Global INitiative for Asthma Guidelines 2006
1993 Global Initiative for Asthma (GINA) formed
1995 goals and objectives were described in NHLBI/WHO workshop report
2002 revised
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

- Asthma is one of the most common chronic diseases worldwide with an estimated 300 million affected individuals.

- Prevalence increasing in many countries, especially in children and range from 1% to 18%.

- A major cause of school/work absence.

- 1% of the total global disease burden.

*Masoli et al. Allergy 2004;59(5):469-78*
Factors that Influence Asthma Development and Expression

Host Factors

- **Genetic**
  - Atopy - IgE, cytokine
  - Airway hyperresponsiveness - chromosome 5

- **Gender** - childhood <14 year M>F, adult F>M

- **Obesity** – Leptin*

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*Beuther et al. Am J Respir Crit Care Med2006;174(2):112-119
Environmental factors

- **Indoor** allergens - mites, cockroaches, house dust
- **Outdoor** allergens
- **Occupational** sensitizers - >300 substances eg. Isocyanates, platinum salts, plants and animal products. High risk in farming and agricultural workers, painting, cleaning, plastic manufacturing
- **Air Pollution**
Tobacco smoke- accelerated decline in lung function. >4 times in infant of smoking mothers

Respiratory Infections- RSV, Para influenza produce symptoms similar to asthma

Measles protect against asthma

Diet- breast feeding protect against asthma

Hygiene hypothesis

#Dezateux et al. Am J Respir Crit Care Med1999;159(2):403-10
*Shaheen et al. Lancet1996;347(9010):1792-1796
##Meer et al. Allergy2005;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 where LFT normal
- 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 diagnosis*

Examination

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

- Lung function test by spirometry or peak expiratory flow meter
- Measurement of airway responsiveness
- Measurements of allergic status to identify risk factors
- Extra measures may be required to diagnose asthma in children 5 years and younger and the elderly
Pulmonary function test continue to be recommended as an aid to diagnosis and monitoring. Show obstructive pattern

**Reversibility** – rapid improvement in FEV$_1$ or PEF measured within minutes after inhalation of SABA or more sustained improvement over days or weeks after effective controller treatment like inhaled glucocorticoids. Significant - >12% or > 200ml but not always
Variability – improvement or deterioration in symptoms and lung function over time e.g. Over days, day to day, month to month or seasonal. PEF >20% significant

Measure of variability of airflow limitation is given increase prominence rather than reversibility

As, most asthma patients will not exhibit reversibility at each assessment
Measurement of airway responsiveness

- Methacholine, histamine, mannitol or exercise challenge test#
- Fall in FEV$_1$ > 20% is diagnostic

Limitation-

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

#Cockroft et al; Clin Rev Allergy Immunol2003;24(1):19-26
Non-invasive markers of airway inflammation

- Sputum eosinophil and neutrophil
- Exhaled nitric oxide and carbon monoxide

Measurement of allergic status

- Skin test
- Specific IgE
Look for alternative diagnosis

_in case of adult and older children_

- Upper airway obstruction and FB
- Hyperventilation syndrome and panic attack
- Vocal cord dysfunction
- Other obstructive lung diseases particularly COPD
- Non obstructive lung diseases e.g. DPLD
- Non respiratory causes of symptoms e.g. LVF
New approach

GINA 2006 emphasize asthma management based on clinical control Rather than classification of patient by severity
- Cost depends on individual patients' level of control and extent of exacerbation.
- Emergency care is more expensive than planned treatment.
- Guideline determined asthma care can be cost effective.
- Well control asthma reduce socio-economic burden.
- more streamlined document that will be useful for busy clinicians
- Updated epidemiological data
- Introduction of concept of difficult to treat asthma
Difficult to treat asthma

- Some patients develop asthma that is difficult to manage.
- Relatively insensitive to glucocorticosteroids.
- Most of them have difficult to treat asthma from the onset rather than progressing from milder asthma.
- Poor compliance, psychological and psychiatric disorders.
Classification based on severity (intermittent, mild, moderate and severe) is now recommended only for research purposes.

Present classification is controlled, partly controlled and uncontrolled.
Emphasis is placed on the concept that the goal of asthma treatment is to achieve and maintain control.

