

Practical approach to the pediatric asthma guidelines: What's new?

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Disclosures

| | Company/Organization | Details |
|---|--|---|
| I am a member of an Advisory Board or equivalent with a commercial organization. | CSL-Behring Sanofi-Genzyme Liffey Biotech Immunology CSO | Advisor for development of therapeutic molecule for allergic hypersensitivities |
| I am a member of a Speaker's Bureau | n/a | |
| I have received payment from a commercial organization (including gifts or other consideration or 'in kind' compensation). | n/a | Puis-je soumettre l'histoire d'Eve |

Objectives

Describe pediatric asthma endotypes

Understand important elements of new CTS and CPS and GINA guidelines for asthma management

Understand new therapies now available and those coming in the near future for pediatric asthma

The Case

- 2 year old boy with first admission to hospital for respiratory distress. Symptoms started with URTI and worsened over the first few days of infection.
- He is treated with bronchodilators and corticosteroids and symptoms resolve.
- He has had one episode previously treated with salbutamol.

What are the possible diagnoses and how is this managed?

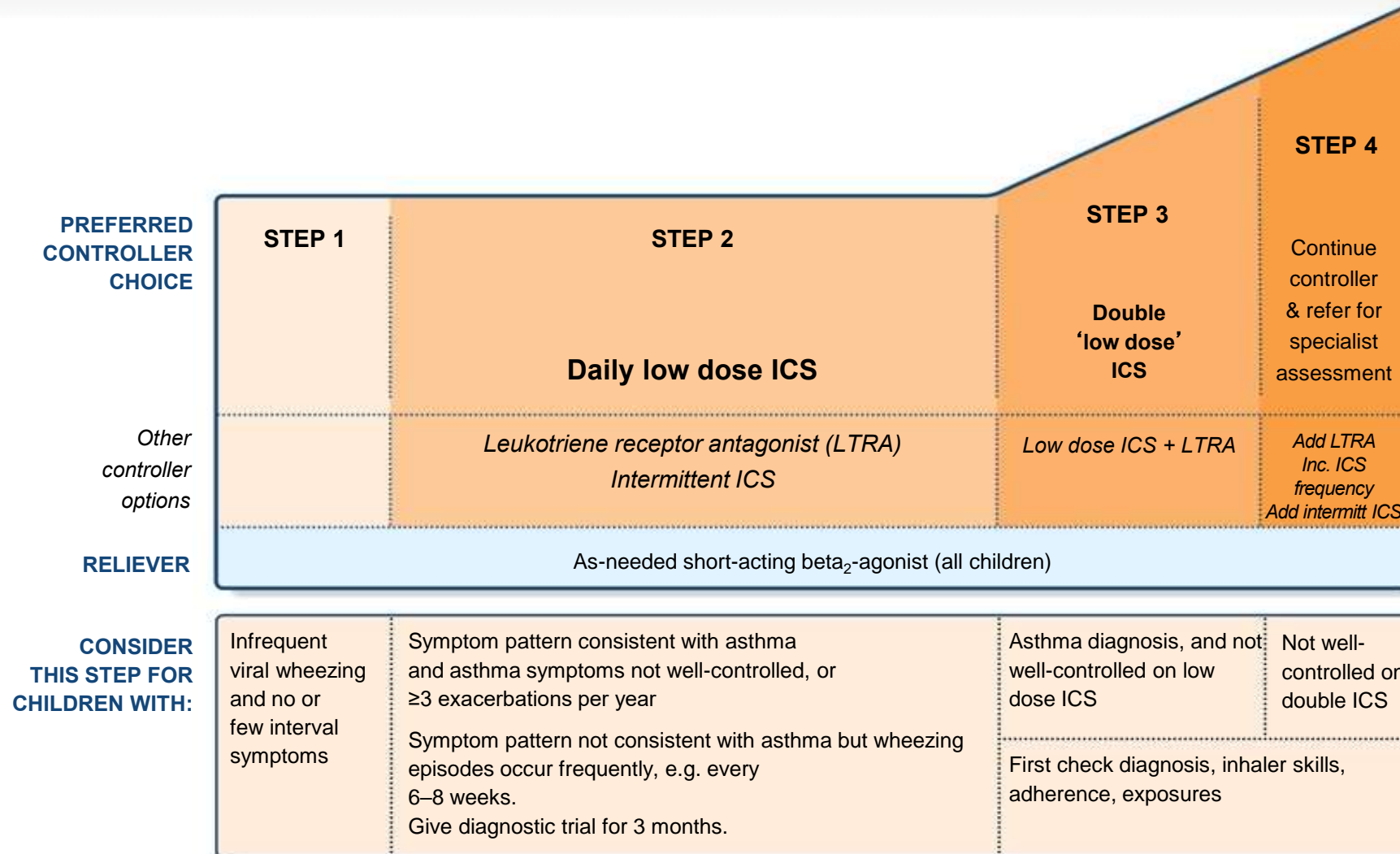
Differential diagnosis:

- viral-induced reactive airways
- CF,PCD
- Anatomical abnormality
- Pneumonia
- GERD

Management?

