BRONCHIAL ASTHMA

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DEFINITION

- Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation, airway hyperresponsiveness and intermittent airway obstruction. It is defined by:
- I. The history of the following respiratory symptoms that vary over time and in intensity:
 - Wheeze
 - Shortness of breath
 - Chest tightness
 - Cough
- 2. Variable expiratory airflow limitation.

DIAGNOSIS

- Variability:
 - History of variable respiratory symptoms
 - Confirmed variable expiratory airflow limitation by lung function tests
 - The greater the variations, or the more occasions excess variation is seen, the more confident the diagnosis
- Airflow limitation:
 - A reduced FEVI may be found with many other lung diseases, but a reduced ratio of FEVI to FVC indicates airflow limitation.
 - The FEVI/FVC ratio is normally > 0.75-0.80, and usually > 0.90 in children.

VARIABILITY IN LUNG FUNCTION

Positive bronchodilator (BD) reversibility test

- Adults: increase in FEV1 of >12% and >200 mL from baseline, 10–15 minutes after 200–400 mcg albuterol or equivalent
- Children: increase in FEV1 of >12% predicted

• Excessive variability in twice-daily PEF over 2 weeks

- Adults: average daily diurnal PEF variability >10%
- Children: average daily diurnal PEF variability > 13%
- Significant increase in lung function after 4 weeks of anti-inflammatory treatment
 - Adults: increase in FEV1 by >12% and >200 mL (or PEF by >20%) from baseline after 4 weeks of treatment, outside respiratory infections

DIFFERENTIAL DIAGNOSIS

12-39 YEARS OLD

- Chronic upper airway cough syndrome
- Vocal cord dysfunction
- Hyperventilation, dysfunctional breathing
- Bronchiectasis
- Cystic fibrosis
- CHD
- Alpha I -antitrypsin deficiency
- Inhaled foreign body

>40 YEARS OLD

- Vocal cord dysfunction
- Hyperventilation, dysfunctional breathing
- COPD
- Bronchiectasis
- Cardiac failure
- Medication-related cough
- Parenchymal lung disease
- Pulmonary embolism
- Central airway obstruction

COUGH-VARIANT ASTHMA

- Chronic cough is their principal, if not only, symptom, associated with airway hyperresponsiveness.
- It is more common in children and often more problematic at night
- Documentation of variability in lung function is important.
- Must be distinguished from other causes of chronic cough

DDX OF CHRONIC COUGH IN ADULTS

- Upper airway cough syndrome (postnasal drip)
- Asthma
- Gastroesophageal reflux
- Laryngopharyngeal reflux
- Respiratory tract infection
- ACE inhibitors
- Chronic bronchitis
- Bronchiectasis
- Lung Cancer
- Nonasthmatic eosinophilic bronchitis

Features that increase probability of asthma	Features that decrease probability of asthma
More than one symptom (wheeze, shortness of breath, cough, chest tightness), especially in adults	Isolated cough with no other respiratory symptoms
Symptoms often worse at night or in the early morning	Chronic production of sputum
Symptoms vary over time and in intensity	Shortness of breath associated with dizziness, light- headedness or peripheral tingling (paresthesia)
Symptoms are triggered by viral infections (colds), exercise, allergen exposure, changes in weather, laughter, or irritants such as car exhaust fumes, smoke or strong smells.	Chest pain
Commencement of respiratory symptoms in childhood, a history of allergic rhinitis or eczema, or a family history of asthma or allergy.	Exercise-induced dyspnea with noisy inspiration.

