



• Proud to be celebrating the 30th year of GINA •

Asthma Management Updates for Respiratory Therapists

Khalid Al Efraij, MBBS, FRCPC, ABIM

Internal Medicine and Pulmonary

Definition

- A heterogeneous disease,
- Chronic airway inflammation.
- History of respiratory symptoms, such as wheeze, shortness of breath, chest tightness and cough, that vary over time and in intensity
- Variable expiratory airflow limitation. Airflow limitation may later become persistent.

Asthma is a chronic inflammatory disease; inflammation is central to exacerbations¹



Bm = basement membrane; Bv = blood vessel; CRTH2 = chemoattractant receptor-homologous molecule expressed on Th2 cells; EoP = eosinophilopoiesis; EOS = eosinophils; Ep = epithelium; IgE = immunoglobulin E; IL = interleukin; ILC2 = type 2 innate lymphoid cells; PAMP = pathogen-associated molecular pattern; SM = smooth muscle; T1 = Type 1 cell; T2 = Type 2 cell; T17 = Type 17 cell; TLR = toll-like receptor; TSLP = thymic stromal lymphopoietin.

1. Global Initiative for Asthma. Updated 2018. www.ginasthma.org. Accessed March 2019; 2. Holgate ST et al. Nat Rev Dis Primers. 2015;1:15025; 3. Wenzel SE. Nat Med. 2012;18:716-725; 4. Peters SP et al. J Allergy Clin Immunol Pract. 2017;5:S15-S24; 5. Mukherjee M et al. World Allergy Organ J. 2014;7:32.

Epidemiology

- 26 million people in the U.S.
- More in Black adults in the U.S.
- More common in female 9.7% vs 6.2% male

National Center for Health Statistics. (2022)





Induced sputum





Diagnosis

2.2 Documented* excessive variability in lung function* (one or more of the following): Positive bronchodilator (BD) responsiveness (reversibility) test Excessive variability in twicedaily PEF over 2 weeks Significant increase in lung function after 4 weeks of anti-inflammatory treatment Positive exercise challenge test Positive bronchial challenge test (usually only for adults) Excessive variation in lung function between visits (good specificity but poor sensitivity)

Global Initiative for Asthma, GINA (2023)



Aaron et al. Am J Respir Crit Care Med (2018) 198, 8: 1012–1020



Am J Respir Crit Care Med Vol 198, Iss 8, pp 1012–1020, Oct 15, 2018

Change in BRD definition



EUROPEAN RESPIRATORY journal

FLAGSHIP SCIENTIFIC JOURNAL OF ERS

ERS/ATS technical standard on interpretive strategies for routine lung function tests

Sanja Stanojevic, David A. Kaminsky, Martin R. Miller, Bruce Thompson, Andrea Aliverti, Igor Barjaktarevic, Brendan G. Cooper, Bruce Culver, Eric Derom, Graham L. Hall, Teal S. Hallstrand, Joerg D. Leuppi, Neil MacIntyre, Meredith McCormack, Margaret Rosenfeld, Erik R. Swenson

Furopean Respiratory Journal 2022 60: 2101499: DOI: 10.1183/13993003.01499-2021

Management

ACQ: Asthma Control Questionnaire; ACT: Asthma Control Test; OCS: oral corticosteroids

Goals of asthma treatment

- Few asthma symptoms
- No sleep disturbance
- No exercise limitation
- Maintain normal lung function
- Prevent flare-ups (exacerbations)
- Prevent asthma deaths
- Minimize medication side-effects (including OCS)
- The patient's goals may be different
- Symptom control and risk may be discordant
 - Patients with few symptoms can still have severe exacerbations

Symptom control (e.g. ACT, ACQ)

Risk reduction



Asthma control

Box 2-2. GINA assessment of asthma control in adults, adolescents and children 6-11 years

Α.	Asthma symptom control					
In f	he past 4 weeks, has the patient had:			Well controlled	Partly controlled	Uncontrolled
•	Daytime asthma symptoms more than twice/week?	Yes□ No□	٦			
•	Any night waking due to asthma?	Yes□ No□		None of	1–2 of	3–4 of
•	SABA* reliever for symptoms more than twice/week?	Yes□ No□	Ì	[–] these	these	these
•	Any activity limitation due to asthma?	Yes□ No□				

ACT

Asthma Control Test



healthline

ACQ-5

Asthma Control Questionnaire - 5 (ACQ-5)

Q1) On average, during the past week, how often were you woken by your asthma during the night?