- One episode responsive to salbutamol???. Does he require inhaled corticosteroids?

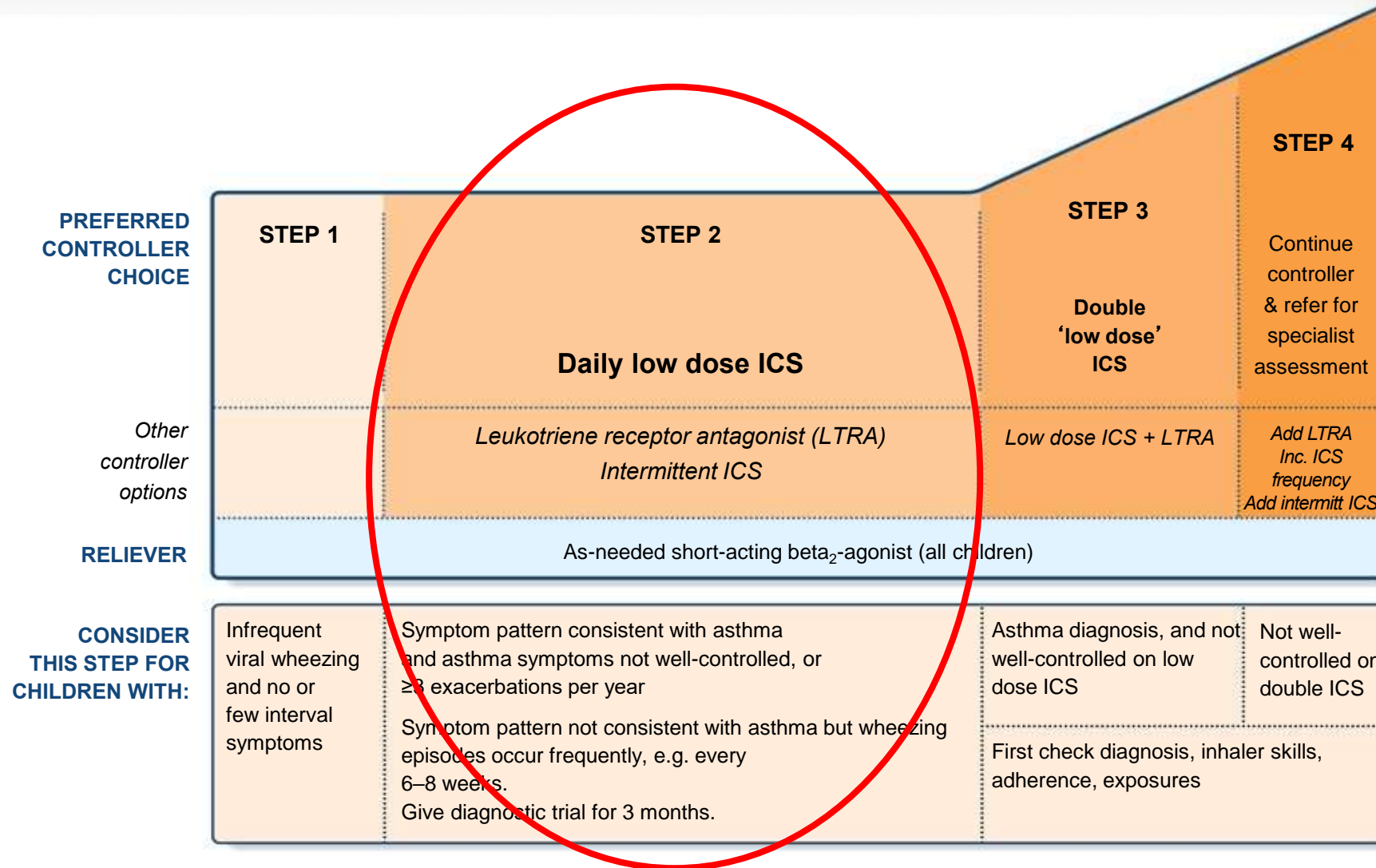
Stepwise approach – pharmacotherapy (children ≤5 years)



Case continues

- Over the next 4 months he is seen frequently at ER with respiratory distress. He is admitted again to hospital and goes to the PICU because of high acuity. Not intubated.
- Each ER visit he is treated with oral dexamethasone.
- All investigations for CF, PCD and other extrinsic causes are negative.

