

Management of asthma

Global Initiative for Asthma Guidelines



Definition

- **A chronic inflammatory disorder of the airways**
- **Many cells and cellular elements play a role**
- **Chronic inflammation is associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing**
- **Widespread, variable, and often reversible airflow limitation**

Burden of asthma

- One of the most common chronic diseases
 - worldwide : estimated 300 million affected
- Prevalence increasing
- Children - 1% to 18%
- Major cause of school / work absence
- 1% of the total global disease burden ¹

Factors influencing asthma

Host Factors :

Genetic - Atopy - IgE

- cytokine

- Airway hyperresponsiveness

- chromosome 5¹

Gender - children < 14 year : M>F

- adult F>M

Obesity – Leptin²

1. Postma et al. *N Engl J Med* 1995;333(14):894-900

2. Beuther et al. *Am J Respir Crit Care Med* 2006;174(2):112-119

Environmental factors

- **Indoor allergens - mites, cockroaches, house dust**
- **Outdoor allergens**
- **Occupational sensitizers-**
Isocyanates, platinum salts, plants and animal products. High risk in farming and agricultural workers, painting, cleaning, plastic manufacturing
- **Air Pollution**

Factors influencing asthma

- Tobacco smoke- accelerated decline in lung function.
 >4 times in infant of smoking mothers¹
- Respiratory Infections- RSV, Para influenza produce symptoms similar to asthma²

1. Dezateux et al. *Am J Respir Crit Care Med* 1999;159(2):403-10

2. Sigurs et al. *Am J Respir Crit Care med* 2000;161(5):1501-7

Factors influencing asthma

- Measles protect against asthma¹
- Diet- breast feeding protect against asthma²
- Hygiene hypothesis³

1. Shaheen et al. *Lancet* 1996;347(9010):1792-1796

2. Friedman et al. *J Allergy Clin Immunol* 2005;115(6):1238-48

3. Meer et al. *Allergy* 2005;60(5):619-625

History

- **Recurrent episodes of wheezing**
- **Troublesome cough at night**
- **Cough or wheeze after exercise**
- **Cough, wheeze or chest tightness after exposure to airborne allergens or pollutants**
- **Colds “go to the chest” or take more than 10 days to clear**

Cough variant asthma

- Chronic cough , more at night
- Variability in lung function or airway hyperresponsiveness
- D/D eosinophilic bronchitis

Other D/D

- ACE inhibitors
- GERD
- Post nasal drips
- Chronic sinusitis
- Vocal cord dysfunction

Exercise induced asthma

- 5-10 min after completing exercise
- Resolve spontaneously within 30-45 min
- Symptoms similar to asthma
- 8 min running protocol is used for diagnosis¹

Examination

- May be normal
- Usually *wheezing* on auscultation
- *Exacerbation* – cyanosis
 - drowsiness
 - difficulty in speaking
 - tachycardia
 - hyperinflated chest
 - use of accessory muscles
 - intercostal recession

Investigation

- **Spirometry or peak expiratory flow**
- **Measurement of airway responsiveness**
- **Measurements of allergic status to identify risk factors**

***Pulmonary function test* : diagnosis and monitoring**

- ***Reversibility* : improvement in FEV₁ or PEF measured within minutes after inhalation of SABA**

**Significant : >12% and > 200ml
not seen in all asthmatics**

- ***Variability* : increase or decrease in symptoms and lung function over time**

PEF >20% significant

variability more important than reversibility

Measurement of airway responsiveness

- Methacholine, histamine, mannitol or exercise challenge test ¹

Fall in $FEV_1 > 20\%$ is diagnostic

Limitation : Limited specificity

positive in allergic rhinitis,
cystic fibrosis, bronchiectasis
and COPD, fatal reaction

Non-invasive markers of airway inflammation

- Sputum eosinophil and neutrophil
- Exhaled nitric oxide¹ and carbon monoxide²

***Allergic status* : Skin test**
Specific IgE

1.Kharitonov S et al. Exhaled and nasal nitric oxide measurement : recommendations. The European Respiratory Society Task Force. *Eur Respir J* 1997;10(7):1683-1693.