PHYSICAL EXAMINATION

- Physical examination in people with asthma is often normal.
- The most frequent abnormality is expiratory wheezing, but this may be absent or only heard on forced expiration.
- Wheezing may also be absent during severe asthma exacerbations, due to severely reduced airflow (so called 'silent chest')

OTHER TESTS

Allergy tests:

- Skin prick test &/or serum IgE
- Mainly used in children <5 years of age
- **FeNO** (Fractional concentration of exhaled Nitric Oxide) :
 - It is modestly associated with levels of sputum and blood eosinophils
 - A finding of FENO >50 parts per billion (ppb) was associated with a good short-term response to ICS
- Bronchial provocation tests:
 - This is most often established with inhaled methacholine, but histamine, exercise, eucapnic voluntary hyperventilation or inhaled mannitol may also be used
 - These tests are moderately sensitive for a diagnosis of asthma but have limited specificity

ASTHMA MANAGEMENT

• The long-term goals of asthma management are:

- To achieve good control of symptoms and maintain normal activity levels
- To minimize future risk of exacerbations, persistent airflow limitation and side-effects.

• Pharmacological categories for long-term treatment :

- Controller medications (maintenance treatment)
- Reliever medications : as-needed relief of breakthrough symptoms and during exacerbations, also for prevention of exercise-induced bronchoconstriction

CONTROLLER MEDICATIONS

- Reduce airway inflammation
- Control symptoms
- Reduce future risks such as exacerbations and decline in lung function.

Can be in the form of:

- Inhaled Corticosteroid (ICS)
- Inhaled Long-Acting Beta Agonist (LABA)
- LTRA
- Other Add-on treatments :
 - Inhaled LAMA (long-acting muscarinic antagonist)
 like Tiotropium
 - Anti Ig-E (Omalizumab)
 - Anti-IL5 (SQ Mepolizumab; IV Reslizumab)
 - Low dose OCS
 - Azithromycin

ASTHMA MANAGEMENT

• Step-wise approach

- Stepping up with uncontrolled symptoms, exacerbations or the presence of risk factors for exacerbations
- Stepping down if symptoms are controlled for at least 3 months AND low risk for exacerbations.

- Always remember to treat modifiable risk factors e.g. obesity, smoking, anxiety
- Advise about nonpharmacological therapies like physical activity, weight loss, avoidance of sensitizers, avoidance of medications that may make asthma worse

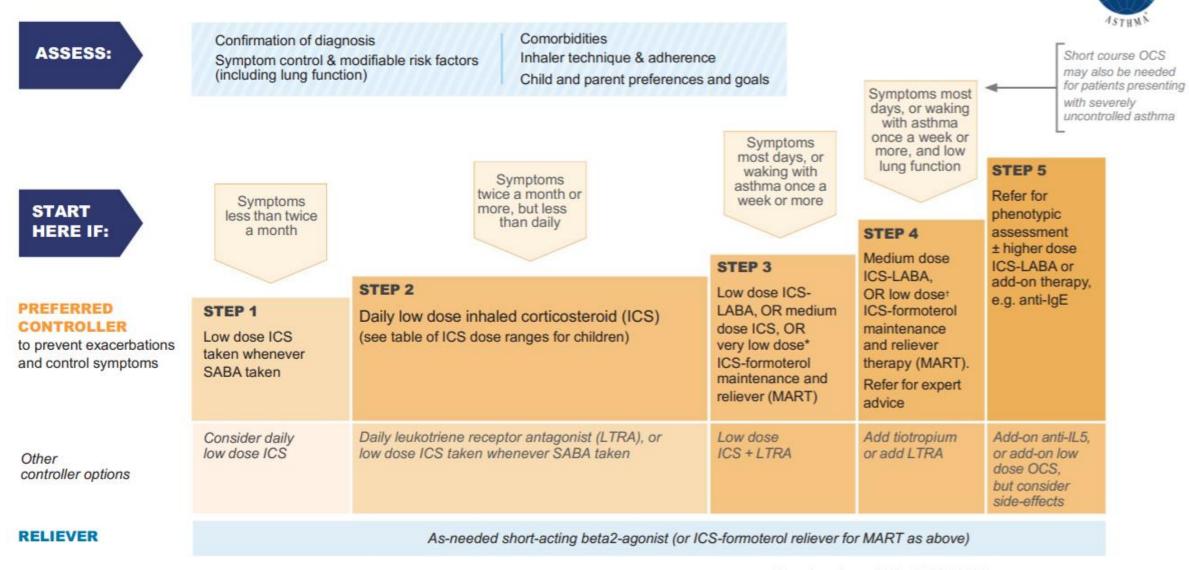
	Adults and adolescents Children 6-11 years		Children 5 years and younger	
Step I	As-needed low-dose ICS- formoterol (Low-dose ICS taken whenever SABA taken)	Low-dose ICS taken whenever SABA taken Daily low-dose ICS	As-needed SABA	
Step II	As-needed low-dose ICS- formoterol Daily low-dose ICS (LTRA, or Low-dose ICS taken whenever SABA taken)	Daily low-dose ICS (LTRA, or Low-dose ICS taken whenever SABA taken)	Daily Low-dose ICS (LTRA, or intermittent ICS)	
Step III	Low-dose ICS-formoterol MART Low-dose ICS-LABA (Medium-dose ICS, or low-dose ICS+LTRA)	 Very Low-dose ICS- Formoterol MART Medium-dose ICS Low-dose ICS-LABA (low-dose ICS+LTRA) 	Double low-dose ICS (Low-dose ICS+LTRA)	
Step IV	Medium-dose ICS-formoterol MART Medium-dose ICS-LABA (add-on tiotropium, or add-on LTRA)	Medium-dose ICS-LABA Low-dose ICS-Formoterol MART (add-on tiotropium, or add-on LTRA) Refer for expert advice	Continue double low-dose ICS and refer for specialist assessment	
Step V	High-dose ICS-Formoterol Add-On LAMA High-dose ICS-LABA (Add-on therapy)	High-dose ICS-LABA +/- add- on therapy		

