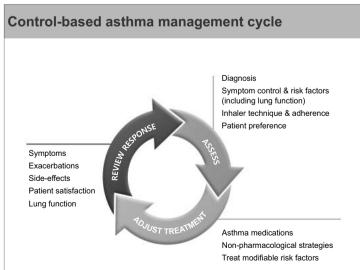
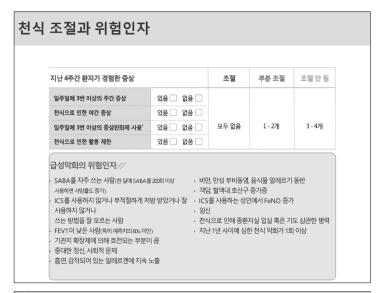
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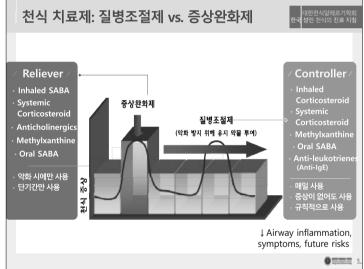
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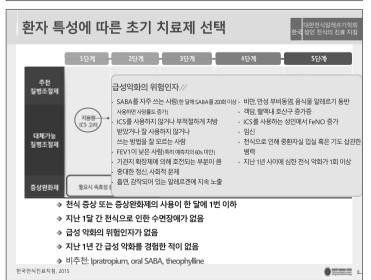
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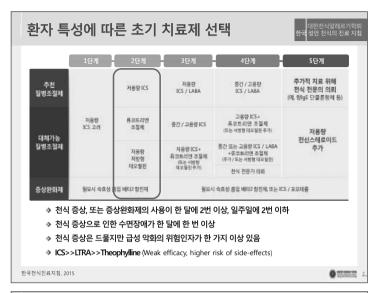


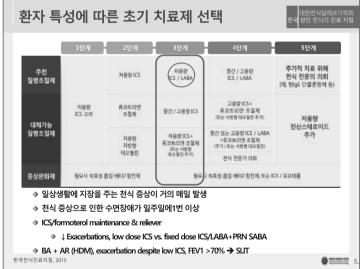


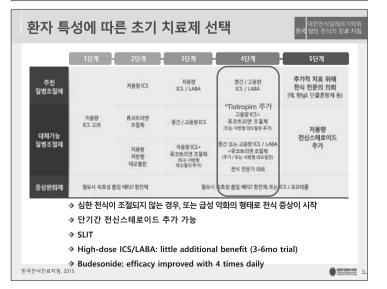


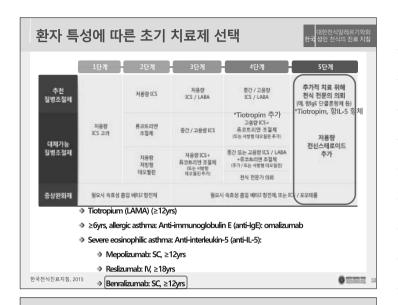












STEP 5 - Severe asthma

- · Sputum guided tx
 - Induced sputum eosinophilia (>3%)
 - ↓Exacerbations, ICS dose
- Low dose oral corticosteroids
 - ≤7.5mg/d, prednisone
 - Only with poor symptom control & frequent exacerbations
 - ↑S/E: ≥3mo → prevention of osteoporosis

Severe asthma

Very few patients are completely resistant to corticosteroids, so ICS remain the mainstay of therapy for difficult-to-treat asthma. Additional therapeutic options include:

- Optimization of ICS/LABA dose: some patients may respond to higher doses of ICS than are routinely recommended for general use³⁴² (Evidence B). However, this carries the risk of systemic side-effects,³³⁹ after some months dose optimization should be pursued by stepping down slowly at 3–6 month intervals; see Box 3-7 (p.49)
- (Evidence IJ).