2. Horvath I, Barnes PJ. Exhaled monoxides in asymptomatic atopic subjects. *Clin Exp Allergy* 1999;29(9):1276-80.

Alternative diagnosis

- **Upper airway obstruction and Foreign body**
- **Hyperventilation syndrome and panic attack**
- **Vocal cord dysfunction**
- **Chronic obstructive pulmonary disease**
- **Diffuse parenchymal lung diseases**
- **Left ventricular failure**

New approach

- GINA 2006 emphasize asthma management based on

clinical control

rather than classification of patient by

severity

- Introduction of concept of difficult to treat asthma

Classification of asthma severity

Classification	Symptoms	Nighttime symptoms	Lung Function
Step 1: Mild Intermittent	≤ 2 / week then Asymptomatic	≤ 2 /month	FEV ₁ or PEF $\geq 80\%$ PEF var $< 20\%$
Step 2: Mild Persistent	>2 /wk, < 1 /day Activity affected	> 2 /month	FEV ₁ or PEF $\geq 80\%$ PEF var: 20-30%
Step 3: Mod Persistent	Daily symptoms Exacerb ≥ 2 /wk	> 1 / week	$60\% < \text{FEV}_1 < 80\%$ PEF var $> 30\%$
Step 4: Sev Persistent	Cont symptoms Frequent exacerb	Frequent	FEV ₁ or PEF $< 60\%$ PEF var $> 30\%$

Levels of Asthma Control

<i>Characteristic</i>	Controlled (All of the following)	Partly controlled (Any present in any week)	Uncontrolled
Daytime symptoms	None (2 or less / week)	More than twice / week	3 or more features of partly controlled asthma present in any week
Limitations of activities	None	Any	
Nocturnal symptoms / awakening	None	Any	
Need for rescue / “reliever” treatment	None (2 or less / week)	More than twice / week	
Lung function (PEF or FEV₁)	Normal	< 80% predicted or personal best (if known) on any day	
Exacerbation	None	One or more / year	

Goals of successful management of asthma

- **Achieve and maintain control of symptoms**
- **Maintain normal activity levels, including exercise**
- **Maintain pulmonary function as close to normal as possible**
- **Prevent asthma exacerbations**
- **Avoid adverse effects from asthma medications**
- **Prevent Asthma mortality**

Asthma management

- 1. Develop patient/doctor partnership**
- 2. Identify and reduce exposure to risk factors**
- 3. Assess, treat and monitor asthma**
- 4. Manage asthma exacerbations**
- 5. Special considerations**

Develop patient/doctor partnership

- **Education**
 - **Include the family and joint setting of goals**
 - **Provide information about asthma**
 - **Provide training on self-management skills**
 - **Follow up and review**
 - **Written action plan**
 - **Improve adherence**

Identify and reduce exposure to risk factors

- **Indoor allergens – domestic mites, furred animals, cockroaches and fungi**
- **Outdoor allergen – pollens and molds**
- **Indoor air pollutants – primary / secondary smoke, nitric oxide, carbon monoxide, carbon dioxide, sulphur dioxide, formaldehyde**
- **Outdoor air pollutants – ozone, nitrogen oxides, acidic aerosols and particulate matter**

Identify and reduce exposure to risk factors

- Occupational exposure
- Food and food additives
- Drugs : aspirin and NSAIDs
- Rhinitis, sinusitis and polyposis
- Obesity
- Emotional stress

Assess, Treat and Monitor Asthma

- **Assessing level of asthma control**
- **Treating to achieve control**
- **Monitoring to maintain control**

Treatment

- **Step 1: as needed reliever medication**
- **Step 2: reliever medication plus a single controller**
- **Step 3: reliever medication plus one or two controllers**
- **Step 4: reliever medication plus two or more controllers**
- **Step 5: reliever medication plus additional controller option**

		TREATMENT STEPS				
		STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
		asthma education				
		environmental control				
		as needed rapid-acting β_2 -agonist	as needed rapid-acting β_2 -agonist			
CONTROLLER OPTIONS		SELECT ONE	SELECT ONE	ADD ONE OR MORE	ADD ONE OR BOTH	
		low-dose ICS*	low-dose ICS <i>plus</i> long-acting β_2 -agonist	medium- <i>or</i> high-dose ICS <i>plus</i> long-acting β_2 -agonist	oral glucocorticosteroid (lowest dose)	
		leukotriene modifier**	medium- <i>or</i> high-dose ICS	leukotriene modifier	anti-IgE treatment	
			low-dose ICS <i>plus</i> leukotriene modifier	sustained-release theophylline		
			low-dose ICS <i>plus</i> sustained-release theophylline			