12+ years Personalized asthma management Assess, Adjust, Review for individual patient needs	E S L	Symptoms Exacerbations Side-effects ung function Patient satisfaction	Assessor Treatment of m and comorbidit Non-pharmaco Asthma medica	risk factors (including lung function) Comorbidities Inhaler technique & adherence Patient preferences and goals Treatment of modifiable risk factors and comorbidities Non-pharmacological strategies Asthma medications (adjust down/up/between tracks) Education & skills training			
				STEP 4	STEP 5		
CONTROLLER and PREFERRED RELIEVER (Track 1). Using ICS-formoterol as reliever reduces the risk of	STEPS 1 – 2 As-needed low dose IC	CS-formoterol	STEP 3 Low dose maintenance ICS-formoterol	Medium dose maintenance ICS-formoterol	Add-on LAMA Refer for phenotypic assessment ± anti-IgE, anti-IL5/5R, anti-IL4R Consider high dose ICS-formoterol		
exacerbations compared with using a SABA reliever	RELIEVER: As-needed low-dose ICS-formoterol						
			STEP 3	STEP 4 Medium/high	STEP 5 Add-on LAMA Refer for phenotypic		
CONTROLLER and ALTERNATIVE RELIEVER (Track 2). Before considering a regimen with SABA reliever, check if the patient is likely to be adherent with daily controller	STEP 1 Take ICS whenever SABA taken	STEP 2 Low dose maintenance ICS	Low dose maintenance ICS-LABA	dose maintenance ICS-LABA	assessment ± anti-IgE, anti-IL5/5R, anti-IL4R Consider high dose ICS-LABA		
	RELIEVER: As-needed short-acting β2-agonist						
Other controller options for either track		Low dose ICS whenever SABA taken, or daily LTRA, or add HDM SLIT	Medium dose ICS, or add LTRA, or add HDM SLIT	Add LAMA or LTRA or HDM SLIT, or switch to high dose ICS	Add azithromycin (adults) or LTRA; add low dose OCS but consider side-effects		