 Oral corticosteroids: some patients with severe asthma may benefit from low dose maintenance OCS treatment¹³⁰
 (Evidence D), but the potential long-term side-effects should be taken into account.²⁰¹ Patients should be monitored for risk of corticosteroid-induced osteoporois, and those expected to be treated for all months should be provided with relevant litestyle counseling and prescription of therapy for prevention of osteoporois (where appropriate). Add-on treatments without phenotyping: In patients selected for uncontrolled symptoms and persistent artiflow limitation despite moderate-high dose ICS and LARA, add-on treatment with the long-acting muscarinic entagonist bronchodilator, tiotropium, showed improved lung function and increased time to first exacerbation.³⁰³ Other add-on controller medications such as theophylline and LTRAs, although suggested for severe asthma, appear in the small number of available studies to be of limited benefit.
- Sputum-guided treatment: in centers with specific expertise in inducing and analyzing sputum, adjusting treatment for severe asthma on the basis of sputum eosinophils may allow corticosteroid dose and/or exacerbation frequency to be reduced. ("Cividence A).
- to be resulted (evidence A).

 Phenotype-guided add-on treatment: patients with severe asthma, uncontrolled on Step 4 treatment, may benefit from phenotyping into categories such as severe allergic, aspirin-exacerbated or eosinophilic asthma. R7.443.500 Patients 20 years with severe allerain asthma with elevated IgE levels may benefit from ornalizumab (anti-IgD hereapy)**82.00 (Evidence A benralizumab) s with severe eosinophilic asthma may benefit from anti-ILS therapy (mepolizumab, resilizumab)) (Evidence B), and LTRAs may be helpful for patients found to be aspirin sensitive to the control of the c
- (Evidence b).

 Mon-pharmacological interventions: bronchial thermoplasty may be helpful in selected patients with severe asthma (Evidence B).

 See p. 51. Carefully controlled this are inportant as a large placebo effect has been seen in studies are inportant as a large placebo effect has been seen in studies to date.

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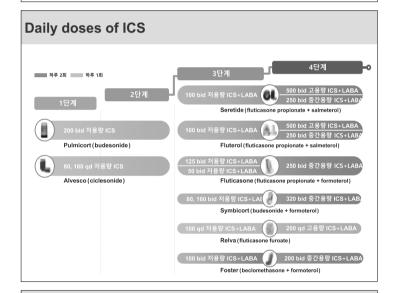
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Daily doses of ICS					
약제	저용량 (μg / 일)	중간용량 (μg / 일)	고용량 (µg / 일)		
Beclomethasone dipropionate (CFC*)	200 - 500	>500 - 1000	>1000		
Beclomethasone dipropionate (HFA**)	100 - 200	>200 - 400	>400		
Budesonide (DPI†)	200 - 400	>400 - 800	>800		
Ciclesonide (HFA**)	80 - 160	>160 - 320	>320		
Fluticasone propionate (DPI† HFA**)	100 - 250	>250 - 500	>500		
Fluticasone furoate	100		200		



Review & Adjust: Step-Up

- Sustained step up (≥2-3mo)
 - Therapeutic trial → review response after 2-3 mo
 - No response → alternative options or referral
- Short-term step-up (1-2 wks)
 - – ↑ICS during viral infection or seasonal allergen exposure (or action plan)
- Day-to-day adjustment
 - ICS/formoterol (SMART or MART)

Review & Adjust: Step-Down

- Well-controlled for 3mo
- · Lung function plateau
- Predictors of loss of control
 - Airway hyperresponsiveness, sputum eosinophilia

Review & Adjust: Step-Down

Current step	Current medication and dose	Options for stepping down	Evidence
Step 5	High dose ICS/LABA plus	Continue high dose ICS/LABA and reduce OCS dose	D
٠.	oral corticosteroids (OCS)	 Use sputum-guided approach to reducing OCS 	В
		Alternate-day OCS treatment	D
		Replace OCS with high dose ICS OCS ↓	D
	High dose ICS/LABA plus other add-on agents	Refer for expert advice	D
Step 4	Moderate to high dose ICS/LABA maintenance	Continue combination ICS/LABA with 50% reduction in ICS component, by using available formulations.	В
	treatment	Discontinuing LABA may lead to deterioration ²¹⁷	A
	Medium dose ICS/formoterol* as maintenance and reliever	 Reduce maintenance ICS/formoterol* to low dose, and continue as- needed low dose ICS/formoterol* reliever 	D
	High dose ICS plus second controller	Reduce ICS dose by 50% and continue second controller ²¹⁶ ICS ↓ 50%	В
Step 3	Low dose ICS/LABA	Reduce ICS/LABA to once daily	D
	maintenance	Discontinuing LABA may lead to deterioration ²¹⁷	Α
	Low dose ICS/formoterol* as maintenance and reliever	Reduce maintenance ICS/formoterol* dose to once daily and continue as-needed low dose ICS/formoterol* reliever	С
	Moderate- or high-dose ICS	Reduce ICS dose by 50% ^{2%} ICS ↓ 50% or qc	A b
Step 2	Low dose ICS	Once-daily dosing (budesonide, ciclesonide, mometasone) ^{216,219}	Α
		Adding LTRA may allow ICS dose to be stepped down ²²⁰	В
		 Insufficient evidence to support step-down to as-needed ICS with SABA²²¹ 	
	Low dose ICS or LTRA	 Consider stopping controller treatment only if there have been no symptoms for 6–12 months, and patient has no risk factors (Box 2-2, 	D
		p17). Provide a written asthma action plan, and monitor closely.	A
		Complete cessation of ICS in adults is not advised as the risk of exacerbations is increased.	^
		exacerbations is increased	

