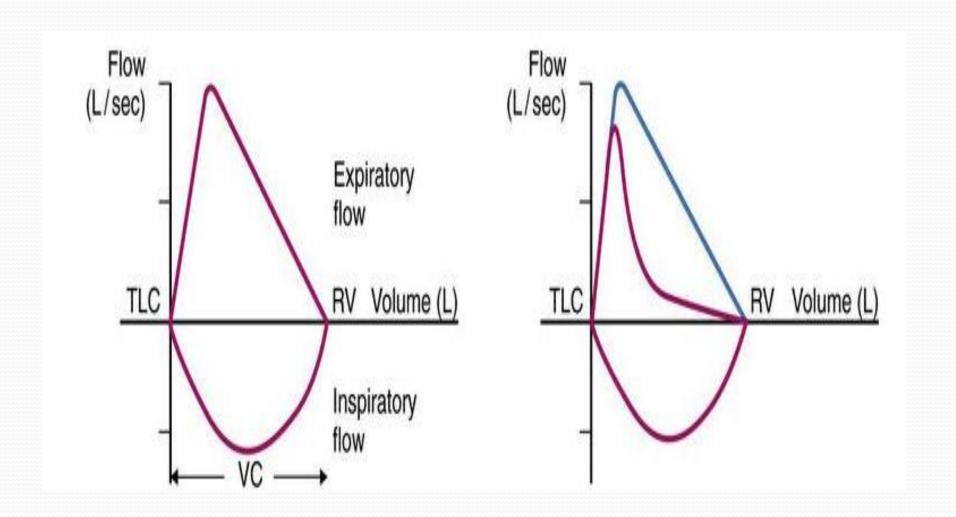
• In contrast to the spirogram, which displays airflow (in L) over time (in sec), the flow-volume loop displays airflow (in L/sec) as it relates to lung volume (in L) during maximal inspiration from complete exhalation (residual volume [RV]) and during maximum expiration from complete inhalation (TLC).

Advantage

The principal advantage of the flow-volume loop is

that it can show whether airflow is appropriate for a

particular lung volume.



• The shape of the flow-volume loop can indicate the location of airflow limitation, such as the large upper airways or smaller distal airways. With common obstructive airflow disorders, such as asthma or emphysema, the disease generally affects the expiratory limb and can reduce the effort-dependent peak expiratory flow as well as subsequent airflows that are independent of effort.

• The descending limb of the expiratory loop is typically concave. In contrast, several unusual anatomic disorders that narrow the large airways can produce a variety of patterns of truncation or flattening of either one limb of the loop (variable upper airway obstruction) or both limbs of the loop (fixed upper airway obstruction).

- Peak expiratory flow measurements are made using a peak flow meter
- PEF measurements should preferably be compared to the patient's own previous best measurement using his/her own peak flow meter.
- PEF is measured first thing in the morning before treatment is taken, when values are often close to their lowest, and last thing at night when values are usually higher
- A 60 L/min (or 20% or more of prebronchodilator PEF) improvement after inhalation of a bronchodilator, or diurnal variation in PEF of more than 20% (with twice daily readings, more than 10%) suggests a diagnosis of asthma.

Asthma action plan and Peak Flow

Green: 80-100% of your personal best

- Your breathing is good.
- · You do not have any early warning signs or asthma symptoms.
 - o. Take all your medicines every day, as your doctor tells you
 - Take your inhaler before exercise, as your doctor tells you.

Yellow: Caution 60-80% of your personal best

- Runny, stuffy nose
- Feel more tired
- Chin or throat itches
- Sneezing
- Restless
- Red or pale face
- Coughing
- Dark circles under your eyes
 - o Use "rescue" medicine
 - o Recheck peak flows after 20-30 minutes
 - Call your doctor, health care professional, or nurse care manager:
 - if your peak flow is not back up to the Green Zone
 - if your peak flow drops into the Yellow Zone again in less that 4 hours.