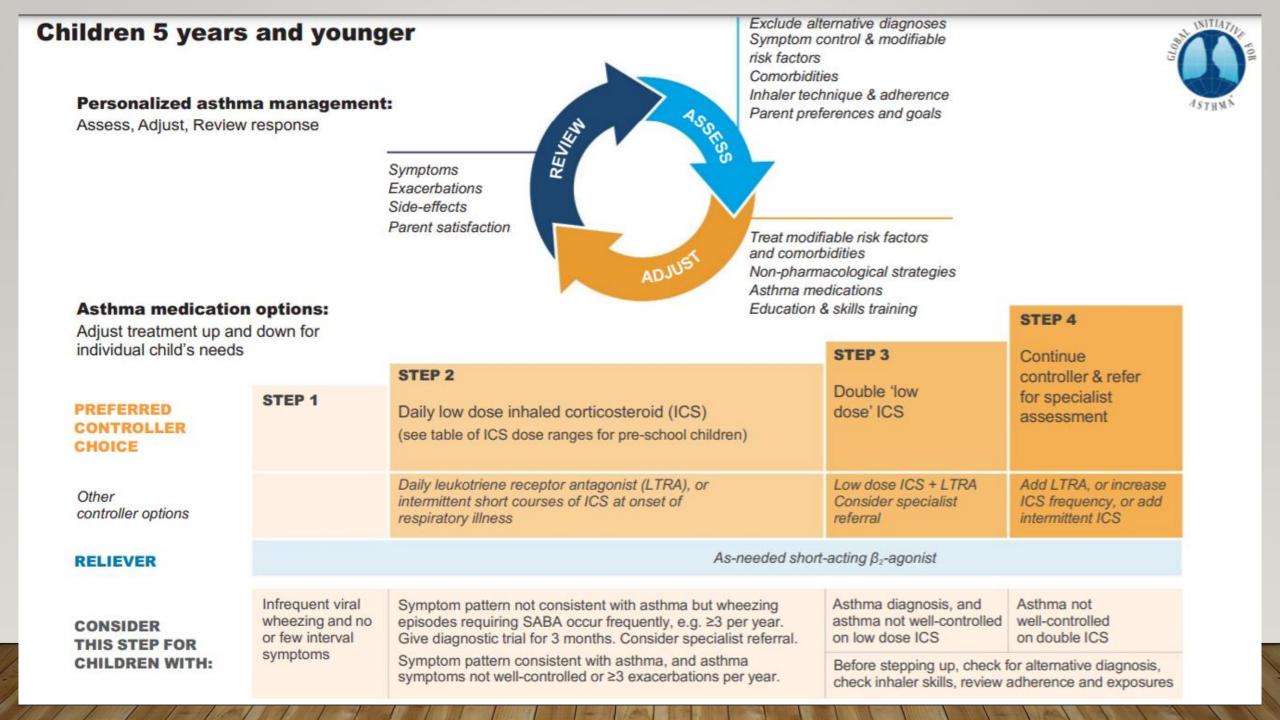
GINA 2021, Box 3-5A

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Children 6-11 years with a diagnosis of asthma



*Very low dose: BUD-FORM 100/6 mcg †Low dose: BUD-FORM 200/6 mcg (metered doses).



GINA TRACK I

- Track I is preferred because using low dose ICS-formoterol as reliever reduces the risk of severe exacerbations compared with regimens with SABA as reliever, with similar symptom control.
- When a patient at any treatment step has asthma symptoms, they use low dose ICSformoterol in a single inhaler for symptom relief
- In Steps 3–5, patients also take ICS-formoterol as their daily controller treatment. Together, this is called 'maintenance and reliever therapy' or 'MART'
- ICS-formoterol should not be used as the reliever in patients prescribed a different ICS-LABA for their controller therapy