Other Therapies

- Allergen Immunotherapy
 - Mild asthma, Allergic sensitization
 - SCIT
 - JSymptom, medication, AHR
 - S/E: anaphylaxis
 - SLIT
 - ↓ICS, exacerbations,
 - S/E: mild oral & GI sx

Other Therapies

- Vaccinations
 - Influenza vaccine
 - Annual, ↓morbidity & mortality
 - Pneumococcal vaccine
 - · Children & elderly asthma
 - ↑Risk of pneumococcal disease
 - Insufficient evidence to recommend routine vaccination in asthmatics

Other Therapies

- · Bronchial thermoplasty
 - Bronchoscopy with radiofrequency pulse
 - Exacerbations: ↑during 3mo → ↓
 - No effect on lung function or symptoms
 - Long-term f/u data is needed (effectiveness, safety)
- · Vitamin D
 - No good-quality evidence

Non-Pharmacological

Intervention	Advice/recommendation (continued on next page)	Evidence
Cessation of smoking and ETS exposure	 At every visit, strongly encourage people with asthma who smoke to quit. Provide access to counseling and smoking cessation programs (if available) 	A
exposure	 Advise parents/carers of children with asthma not to smoke and not to allow smoking in rooms or cars that their children use 	A
	Strongly encourage people with asthma to avoid environmental smoke exposure	В
	 Assess smokers/ex-smokers for COPD or overlapping features of asthma and COPD (asthma— COPD overlap, ACO, Chapter 5, p.89), as additional treatment strategies may be required 	D
	Encourage people with asthma to engage in regular physical activity for its general health benefits.	A
	Provide advice about prevention and management of exercise-induced bronchoconstriction (p50)	A
	 Regular physical activity improves cardiopulmonary fitness, but confers no other specific benefit on lung function or asthma symptoms, with the exception of swimming in young people with asthma 	В
	There is little evidence to recommend one form of physical activity over another	D
Avoidance of occupational exposures	Ask all patients with adult-onset asthma about their work history and other exposures	A
	 In management of occupational asthma, identify and eliminate occupational sensitizers as soon as possible, and remove sensitized patients from any further exposure to these agents 	A
	 Patients with suspected or confirmed occupational asthma should be referred for expert assessment and advice, if available 	А
Avoidance of medications that may make	 Always ask about asthma before prescribing NSAIDs, and advise patients to stop using them if asthma worsens 	A
asthma worse	Always ask people with asthma about concomitant medications	D
	 Aspirin and NSAIDs (non-steroidal anti-inflammatory drugs) are not generally contraindicated unless there is a history of previous reactions to these agents (see p.69) 	A
	 Decide about prescription of oral or intra-ocular beta-blockers on a case-by-case basis. Initiate treatment under close medical supervision by a specialist 	D
	 If cardioselective beta-blockers are indicated for acute coronary events, asthma is not an absolute contra-indication, but the relative risks/benefits should be considered 	D

