1 Hour Session and **Role of Allergy Testing & Allergy Control Measures in Improving Outcomes in Asthma**

March 19, 2021

12:00pm-1:00pm

OneCare Vermont

onecarevt.org

Title of Program: OneCare Vermont: Knowledge Hour Session

Title of Talk: Role of Allergy Testing & Allergy Control Measures in Improving Outcomes in Asthma

Speaker/Moderator: Dr. Cristina Carter, Dr. Norman Ward

Planning Committee Members: Dr. Norman Ward, Lindsay Morse, Adrienne Gil, Tawnya Safer

Date: March 19, 2021 Noon to 1:00pm

Workshop #: 21-267-08

Claiming Instructions

OneCare Vermont: Knowledge Hour Session - Dr. Cristina Carter with Timberlane Asthma and Allergy Associates
03/19/2021

Use the following link to access the claiming app, or scan the QR code below.

Claiming App:
http://www.highmarksce.com/uvmmed/index.cfm?do=ip.claimCreditApp&eventID=15981

Learning Objectives

1. Define the pathophysiology of allergic asthma
2. Appreciate the role of allergy testing in identifying environmental risk factors for allergic asthma
3. Identify allergy control measures to improve allergic asthma control, including allergen immunotherapy
4. Recognize the role of allergy testing and allergy control measures in improving outcomes in allergic asthma

DISCLOSURE:
Is there anything to disclose? ☐ Yes or ☒ No
Please list the Potential Conflict of Interest (*if applicable*): ****

☒ All Potential Conflicts of Interest have been resolved prior to the start of this program.
Yes or No (*If no, credit will not be awarded for this activity.)*
(CMIE staff members do not have any interests to disclose)

All recommendations involving clinical medicine made during this talk were based on evidence that is accepted within the profession of medicine as adequate justification for their indications and contraindications in the care of patients. ☒ Yes

COMMERCIAL SUPPORT ORGANIZATIONS *(if applicable)*: This activity is free from any commercial support

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The University of Vermont designates this internet live activity for a maximum of 1 *AMA PRA Category 1 Credit(s)*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

This program has been reviewed and is acceptable for up to 1 Nursing Contact Hours

Welcome

Norman Ward, MD
Chief Medical Officer

Agenda:

Session held via Microsoft Teams

	Presenter	Time
Noon-12:05pm	**Norman Ward, MD** Chief Medical Officer, OneCare Vermont Introduction & Session Logistics	5 Minutes
12:05pm-12:45pm	**Dr. Cristina Carter** Clinical Assistant Professor Department of Pediatrics UNIVERSITY OF VERMONT Larner College of Medicine Timber Lane Allergy & Asthma Associates, PC	40 Minutes
12:45pm-1:00pm	**Q&A**	15 Minutes

Presenter Bio: Dr. Cristina Carter

Cristina Carter, MD is a board certified allergist immunologist at Timber Lane Allergy & Asthma Associates in South Burlington, VT and a Clinical Associate Professor in Pediatrics at University of Vermont. She attended New York University School of Medicine, and completed her pediatric residency at Children's National Medical Center in Washington, DC. She then completed her fellowship training at the National Institutes of Health in Bethesda, MD in pediatric and adult allergy and immunology. Her clinical interests include food allergy, urticaria / angioedema, asthma and primary immunodeficiency. She sees both children and adults in clinical practice.

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1. Define the pathophysiology of allergic asthma
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Accreditation Designation Statement

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As a Jointly Accredited Organization, The Robert Larner College of Medicine at the University of Vermont is approved to offer social work continuing education by the Association of Social Work Boards (ASWB) Approved Continuing Education (ACE) program. Organizations, not individual courses, are approved under this program. State and provincial regulatory boards have the final authority to determine whether an individual course may be accepted for continuing education credit. The University of Vermont maintains responsibility for this course. Social workers completing this course receive 1 continuing education credits.

This activity was planned by and for the healthcare team, and learners will receive 1Interprofessional Continuing Education (IPCE) credit for learning and change.