Red: Danger Below 60% of your personal best

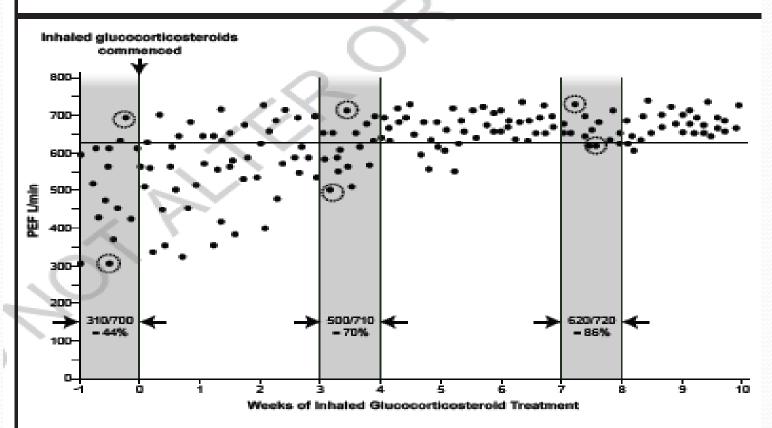
- Cough, more at night
- Wheezing
- Chest feels tight or hurts
- · Breathing faster than normal
- Get out of breath easily
 - Use your quick-relief medicine by inhaler or nebulizer right away!
 - o Call your doctor or 911 NOW

PEF Variability

• Diurnal PEF variability is defined as the amplitude (the difference between the maximum and the minimum value for the day), expressed as a percentage of the mean daily PEF value, and averaged over 1-2 weeks.

 Another method of describing PEF variability is the minimum morning pre-bronchodilator PEF over 1 week, expressed as a percent of the recent best (Min%Max).

Figure 2-2. Measuring PEF Variability*



*PEF chart of a 27-year-old man with long-standing, poorly controlled asthma, before and after the start of inhaled glucocorticosteroid treatment. With treatment, PEF levels increased, and PEF variability decreased, as seen by the increase in Min%Max (lowest morning PEF/highest PEF %) over 1 week.

Limitations of Spirometry and PEFR

- Both are reproducible, but effort-dependent.
- Ethnic differences in spirometric values have been demonstrated, appropriate predictive equations for FEV1 and FVC should be established for each patient.
- Spirometry lacks sensitivity as most asthma patients will not exhibit reversibility at each assessment, particularly those on treatment.
- PEF can underestimate the degree of airflow limitation, particularly as airflow limitation and gas trapping worsen.

Measurement of Airway Responsiveness

- Airways responsiveness is measured by means of :
 BRONCHIAL PROVOCATION TEST
- Bronchial Provocation test may be :
 - Direct
 - Indirect

Direct Test: Is performed with histamine and methacholine. Histamine act via H₁ receptors and cause constriction of the bronchial smooth muscles, whereas methacholine act via M₃ receptor causing bronchoconstriction.

Measurement of Airway Responsiveness Contd.

Direct tests include:-

1. Histamine challenge test:

Histamine challenge test is considered positive if the fall in FEV₁ (often 20%) occurs at a dose of less than or equal to 8 mg/ml with histamine.

2. Methacholine challenge test:

Negative test results at 16mg/ml has been promoted as a rule out test for clinical current asthma. However, recent studies suggest that negative methacholine test should not be relied upon to rule out asthma. A positive methacholine test with negative mannitol testing / exercise testing is more indicative of airway injury and remodelling then current active asthma.

Measurement of Airway Responsiveness Contd.

Indirect Testing : Various methods that can be used for indirect testing are as follows:-

- 1. Exercise
- 2. Adenosine Monophosphate
- 3. Eucapnic Voluntary hyperapnoea
- 4. Hypertonic saline
- 5. Dry powder mannitol

The indirect agents does not act via a specific receptors, there is no direct effect on bronchial smooth muscles. They cause the inflammatory cells to release mediators for e.g. histamine, leukotrienes. Hence, they are more specific in asthma diagnosis.

Measurement of Airway Responsiveness Contd.