0 = never

Response:

Response:

1 = hardly ever

- 2 = a few times
- 3 = several times
- 4 = many times
- 5 = a great many times
- 6 = unable to sleep because of asthma

Q2) On average, during the past week, how bad were your asthma symptoms when you woke up in the morning?

0 = no symptoms

1 = very mild symptoms

- 2 = mild symptoms
- 3 = moderate symptoms
- 4 = quite severe symptoms
- 5 = severe symptoms
- 6 = very severe symptoms

Q3) In general, during the past week, how limited were you in your activities because of your asthma?

0 = not limited at all

- 1 = very slightly limited
- 2 = slightly limited
- 3 = moderately limited
- 4 = very limited
- 5 = extremely limited
- 6 = totally limited

Q4) In general, during the past week, how much shortness of breath did you experience because of your asthma?

- 0 = none
- 1 = very little
- 2 = a little
- 3 = a moderate amount
- 4 = quite a lot
- 5 = a great deal
- 6 = a very great deal

Q5) In general, during the past week, how much of the time did you wheeze?

0 = not at allResponse:1 = hardly any of the time2 = a little of the time3 = a moderate amount of the time4 = a lot of the time5 = most of the time6 = all of the time

Response:

Response:

SABA use and need for future acute asthma health care

Patients prescribed ≥3 SABAS per year have an increased risk of hospitalisation/OCS prescriptions compared with patients prescribed 0– 2 SABAs



*Adjusted for year 2002 use in the predictive validity cohort (n=62369)

Study based on survey of 2250 maintenance organisations members (construct validity sample) and predictive validity sample (n=62369) from the Southern California Kaiser Permanente asthma database.

Number of hospitalisations and ED visit were compared against SABA canisters dispensed in 12 months. Asthma ED visits and hospitalisations were combined into the single outcome of emergency hospital care for asthma, defined as at least one hospitalisation or ED visit for asthma

ED = emergency department; OCS = oral corticosteroid; SABA = short-acting β_2 -agonist.

Schatz M et al. J Allergy Clin Immunol. 2006;117:995-1000.

Patients with mild asthma are at risk of

exacerbations ¹⁻⁶

19–36% of patients with mild asthma experience a exacerbation every

year¹⁻⁶

Study	Study type	Definition of exacerbation	Total number of patients	% experiencing an exacerbation within previous 12m
O'Byrne et al 1 (ODTIMA)*	Randomised	Severe exac: OCS use, hospitalisation/	Group A (placebo) –237	33.3
	clinical trial	decrease from baseline in morning PEF on 2 consecutive days	Group B (budesonide 200 μg) – 317	33.8
Price et al ² (REALISE)	Quantitative questionnaire	Acute exac:≥1 course of OCS in	Reliever only – 1419	26.1
FILE EL AL- (NEALISE)		the previous 12 months	Single-drug preventer inhaler –1923	29.2
Ding et al. ³	Observational survey	Physician confirmed worsening of symptoms	1115	19
Placem at al 4 [†]	Population-based ≤300 mg OCS, A&E visit or BTS Step 1 -		BTS Step 1 – 86360	31
cohort study hospitalisation		BTS Step 2 – 54773	36	
O'Byrne et al. ⁵ (SYGMA 1)	Randomised clinical trial	Severe exac: ≥3 days OCS use, hospitalisation or ED visit	3836	19.7
Bateman et al. ⁶ (SYGMA 2)	Randomised clinical trial	Severe exac: ≥3 days OCS use, hospitalisation or ED visit	4176	22

*Group A patients (n=698) were prescribed daily placebo, budesonide 200 µg or budesonide 200 µg + formoterol 9 µg. Group B patients (n=1272) were prescribed budesonide 200 µg with or without formoterol 9 µg. The table presents the results for one group in each arm – Group A (placebo) and Group B (budesonide 200 µg).

[†]Patients were stratified according to age – <5 years, 5–17 years, 18–54 years and ≥55 years. The table reports the results for the 18–54 years group.