**Asthma control** is defined as:

- No (twice or less/week) day time symptoms
- No limitation of daily activities
- No nocturnal symptoms or awakening
- No (≤2/week) need for reliever medication
- Normal or near normal lung function results
- No exacerbation
Treatment

Role of several medications have evolved since previous version of the report
Medications

**Controller**
- Inhaled glucocorticosteroids
- Leukotriene modifiers
- Long-acting inhaled β2-agonists
- Systemic glucocorticosteroids
- Theophylline
- Cromones
- Long-acting oral β2-agonists
- Anti-IgE (omalizumab)

**Reliever**
- Rapid-acting inhaled β2-agonists - salbutamol, terbutaline, fenoterol, reproterol and pirbuterol
- Systemic glucocorticosteroids
- Anticholinergics - ipratropium bromide and oxitropium bromide
- Theophylline
- Short-acting oral β2-agonists
Oral anti allergic compounds

E.g. tranilast, repirinlast, tazanolast

Very limited role

Other controller therapies

Methotrexate

Cyclosporin

Gold

Macrolide

troleandomycine
Allergen-specific Immunotherapy

- Greatest benefit of specific immunotherapy using allergen extracts has been obtained in the treatment of allergic rhinitis.
- The role of specific immunotherapy in asthma is limited.
- Specific immunotherapy should be considered only after strict environmental avoidance and pharmacologic intervention, including inhaled glucocorticosteroids, have failed to control asthma.

Perform only by trained physician.
Changes in medication approach

Recent data indicating an increase risk of asthma related death associated with long acting $\beta_2$ agonists (salmeterol) and should not be used as monotherapy. Only be used with an appropriate dose of inhaled corticosteroid.

Leukotriene modifier now have a more prominent role.
Monotherapy with cromones is no longer an alternative to low dose inhaled glucocorticoids to adults.

Increase use of rapid-acting inhaled β₂-agonists is an indication of poor asthma control.
Change in equipotent daily dose of inhaled glucocorticoids for both adults and children

<table>
<thead>
<tr>
<th></th>
<th>Low adult (μg)</th>
<th>Low children</th>
<th>Med. adult</th>
<th>Med. children</th>
<th>High adult</th>
<th>High children</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beclolemethasone</strong></td>
<td>200-500</td>
<td>100-200</td>
<td>500-1000</td>
<td>200-400</td>
<td>1000-2000</td>
<td>&gt;400 new</td>
</tr>
<tr>
<td></td>
<td>200-500</td>
<td>100-250</td>
<td>250-500</td>
<td></td>
<td>&gt;1000</td>
<td>&gt;500 old</td>
</tr>
<tr>
<td><strong>Budesonide</strong></td>
<td>200-400</td>
<td>100-200</td>
<td>400-800</td>
<td>200-400</td>
<td>800-1600</td>
<td>&gt;400</td>
</tr>
<tr>
<td></td>
<td>200-600</td>
<td>100-200</td>
<td>600-1000</td>
<td></td>
<td>&gt;1000</td>
<td>&gt;600</td>
</tr>
<tr>
<td><strong>Ciclosonide</strong></td>
<td>80-160</td>
<td>80-160</td>
<td>160-320</td>
<td>160-320</td>
<td>320-1280</td>
<td>&gt;320</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fluticasone</strong></td>
<td>100-250</td>
<td>100-200</td>
<td>250-500</td>
<td>200-500</td>
<td>500-1000</td>
<td>&gt;500</td>
</tr>
<tr>
<td></td>
<td>100-250</td>
<td>100-200</td>
<td>200-400</td>
<td></td>
<td>&gt;400</td>
<td></td>
</tr>
</tbody>
</table>
Change in asthma management

Previous *six* part asthma management program is changed to *five* component –

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
Component 1 reflects that control of asthma require:

- 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
Factors Involved in Non-Adherence

**Medication Usage**
- Difficulties associated with inhalers
- Complicated regimens
- Fears about, or actual side effects
- Cost
- Distance to pharmacies

**Non-Medication Factors**
- Misunderstanding/lack of information
- Fears about side-effects
- Inappropriate expectations
- Underestimation of severity
- Attitudes toward ill health
- Cultural factors
- Poor communication
Component 2: 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 etc
- **Outdoor air pollutants** – ozone, nitrogen oxides, acidic aerosols and particulate matter
- **Influenza vaccination**
- Occupational exposure
- Food and food additives – sulphites in food and drug preservatives found in processed potatoes, shrimp, dried fruits, bear and wine. Other dietary substances like – yellow dye tartazine, benzoate and monosodium glutamate
- Drugs – aspirin and NSAIDs
- Obesity
- Emotional stress
- Other factors – Rhinitis, sinusitis and polyposis
## Component 3: Assess, Treat and Monitor Asthma