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Intervention	Advice/recommendation	Evidence
Healthy diet	Encourage patients with asthma to consume a diet high in fruit and vegetables for its general health benefits	A
Avoidance of indoor allergens	Allergen avoidance is not recommended as a general strategy in asthma	A
noor anigens	For sensitized patients, there is indoor allergen avoidance Limited of clinical benefit for asthma with single-strategy of clinical benefit for asthma with single-strategy.	A
	 Remediation of dampness or mold in homes reduces asthma symptoms and medication use in adults 	Α
	 For patients sensitized to house dust mite and/or pets, there is limited evidence of olinical benefit for asthma with multi-component avoidance strategies (only in children) 	В
	 Allergen avoidance strategies are often complicated and expensive, and there are no validated methods for identifying those who are likely to benefit 	D
Weight reduction	Include weight reduction in the treatment plan for obese patients with asthma 2/wk aerobic 8	
Allergen immunotherapy	 For adult patients with allergic rhinitis and sensitized to HDM, with exacerbations despite low to high dose ICS, consider adding sublingual immunotherapy (SLIT), provided FEV₁ is >70% predicted 	for sex co
	 Compared to pharmacological and avoidance options, potential benefits of allergen immunotherapy. (SCIT or SUIT) must be weighed against the risk of adverse effects and the inconvenience and cost of the prolonged course of therapy, including for SCIT the minimum half-hour wait required after each injection. 	
Breathing exercises	Breathing exercises may be a useful supplement to asthma pharmacotherapy	В
Avoidance of indoor air pollution	 Encourage people with asthma to use non-polluting heating and cooking sources, and for sources of pollutants to be verted outdoors where possible 	В
Vaccinations	 People with asthma, particularly children and the elderly, are at higher risk of pneumococcal disease, but there is insufficient evidence to recommend routine pneumococcal vaccination in people with asthma 	В
	 Advise patients with moderate-severe asthma to have an influenza vaccination every year, or at least when vaccination of the general population is advised 	D
Bronchial thermoplasty	 For highly-selected adult patients with uncontrolled asthma despite use of recommended therapeutic regimens and referral to an asthma specialty center (Step 5), bronchial thermoplasty is a potential treatment option in some countries. 	В
	 Causion should be used in selecting patients for this procedure, as the number of studies is small, and people with chronic sinus disease, frequent chest infections or FEV₁ ~80% predicted were excluded. 	D
Avoidance of outdoor allergens	 For sensitized patients, when pollen and mold counts are highest, closing windows and doors, remaining indoors, and using air conditioning may reduce exposure to outdoor allergens 	D

Non-Pharmacological

Intervention	Advice/recommendation	Evidence
Dealing with emotional stress	 Encourage patients to identify goals and strategies to deal with emotional stress if it makes their asthma worse 	D
	 There is insufficient evidence to support one stress-reduction strategy over another, but relaxation strategies and breathing exercises may be helpful 	В
	Arrange a mental health assessment for patients with symptoms of anxiety or depression	D
Avoidance of outdoor air pollutants/	 In general, when asthma is well-controlled, there is no need for patients to modify their lifestyle to avoid unfavorable outdoor (air pollutants, weather). 	D
weather conditions	 It may be helpful during unfavorable environmental conditions (very cold weather, low humidity or high air pollution) to avoid stremous outdoors physical activity and stay indoors in a climate- controlled environment; and during viral infections to avoid polluted environment. 	D
Avoidance of foods and food chemicals	 Food avoidance should not be recommended unless an allergy or food chemical sensitivity has been clearly demonstrated, usually by carefully supervised oral challenges 	D
	For confirmed food allergy, food allergen avoidance may reduce asthma exacerbations	D
	 If food chemical sensitivity is confirmed, complete avoidance is not usually necessary, and sensitivity often decreases when asthma control improves 	D

Indications for Referral

- Patient has symptoms of chronic infection, or features suggesting a cardiac or other non-pulmonary cause (8or 1-3, p.20) (immediate referral recommended)
 Diagnosis is unclear en after a tisk of therapy with ICS or systemic corticosteroids
 Patients with features of took asthma and COPO, if there is doubt about priorities for treatment

 Suspected occupational asthma

Refer for confirmatory testing and identification of sensitizing or initiant agent, specific advice about eliminating exposure and pharmacological treatment. See specific guidelines (e.g. ³) for details.

Persistent uncontrolled asthma or frequent exacerbations

- Patient's symptoms remain uncontrolled, or patient has ongoing exacerbations or low lung function despite correct inhales technique and good adherence with 58p4 treatment (moderate or high-dose ICSL-ILBA, Box 3-5, p-43). Before referral, depending on the cinical context, (damping and team formation less factors; 60b; 22-2, p-28; Box 3-6, p-50) and comorbidities (p-62).