A&E = Accident & Emergency; ED = Emergency Department; exac = exacerbation; m= month; OCS = oral corticosteroid; PEF = peak expiratory flow

1. O'Byrne PM et al. Am J Resp Crit Care Med. 2001;164:1392-1397; 2. Price D et al. NPJ Prim Care Resp Med. 2014;24:14009; 3. Ding B et al. Adv Ther. 2017;34:1109-1127; 4. Bloom Cl et al. Thorax. 2018;73:313-320; 5. O'Byrne PM et al. N Engl J Med. 2018;378:1865-1876; 6. Bateman ED et al. N Engl J Med. 2018;378:1877-1887.



Confirmation of diagnosis if necessary Symptom control & modifiable risk factors (see Box 2-2) Comorbidities Inhaler technique & adherence Patient (and parent/caregiver) preferences and goals

Symptoms Exacerbations Side-effects Lung function Comorbidities Patient (and parent/ caregiver) satisfaction ADJUST

Treatment of modifiable risk factors and comorbidities Non-pharmacological strategies Asthma medications (adjust down/up/ between tracks) Education & skills training

GINA 2023 – Adults & adolescents 12+ years

Personalized asthma management Assess, Adjust, Review for individual patient needs



simpler regimen

© Global Initiative for Asthma, www.ginasthma.org Box 3-12

Reliever doses of ICS-formoterol - how much can be taken?



- For ICS-formoterol with 6 mcg (4.5 mcg delivered dose) of formoterol, take 1 inhalation whenever needed for symptom relief
- Another inhalation can be taken after a few minutes if needed
- Maximum total number of inhalations in any single day (as-needed + maintenance)
 - Budesonide-formoterol: maximum 12 inhalations* for adults, 8 inhalations for children, based on extensive safety data (*Tattersfield et al, Lancet 2001; Pauwels et al, ERJ 2003*)
 - Beclometasone-formoterol: maximum total 8 inhalations in any day (Papi et al, Lancet Respir Med 2013)
- Emphasize that most patients need far fewer doses than this!
- For pMDIs containing 3 mcg formoterol (2.25 mcg delivered dose), take 2 inhalations each time

*For budesonide-formoterol 200/6 [delivered dose 160/4.5 mcg], 12 inhalations gives 72 mcg formoterol (54 mcg delivered dose)



Inhaler choice and environmental considerations

- Inhaled corticosteroids markedly reduce the risk of asthma exacerbations and death
 - But limited availability and access in low and middle income countries
- Many inhaler types available, with different techniques
- Some inhalers are not suitable for some patients. For example:
 - DPIs are not suitable for children ≤5 years and some elderly
 - pMDIs difficult for patients with arthritis or weak muscles
 - Capsule devices are difficult for patients with tremor
- Most patients don't use their inhaler correctly
 - More than one inhaler \rightarrow more errors
- Incorrect technique → more symptoms → worse adherence
 → more exacerbations → higher environmental impact
- Propellants in current pMDIs have 25x global warming potential compared with dry powder inhalers
 - New propellants are being developed but not yet approved
- Choice of inhaler is important!







Inhaler technique



Sanchis J. et al; Chest. 2016 Aug 1;150(2):394-406.



Figure 2: Device selection algorithm. Reproduced with permission from [28]. DPI, dry powder inhaler; pMDI, pressurized metered-dose inhaler; BA, breath-actuated; SMI, soft mist inhaler.

Kaplan A et al. Canadian Respiratory Journal, 2018, Article ID 9473051.

Inhaler choice and environmental considerations

- First, what is the right medication for this patient?
 - Control symptoms and reduce exacerbations
 - Urgent healthcare and hospitalization have a heavy environmental burden
- Which inhaler(s) can the patient access for this medication?
 - Low/middle income countries often have limited choice and access
 - Cost of inhalers is a major burden
- Which of these inhalers can the patient use correctly?
 - Incorrect technique → more exacerbations
- What are the environmental implications of these inhaler(s)?
 - Manufacture
 - Propellant (for pMDIs)
 - Recycling potential
- Is the patient satisfied with the treatment and the inhaler?
 - Consider the patient's environmental priorities
 - Avoid 'green guilt', which may contribute to poor adherence
 - Check inhaler technique frequently





For this patient, which is the right class of medication?





inhaler(s)?