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Controlled</th>
<th>Partly controlled (Any one present in any week)</th>
<th>Uncontrolled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daytime symptoms</td>
<td>None (2 or less / week)</td>
<td>More than twice / week</td>
<td></td>
</tr>
<tr>
<td>Limitations of activities</td>
<td>None</td>
<td>Any</td>
<td>3 or more features of partly controlled asthma present in any week</td>
</tr>
<tr>
<td>Nocturnal symptoms / awakening</td>
<td>None</td>
<td>Any</td>
<td></td>
</tr>
<tr>
<td>Need for rescue / “reliever”</td>
<td>None (2 or less / week)</td>
<td>More than twice / week</td>
<td></td>
</tr>
<tr>
<td>treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung function (PEF or FEV₁)</td>
<td>Normal</td>
<td>&lt; 80% predicted or personal best (if known) on any day</td>
<td></td>
</tr>
<tr>
<td>Exacerbations</td>
<td>None</td>
<td>One or more per day</td>
<td>One in any</td>
</tr>
</tbody>
</table>
Treatment steps –

- **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

**REDUCE**

**STEP 1**
- asthma education

**STEP 2**
- environmental control

**STEP 3**
- as needed rapid-acting β₂-agonist

**STEP 4**
- as needed rapid-acting β₂-agonist

**STEP 5**

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**INCREASE**

**SELECT ONE**
- low-dose ICS
- leukotriene modifier

**SELECT ONE**
- low-dose ICS plus long-acting β₂-agonist
- medium- to high-dose ICS plus long-acting β₂-agonist

**ADD ONE OR MORE**
- medium- to high-dose ICS
- leukotriene modifier

**ADD ONE OR BOTH**
- oral glucocorticosteroid (lowest dose)
- anti-IgE treatment

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*Inhaled glucocorticosteroids

** receptor antagonist or synthesis inhibitors
Stepping down

When controlled on medium- to high-dose inhaled glucocorticosteroids: 50% dose reduction at 3 month intervals *

When controlled on low-dose inhaled glucocorticosteroids: switch to once-daily dosing

Maintain control at lowest possible step and lowest dose

*Hawkins et al. BMJ 2003; 326(7399): 1115
Stepping up

- Need for repeated dosing over more than one/two days signals need for possible increase in controller therapy

Use of a combination rapid and long-acting inhaled β2-agonist (e.g., formoterol) and an inhaled glucocorticosteroid (e.g., budesonide) in a single inhaler both as a controller and reliever is effecting in maintaining a high level of asthma control and reduces exacerbations**

Temporarily doubling the dose of inhaled glucocortico-steroids is not effective, and is not recommended. A four fold rise or more is equal to short course of oral steroids *

**Rabe et al. Chest 2006;129(2):246-256
Exacerbations of asthma are episodes of progressive increase in shortness of breath, cough, wheezing, or chest tightness.
Patient with high risk

