L’asma in età pediátrica. Concetti basici.

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SAPIENZA UNIVERSITÀ DI ROMA

SISTEMA SANITARIO REGIONALE
AZIENDA OSPEDALIERO-UNIVERSITARIA SANT’ANDREA

Definizione

Descrizione

- Comune (dal 1% al 18% secondo il paese), in Italia circa il 12%
- Multipli fattori scatenanti (virosi, allergeni, irritanti, cambiamenti climatici, esercizio, risata, ecc).
- Sintomi e limitazione di flusso: risoluzione spontanea oppure dopo terapia
- Periodi di “quiete” di durata variabile, talvolta esacerbazioni che possono essere gravi
- Iperreattività e infiammazione delle VA possono persistere in pazienti asintomatici o con FR normale, ma possono migliorare dopo terapia.

Diagnosi di asma

- Anamnesi consistente + dimostrata limitazione variabile di flusso (BDR, bronchial challenge)
- Prima i tests di FR, poi la terapia (testare durante la terapia è fuorviante)
- Strategie addizionali/alternative in casi speciali (trattati, non collaboranti, disagio socio-ec.)
- Infiammazione e reattività delle VA: non necessarie né sufficienti per fare diagnosi di asma (supportano ma non sostituiscono la clinica).
- Fenotipi diversi (clusters di caratteristiche demografiche, cliniche, fisiopatologiche) che non correlano in maniera stretta con processi patologici specifici o risposte alla terapia.

Diagnosi differenziale

- Sintomi alte VA (rinite)
- Wheezing Improvviso, unilaterale (corpo estraneo)
- Capogiro, parestesie, sospiri (iperventilazione, respiro disfunzionale)
- Infezioni ricorrenti, tosse grassa (bronchiectasie)
- Idem + sinusiti (PCD)
- Tosse eccessiva, produzione di muco, sintomi GI (FC)
- Rumori cardiaci, soffi (cardiopatia congenita)
- Dispnea, anamnesi familiare di enfisema precoce (deficit di Alfa-1-antitripsina)
- Prematurità, sintomi dalla nascita (BPD)

Fenotipi comuni

Asma allergico (frequente inizio nell'infanzia, anamnesi personale o familiare di «AD», «AR», «FA»; espettorato usualmente eosinofilico, rispondono a corticosteroidi)

Asma non allergico (profilo cellulare dello espettorato neutrofilico, eosinofilico o paucigranulocitico; scarsa risposta a corticosteroidi)

Asma d'insorgenza in età adulta (>sesso F, frequente non allergia, richiedono > dosi di corticosteroidi (resistenza parziale), da escludere asma occupazionale

Asma con limitazione di flusso persistente (sviluppata in alcuni asmatici di lunga durata, ostruzione persistente e poco reversibile. Rimodelamento delle V.A.?)

Asma con obesità (spesso molto sintomatici con scarsa infiammazione eosinofilica delle VA).

	Description	Findings in children	Therapy
T2-high	High concentrations of Th2 cytokines (IL-4, IL-5, and IL-13); biomarkers include airway and blood eosinophils, FeNO, and periostin	Children with severe asthma are predominantly eosinophilic, although Th2 cytokines might not be elevated	Steroid responsive; consider anti-IgE or anti-IL-4, anti-IL-5, or anti-IL-13 therapeutics
T2-low	Low concentrations of eosinophils, often associated with airway neutrophilia	Little evidence exists for T2-low asthma in children; airway neutrophils might be protective; airway neutrophilia can be associated with infection	Macrolide antibiotics might be beneficial, although little evidence exists
Persistent airflow limitation	Low FEV_1 or FEV_1/FVC ratio after the use of a bronchodilator and a steroid trial	25% of children with severe asthma have persistent airflow limitation; associated with an increase in airway smooth muscle	Optimise long-acting bronchodilators; titrate steroids down to lowest dose to control symptoms
Atopic	Sensitisation to aeroallergens and elevated IgE	Most children are atopic and have comorbid atopic diseases	Steroid responsive; consider T2-targeted therapies

Phenotypes in children with severe asthma

- Pijnenburg MW, Fleming L. Advances in understanding and reducing the burden of severe asthma in children. Lancet Respir Med. 2020 Oct;8(10):1032-1044. doi: 10.1016/S2213-2600(20)30399-4. Epub 2020 Sep 7. PMID: 32910897.

Il problema della diagnosi nei bambini ≤5 anni

- Il wheezing è comune e spesso associato a virosi
- Fenotipi basati sui sintomi o sull'andamento (time-trend): utilità clinica incerta
- Se il wheezing è ricorrente, maggiore probabilità di asma se:

-sintomi non solo indotti da infezioni

-sensibilizzazione allergica o malattia associata (AR, AD) o genitori asmatici

-risposta clinica a farmaci di controllo (2-3 mesi) o ricaduta dopo cessazione

Probabilità di asma nei pazienti di età ≤5 anni (GINA 2022). ***NB: I sintomi possono cambiare nel tempo.***			
	Scarsa	**Moderata**	**Alta**
Sintomi durante "URTI"[1]	<10 gg	>10 gg	>10gg
Episodi annui[2]	2-3	>3	>3
Sintomi tra episodi[1]	assenti	occasionali	Frequenti (gioco, risata)
Allergia	assente	assente	Si, e/o asma genitori
[1]tosse, sibili, dispnea. [2]oppure episodi severi con o senza peggioramento notturno.			