GINA TRACK II

- This is an alternative approach for adults and adolescents if Track I is not possible, or is not preferred by a patient with no exacerbations on their current therapy
- In Step I, the patient takes a SABA and a low dose ICS together for symptom relief when

symptoms occur, in a combination inhaler, or with the ICS taken right after the SABA

• In Steps 2–5, the patient takes ICS-containing controller medication regularly every day, and uses a SABA (alone) for symptom relief

INITIATING TREATMENT FOR ASTHMA

• Start treatment with step 1 if:

- Asthma symptoms or need for SABA less than twice a month AND
- No waking due to asthma in last month AND
- No risk factors for exacerbations (including normal lung function)

• Start treatment with step 2 in the following cases:

- Infrequent asthma symptoms, but the patient has one or more risk factors for exacerbations
- Asthma symptoms or need for SABA between twice a month and twice a week, or patient wakes due to asthma
 once or more a month
- Asthma symptoms or need for SABA more than twice a week

INITIATING TREATMENT FOR ASTHMA, CONT'D

• Start treatment with step 3 if:

• Troublesome asthma symptoms most days; or waking due to asthma once a week or more, especially if any risk factors exist

• Start treatment with step 4 if:

- Troublesome asthma symptoms most days; or waking due to asthma once a week or more, and low lung function
- Short course of OCS may be needed at presentation

ASTHMA SEVERITY

It can be assessed when the patient has been on regular controller treatment for several months:

- Mild Asthma :asthma that is well controlled with Step 1 or Step 2 treatment
- Moderate Asthma: asthma that is well controlled with Step 3 treatment
- Severe Asthma : asthma that requires Step 4 or 5 treatment to prevent it from becoming 'uncontrolled', or asthma that remains 'uncontrolled' despite this treatment.

FOLLOW UP

- Patients should be seen I-3 months after starting treatment and every 3-I2 months thereafter:
 - To monitor their symptom control
 - To check for risk factors and occurrence of exacerbations,
 - To document the response to any treatment changes.
- Always before stepping up in treatment:
 - Confirm that the symptoms are due to asthma
 - Check for common problems such as incorrect inhaler technique, poor adherence, and environmental exposures.

ASTHMA ASSESSMENT

- Assessment of asthma control over the last 4 weeks
- Assess for treatment issues such as
 - Current treatment step
 - Inhaler technique and adherence
 - Side-effects
 - Comorbidities (Rhinitis, GER, obesity, OSA, depression and anxiety)
- Assess for asthma severity (retrospectively) from the level of treatment required to control symptoms and exacerbations.
- Lung function is an important part of the assessment of future risk; it should be measured at the start of treatment, after 3-6 months of treatment (to identify the patient's personal best), and periodically thereafter (every 1-2 years) for ongoing risk assessment.

ASSESSMENT OF ASTHMA CONTROL

Symptom control

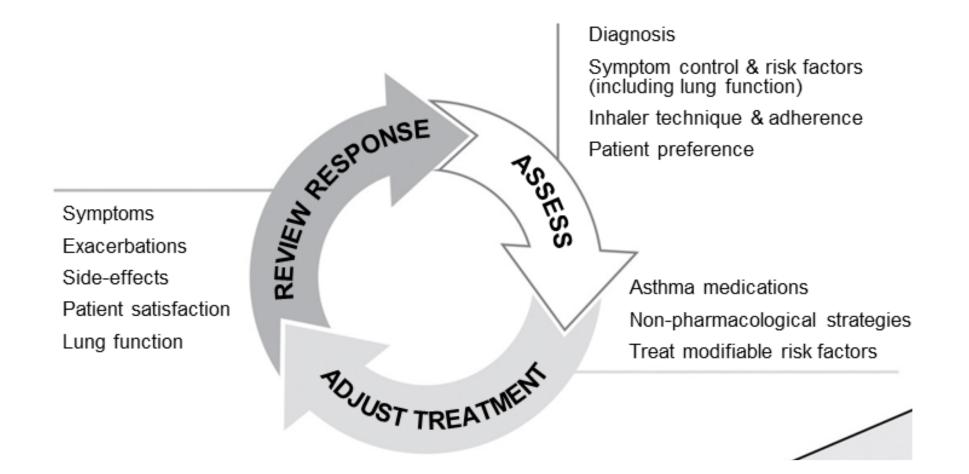
- The frequency of daytime and night-time asthma symptoms and reliever use
- Activity limitation