- H/O near fatal asthma require intubation and mechanical ventilation
- H/O hospitalization or emergency visit in past years
- Currently or recently use oral glucocorticosteroids
- Not currently using inhaled glucocorticosteroids
- Over dependant on SABA
- Psychiatric disease or psychosocial problems
- Noncompliance
<table>
<thead>
<tr>
<th></th>
<th>mild</th>
<th>moderate</th>
<th>Severe</th>
<th>Respi. Arrest</th>
</tr>
</thead>
<tbody>
<tr>
<td>breathlessness</td>
<td>Can lie down</td>
<td>sitting</td>
<td>Hunch forward</td>
<td></td>
</tr>
<tr>
<td>Talk in</td>
<td>sentences</td>
<td>phrases</td>
<td>words</td>
<td></td>
</tr>
<tr>
<td>alertness</td>
<td>May be agitated</td>
<td>Usually agitated</td>
<td>Usually agitated</td>
<td>Drowsy / confused</td>
</tr>
<tr>
<td>RR</td>
<td>increased</td>
<td>increased</td>
<td>&gt; 30/min</td>
<td></td>
</tr>
<tr>
<td>Acc. Muscle /retraction</td>
<td>Usually not</td>
<td>usually</td>
<td>Usually</td>
<td>Paradoxical Abd move.</td>
</tr>
<tr>
<td>wheeze</td>
<td>Moderate</td>
<td>loud</td>
<td>Usually loud</td>
<td>absent</td>
</tr>
<tr>
<td>Pulse/min</td>
<td>&lt;100</td>
<td>100-120</td>
<td>&gt; 120</td>
<td>bradycardia</td>
</tr>
<tr>
<td>Pulsus paradoxus</td>
<td>absent</td>
<td>May be present</td>
<td>Often +</td>
<td>Absent due to fatigue</td>
</tr>
<tr>
<td>PEF- post bronchodilator</td>
<td>&gt;80%</td>
<td>60-80%</td>
<td>&lt;60% or response &lt;2hr</td>
<td></td>
</tr>
<tr>
<td>PaO2(on air) or PaCO2</td>
<td>Normal &lt; 45mm Hg</td>
<td>&gt;60 mm Hg &lt;45mm Hg</td>
<td>&lt;60 mm Hg &gt;45 mm Hg</td>
<td></td>
</tr>
<tr>
<td>SaO2%</td>
<td>&gt;95%</td>
<td>91-95%</td>
<td>&lt;90%</td>
<td></td>
</tr>
</tbody>
</table>
**Initial assessment**

- History, examination, SpO$_2$, ABG

**Initial treatment**

- O$_2$ 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**

Cont.
<table>
<thead>
<tr>
<th>Moderate episodes</th>
<th>Severe episodes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PEF 60 – 80%</strong></td>
<td>Risk factor for near fatal asthma</td>
</tr>
<tr>
<td>personal best</td>
<td>PEF &lt;60%</td>
</tr>
<tr>
<td>Moderate symptoms</td>
<td>Severe symptom at rest, chest retraction</td>
</tr>
<tr>
<td>Accessory muscle use</td>
<td>No improvement</td>
</tr>
<tr>
<td>Treatment:</td>
<td>Treatment:</td>
</tr>
<tr>
<td>O2, inhaled β2 agonist &amp; inhaled anticholinergics every 60min, oral glucocorticosteroids</td>
<td>O2, Inhaled β2 agonist &amp; anticholinergics, systemic glucocorticosteroids</td>
</tr>
<tr>
<td>cont. for 1-3 hrs</td>
<td>cont. for 1-3 hrs</td>
</tr>
</tbody>
</table>

Reassess after 1-2 hrs
<table>
<thead>
<tr>
<th>Good response</th>
<th>Incomplete response</th>
<th>Poor response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal physical examination &gt;70%, SpO2 &gt;90%</td>
<td>Risk factor for near fatal asthma, mild to mod signs, PEF &lt; 60%, SpO2 &lt;90%</td>
<td>Risk factors+, severe symptoms- drowsiness, confused, PEF &lt; 30%, PCO2 &gt; 45, PO2 &lt;60</td>
</tr>
<tr>
<td>Home treatment</td>
<td>Admit to acute care setting O2, β2 agonist, anti cholinergics, systemic steroids, I.V. MgSO4 Assess after 6-12 hr improve/not</td>
<td>Admit to intensive care O2, β2 agonist, anti cholinergics, systemic steroids, consider I.V. β2 agonist, I.V. theophyllines, intubation and mechanical ventilation</td>
</tr>
</tbody>
</table>
Component 5: Special considerations are required to manage asthma in relation to:

- **Pregnancy** - 1/3 worse, 1/3 less severe and 1/3 unchanged *. Poor control leads to increase perinatal mortality, prematurity and LBW.

  Monitored use of theophylline, inhaled glucocorticosteroids, β2 agonist and leucotriene modifiers are safe.

- **Surgery** - systemic glucocorticoids coverage during the surgical period and reduce rapidly 24hr after surgery for wound healing.

- Rhinitis, sinusitis, and nasal polyps
- Occupational asthma- complete avoidance of the relevant exposure
- Respiratory infections
- Gastroesophageal reflux
- Aspirin-induced asthma- in minute to hrs patient experience vasomotor rhinitis and rhinorrhoea, attack of asthma and may lead to violent bronchospasm and even respiratory arrest
- Anaphylaxis and Asthma- epinephrine is the bronchodilator of choice
Conclusion

Asthma can be effectively controlled in most patients 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...