- Castro-Rodríguez JA, Holberg CJ, Wright AL, Martinez FD. A clinical index to define risk of asthma in young children with recurrent wheezing. Am J Respir Crit Care Med. 2000;162:1403-1406

Table 1. A CLINICAL INDEX TO DEFINE ASTHMA RISK*

Major Criteria	Minor Criteria
1. Parental MD asthma†	1. MD allergic rhinitis§
2. MD eczema‡	2. Wheezing apart from colds
	3. Eosinophilia (⩾ 4%)

*Loose index for the prediction of asthma: Early wheezer plus at least one of two major criteria or two of three minor criteria. Stringent index for the predication of asthma: Early frequent wheezer plus at least one of two major criteria or two of three minor criteria.

†History of a physician diagnosis of asthma.

‡ Physician diagnosis of atopic dermatitis as reported in questionnaires at ages 2 or 3.

§ Physician diagnosis of allergic rhinitis as reported in questionnaires at ages 2 or 3.

- Chang TS, Lemanske RF Jr, Guilbert TW, Gern JE, Coen MH, Evans MD, et. al. Evaluation of the modified asthma predictive index in highrisk preschool children. J Allergy Clin Immunol Pract. (2013) 1:152–6.
- doi: 10.1016/j.jaip.2012.10.008

Stringent API			
Primary	Early frequent wheezer (≥3 on 1–5 rating scale)		
AND			
Secondary	At least 1 major:	OR	At least 2 minor:
	Parental physician-diagnosed asthma		Wheezing unrelated to colds
	Physician-diagnosed atopic dermatitis		Eosinophils ≥4% in circulation
			Physician-diagnosed allergic rhinitis
mAPI			
Primary	≥4 wheezing episodes in a year		
AND			
Secondary	At least 1 major:	OR	At least 2 minor:
	Parental physician-diagnosed asthma		Wheezing unrelated to colds
	Physician-diagnosed atopic dermatitis		Eosinophils ≥4% in circulation
	Allergic sensitization to at least one aeroallergen		Allergic sensitization to milk, egg, or peanuts

Conferma funzionale della diagnosi (tests)

- -Spirometria basale e dopo broncodilatatore
- -Challenge bronchiale (preferibile test da sforzo)
- -FeNO?
- -Alternativi: Impedenzometria (FOT: Rrs, Xrs) o RINT, basale e dopo BD.
- Altri tests: volumi polmonari (dil. o plet.), distribuzione della ventilazione (LCI, M1/M0, M2/M0, Sacin, Scond, ecc), DLCO. Più utili per valutare la prognosi ed escludere patologie coesistenti o alternative.

Inquadramento del fenotipo

Tests allergometrici (SPT, IgE tot e specifiche, frazioni molecolari)

Cellularità (sangue, espettorato, BAL)

FeNO

Valutazione del controllo e della severità della malattia

Controllo dei sintomi nelle ultime 4 settimane (criteri GINA, pazienti ≥6 anni)				
	S/N	Controllato	Controllo parziale	Non controllato
Sintomi diurni > 2 v/sett.		Tutte: N	1-2: S	3-4: S
Risvegli notturni per asma				
Uso SABA per sintomi > 2 v/sett.*				
Limitazione attività per asma				
**Non include SABA pre-esercizio fisico né ICs-LABA "as needed".*				

ASMA CONTROL TEST ≥12 ANNI:

1. Nelle ultime 4 settimane, quanto spesso l'asma ti ha impedito di fare tutto ciò che avresti fatto di solito a scuola o a casa?
   Sempre Molto spesso A volte Raramente Mai

2. Nelle ultime 4 settimane, quanto spesso hai avuto il fiato corto?
   Più di 1 volta/die 1 volta/die 3-6 volte a settimana 1-2 volte a settimana Mai

3. Nelle ultime 4 settimane, quanto spesso i sintomi dell'asma (fischi, tosse, fiato corto, costrizione o dolore al petto) ti hanno svegliato di notte?
   4 o + notti a settimana 2-3 notti a settimana 1-2 volte a settimana 1 volta a settimana Mai

4. Nelle ultime 4 settimane, quanto spesso hai usato il farmaco di emergenza (Ventolin o Broncovaleas) per inalazione o per aerosol?
   3 o più volte al giorno 1 o 2 volte al giorno 2 o 3 volte a settimana 1 volta a settimana Mai

5. Nelle ultime 4 settimane, quanto credi di aver tenuto sotto controllo la tua asma?
   Per niente Scarsamente Abbastanza Ben sotto controllo Completamente

PUNTEGGIO ACT: .....
(1-5 per ogni domanda)

NB:
Ben controllato ("mai" a tutte le domande): 25.
Controllo parziale: 20-24.
Non controllato: inferiore a 20.

MINI PAEDIATRIC ASTHMA QUALITY OF LIFE QUESTIONNAIRE (MiniPAQLQ). Da compilare in intervista al bambino.