Future risk of adverse outcomes

- Exacerbations
- Persistent airflow limitation
- Medication side-effects

UNCONTROLLED ASTHMA

- Poor inhaler technique (up to 80% of community patients): watch patient using inhaler, recheck every visit
- Poor medication adherence:
 - Have empathic discussion to identify this.
 - Check the date of the last controller prescription or the date and dose counter on the inhaler.
- **Incorrect diagnosis** of asthma, with symptoms due to alternative conditions : confirm diagnosis of asthma
- **Comorbidities** and complicating conditions: check and manage them
- Ongoing exposure to sensitizing or irritant agents in the home or work environment or the use of NSAIDS or BB



OTHER THERAPIES

- Allergen Immunotherapy:
 - May be an option if allergy plays a prominent role, e.g. asthma with allergic rhinoconjunctivitis.
- Vaccinations
 - Influenza contributes to some acute asthma exacerbations, and patients with asthma are advised to receive an influenza vaccination every year
 - People with asthma, are at higher risk of pneumoccal disease, however there is insufficient evidence to recommend routine pneumococcal vaccination in people with asthma
- Bronchial Thermoplasty
 - Potential treatment option at Step 5 in some countries
- Vitamin D
 - Low serum levels of Vitamin D are linked to impaired lung function, higher exacerbation frequency and reduced corticosteroid response

SELF MONITORING

- Patients should be trained to keep track of their symptoms (with or without a diary), and notice and take action if
 necessary when symptoms start to worsen.
- PEF monitoring may sometimes be useful:
- Short-term monitoring
 - Following an exacerbation, to monitor recovery.
 - Following a change in treatment, to help in assessing whether the patient has responded.
 - If symptoms appear excessive (for objective evidence of degree of lung function impairment).
 - To assist in identification of occupational or domestic triggers for worsening asthma control
- **Long-term** monitoring
 - For earlier detection of exacerbations, mainly in patients with poor perception of airflow limitation.
 - For patients with a history of sudden severe exacerbations.
 - For patients who have difficult-to-control or severe asthma

EXACERBATIONS

- Exacerbations represent an acute or sub-acute progressive worsening in symptoms and lung function from the patient's usual status.
- Exacerbations usually occur in response to:
 - Exposure to an external agent (e.g. viral URTI, pollen or pollution) and/or
 - Poor adherence with controller medication.

RISK FACTORS FOR EXACERBATIONS

- Poor symptom control
- History of $\geq I$ exacerbations in the previous year
- Ever intubated or in ICU for asthma
- Poor adherence or incorrect inhaler technique
- Smoking
- Blood or sputum eosinophilia
- High SABA use
- Inadequate ICS

- Low FEVI, especially if <60% predicted
- Higher bronchodilator reversibility
- Major psychological or socioeconomic problems
- Exposures: allergen exposure if sensitized
- Comorbidities: obesity; chronic rhinosinusitis; confirmed food allergy
- Elevated FENO (in adults with allergic asthma taking ICS)
- Pregnancy

RISK FACTORS FOR ASTHMA-RELATED DEATH

- A history of near-fatal asthma requiring intubation and mechanical ventilation
- Hospitalization or emergency care visit for asthma in the past year
- Currently using or having recently stopped using OCS
- Not currently using ICS
- Over-use of SABAs,(> one 200mg canister of salbutamol monthly)
- A history of psychiatric disease or psychosocial problems
- Poor adherence with asthma medications
- Food allergy in a patient with asthma