 Patient has flequent estiman-everlated health care utilization (e.g. multiple ED visits or urgent primary care visits).
- Any risk factors for asthma-related death (see Box 4-1, p.75)

Near-datal asthma attack (ICU admission, or mechanical ventilation for asthma) at any time in the past
 Anaphylaxis or confirmed food allergy in a patient with asthma

Evidence of, or risk of, significant treatment side-effects

- Patients with significant side-effects from treatment
 Need for long-term and controstered use
 Frequent courses of and controstereds (e.g., two or more courses a year)
 Symptoms suggesting complications or sub-types of ast
- e.g. aspirin-exacerbeted respiratory disease (p.69); allergic bronchopulmonary aspergillosis
 Additional reasons for referral in children 6-11 years

- Doubth about diagnosis of reterral in crimitate in 1 years

 Doubth about diagnosis of safetime e.g. respiratory symptoms are not responding well to treatment in a child who
 was born prematurely

 Symptoms or exacerbations remain uncontrolled despite moderate dose ICS (Box 3-6B, p.44) with correct inhaler
 fermingue and good adherence

 Suspected side-fetchs of reatment (e.g. growth delay)

 Asthma and confirmed food allergy

Self-management Inhaler skill - Misuse 70-80% Choose the most appropriate inhaler device for the patient before prescribing. Consider the medication options (Box 3-5, p.43), the available devices, patient skills and cost. If different options are available, encourage the patient to participate in the choice For pMDIs, use of a spacer improves delivery and (with ICS) reduces the potential for side-effects Ensure that there are no physical barriers, e.g., arthrifts, that limit use of the inhaler Avoid use of multiple different inhaler types where possible, to avoid confusion CHECK Check inhaler technique at every opportunity Ask the patient to show you how they use their inhaler (don't just ask if they know how to use it) Identity any errors using a device-specific checklist CORRECT Show the patient how to use the device correctly with a physical demonstration, e.g. using a placebo inhaler Check technique again, paying attention to problematic steps. You may need to repeat this process 2–3 times. 233 Only consider an alternative device if the patient cannot use the inhaler correctly after several repeats of training Re-check inhaler technique frequently. After initial training, errors often recur within 4–6 weeks. 234 CONFIRM Clinicians should be able to demonstrate correct technique for each of the inhalers they prescribe Pharmacists and nurses can provide highly effective inhaler skills training^{255,234} **Adherence** Factors contributing to poor adherence How to identify poor adherence in clinical practice Medication/regimen factors Ask an empathic question Difficulties using inhaler device (e.g. arthritis) Burdensome regimen (e.g. multiple times per viedge the likelihood of incomplete adherence and encourage an open non-judgemental discussion Examples are: In the last 4 weeks, how many days a week have you been taking it — not at all, 1, 2, 3 or more days a week?²⁵¹ Multiple different inhalers Unintentional poor adherence Misunderstanding about instructions Misunderstanding about in Forgetfulness Absence of a daily routine Cost 'Do you find it easier to remember your inhaler in the morning or the evening? Check medication usage Check the date of the last controller prescription Intentional poor adherence Perception that treatment is not necessary Denial or anger about asthma or its treatment Inappropriate expectations Check the date and dose counter on the inhaler In some health systems, prescribing and dispensing frequency can be monitored electronically by clinicians Concerns about side-effects (real or perceived) and/or pharmacists See review articles for more detail. 128,252 Stigmatization Cultural or religious issues Examples of successful adherence interventions Shared decision-making for medication/dose choice Inhaler reminders for missed doses^{248,247} Prescribing ICS once-daily versus twice-daily²⁵³ Home visits for a comprehensive asthma program by an asthma nurse²⁴¹ **Asthma Information** • Verbal → Written or pictorial information http://www.kaaf.org/ Self-monitoring (sx & PEF) Action plan · Regular review of control, treatment, skills Goal: To provide the person with asthma, their family and other carers with suitable information and training to manage their asthma in partnership with their health care providers Content · Focus on the development of the partnership Asthma diagnosis Accept that this is a continuing process Rationale for treatment, and differences between Share information 'relievers' and 'controllers' Potential side-effects of medication Adapt the approach to the patient's level of health literacy (Box 3-1, p.37) Prevention of symptoms and flare-ups · How to recognize worsening asthma and what actions