NELL'ULTIMA SETTIMANA QUANTO TI HA DATO FASTIDIO:

		moltissimo fastidio	molto fastidio	abbastanza fastidio	un pò fastidio	poco fastidio	quasi nessun fastidio	nessun fastidio
1.	La tosse	1	2	3	4	5	6	7
2.	Il respiro con il fischio	1	2	3	4	5	6	7
3.	Avere difficoltà a respirare	1	2	3	4	5	6	7

NELL'ULTIMA SETTIMANA QUANTE VOLTE:

		sempre	quasi sempre	spesso	qualche volta	una volta ogni tanto	quasi mai	mai
4.	Ti sei sentito senza fiato	1	2	3	4	5	6	7
5.	Ti sei sentito stanco	1	2	3	4	5	6	7
6.	Hai avuto difficoltà a dormire la notte a causa dell'asma	1	2	3	4	5	6	7
7.	Ti sei sentito a disagio, nervoso a causa dell'asma	1	2	3	4	5	6	7
8.	Ti sei sentito in ansia, preoccupato o agitato a causa dell'asma	1	2	3	4	5	6	7
9.	Ti sei sentito di cattivo umore o hai perso la pazienza a causa dell'asma	1	2	3	4	5	6	7
10.	Non ti sei sentito come gli altri o ti sei sentito lasciato da parte a causa dell'asma	1	2	3	4	5	6	7

NELL'ULTIMA SETTIMANA QUANTO TI HA DATO FASTIDIO L'ASMA:

		moltissimo fastidio	molto fastidio	abbastanza fastidio	un pò fastidio	poco fastidio	quasi nessun fastidio	nessun fastidio
11.	Nel fare delle attività fisiche (come ad esempio correre, nuotare, fare ginnastica, camminare in salita/salire le scale e andare in bicicletta)	1	2	3	4	5	6	7
12.	Nello stare con degli animali (come ad esempio nel giocare con degli animali domestici o nel prenderti cura degli animali)	1	2	3	4	5	6	7
13.	Nel fare attività con i tuoi amici o con la tua famiglia (come ad esempio giocare durante l'intervallo e fare delle cose con i tuoi amici o con la tua famiglia)	1	2	3	4	5	6	7

Sintomi: domande 1-6; sfera emotiva: domande 7-10 ; limitazione delle attività: domande 11-13.

Rischio esacerbazioni

- Mancato controllo dei sintomi (principale rischio)
- Altri fattori di rischio anche in asmatici con sintomi scarsi:

-abuso di SABA, uso inadeguato/mancante di ICs, tecnica inadeguata, non aderenza

-comorbidità: obesità, rinite/sinusite cronica, GERD, FA, gravidanza

-esposizioni: allergeni, fumo sigaretta (ed e-sigarette), inquinanti ambientali.*

-contesto: disagio socioeconomico e /o psicologico rilevanti

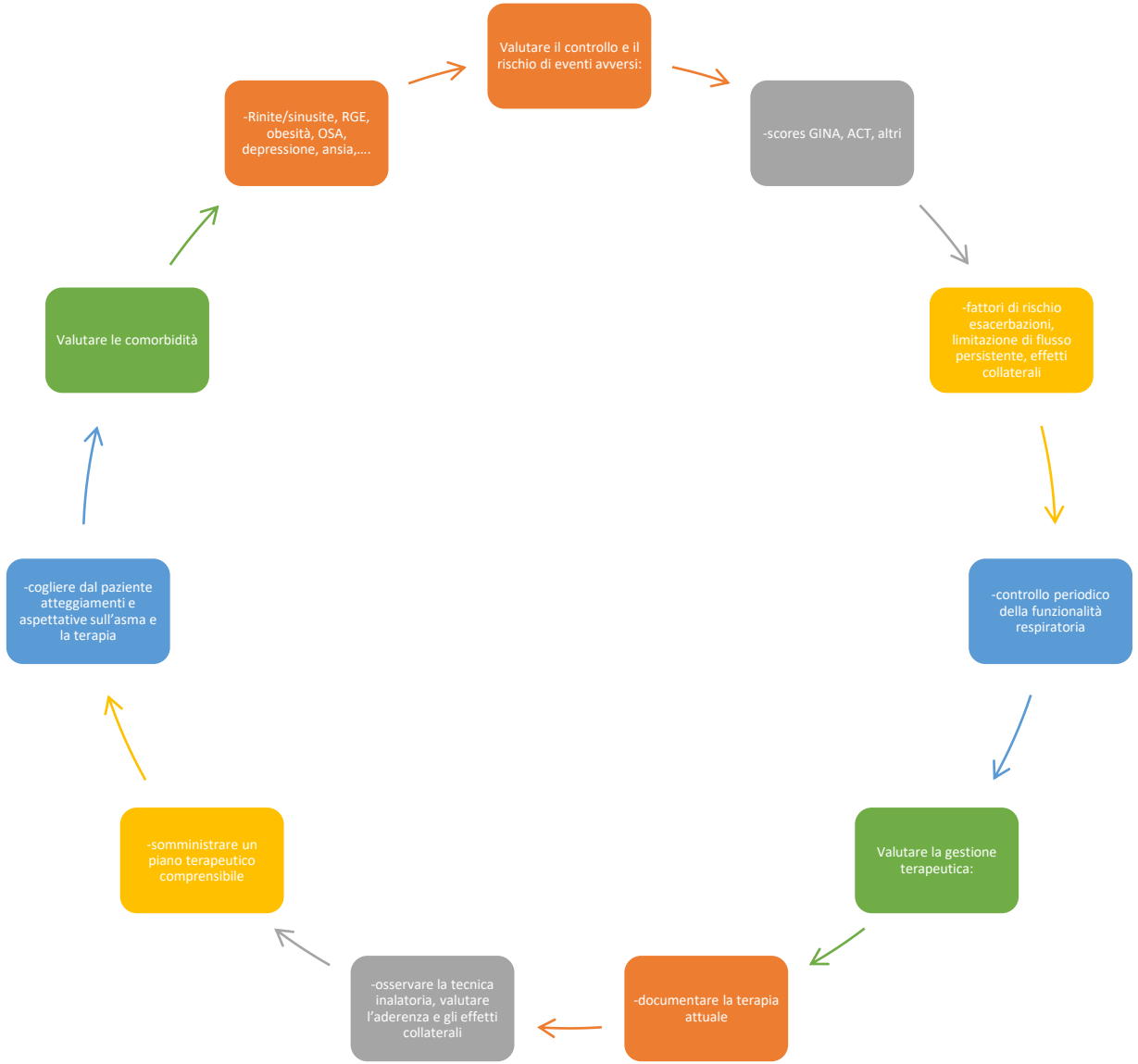
-ridotta funzionalità respiratoria (FEV1<60%) e marcata broncoreattività (BD, challenge)