SELF-MANAGEMENT OF EXACERBATIONS

- Repeated dosing with inhaled SABA
- ICS should be increased (at least doubled) when there is a clinically important change from the patient's usual level of asthma control and this dose increase should be maintained for 2-4 weeks
- For patients on combination ICS/formoterol inhaler dose may be increased up to a maximum total formoterol dose of 72 mcg/day
- Patient should be instructed to see his doctor within I-2 weeks of the exacerbation to assess for symptom control and identify the potential cause of the exacerbation.
- Start OCS and Contact a doctor immediately if:
 - PEF<60% best
 - Not improving after 48 hours

MANAGEMENT OF EXACERBATIONS IN PRIMARY CARE

 Assess exacerbation severity and risk factors of asthma-related death concurrently with the prompt initiation of therapy

History

- Timing of onset and cause (if known) of the present exacerbation
- Severity of asthma symptoms, including any limiting exercise or disturbing sleep
- Any symptoms of anaphylaxis
- Any risk factors for asthma-related death
- All current reliever and controller medications, including doses and devices prescribed, adherence pattern, any recent dose changes, and response to current therapy.

PHYSICAL EXAMINATION

- Signs of exacerbation severity and vital signs (e.g. level of consciousness, temperature, PR, RR, BP, ability to complete sentences, use of accessory muscles, wheeze.)
- Complicating factors (e.g. anaphylaxis, pneumonia, pneumothorax)
- Signs of alternative conditions that could explain acute breathlessness (e.g. cardiac failure, upper airway dysfunction, inhaled foreign body or pulmonary embolism).

EXACERBATION SEVERITY

Mild-Moderate

Severe

- Talks in phrases
- Prefers sitting to lying
- Increased RR
- Not agitated
- No use of accessory muscles
- PR 100-120 bpm
- O2 saturation (room air) 90-95% (>95% in young children)
- PEF >50% predicted or best

Talks in words

- Sits hunched forwards
- RR> 30/min
- Agitated
- Accessory muscles in use
- PR>120 bpm ((>200 bpm(0-3 years), >180 bpm(4-5 years))
- O2 saturation (room air) < 90% (<92% in young children)
- PEF</= 50% predicted or best

TREATING MILD-MOD EXACERBATION

- Repeated administration of inhaled SABA
 - 4-10 puffs every 20 minutes for the 1st hour
 - Then continue with as-needed SABA
 - Delivery of SABA via a pMDI and spacer or a DPI leads to a similar improvement in lung function as delivery via nebulizer
- Controlled oxygen therapy (titrated against pulse oximetry)
 - The aim is to maintain O2 sat at 93–95% (94–98% for children)
- Systemic corticosteroids
 - The recommended dose for adults is I mg prednisolone/kg/day (I-2 mg/kg/day in children)
 - Continued for 5–7 days (3-5 days in young children) with no need for tapering

TREATING MILD-MOD EXACERBATION, CONT'D

- Response of symptoms, oxygen saturation and lung function should be reviewed after 1 hour.
- Ipratropium bromide treatment is recommended only for severe exacerbations
- Intravenous magnesium sulfate should be considered for patients with severe exacerbations not responding to initial treatment.

TREATING MILD-MOD EXACERBATION, CONT'D

- Increase the dose of controller medications for 2-4 weeks, in young children continue to take the prescribed dose during and after an exacerbation
- Chest X-ray is not routinely recommended.
- Antibiotics should not be routinely prescribed
- Schedule a follow-up visit within I week after an exacerbation.