OneCare Vermont
Asthma / COPD Learning Collaborative: Allergies & Allergic Asthma

CRISTINA CARTER, MD
CLINICAL ASSISTANT PROFESSOR
DEPARTMENT OF PEDIATRICS
UNIVERSITY OF VERMONT LARNER COLLEGE OF MEDICINE
TIMBER LANE ALLERGY & ASTHMA ASSOCIATES, PC

MARCH 19TH, 2021

Learning Objectives

- Define the pathophysiology of allergic asthma
- Recognize the role of allergy testing in identifying environmental risk factors for allergic asthma
- Identify allergy control measures to improve allergic asthma control, including allergen immunotherapy

Case

- 26-year-old female with a history of mild intermittent asthma is seen for her yearly physical.
- Chief complaint: difficulty breathing
  - Previous note:
    - Albuterol 2 puffs PRN exercise and with viral infections.

Case

- *What does this difficulty breathing feel like to you? Where is it coming from?*
  - *It's coming from my chest. My chest feels tight. I have trouble taking deep breaths in. I also seem to be more congested than usual, but that feels different.*
- *Do you have a cough, and is it dry or productive?*
  - *Oh yes, I have a dry cough throughout the day, and sometimes it wakes me up at night.*
- *What seems to trigger it?*
  - *I've noticed that when I'm at work, it seems a little less severe. After an hour of getting home, or on the the weekends, it's really bad.*
- *When did this start, and how frequently do you have symptoms?*
  - *It started pretty abruptly, about 2 months ago, after I moved in with my new roommate. I'm having symptoms every day.*
- *How often are you using albuterol? Do you wake up night coughing?*
  - *I use albuterol every day at night before bed. I wake up maybe once a week coughing.*