-elevati marcatori TH2: eosinofilia, FeNO (soprattutto se già in terapia con ICs)

-anamnesi di intubazione/UTIC nella vita, ≥1 esacerbazione negli ultimi 12 mesi

*Indagare sull'andamento nella stagione precedente

Follow-up del paziente asmatico



Ha il nostro paziente un “asma severo”?

- Terapia antinfiammatoria insufficiente, anche a dosi elevate
- Controllo della malattia insoddisfacente
- Esacerbazioni di asma persistenti
- Funzionalità respiratoria ridotta

Definition of severe asthma for patients aged ≥6 years

- **Asthma which requires treatment with guidelines suggested medications for GINA steps 4–5 asthma (high dose ICS# and LABA or leukotriene modifier/theophylline) for the previous year or systemic CS for ≥50% of the previous year to prevent it from becoming "uncontrolled" or which remains "uncontrolled" despite this therapy**

#: age-specific

- **Uncontrolled** asthma defined as **at least one** of the following:

1) Poor symptom control: ACQ consistently ≥ 1.5 or ACT<20 (or ''not well controlled'' by NAEPP/GINA guidelines)

2) Frequent severe exacerbations: two or more bursts of systemic CS (≥ 3 days each) in the previous year

3) Serious exacerbations: at least one hospitalisation, ICU stay or mechanical ventilation in the previous year

4) Airflow limitation: after appropriate bronchodilator withhold FEV1 <80% predicted (in the face of reduced FEV1/FVC defined as less than the lower limit of normal)

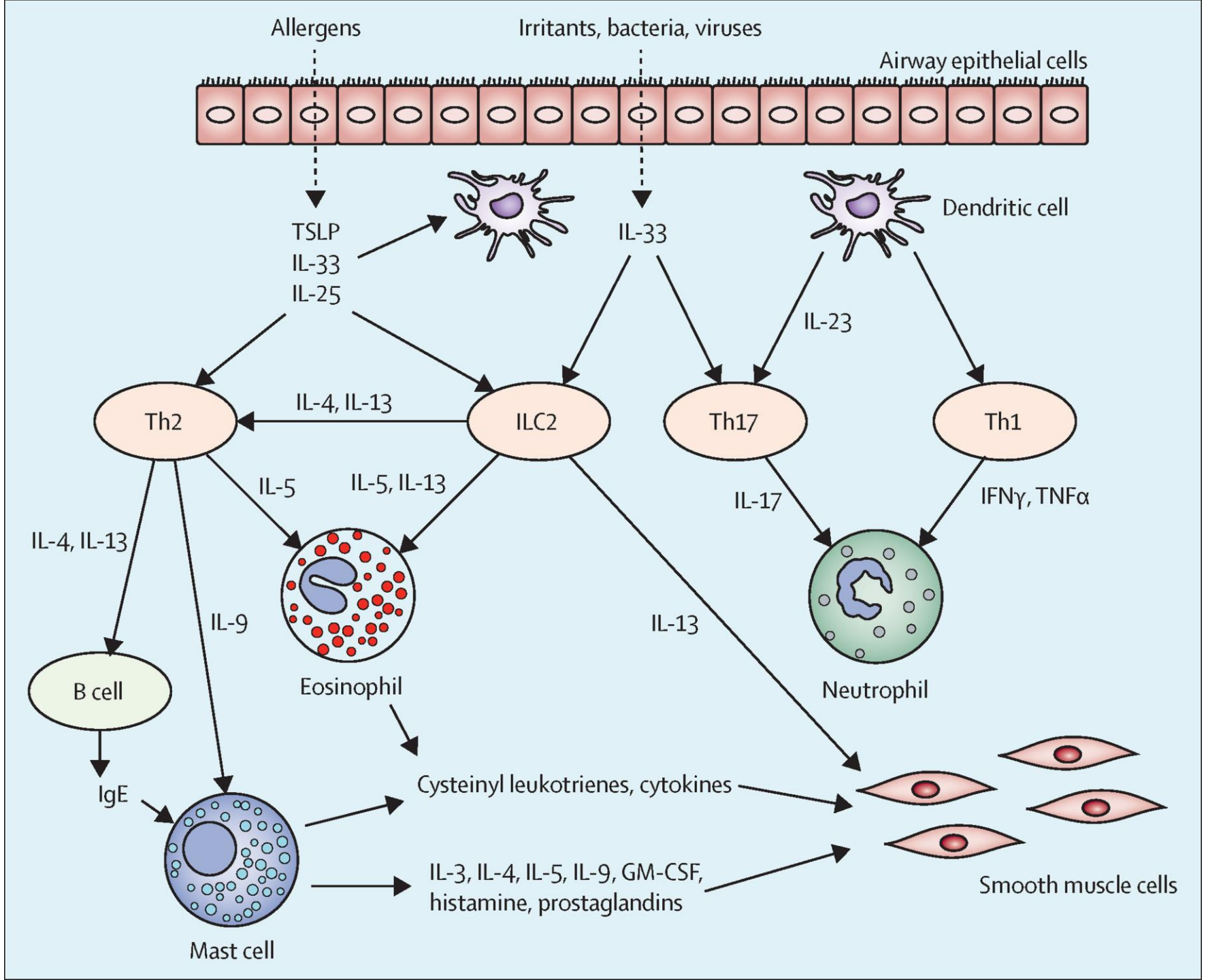
- **Controlled** asthma that worsens on tapering of these high doses of ICS or systemic CS (or additional biologics)