BRONCHIAL ASTHMA IN YOUNG CHILDREN

- Asthma is the most common chronic disease of childhood
- Features suggesting a diagnosis of asthma in children <5 years:
 - Prolonged cough, wheezes and breathlessness for >10 days during URTI, or severe symptoms
 - Recurrent cough and wheezy episodes (3 or more per year)
 - Between episodes may have cough, wheeze or heavy breathing that may be worse at night, occurring with exercise, laughing, crying or exposure to tobacco smoke or air pollution in the absence of an apparent respiratory infection

FEATURES SUGGESTING A DIAGNOSIS OF ASTHMA IN CHILDREN, CONT'D

- Reduced activity compared with other children; tires earlier during walks (wants to be carried)
- Past or FHx of allergic disease (atopic dermatitis or allergic rhinitis), asthma in first-degree relatives
- Clinical improvement with therapeutic trial with low dose ICS and asneeded SABA

COMMON DDX IN CHILDREN

- Recurrent viral URTI
- GER
- Foreign body aspiration
- Tracheomalacia
- TB
- CHD
- CF and Primary Ciliary Dyskinesia
- Vascular ring
- Bronchopulmonary Dysplasia

TESTS TO ASSIST IN DX

- Therapeutic trial
- Test for atopy (skin prick testing or allergen-specific Ig E.)
- CXR (if in doubt about Dx, to R/O structural lesions)
- Lung function tests have limited role in the dx of asthma in this age
- Exhaled nitric oxide (FeNO)

MANAGEMENT

- Wheezing episodes in young children should be treated initially with inhaled SABA
- A trial of controller therapy should be given if the symptom pattern suggests asthma and/or wheezing episodes are frequent (the need for inhaled SABA more than every 6-8 weeks) or severe.
- Response to treatment should be reviewed before deciding whether to continue it. If no response is observed, consider alternative diagnoses.
- Review the need for asthma treatment frequently, as asthma-like symptoms remit in many young children

- The preferred inhaler device is pMDI with a valved spacer (with face mask in children <4years and mouthpiece for those 4-5year)
- The minimum effective dose of ICS to maintain good asthma control should be used.
- The child's height should be measured and recorded at least yearly, as growth velocity may be lower in the first 1-2 years of ICS treatment, and poorly-controlled asthma can affect growth.

PRIMARY PREVENTION OF ASTHMA

For children, 'window of opportunity' exists in utero and in early life for the prevention of asthma:

- Avoid exposure to environmental tobacco smoke during pregnancy and the 1st year of life
- Reduce maternal obesity and weight gain during pregnancy which pose an increased risk for asthma in children
- Encourage vaginal delivery (the Hygiene Hypothesis)
- Advise breast-feeding
- Where possible, avoid use of paracetamol (acetaminophen) and broad-spectrum antibiotics during the first year of life.

COVID-19 AND ASTHMA

- People with asthma do not appear to be at increased risk of acquiring COVID-19, and systematic reviews have not shown an increased risk of severe COVID-19 in people with well-controlled, mild-to-moderate asthma
- Overall, people with well-controlled asthma are not at increased risk of COVID-19-related death. However, the risk of COVID-19 death was increased in people who had recently needed OCS for their asthma and in hospitalized patients with severe asthma
- In 2020, many countries saw a reduction in asthma exacerbations and influenza-related illness. The reasons are not precisely known, but may be due to handwashing, masks and social/physical distancing that reduced the incidence of other respiratory infections, including influenza

COVID-19 AND ASTHMA MEDICATIONS

- Advise patients to continue taking their prescribed asthma medications, particularly ICS
- Make sure that all patients have a written asthma action plan, advising them to increase controller and reliever medication when asthma worsens and take a short course of OCS when appropriate for severe asthma exacerbations
- Avoid nebulizers where possible, to reduce the risk of spreading virus; pressurized MDI via a spacer is preferred except for life-threatening exacerbations

ASTHMA AND VACCINATION

- At present, based on the risks and benefits, and with the above caution, GINA recommends COVID-19 vaccination for people with asthma
- Remind people with asthma to have an annual influenza vaccination. A gap of 14 days between COVID-19 vaccination and influenza vaccination is recommended by CDC

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