Disadvantages of bronchial provocation test:

- 1. They are not specific.
- 2. They does not necessarily reflect the presence of inflammatory cells.
- 3. Many healthy people may show bronchial hyperresponsiveness to histamine.

Measurement of Allergic Status

- The components of an allergic evaluation include a detailed history of the patient's environment and possible triggers, followed by tests of allergic sensitivity
- Sensitivity to a particular allergen (or the presence of specific IgE antibody) can be verified by skin tests or in vitro serum antibody studies.
- They are simple and rapid to perform, and have a low cost and high sensitivity but low specificity.

BLOOD TESTS

- Peripheral blood eosinophilia (greater than 4 percent or 300 to 400 per cu.mm) may be seen in both allergic and non allergic asthmatics and may be used to support a diagnosis of asthma.
- High eosinophil counts (greater than 800 per cu.mm) suggest the presence of other disorders, such as ABPA, Churg-Strauss syndrome, tropical eosinophilia, and Loeffler's sndrome.
- Measurement of specific IgE in serum lacks specificity and measurement of total IgE in serum has no value as a diagnostic test for atopy.

OTHER LAB STUDIES

- Sputum eosinophil counts have been shown to predict clinical outcomes, particularly exacerbations when corticosteroids are withdrawn, but more research needs to be done.
- On chest radiograph non specific radiographic findings, such as overinflation, prominent hilar vessels, and bronchial wall thickening may be seen.
- Computed tomography may demonstrate atelectasis, bronchial wall thickening, or mucus impaction.
- Levels of exhaled nitric oxide (FeNO) and carbon monoxide (FeCO) have been suggested as non-invasive markers of airway inflammation in asthma

Differential diagnoses include:

- Infants and Children
 - Upper airway diseases
 - Allergic rhinitis and sinusitis
 - Obstructions involving large airways
 - Foreign body in trachea or bronchus
 - Vocal cord dysfunction
 - Vascular rings or laryngeal webs
 - Laryngotracheomalacia, tracheal stenosis, or bronchostenosis
 - Enlarged lymph nodes or tumor

Obstructions involving small airways

- Viral bronchiolitis or obliterative bronchiolitis
- Cystic fibrosis
- Bronchopulmonary dysplasia
- Heart disease

Other causes

- Recurrent cough not due to asthma
- Aspiration from swallowing mechanism dysfunction or gastroesophageal reflux
- Medication induced

- Adults
 - COPD (e.g., chronic bronchitis or emphysema)
 - Congestive heart failure
 - Pulmonary embolism
 - Mechanical obstruction of the airways (benign and malignant tumours)
 - Pulmonary infiltration with eosinophilia
 - Cough secondary to drugs (e.g., angiotensin-converting enzyme (ACE) inhibitors)
 - Vocal cord dysfunction

DIAGNOSIS OF ASPIRIN INDUCED ASTHMA

- AIA is diagnosed by in vivo testing using placebocontrolled oral challenges of persons suspected of having this disorder.
- This testing can be performed according to published protocols using single-blind or double-blind approaches.
- These protocols generally begin with a 3-mg dose of aspirin, although higher initial doses (30 mg) have been recently advocated since, if reactions occur at this dose, they are easily treated.

- The dosage is then increased to a maximum of 650 mg over a 3-day period. Spirometric pulmonary function is monitored serially during the challenge to assess the degree of bronchial constriction.
- An alternative to oral challenge, used in some centers for the diagnosis of AIA, is the inhalation of stabilized lysineaspirin, followed by serial lung function measurements, or nasal provocation with aspirin or lysine-aspirin followed by serial rhinomanometry or acoustic rhinometry.

Diagnosis of Aspirin-Induced Asthma: Aspirin (ASA) Challenge Protocols

Single-Blind Oral 3-Day Aspirin Challenge

Test days 2 3

 0
 Placebo
 ASA 30 mg
 ASA 100–150 mg

 3 h
 Placebo
 ASA 45–60 mg
 ASA 150–325 mg

 6 h
 Placebo
 ASA 60–100 mg
 ASA 325–650 mg

Double-Blind Oral Aspirin Challenge

Time

Both tester and patient are blinded to eliminate potential bias.