"International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma." Chung KF, Wenzel SE, Brozek JL, Bush ZA, Castro M, et al. *Eur Respir J* 2014; 43: 343-373. Eur Respir J. 2018 Jul 27;52(1):1352020. doi: 10.1183/13993003.52020-2013. Erratum for: Eur Respir J. 2014 Feb;43(2):343-73. PMID: 30054347.

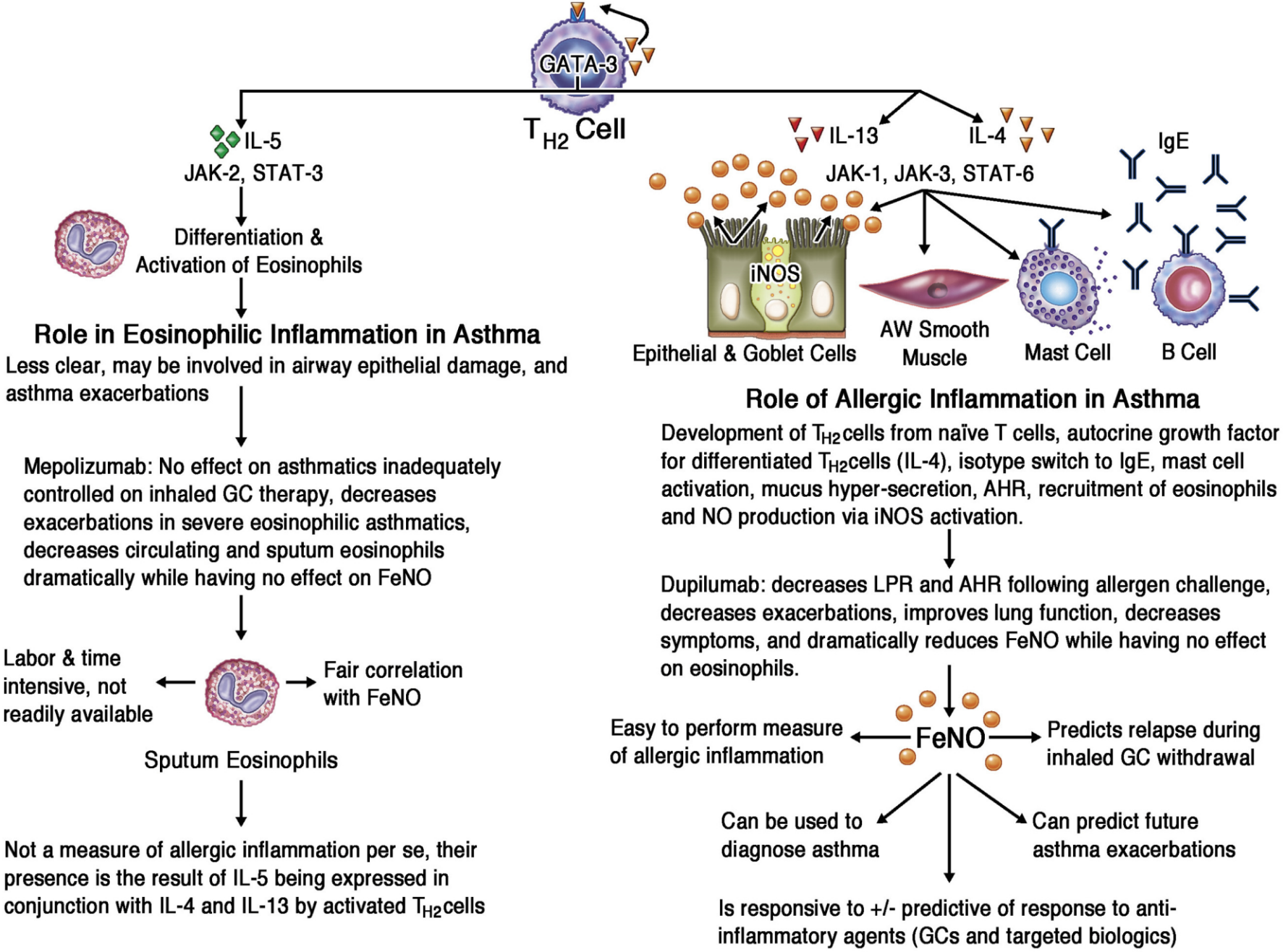
Inhaled corticosteroid	Threshold daily dose in µg considered as high	
	Age 6–12 years	Age >12 years
Beclomethasone dipropionate	≥800 (DPI or CFC MDI) ≥320 (HFA MDI)	≥2000 (DPI or CFC MDI) ≥1000 (HFA MDI)
Budesonide	≥800 (MDI or DPI)	≥1600 (MDI or DPI)
Ciclesonide	≥160 (HFA MDI)	≥320 (HFA MDI)
Fluticasone propionate	≥500 (HFA MDI or DPI)	≥1000 (HFA MDI or DPI)
Mometasone furoate	≥500 (DPI)	≥800 (DPI)
Triamcinolone acetonide	≥1200	≥2000

CFC: chlorofluorocarbon, HFA: hydrofluoroalkane. DPI: dry powder inhaler; MDI: metered-dose inhaler

"International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma." Chung KF, Wenzel SE, Brozek JL, Bush ZA, Castro M, et al. *Eur Respir J* 2014; 43: 343-373. Eur Respir J. 2018 Jul 27;52(1):1352020. doi: 10.1183/13993003.52020-2013. Erratum for: Eur Respir J. 2014 Feb;43(2):343-73. PMID: 30054347.