*inhaled glucocorticosteroids

** receptor antagonist or synthesis inhibitors

Medications

Controller

- Inhaled glucocorticosteroids
- Leukotriene modifiers
- Long-acting inhaled β 2-agonists
- Systemic steroids
- Theophylline
- Cromones
- Long-acting oral β 2-agonists
- Anti-IgE

Reliever

- Rapid-acting inhaled β 2-agonists
- Systemic steroids
- Anticholinergics – ipratropium bromide and oxitropium bromide
- Theophylline
- Short-acting oral β 2-agonists

Equipotent daily dose of inhaled glucocorticoids for both adults and children

	Low adult (μ gm)	Low children	Med. adult	Med. children	High adult	High children
Beclomethason	200-500 200-500	100-200 100-250	500-1000 500-1000	200-400 250-500	1000-2000 >1000	>400 new >500 old
Budesonide	200-400 200-600	100-200 100-200	400-800 600-1000	200-400 200-600	800-1600 >1000	>400 >600
Ciclesonide	80-160	80-160	160-320	160-320	320-1280	>320
Fluticasone	100-250 100-250	100-200 100-200	250-500 250-500	200-500 200-400	500-1000 500-1000	>500 >400

Stepping down

- When controlled on medium - to high - dose inhaled glucocorticosteroids : 50% dose reduction at 3 month intervals ¹
- When controlled on low - dose inhaled glucocorticosteroids : switch to once - daily dosing
- Maintain control at lowest possible step and lowest dose
- Controller treatment stopped if on lowest dose and no symptoms for 1 year

Stepping up

- Use of combination rapid and long-acting inhaled β_2 -agonist and inhaled glucocorticosteroid in a single inhaler both as a controller and reliever is effective in maintaining a high level of asthma control and reduces exacerbations¹
- Temporarily doubling the dose of inhaled glucocortico-steroids is not effective.
A four fold rise or more is equal to short course of oral steroids ²

1. Rabe et al. *Chest* 2006;129(2):246-256

2. Reddel et al. *Eur Respir J* 2006;28(1):182-199

Difficult to treat asthma

- **Insensitive to glucocorticosteroids**
- **Difficult to treat asthma from onset rather than progressing from milder asthma :**
 - poor compliance**
 - psychological**
 - psychiatric disorders**

Difficult asthma

Diseases that mimic asthma :

COPD

bronchiectasis , cystic fibrosis

CHF – diastolic dysfunction

upper airway obstruction

aspiration or foreign body

neuromuscular weakness

vocal cord dysfunction

hyperventilation / panic attack

Difficult to treat asthma

- **Confirm the diagnosis**
- **Confirm compliance with treatment :**
incorrect or inadequate
- **Consider current or past smoking :**
reduces effectiveness of steroids
- **Comorbidities : chronic sinusitis**
GERD
OSA
psychological disorders

Manage Asthma Exacerbations

- Exacerbations are episodes of progressive increase in shortness of breath, cough, wheezing, or chest tightness
- Characterized by decrease in expiratory airflow:
 - ↓ in PEF or FEV1
- Primary therapy : rapid acting bronchodilator
 - systemic steroids
 - oxygen supplementation

	mild	moderate	Severe	Respi. Arrest
breathlessness	Can lie down	sitting	Hunch forward	
Talk in	sentences	phrases	words	
alertness	May be agitated	Usually agitated	Usually agitated	Drowsy / confused
RR	increased	increased	> 30/min	
Acc. Muscle /retraction	Usually not	usually	Usually	Paradoxical Abd move.
wheeze	Moderate	loud	Usually loud	absent
Pulse/min	<100	100-120	> 120	bradycardia
Pulsus paradoxus	absent	May be present	Often +	Absent due to fatigue
PEF- post bronchodilato	>80%	60-80%	<60% or response <2hr	
PaO2(on air) or PaCO2	Normal < 45mm Hg	>60 mm Hg <45mm Hg	<60 mm Hg >45 mm Hg	
SaO2%	>95%	91-95%	<90%	

Initial assessment

- History, examination, SpO₂, ABG (if PEF 30 – 50%)



Initial treatment

- O₂ to keep saturation >90% (children >95%)
- Inhaled SABA
- Systemic glucocorticosteroids (if no rapid response, pt is on oral steroids or severe episodes)
- Sedation contraindicated