Stepwise approach – pharmacotherapy (children ≤5 years)



Children aged ≤ 5 years – key changes

- Home management of intermittent viral-triggered wheezing
 - Preemptive episodic high-dose episodic ICS may reduce progression to exacerbation (*Kaiser Pediatr 2016*)
 - However, this has a high potential for side-effects, especially if continued inappropriately or is given frequently
 - Family-administered high dose ICS should be considered only if the health care provider is confident that the medications will be used appropriately, and the child closely monitored for side-effects
- Emergency department management of worsening asthma
 - Reduced risk of hospitalization when OCS are given in the emergency department, but no clear benefit in risk of hospitalization when given in the outpatient setting (*Castro-Rodriguez Pediatr Pulm 2016*)

'Low dose' inhaled corticosteroids (mcg/day) for children ≤5 years – updated 2018

| Inhaled corticosteroid | Low daily dose, mcg (with lower limit of age-group studied) |
|----------------------------------|--|
| Beclometasone dipropionate (HFA) | 100 (ages ≥5 years) |
| Budesonide (nebulized) | 500 (ages ≥1 year) |
| Fluticasone propionate (HFA) | 100 (ages ≥4 years) |
| Mometasone furoate | 110 (ages ≥4 years) |
| Budesonide (pMDI + spacer) | Not sufficiently studied in this age group |
| Ciclesonide | Not sufficiently studied in this age group |
| Triamcinolone acetonide | Not sufficiently studied in this age group |

- This is not a table of equivalence
- A low daily dose is defined as the lowest approved dose for which safety and effectiveness have been adequately studied in this age group

Children aged ≤ 5 years – newer recommendations

- Step 2 (initial controller treatment) for children with frequent viral-induced wheezing and with interval asthma symptoms
 - A trial of regular low-dose ICS should be undertaken first
 - As-needed (prn) or episodic ICS may be considered
 - The reduction in exacerbations seems similar for regular and high dose episodic ICS
(Kaiser Pediatr 2015)
 - LTRA is another controller option
- Step 3 (additional controller treatment)
 - First check diagnosis, exposures, inhaler technique, adherence
 - Preferred option is medium dose ICS
 - Low-dose ICS + LTRA is another controller option
 - Blood eosinophils and atopy predict greater short-term response to moderate dose ICS than to LTRA *(Fitzpatrick JACI 2016)*
 - Relative cost of different treatment options in some countries may be relevant to controller choices

Case continues

- He is started on regular ICS: ciclesonide, monteleukast, salbutamol.
- 2 more visits to ER-changed to salmeterol/fluticasone.
- 2 months later, another visit to ER and admission to PICU.
- Changed to mometasone and fomoterol. Needs Ventolin with every URTI. Now has had 7 courses of oral corticosteroids.
- AM cortisol depressed. Mother is given additional prescriptions for dexamethasone to start immediately at first sign of distress.
- WHAT NOW?

Adherence

- Focus on assessment and reassessment with patient communication the key component for compliance and success
- 30-70% of prescribed doses of ICS actually used
- Most basic form of non-compliance is “misunderstanding of basic medical advice”
 - Occurs in patients with little to no asthma education
- Barriers to good communication
 - Lack of time/distractions
 - Misunderstanding of parental goals / concerns
 - Reluctance to question physicians
 - Language and jargon