Pijnenburg MW, Fleming L. Advances in understanding and reducing the burden of severe asthma in children. Lancet Respir Med. 2020 Oct;8(10):1032-1044. doi: 10.1016/S2213-2600(20)30399-4. Epub 2020 Sep 7. PMID: 32910897.



Spahn JD, Malka J, Szefler SJ. Current application of exhaled nitric oxide in clinical practice. J Allergy Clin Immunol. 2016 Nov;138(5):1296-1298. doi: 10.1016/j.jaci.2016.09.002. Epub 2016 Sep 21. PMID: 27664377.

Monoclonal antibodies (T2-type severe asthma in children)

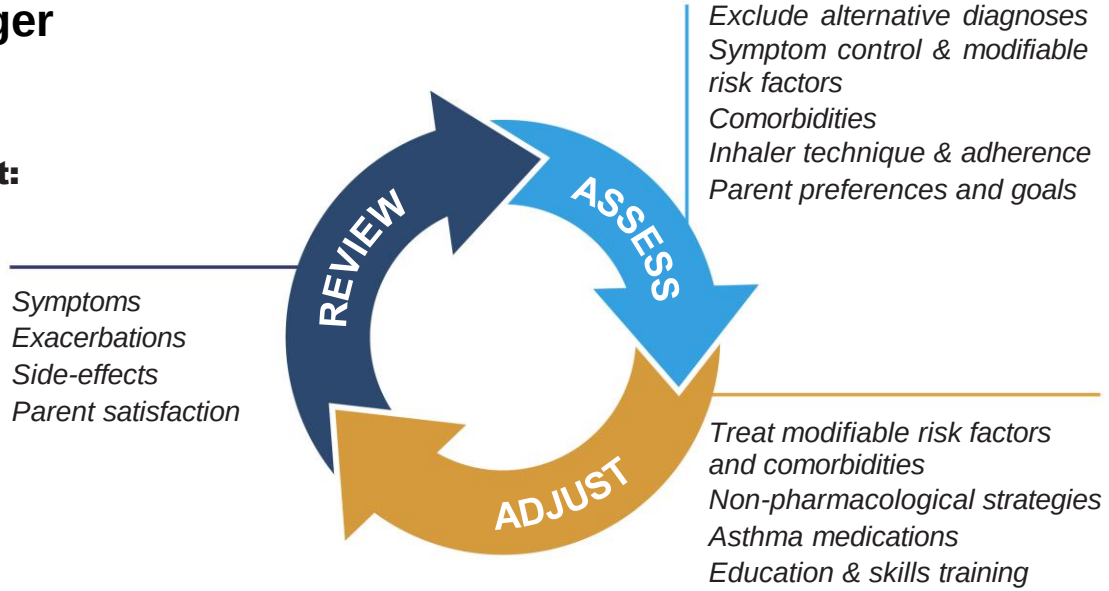
- target IL-5 (mepolizumab[1], reslizumab) or its receptor IL-5Rα (benralizumab)
- anti-IgE antibody (omalizumab[1])
- anti-IL-4Rα/IL13 (dupilumab[1])
- anti-TSLP (tezepelumab[2])