GINA 2023 from Box 3-21

© Global Initiative for Asthma, www.ginasthma.org

Action plan for MART with ICS-formoterol



A Practical Guide to Implementing SMART in	Con Vr Province			
Asthma Management	My Asthma Action Plan	Name:	Action plan provided by:	
Helen K. Reddel, MB, BS, PhD ^{a,} , Eric D. Bateman, MB, ChB, MD ^{b,} , Michael Schatz, MD, MS ^o , Jerry A. Krishnan, MD, PhD ^d , and Michelle M. Cloutier, MD ^a Sydney, Australia; Cape Town, South Africa Chicago, Ill; and Farmington, Com	For Single Inhaler Maintenance and Reliever Therapy (SMART) with budesonide/formoterol	Date: Usual best PEF:L/min (if used)	Doctor: Doctor's phone:	
Reddel et al. JACI in Practice 2022: 10: S31-s38	Normal mode	Asthma Flare-up A	sthma Emergency	
This article includes a writable action plan template That can be modified for other combination ICS-formoterol inhalers, and for as-needed-only ICS-formoterol For additional action plans with ICS-formoterol reliever, see National Asthma Council Australia Action plan library www.nationalasthma.org.au/health- professionals/asthma-action-plans	My SMART Asthma Treatment is: budesonide/formoterol 160/4.5 (12 years or older) budesonide/formoterol 80/4.5 (4-11 years) My Regular Treatment Every Day: (Write in or circle the number of doses prescribed for this patient) Take [1, 2] inhalation(s) in the morning and [0, 1, 2] inhalation(s) in the evening, every day Reliever Use 1 inhalation of budesonide/formoterol whenever needed for relief of my asthma symptoms I should always carry my budesonide/formoterol inhaler I can take part in normal physical activity without asthma symptoms AND I do not wake up at night or in the morning because of asthma	 If over a Period of 2-3 Days: My asthma symptoms are getting worse OR NOT improving OR I am using more than 6 budesonide/formoterol reliever inhalations a day (if aged 12 years or older) or more than 4 inhalations a day (if aged 4-11 years) I should: Continue to use my regular everyday treatment PLUS 1 inhalation budesonide/formoterol whenever needed to relieve symptoms Start a course of prednisolone Contact my doctor Contact my doctor Takedays ORdays Or	 Signs of an Asthma Emergency: Symptoms getting worse quickly Extreme difficulty breathing or speaking Little or no improvement from my budesonide/formoterol reliever inhalations If I have any of the above danger signs, I should dial for an ambulance and say I am having a severe asthma attack. While I am waiting for the ambulance start my asthma first aid plan: Sit upright and stay calm. Take 1 inhalation of budesonide/formoterol (up to a maximum of 6 inhalations on a single occasion). If only albuterol is available, take 4 puffs as often as needed until help arrives. Start a course of prednisolone tablets (as directed) while waiting for the ambulance. Even if my symptoms appear to settle quickly, I should see my doctor immediately after a serious attack.	

Modified from Australian action plan with permission from National Asthma Council Australia and AstraZeneca Australia

Uncontrolled Asthma

Assess potential reasons of poor control, and correct if indicated

Assess adherence

Assess inhalation technique

Assess environmental, including occupational, exposures

Assess key potential co-morbidities or alternative diagnoses, and if suspected, investigate/treat

Rhinosinusitis

Gastro-esophageal reflux. Vocal cord dysfunction (VCD) Anxiety and depression Consider less frequent co-morbidities or alternative diagnosis Immunodeficiency Cystic fibrosis Tracheobronchomalacia or other suspected airway abnormalities Non CF bronchiectasis Vasculitis Allergic pulmonary aspergillosis Atypical mycobacteria infections

J Mark FitzGerald, et al. CANADIAN JOURNAL OF RESPIRATORY, CRITICAL CARE, AND SLEEP MEDICINE 2017, VOL. 1, NO. 4, 199–221

Severe Asthma

What proportion of adults have severe asthma?





Data from Hekking et al, JACI 2015

ICS: inhaled corticosteroids; LABA: long-acting beta2-agonist; OCS: oral corticosteroids

Asthma Pathophysiology



Guy G. Brusselle, et al, N Engl J Med 2022; 386:157-171

Biomarkers

Type 2 inflammation

- Blood eosinophils ≥150/µl and/or
- FeNO ≥20 ppb and/or
- Sputum eosinophils ≥2%, and/or
- Asthma is clinically allergendriven

(Repeat blood eosinophils and FeNO up to 3x, at least 1-2 weeks after OCS or on lowest possible OCS dose)



Guy G. Brusselle, et al, N Engl J Med 2022; 386:157-171

Acute Exacerbation



Global Initiative for Asthma, GINA (2023)

Questions?