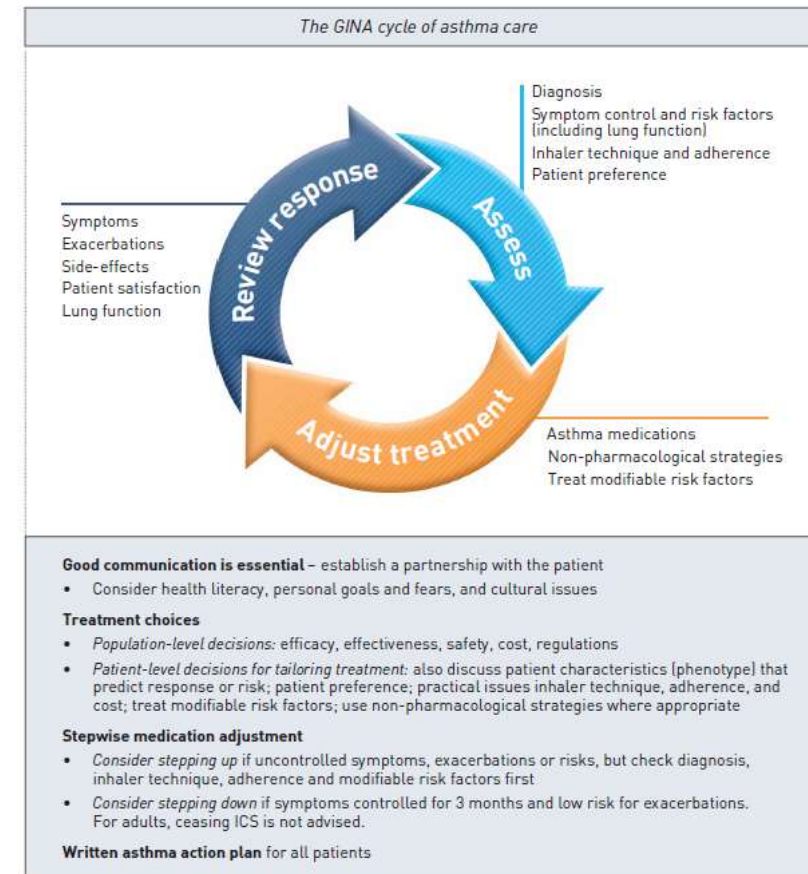
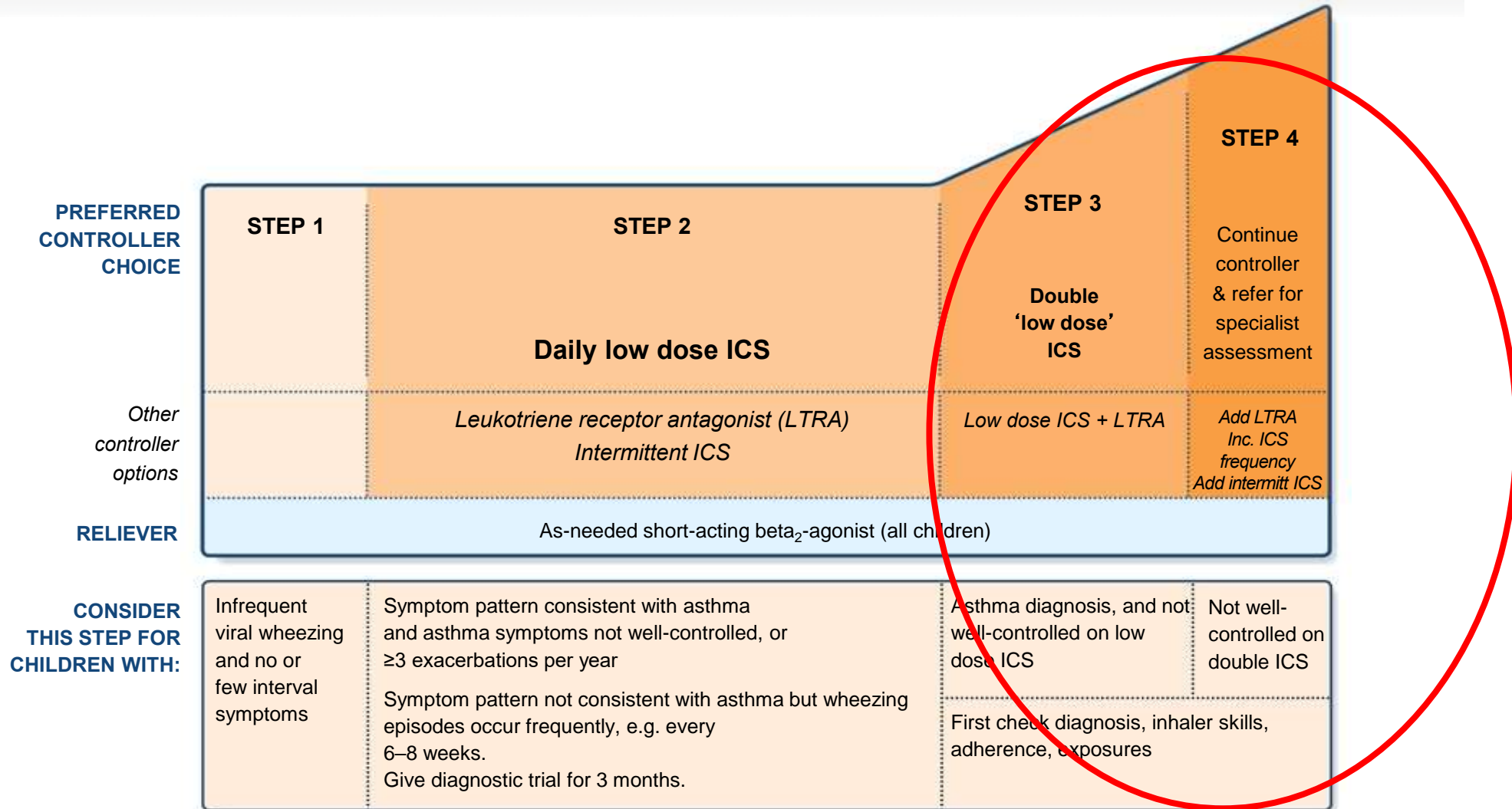


FIGURE 1 The Global Initiative for Asthma (GINA) control-based cycle of asthma care. This figure highlights key priorities in management of asthma in the GINA global asthma strategy. Further details can be found in boxes 3-3 and 3-5 in the full GINA 2015 report (“Global Strategy for Asthma Management and Prevention”), available online (www.ginasthma.org). ICS: inhaled corticosteroids. Figure modified with permission of GINA.