to take; how and when to seek medical attention

Management of comorbidities

Develop shared goals

Comorbidities • GERD - Possible cause of dry cough - Symptomatic reflux should be treated - No anti-reflux therapy unless symptomatic · No significant benefit for asthma outcomes Comorbidities Rhinitis, sinusitis, nasal polyp - Link between upper & lower airways • 80% asthma → rhinitis • 10-40% AR → asthma Chronic (≥12wks) rhinosinusitis /c polyps → ass, with severe asthma -Mx• INS: only symptom control, not asthma control **Special settings** Exercise-induced bronchoconstriction (EIB) - SABA before exercise • Symptoms only after exercise & no risk factors • Regular use (>1/d) \rightarrow tolerance - LTRA: alternative pre-exercise tx - Training, sufficient warm-up - Regular controller (ICS or LTRA) • Symptoms unrelated to exercise & risk factors

Special settings · The elderly - Side-effects • β2-agonist: cardiotoxicity • Steroid: skin bruising, osteoporosis, cataracts • Theophylline: \clearance - Other medications: drug interactions - Arthritis, muscle weakness, impaired vision, inspiratory flow, cognitive function - Check inhaler technique **Special settings** Surgery – ↑Peri-operative risk • Asthma (X) vs. COPD, Asthma with↓FEV1 (O) Achieve good control · Severe asthma, uncontrolled sx, exacerbation hx, fixed airflow limitation - Maintain regular controller - Emergency op Hydrocortisone - Long-term high-dose ICS, OCS ≥2wks in 6mo **Special settings** Aspirin-exacerbated respiratory disease - Triad • Chronic rhinosinusitis /c nasal polyps Asthma · Aspirin hypersensitivity - 7% in asthma, 15% in severe asthma - Diagnosis: aspirin challenge · High risk of severe reaction, resuscitation capabilities - Management: avoid aspirin or NSAIDS · Cox-2 inhibitor or AAP • ICS, LTRA, desensitization (daily aspirin tx)

Asthma Exacerbations

- Exacerbation = flare-up
 - ↑Symptoms (shortness of breath, cough, wheezing, chest tightness)
 - ↓Lung function (PEF or FEV1)
- · Asthma-related death

- A history of near-fatal asthma requiring intubation and mechanical ventilation³⁵¹
 Hospitalization³⁵¹ or emergency care visit for asthma in the past year
 Currently using not having recently stopped using oral corticosteroids (a marker of event severity)³⁵¹
 Not currently using inhaled corticosteroids^{35,351}
 Over-use of SABAs, especially use of more than one canister of salbutamol (or equivalent) monthly^{60,352}
 A history of psychiatric disease or psychosocial problems,⁵⁰
 Poor adherence with asthma medications and/or poor adherence with (or lack of) a written asthma action plan⁶⁵
 Food allergy in a patient with asthma^{29,250}

Self mx with action plan

Effective asthma self-management education requires: · Self-monitoring of symptoms and/or lung function If PEF or FEV1 <60% best, or not improving after 48 hours Written asthma action plan Regular medical review All patients Continue controller Add prednisolone 40-50 mg/day Contact doctor Review response