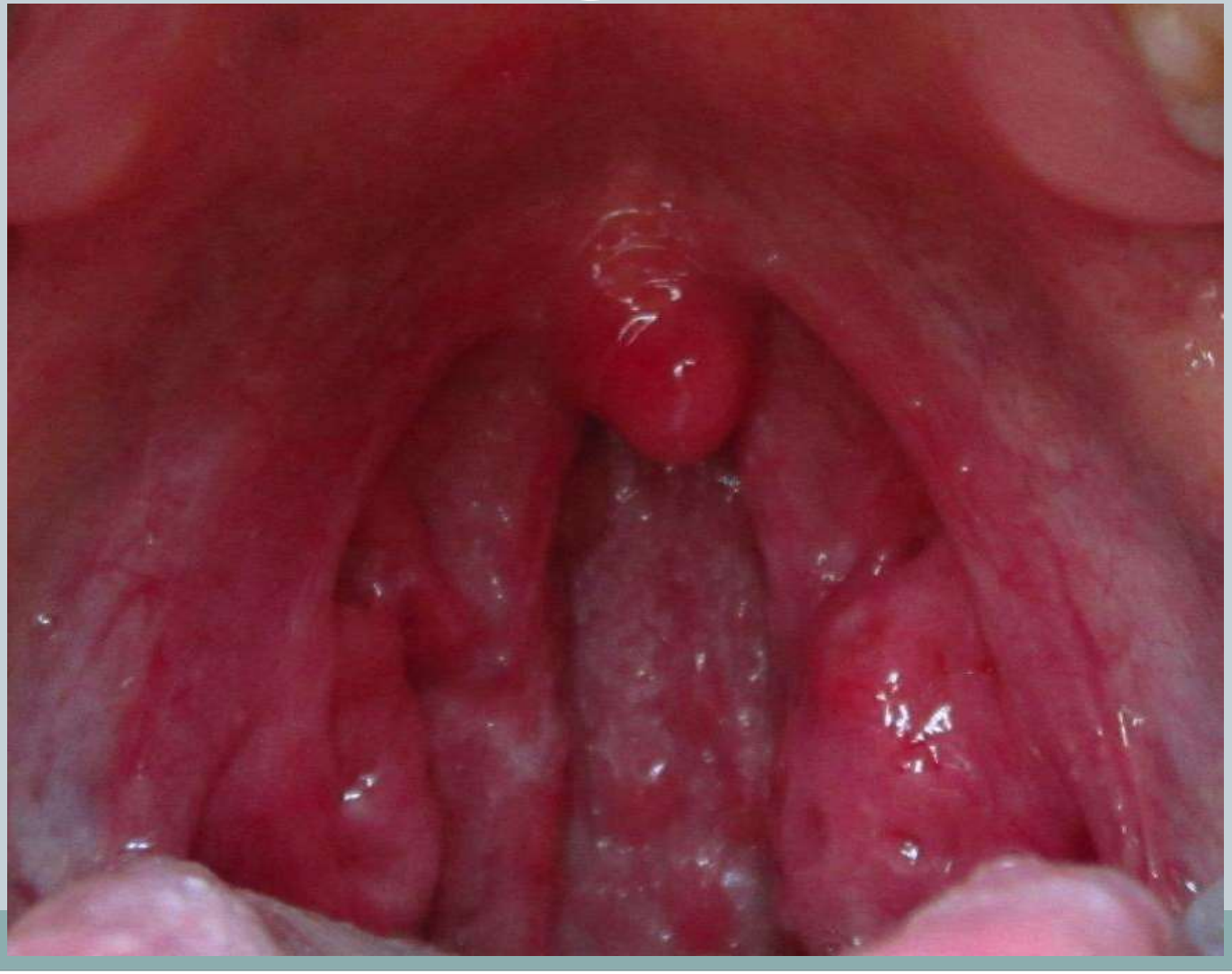
Case

- PMH:
  - Seasonal allergies – Zyrtec in spring and summer months
  - Atopic dermatitis – improved in teen years
- PSH:
  - Appendectomy at age 12
- Social history:
  - Lives with a new roommate, moved in about 2 months ago. Roommate has a dog and a cat. Older home, carpeted. Forced air.
- Medications:
  - IUD, Zyrtec PRN, albuterol PRN

Case

- PE:
  - Gen: NAD
  - HEENT: **Mild conjunctival injection**, normal TMs, **+cobblestoning posterior oropharynx**, no LAD
  - Resp: **Expiratory wheezing lower lung fields bilaterally**
  - CV: RRR, no m/r/g
  - GI: soft, NTND, no HSM
  - Skin: Clear

Cobblestoning in Posterior Oropharynx



Now What?

- Based on her history & exam, you believe her difficulty breathing is due to asthma
- Classify her asthma severity to then decide on an appropriate treatment course.

INITIAL VISIT: CLASSIFYING ASTHMA SEVERITY AND INITIATING THERAPY

(in patients who are not currently taking long-term control medications)

Level of severity (Columns 2–5) is determined by events listed in Column 1 for both impairment (frequency and intensity of symptoms and functional limitations) and risk (of exacerbations). Assess impairment by patient's or caregiver's recall of events during the previous 2–4 weeks; assess risk over the last year. Recommendations for initiating therapy based on level of severity are presented in the last row.

Components of Severity		Intermittent			Persistent								
					Mild			Moderate			Severe		
		Ages 0–4 years	Ages 5–11 years	Ages ≥12 years	Ages 0–4 years	Ages 5–11 years	Ages ≥12 years	Ages 0–4 years	Ages 5–11 years	Ages ≥12 years	Ages 0–4 years	Ages 5–11 years	Ages ≥12 years
Impairment	Symptoms	≤2 days/week			>2 days/week but not daily				Daily		Throughout the day		
	Nighttime awakenings	0	≤2x/month		1–2x/month	3–4x/month		3–4x/month	>1x/week but not nightly		>1x/week	Often 7x/week	
	SABA* use for symptom control (not to prevent EIB*)	≤2 days/week			>2 days/week but not daily	>2 days/week but not daily and not more than once on any day			Daily		Several times per day		
	Interference with normal activity	None			Minor limitation			Some limitation			Extremely limited		
	Lung function		Normal FEV_1 between exacerbations	Normal FEV_1 between exacerbations									
	→ FEV_1* (% predicted)	Not applicable	>80%	>80%	Not applicable	>80%	>80%	Not applicable	60–80%	60–80%	Not applicable	<60%	<60%
	→ FEV_1/FVC*		>85%	Normal†		>80%	Normal†		75–80%	Reduced 5%†		<75%	Reduced >5%†
Risk	Asthma exacerbations requiring oral systemic corticosteroids‡	0–1/year			≥2 exacerb. in 6 months, or wheezing ≥4x per year lasting >1 day AND risk factors for persistent asthma	≥2/year		*Generally, more frequent and intense events indicate greater severity.*					
		*Consider severity and interval since last asthma exacerbation. Frequency and severity may fluctuate over time for patients in any severity category. Relative annual risk of exacerbations may be related to FEV_1.**											
Recommended Step for Initiating Therapy *(See "Stepwise Approach for Managing Asthma Long Term," page 7)* *The stepwise approach is meant to help, not replace, the clinical decisionmaking needed to meet individual patient needs.*		Step 1			Step 2			Step 3	Step 3 medium-dose ICS* option	Step 3	Step 3	Step 3 medium-dose ICS* option or Step 4	Step 4 or 5
								Consider short course of oral systemic corticosteroids.					
		In 2–6 weeks, depending on severity, assess level of asthma control achieved and adjust therapy as needed. For children 0–4 years old, if no clear benefit is observed in 4–6 weeks, consider adjusting therapy or alternate diagnoses.											