Follow-up after an asthma exacerbation

- Follow up all patients regularly after an exacerbation, until symptoms and lung function return to normal
 - Patients are at increased risk during recovery from an exacerbation
- The opportunity
 - Exacerbations often represent failures in chronic asthma care, and they provide opportunities to review the patient's asthma management
- At follow-up visit(s), check:
 - The patient's understanding of the cause of the flare-up
 - Modifiable risk factors, e.g. smoking
 - Adherence with medications, and understanding of their purpose
 - **SABA is being taken only as-needed, not regularly**
 - Inhaler technique skills
 - Written asthma action plan

Stepwise approach – pharmacotherapy (children ≤5 years)



Exhaled nitric oxide (FeNO)

- FeNO is becoming more widely available in some countries
- All sections on FeNO have been reviewed and updated
 - Updated to reflect new meta-analyses (*Petsky Cochrane 2016; Petsky Cochrane 2016*) that separately analyzed studies in which the control algorithm was reasonably close to current clinical recommendations, and therefore provided a clinically relevant comparator
 - Children/adolescents: FENO-guided treatment was associated with significantly fewer exacerbations and lower exacerbation rate than treatment based on current guidelines
- In children ≤ 5 years with recurrent coughing and wheezing
 - Elevated FeNO recorded >4 weeks from any URTI predicts physician-diagnosed asthma at school age (*Singer 2013*)
 - Elevated FeNO at age 4 increases the odds for wheezing, physician-diagnosed asthma and ICS use by school age, independent of clinical history and presence of specific IgE (*Caudri JACI 2010*)

No more
options???

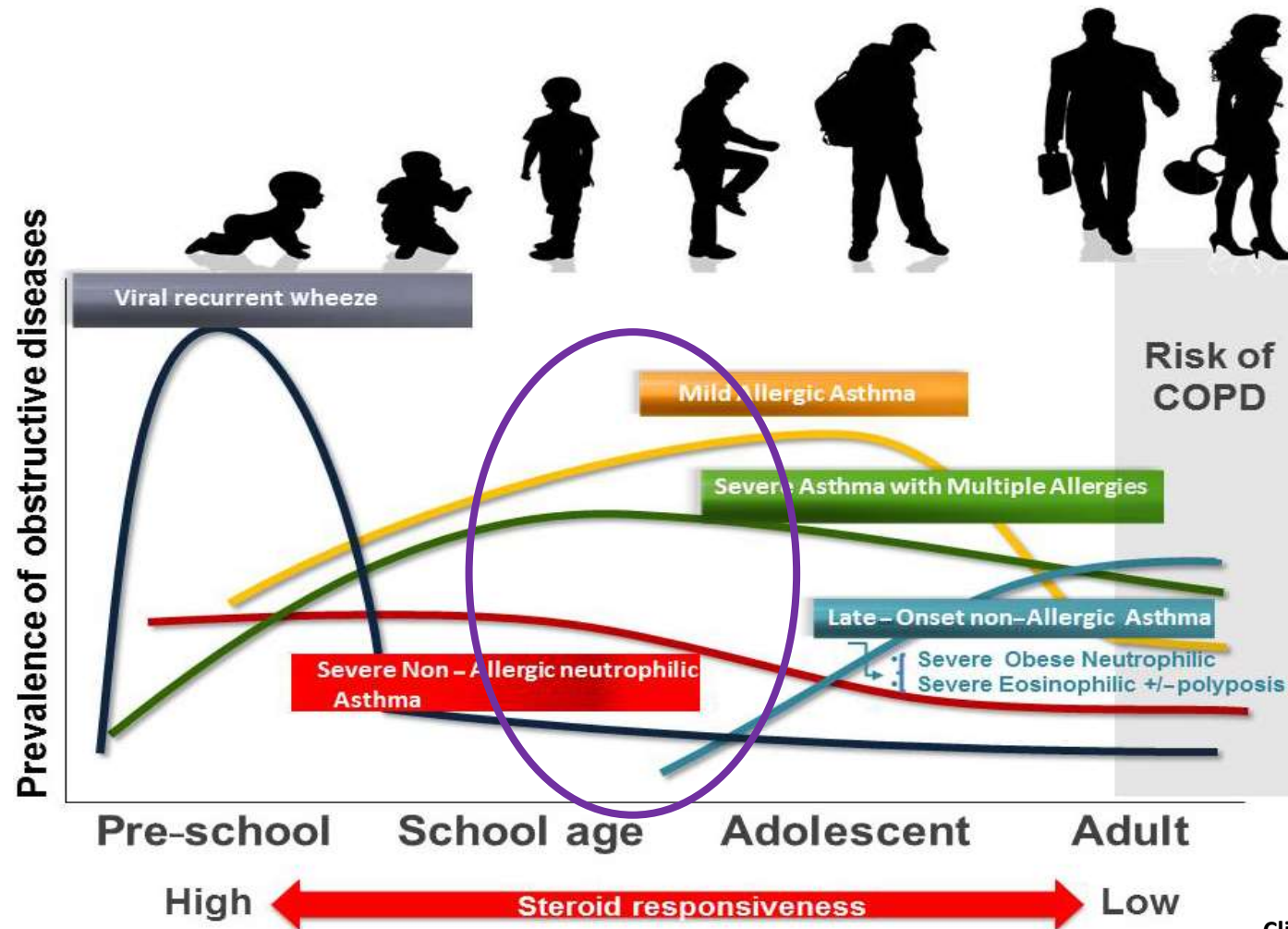
- Child is now age 3.
- He has signs and symptoms of steroid toxicity.
- He is adrenally suppressed.
- He has had 3 visits to the PICU