EARLY OR MILD

LATE OR SEVERE

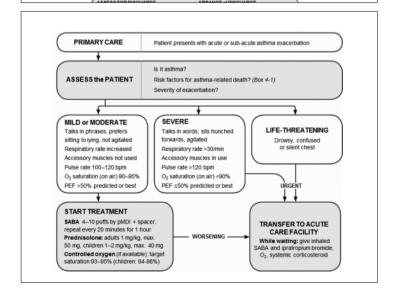
Self mx with action plan

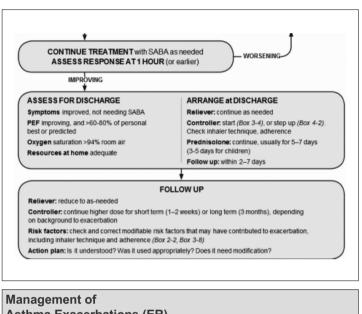
Medication	Short-term change (1-2 weeks) for worsening asthma	Evidence Level
Increase usual reliever:		
Short-acting beta2-agonist (SABA)	Increase frequency of SABA use For pMDI, add spacer	A
Low dose ICS/formoterol *	Increase frequency of reliever use (maximum formoterol total 72 mcg/day)	Α
Increase usual controller:		
Maintenance and reliever ICS/formoterol *	Continue maintenance ICS/formoterol and increase reliever ICS/formoterol as needed* (maximum formoterol total 72 mcg/day)	Α
Maintenance ICS with SABA as reliever	At least double ICS; consider increasing ICS to high dose (maximum 2000 mcg/day BDP equivalent)	В
Maintenance ICS/formoterol with SABA as reliever	Quadruple maintenance ICS/formoterol (maximum formoterol 72 mcg/day)	В
Maintenance ICS/other LABA, with SABA as reliever	Step up to higher dose formulation of ICS/other LABA, or consider adding a separate ICS inhaler (to maximum total 2000 mcg/day BDP equivalent)	D
Add oral corticosteroids (O	CS) and contact doctor	
OCS (prednisone or prednisolone)	Add OCS for severe exacerbations (e.g. PEF or FEV $_1\!<\!60\%$ personal best or predicted), or patient not responding to treatment over 48 hours	Α
	Adults: prednisolone 1 mg/kg/day (maximum 50 mg) usually for 5-7 days. Children: 1-2 mg/kg/day (maximum 40 mg) usually for 3-5 days.	D
	Tapering is not needed if OCS are prescribed for <2 weeks	В

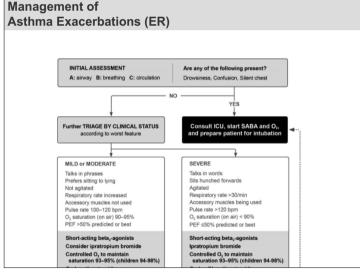
Oral corticosteroids

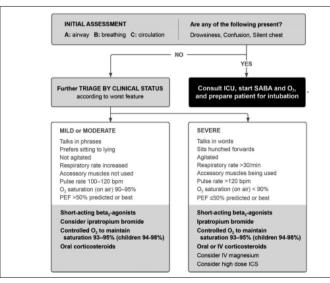
- 40-50mg/d, 5-7days (children 6-11: 1-2mg/kg/d, max 40mg/d)
- Fail to respond to ↑reliever & controller for 2-3days
- Deteriorate rapidly
- PEF or FEV1 <60% of personal best or predicted value
- History of sudden severe exacerbations

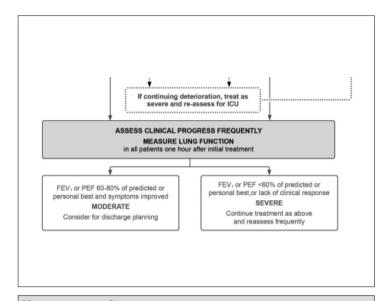
Management of Asthma Exacerbations (primary care) PRIMARY CARE Patient presents with acute or sub-acute asthma exacerbation Is a ashma? Risk bacters for asthma-related death? (Box 4-1) Severity of exacerbation? MILD or MODERATE Takes primaries, grafters usiting to lying, not agitated Respiratory rate increased Recessory muscles not used Puter rate 100-120 gae Question and 100-120 gae Ques











Management of Asthma Exacerbations

Oral confloosteroids (OCS)
Prescribe at least a 5-7 day course of OCS for adults (prednisolone or equivalent 1 mg/kg/day to a maximum of 50 mg/day) and 3–5 days for children (1–2 mg/kg/day to a maximum of 40 mg). For patients considered at risk of poor adherence, inframuscular corticosteroids may be considered ³²³ (Evidence B).

Reliever medication
Transfer patients back to as-needed rather than regular reliever medication use, based on symptomatic and objective improvement. If pratrophum bromide was used in the emergency department or hospital, it may be quickly discontinued, as it is unlikely to provide ongoing benefit.

Inhaled corticosteroids (ICS)

Initiate ICS prior to discharge, if not previously prescribed (Box 3-4, p.42). Patients currently prescribed ICS-containing medication should generally have their treatment stepped up for 2–4 weeks (Box 4-2, p.77) and should be reminded about the importance of adherence with daily use.

Risk factors that contributed to the exacerbation

Identify factors that may have contributed to the exacerbation and implement strategies to reduce modifiable risk factors (Box 3-8, p.50). An exacerbation severe enough to require hospitalization may follow irritant or allergen exposure, inadequate long-term treatment, problems with adherence, and/or lack of a written asthma action plan, as well as unavoidable factors such as viral respiratory infections.