AGES 12+ YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

Treatment	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 12+ Years				
	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6 ■
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA or PRN concomitant ICS and SABA ▲	Daily and PRN combination low-dose ICS-formoterol ▲	Daily and PRN combination medium-dose ICS-formoterol ▲	Daily medium-high dose ICS-LABA + LAMA and PRN SABA ▲	Daily high-dose ICS-LABA + oral systemic corticosteroids + PRN SABA
Alternative		Daily LTRA* and PRN SABA or Cromolyn,* or Nedocromil,* or Zileuton,* or Theophylline,* and PRN SABA	Daily medium-dose ICS and PRN SABA or Daily low-dose ICS-LABA, or daily low-dose ICS + LAMA, ▲ or daily low-dose ICS + LTRA,* and PRN SABA or Daily low-dose ICS + Theophylline* or Zileuton,* and PRN SABA	Daily medium-dose ICS-LABA or daily medium-dose ICS + LAMA, and PRN SABA ▲ or Daily medium-dose ICS + LTRA,* or daily medium-dose ICS + Theophylline,* or daily medium-dose ICS + Zileuton,* and PRN SABA	Daily medium-high dose ICS-LABA or daily high-dose ICS + LTRA,* and PRN SABA	
		Steps 2–4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherapy in individuals ≥ 5 years of age whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy ▲			Consider adding Asthma Biologics (e.g., anti-IgE, anti-IL5, anti-IL5R, anti-IL4/IL13)**	

Assessment & Plan

- Assessment:
  - Moderate persistent asthma with an acute exacerbation
- Plan:
  - Prednisone taper
  - Symbicort 80 mcg/ 4.5 mcg, 2 puffs BID with spacer
  - For rescue inhaler:
    - Albuterol PRN cough / chest tightness
    - Use Symbicort for a maximum total daily maintenance and rescue dose of 12 puffs (for her, 8 puffs max per day)
  - Referral to an allergy specialist for an allergy & asthma evaluation

At the Allergist's Office…

Skin Prick Testing

Allergen New List 5.0

TLAAA ID: 43532-1 Percutaneous Device HS Quintip Performed by: See Note

Aeroallergens

Allergen	PC	ID
Timothy	0	
June	0	
Rye	0	
Sage	10/	
S. Ragwd	0	
G. Ragwd	0	
Lamb's Q	0	
Mugwort	10/	

Aeroallergens

Allergen	PC	ID
E. Plant.	0	
Pigweed	0	
Sorrell	0	
Nettle	0	
Oak	10/	
Maple	3/1	
Hickory	0	
Ash	0	

Aeroallergens

Allergen	PC	ID
Poplar	2	
Willow	3/5	
Elm	0	
Birch	15/	
Alder	5/2	
E Ced	0	
DP	15/	
DF	10/	

Aeroallergens

Allergen	PC	ID
Cat Gly	5/1	
Cat AP	10/	
Feather	0	
Dog AP	5/1	
Dog ALK	0	
Horse	0	
Mouse	0	
Fusariu	0	

Aeroallergens

Allergen	PC	ID
Alternaria	0	
Aspergill.	0	
Helminth.	0	
Penicil.	0	
Cladosp.	0	
Rhizopus	0	
Diluent	0	
Histamine	5/1	