- We are out of guidelines....

Can we treat him like an older child?

- Does he have allergic asthma?
 - no allergies identified, total IgE 62
- Does he have viral-induced reactive airways?
 - All exacerbations associated with URTI
 - NPA consistently +ve for different viruses during hospitalizations
- Treatment options?

Clinical phenotypes in asthma during childhood: Does this change management?



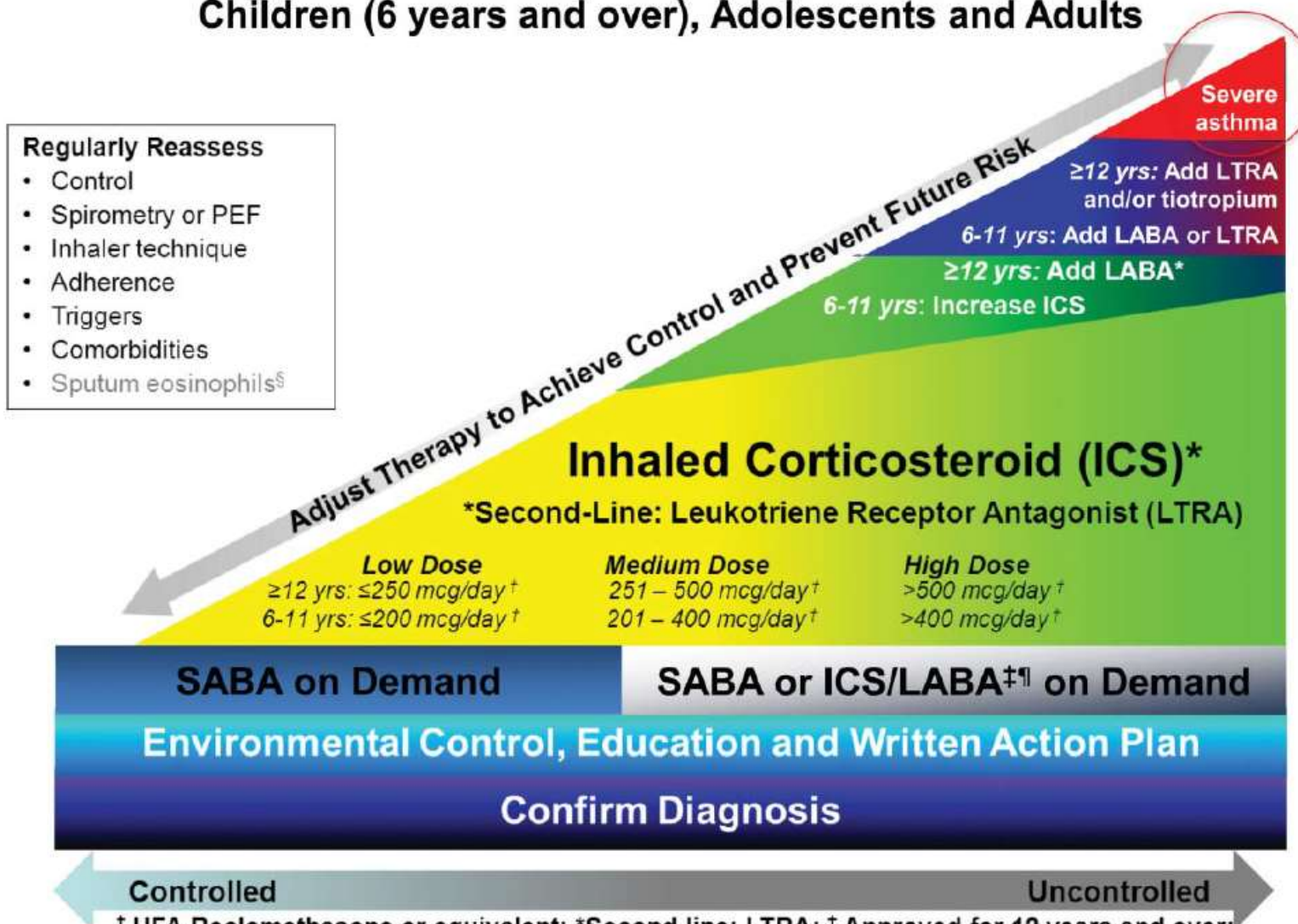
A recent study of pediatric fatal asthma showed mucous plugging of small airways and strong presence of eosinophils were hallmark pathological findings, suggesting fatal disease may be more of an “acute” event. (Malmstrom et al 2017)