[1] common use in children and adolescents

[2] currently investigated for its pediatric use

Children 5 years and younger

Personalized asthma management:
Assess, Adjust, Review response

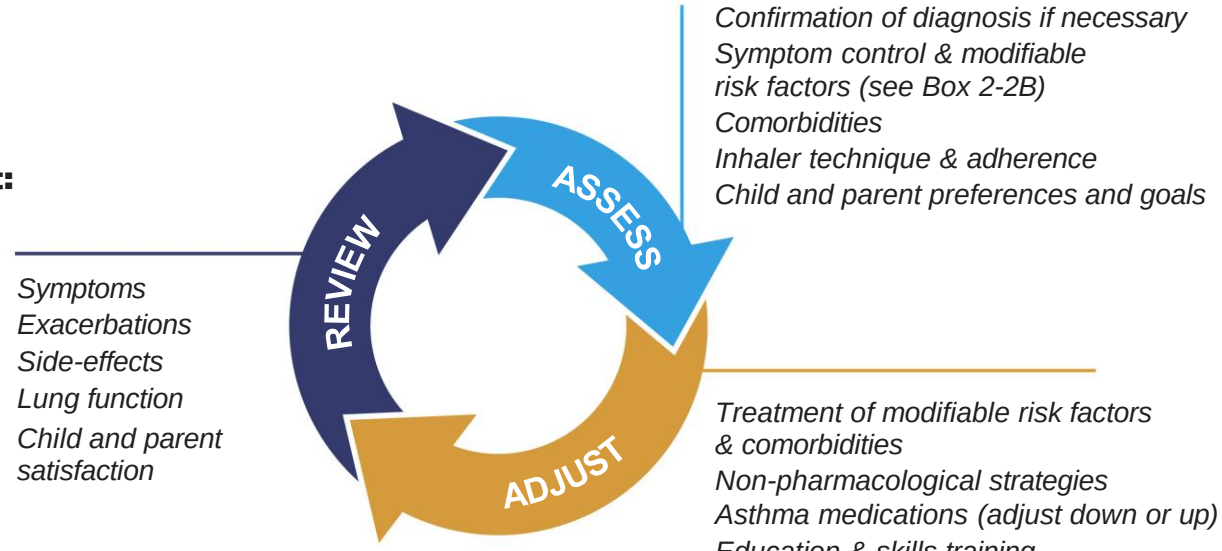


Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4
PREFERRED CONTROLLER CHOICE		Daily low dose inhaled corticosteroid (ICS) (see table of ICS dose ranges for pre-school children)	Double 'low dose' ICS	Continue controller & refer for specialist assessment
Other controller options (limited indications, or less evidence for efficacy or safety)	*Consider intermittent short course ICS at onset of viral illness*	*Daily leukotriene receptor antagonist (LTRA), or intermittent short course of ICS at onset of respiratory illness*	*Low dose ICS + LTRA Consider specialist referral*	*Add LTRA, or increase ICS frequency, or add intermittent ICS*
RELIEVER	As-needed short-acting beta$_2$-agonist			
CONSIDER THIS STEP FOR CHILDREN WITH:	Infrequent viral wheezing and no or few interval symptoms	Symptom pattern not consistent with asthma but wheezing episodes requiring SABA occur frequently, e.g. ≥3 per year. Give diagnostic trial for 3 months. Consider specialist referral. Symptom pattern consistent with asthma, and asthma symptoms not well-controlled or ≥3 exacerbations per year.	Asthma diagnosis, and asthma not well-controlled on low dose ICS Before stepping up, check for alternative diagnosis, check inhaler skills, review adherence and exposures	Asthma not well-controlled on double ICS

Children 6-11 years

Personalized asthma management:
Assess, Adjust, Review



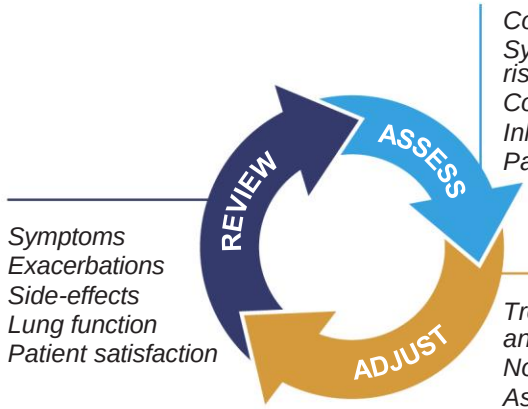
Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms	Low dose ICS taken whenever SABA taken	Daily low dose inhaled corticosteroid (ICS) (see table of ICS dose ranges for children)	Low dose ICS-LABA, OR medium dose ICS, OR very low dose* ICS-formoterol maintenance and reliever (MART)	Medium dose ICS-LABA, OR low dose† ICS-formoterol maintenance and reliever therapy (MART). Refer for expert advice	Refer for phenotypic assessment ± higher dose ICS-LABA or add-on therapy, e.g. anti-IgE, anti-IL4R
Other controller options (limited indications, or less evidence for efficacy or safety)	*Consider daily low dose ICS*	*Daily leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken*	*Low dose ICS + LTRA*	*Add tiotropium or add LTRA*	*Add-on anti-IL5 or, as last resort, consider add-on low dose OCS, but consider side-effects*
RELIEVER	As-needed short-acting beta$_2$-agonist (or ICS-formoterol reliever in MART in Steps 3 and 4)				

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

Adults & adolescents 12+ years

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



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

Symptoms
Exacerbations
Side-effects
Lung function
Patient satisfaction

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

CONTROLLER and **PREFERRED RELIEVER**
(Track 1). Using ICS-formoterol as reliever reduces the risk of exacerbations compared with using a SABA reliever

STEPS 1 – 2	STEP 3	STEP 4	STEP 5
As-needed low dose ICS-formoterol	Low dose maintenance ICS-formoterol	Medium dose maintenance ICS-formoterol	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-formoterol, ± anti-IgE, anti-IL5/5R, anti-IL4R, anti-TSLP
RELIEVER: As-needed low-dose ICS-formoterol			

See GINA severe asthma guide

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	STEP 2	STEP 3	STEP 4	STEP 5
Take ICS whenever SABA taken	Low dose maintenance ICS	Low dose maintenance ICS-LABA	Medium/high dose maintenance ICS-LABA	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-LABA, ± anti-IgE, anti-IL5/5R, anti-IL4R, anti-TSLP
RELIEVER: As-needed short-acting beta$_2$-agonist				

Other controller options for either track (limited indications, or less evidence for efficacy or safety)	*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. As last resort consider adding low dose OCS but consider side-effects*

GINA 2022, Box 3-5A

European Respiratory Society clinical practice guidelines for the diagnosis of asthma in children aged 5–16 years

Erol A. Gaillard[1,2], Claudia E. Kuehni[3,4], Steve Turner[5], Myrofora Goutaki[3,4], Karl A. Holden[1], Carmen C.M. de Jong[3], Christiane Lex[6], David K.H. Lo[1,2], Jane S. Lucas[7,8], Fabio Midulla[9], Rebeca Mozun[3], Giorgio Piacentini[10], David Rigau[11], Bart Rottier[12,13,14], Mike Thomas[15], Thomy Tonia[3], Jakob Usemann[16,17], Ozge Yilmaz[18], Angela Zacharasiewicz[19] and Alexander Moeller[17]

Cite this article as: Gaillard EA, Kuehni CE, Turner S, *et al*. European Respiratory Society clinical practice guidelines for the diagnosis of asthma in children aged 5–16 years. *Eur Respir J* 2021; 58: 2004173 [DOI: 10.1183/13993003.04173-2020].