Bronchial Challenge with Lysine-Aspirin

Гime	Challenge
(Min)	(Lysine-aspirin in mg/ml)
0	Placebo
45	Placebo
90	11.25
135	22.5
180	45
225	90
270	180
315	360
350	360 (10 breaths)

Patients receive four breaths of all doses of lysine-aspirin unless otherwise indicated.

DIAGNOSIS OF EXERCISE INDUCED ASTHMA

- The diagnosis of EIA is most accurately established by employing validated exercise protocols coupled with pulmonary function testing.
- However, presumptive diagnosis can be made on the basis of history and physical examination.
- Important points in the clinical history include the:
- Level and type of exercise that provokes asthma,
- The timing of symptom onset,
- The situation that modifies the onset of symptoms and the precise symptoms experienced.

Physiological Documentation

- Two basic methods of provocation have been used, exercise and the inhalation of dry air (isocapnic hyperventilation, ISH).
- Exercise provocation, can be performed on an ergometer or a treadmill and leads to significantly greater increases in heart rate, metabolic rate, and oxygen consumption.
- ISH is preferred over exercise provocation since oxygen consumption and heart rate are not increased with ISH.
- As a result, ISH is useful in differentiating EIA from occult cardiac disease and is especially valuable when elderly or cardiac patients are being evaluated.

Isocapnic Hyperventilation

- The most commonly used protocol for the diagnosis of EIA is that published by O'Byrne et al and modified by Phillips et al.
- This protocol registers changes in pulmonary function in response to varying rates of ventilation using dry air which contains a fixed CO₂ content of 4.9 percent to maintain isocapnia.
- Each ventilatory challenge is performed for 3 min; spirometry is performed at intervals thereafter (usually 2, 5, and 10 min after the end of hyperventilation). Serial increase in hyperventilation is continued until maximal voluntary ventilation is reached.
- If the FEV1 falls 10 to 20 percent after provocation, the test is considered positive, confirming the diagnosis of EIA.

Differential Diagnosis of Exercise-Induced Asthma

Cardiac Disease

Coronary ischemia

Mitral valve prolapse

Atrial myxoma

Cardiomyopathy

Arrythmias

Functional abnormalities

Vocal cord dysfunction

Panic disorders

General

Deconditioning

Anemia

Lung disease

Fixed airway obstruction

Interstitial lung disease

Exercise-induced cough

STEROID RESISTANT ASTHMA

- Patients usually have persistent asthma that is difficult to control and is characterized by nocturnal exacerbations, chronic airflow limitation (FEV1 < 70% of predicted), and a poor clinical response, as well as a poor spirometric response to corticosteroid therapy.
- A poor response is usually defined as an inability of the patient's lung function to improve following at least seven to 14 days of high-dose (at least 40 mg daily) oral corticosteroid therapy.
- This is measured by a lack of improvement in the morning pre bronchodilator FEV1 of less than 15% from baseline.

DIAGNOSIS OF ASTHMA IN

CHILDREN

- The diagnosis of asthma in early childhood is based on clinical judgment and an assessment of symptoms and physical findings.
- Three categories of wheezing have been described in children 5 years and younger:
- Transient early wheezing, which is often outgrown in the first 3 years. This is often associated with prematurity and parental smoking.
- 2. Persistent early-onset wheezing (before age 3), *These* children typically have recurrent episodes of wheezing associated with acute viral respiratory infections, have no evidence of atopy

 Late-onset wheezing/asthma- These children have asthma which often persists throughout childhood and into adult life.

 They typically have an atopic background, often with eczema, and airway pathology is characteristic of asthma.

- The following categories of symptoms are highly suggestive of a diagnosis of asthma:
- Frequent episodes of wheeze (more than once a month)
- Activity-induced cough or wheeze
- Nocturnal cough in periods without viral infections
- Absence of seasonal variation in wheeze
- Symptoms that persist after age 3
- The presence of a wheeze before the age of 3, and the presence of one major risk factor (parental history of asthma or eczema) or two of three minor risk factors (eosinophilia, wheezing without colds, and allergic rhinitis) has been shown to predict the presence of asthma in later childhood.