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2017 Asthma Management Continuum Children (6 years and over), Adolescents and Adults



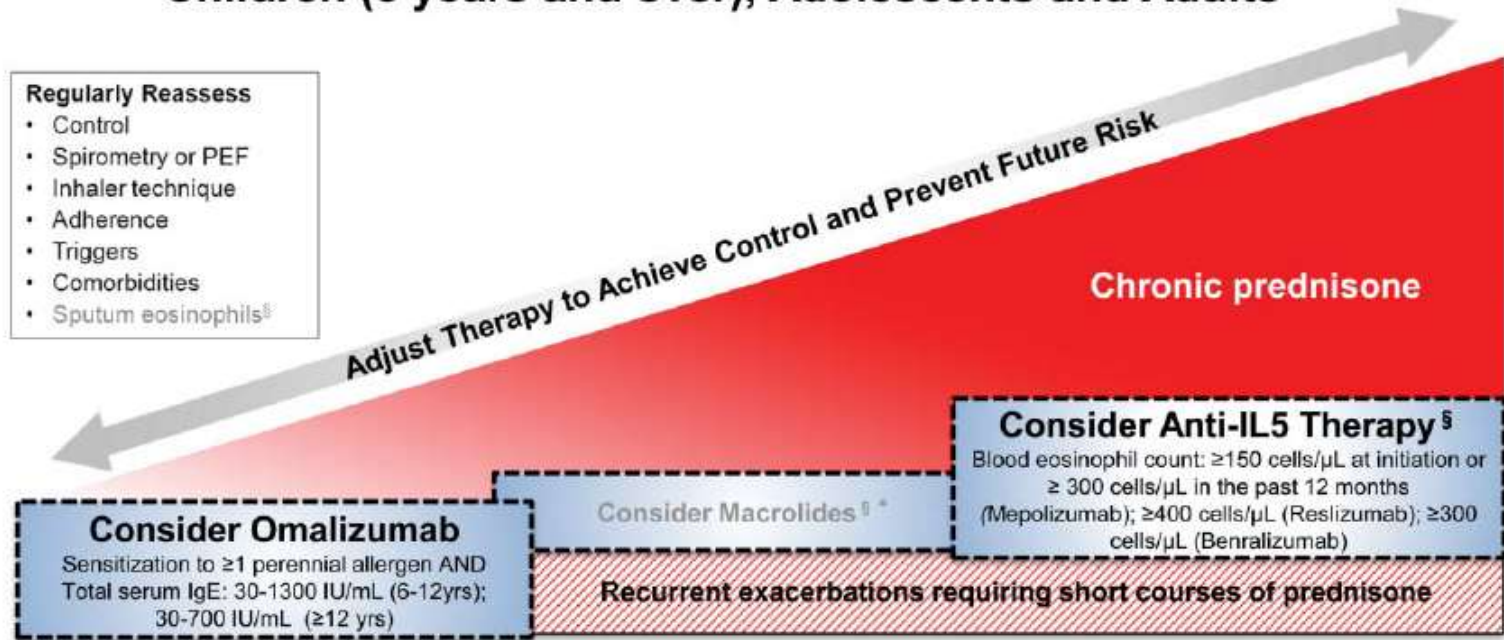
[†] HFA Beclomethasone or equivalent; *Second-line: LTRA; [‡] Approved for 12 years and over;