TABLE 2 Evidence-based recommendations for the use of each of the tests considered for asthma diagnosis in children aged 5–16 years in primary, secondary or tertiary care

	Recommendation	Remarks
PICO 1. In children aged 5–16 years under investigation for asthma, should the presence of the symptoms wheeze, cough and breathing difficulty be used to diagnose asthma?	• The task force recommends against diagnosing asthma based on symptoms alone (strong recommendation against the intervention, moderate quality of evidence)	• Recurrent wheeze, cough and breathing difficulty are key symptoms of asthma. The task force considers a history of recurrent reported wheeze or wheeze on auscultation as the most important symptom of asthma • Children with chronic cough (*i.e.* cough for >4 weeks) as the only symptom are unlikely to have asthma and should be investigated according to the ERS guidelines for chronic cough in children [32] and a referral for further investigations to exclude differential diagnoses should be considered

European Respiratory Society clinical practice guidelines for the diagnosis of asthma in children aged 5–16 years

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PICO 2. In children aged 5–16 years under investigation for asthma, should an improvement in symptoms following a trial of preventer medication be used to diagnose asthma?	• The task force recommends against using an improvement in symptoms after a trial of preventer medication alone to diagnose asthma (conditional recommendation against the intervention, based on clinical experience)	• The task force did not find any evidence for or against a trial of preventer medication to diagnose asthma in children aged 5–16 years • Despite the lack of evidence, based on clinical experience, the task force members agreed that a trial of preventer medication can be considered; but only in symptomatic children with abnormal spirometry and negative bronchodilator response. In such cases, the objective tests spirometry and, if indicated, BDR should be repeated after 4–8 weeks
PICO 3. In children aged 5–16 years under investigation for asthma, should spirometry testing be used to diagnose asthma?	• The task force recommends spirometry as part of the diagnostic work-up of children aged 5–16 years with suspected asthma (strong recommendation for the intervention, moderate quality of evidence)	• An FEV_1/FVC <LLN or <80%, or an FEV_1 <LLN or <80% pred should be considered supportive of an asthma diagnosis. It is important to be aware that not all children are able to perform a sufficient FVC manoeuvre, resulting in a false normal FEV_1/FVC ratio • A normal spirometry result does not exclude asthma

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PICO 4. In children aged 5–16 years under investigation for asthma, should BDR testing be used to diagnose asthma?	• The task force recommends BDR testing in all children with FEV_1 <LLN or <80% pred and/or FEV_1/FVC <LLN or <80% (strong recommendation for the intervention, based on clinical experience)	• Consider an increase in FEV_1 ⩾12% and/or ⩾200 mL following inhalation of 400 μg SABA as diagnostic of asthma • BDR <12% does not exclude asthma • Most task force members consider BDR testing when baseline spirometry is normal if the clinical history is strongly suggestive of asthma
PICO 5. In children aged 5–16 years under investigation for asthma, should F_{eNO} testing be used to diagnose asthma?	• The task force recommends measurement of F_{eNO} as part of the diagnostic work-up of children aged 5–16 years with suspected asthma (strong recommendation for the intervention, moderate quality of evidence)	• A F_{eNO} value ⩾25 ppb in a child with asthma symptoms should be considered as supportive of a diagnosis of asthma • A F_{eNO} value <25 ppb does not exclude asthma

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PICO 6. In children aged 5–16 years under investigation for asthma, should PEFR variability be used to diagnose asthma?	• The task force recommends against PEFR variability testing as the primary objective test on its own to diagnose asthma in children aged 5–16 years (conditional recommendation against the intervention, moderate quality of evidence)	• Other objective tests are preferred, but a PEFR variability test can be considered in healthcare settings lacking other objective tests • If a PEFR variability test is used the result should be based on 2 weeks of measurements, ideally using electronic peak flow meters • A cut-off of ⩾12% in PEFR variability should be considered a positive test • A PEFR variability of <12% does not exclude asthma
PICO 7. In children aged 5–16 years under investigation for asthma, should allergy testing be used to diagnose asthma?	• The task force recommends against the use skin-prick tests to aeroallergens as diagnostic tests for asthma (strong recommendation against the intervention, moderate quality of evidence) • The task force recommends against the use of serum total and specific IgE tests as diagnostic tests for asthma (strong recommendation against the intervention, moderate quality of evidence)	

Conclusioni

La diagnosi di asma in età pediatrica spesso è semplice, ma deve essere sempre basata sulla clinica. Gli accertamenti sono utili e qualora positivi supportano la diagnosi. Accertamenti negativi non consentono di escludere la diagnosi.

Il follow-up è fondamentale, da aggiustare in maniera dinamica (caratteristiche del pazienti, rischio, difficoltà socioeconomiche o psicologiche, adolescente con autogestione errata o fumatore)

Ascoltare, spiegare, verificare la comprensione della terapia e della sua pertinenza. Comunicare. Il successo della gestione della malattia dipende in gran parte dalla capacità educativa del pediatra