 A useful method for confirming the diagnosis of asthma in children 5 years and younger is a trial of treatment with short-acting bronchodilators and inhaled glucocorticosteroids.

 Marked clinical improvement during the treatment and deterioration when treatment is stopped supports a diagnosis of asthma.

CLASSIFICATION

 Asthma has been classified as extrinsic or intrinsic, depending on the suspected role of allergens as etiologic factors.

 Atopic subjects are considered to have extrinsic asthma, while non atopic subjects have intrinsic asthma.

LIMITATIONS

- It does not aid in establishing an etiologic diagnosis nor does it help in defining treatment strategies.
- The presence of atopy, often defined by the presence of skin test sensitivity to aeroallergens, does not, by itself, indicate that allergens are important triggers of asthma, since a large percentage of skin-sensitive persons report no allergic symptoms

 Classifying patients as having intrinsic asthma is problematic also, since it implies that all possible allergens in the environment have been excluded as etiologic factors.

 Exercise and viral respiratory infections may play a more prominent role than allergens as triggers of symptoms in some atopic subjects.

PREVIOUS GINA CLASSIFICATION

	Symptoms/Day	Symptoms/Night	PEF or FEV ₁	PEF variability
STEP 1	< 1 time a week	= 2 times a month</td <td>>/= 80%</td> <td>< 20%</td>	>/= 80%	< 20%
Intermittent	Asymptomatic and normal PEF between attacks			
STEP 2	> 1 time a week but < 1 time a day	> 2 times a month	>/= 80%	20-30%
Mild Persistent	- I time a day			
	Attacks may affect activity			
STEP 3	Daily	> 1 time a week	60%-80%	> 30%
Moderate Persistent	Attacks affect activity			
STEP 4	Continuous	Frequent	= 60%</td <td>> 30%</td>	> 30%
Severe Persistent	Limited physical activity			

LIMITATIONS

• The main limitation of this previous method of classification of asthma severity was its poor value in predicting what treatment would be required and what a patient's response to that treatment might be.

CURRENT GINA CLASSIFICATION

Figure 2-4. Levels of Asthma Control

Characteristic	Controlled (All of the following)	Partly Controlled (Any measure present in any week)	Uncontrolled		
Daytime symptoms			Three or more features		
Limitations of activities	None	Any	of partly controlled asthma present in		
Nocturnal symptoms/awakening	None	Any	any week'†		
Need for rellever/ rescue treatment	Twice or less/week	More than twice/week			
Lung function (PEF or FEV ₁)‡	Normal	<80% predicted or personal best (if known)			

B. Assessment of Future Risk (risk of exacerbations, instability, rapid decline in lung function, side-effects)

Features that are associated with increased risk of adverse events in the future include:

Poor clinical control, frequent exacerbations in past year, ever admission to critical care for asthma, low FEV₁, exposure to cigarette smoke, high dose medications.

^{*} Any exacerbation should prompt review of maintenance treatment to ensure that it is adequate.

[†] By definition, an exacerbation in any week makes that an uncontrolled asthma week.

[‡] Lung function testing is not reliable for children 5 years and younger.

SUMMARY

- A clinical diagnosis of asthma is often prompted by symptoms such as episodic breathlessness, wheezing, cough, and chest tightness.
- Measurements of lung function (spirometry or peak expiratory flow) provide an assessment of the severity of airflow limitation, its reversibility, and its variability, and provide confirmation of the diagnosis of asthma.
- Extra measures may be required to diagnose asthma in children 5 years and younger and in the elderly, and occupational asthma.

 Asthma has been classified by severity in previous reports. However, asthma severity may change over time, and depends not only on the severity of the underlying disease but also its responsiveness to treatment.

• To aid in clinical management, a classification of asthma by level of control is recommended.

THANKS