[¶] Using a formulation approved for use as a reliever;

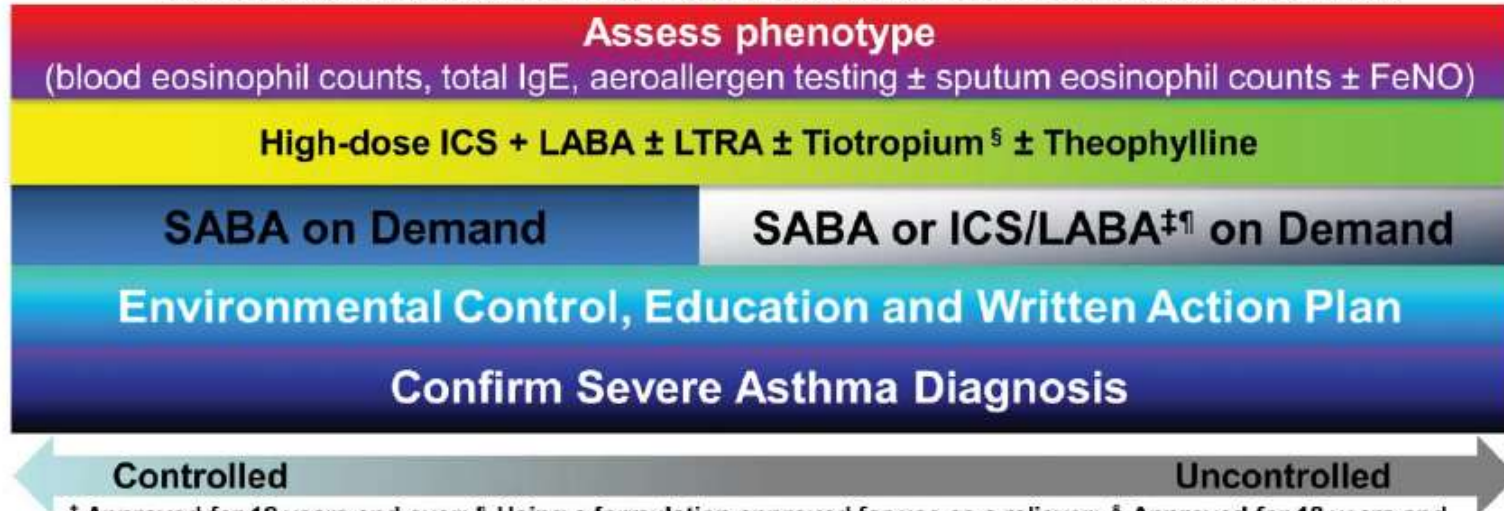
[§] In adults 18 years and over with moderate to severe asthma.

2017 Severe Asthma Management Continuum Children (6 years and over), Adolescents and Adults

- Regularly Reassess**
- Control
 - Spirometry or PEF
 - Inhaler technique
 - Adherence
 - Triggers
 - Comorbidities
 - Sputum eosinophils[§]



Tailor therapy based upon phenotype (order of presentation of medications does not imply a recommended sequence) for their use.



[‡] Approved for 12 years and over; [†] Using a formulation approved for use as a reliever; [§] Approved for 18 years and over; * Limited evidence and risk of QTc prolongation, MAIC infection, antibiotic resistance and hearing impairment;

He does not qualify for biologic therapy under current recommendations because these medications have not been trialed in children for asthma under the age of 6 years.

Options?



Reactive airways results from excessive or inappropriate immune activation in the airways. In this case, this activation appears to be stimulated by acute viral illness.



Anti-inflammatories stabilize his airways but at a cost.



What about IVIg?

Immunomodulatory doses of IVIg have been used in severe asthma



In this child IVIg was started, given every month. He is now well controlled only with ciclesonide and prn salbutamol-used occasionally.

But at what cost? He develops migraine type headaches for 2 days following each IVIg infusion-refractory to treatment. Mother feels this is a better outcome than PICU again.

Summary

New GINA guideline for children <5 years suggest:

- 1. Assess compliance at each visit
- 2. Intermittent ICS may be considered (although data supporting this is very limited-not recommended in Canadian guidelines)
- 3. Newer suggestions to escalate to increasing doses of ICS plus add on therapies such as leukotriene antagonists if control not achieved.
- 4. LABA addition when control not sufficient
- Goal is control. Prognosis-unknown.
- Trials for biologics not likely to be done in younger children any time soon.

- <https://ginasthma.org/2018-gina-report-global-strategy-for-asthma-management-and-prevention>
- <https://cts-sct.ca/guideline-library>
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