Reassess after 1 hr

Moderate episodes	Severe episodes
PEF 60 – 80% personal best	Risk factor for near fatal asthma
<p>Moderate symptoms</p> <p>Accessory muscle use</p> <p><i>Treatment:</i></p> <p>O₂ , inhaled β₂ agonist & inhaled anticholinergics every 60min, oral steroids cont. R_x for 1-3 hrs</p>	<p>PEF <60%</p> <p>Severe symptom at rest, chest retraction</p> <p>No improvement</p> <p><i>Treatment:</i></p> <p>O₂, Inhaled β₂ agonist & anticholinergics, systemic steroids, I.V. MgSO₄</p>

Reassess after 1-2 hrs

Good	Incomplete	Poor response
<p data-bbox="47 157 399 385">Normal O/E PEF > 70% , SpO₂ > 90%</p>	<p data-bbox="514 157 1094 478">Risk factor, mild to mod signs, PEF < 60%, SpO₂ < 90%</p>	<p data-bbox="1247 157 1761 535">Risk factors , drowsiness, confused, PEF < 30%, PCO₂ > 45, PO₂ < 60</p>
<p data-bbox="47 606 342 735">Home treatment</p>	<p data-bbox="514 606 1209 1078">Admit to acute care setting O₂, β₂ agonist, anti cholinergics, systemic steroids, I.V. MgSO₄ Assess after 6-12 hr</p> <p data-bbox="599 1199 1132 1263">← improve / not →</p>	<p data-bbox="1247 606 1837 1363">Admit to intensive care O₂, β₂ agonist, anti cholinergics, systemic steroids, I.V. β₂ agonist, I.V. theophyllines, intubation and mechanical ventilation</p>

Criteria for discharge

- **Post treatment FEV1 / PEF 40 – 60%**
- **Minimum of 7 day course of oral steroids**
- **Check inhaler technique**
- **Identify precipitating factors and strategies for future avoidance**

Special situations

- **Pregnancy - 1/3 worse**

 - 1/3 less severe**

 - 1/3 unchanged ¹**

 - Poor control leads to increase perinatal mortality, prematurity and LBW**

Monitored use of theophylline, inhaled steroids, β 2 agonist and leukotriene modifiers are safe

Special situations

- ***Surgery*** -
systemic glucocorticoids coverage during the surgical period and reduce rapidly 24hr after surgery for wound healing
- ***Occupational asthma*** -
complete avoidance of the relevant exposure
- ***Gastro esophageal reflux***
- ***Aspirin-induced asthma*** - avoid NSAIDS

Unstable asthma

- ***Premenstrual asthma*** : timing coincides with fall in progesterone secretion
 - Corticosteroid resistance
 - Mood disturbances
 - Altered β_2 receptor dysfunction
 - treat with i.m progesterone
- ***Corticosteroid resistant*** : \uparrow in FEV1 $<$ 15%
in spite of 30 – 40 mg of steroids for 2 wks
R_x - stop steroids, long acting β_2 agonists,
NF- κ B inhibitor, p38MAP inhibitor,
antioxidants , theophylline*

Unstable asthma

- ***Brittle asthma*** : 1. persistent and chaotic variability in PEF
(40% diurnal for 50% time)
2. sporadic sudden fall in PEF in well controlled
- ***Treatment*** : Type 1 – treat with β 2 agonist terbutaline (3 – 12 mg in 24 hrs)
Type 2 – due to food allergy – treat with adrenaline infusion or nebulisation

Newer therapies for asthma*

- ***Ciclesonide*** : metabolised locally
less systemic effects
improved safety margin
reduced airway response to adenosine
- ***Theophylline*** : PDE 4 inhibitor – selective
inhibits bronchoconstriction,
oedema, airway smooth muscle
proliferation, excitatory non
adrenergic , non cholinergic
neurotransmission

Newer therapies for asthma*

- ***Allergen immunotherapy / desensitisation :***
 - upregulation of TH1 cytokines
 - downregulation of TH2 cytokines
 - allergen derived peptide immunotherapy,
 - immunostimulatory CpG oligonucleotide, DNA vaccines, mycobacterial vaccine
 - Have ↓ IgE binding and ↑ immunogenicity
- ***Cytokine modulation strategies***– IL-10, IL-12, anti IL-5 antibody, IL-4 antagonist, IL-13 antagonist
- ***Omalizumab(anti IgE)***– humanised monoclonal antibody against high affinity FcεR1 portion of IgE.

Conclusion

- **Asthma can be effectively controlled by intervening to suppress and reverse inflammation as well as treating bronchoconstriction and related symptoms**
- **Although there is no cure for asthma, appropriate management that includes a partnership between the physician and the patient/family most often results in the achievement of control**

All the best...