Mixes ID

Tree Mix 1
Tree Mix 2
Tree Mix 3
Grass Mix
Mite Mix

Mixes ID

Weed Mix A
Weed Mix B
Weed Mix C
Weed Mix D
Mold Mix A
Mold Mix B

Other Allergens

	PC	ID
Rabbit		
Hamster		
G. Pig		
Rat		

Other Allergen

	PC	ID
Gerbil		
Parakeet		
CRoach		
Cow		

Other Allergen

	PC	ID
Boxeld	5/1	
Mulber	3/5	
Sycam	2/5	
Cocklb	0	

Common Foods Percutaneous

Peanut	Hazelnut
Walnut	Pistachio
Almond	Brazil nut
Peacn	Soy
Cashew	Wheat

Common Foods Percutaneous

Shrimp	Oyster
Lobster	Milk
Crab	Casein
Clam	Egg Whole
Scallop	Egg white

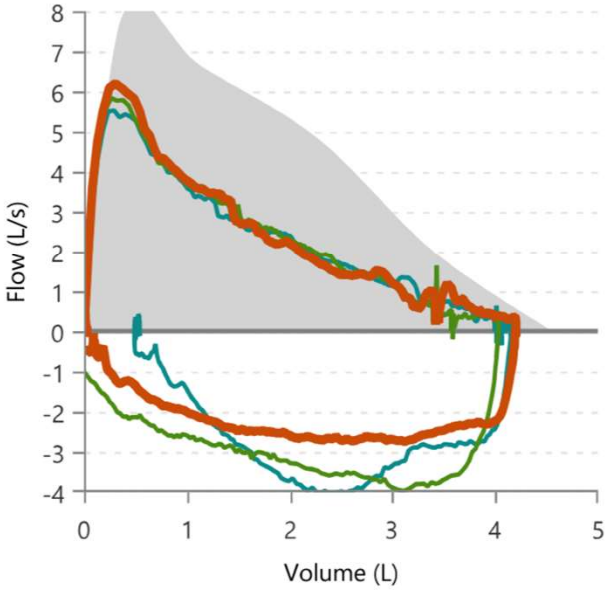
Foods Percutaneous

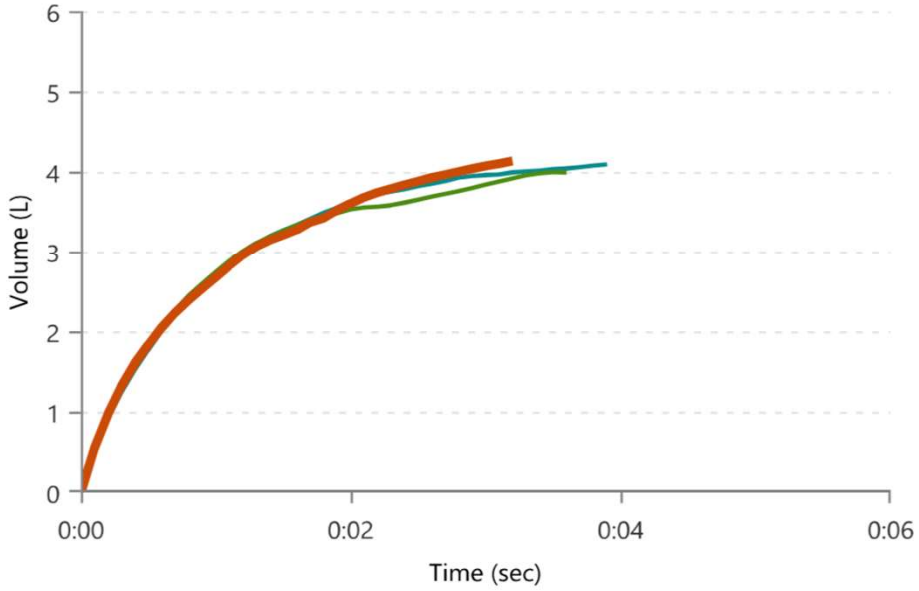
Skin Tests. Physician's Interpretation.

Positive to: ☑ dust mites ☑ cat ☑ dog ☐ other animals ☑ tree ☐ grass ☑ weed ☐ mold

LLN: 70%

FVC





		Pred.	Best	% Pred.	#1	#2	#3
FEV1/FVC	%	84.86	66.12	78%	66.43	68.89	64.78
FVC	L	4.55	4.20	92%	4.15	4.03	4.20
FEV1	L	3.81	2.78	73%	2.76	2.78	2.72
FEF 25-75	L/sec	3.88	1.84	47%	1.94	2.08	1.84
PEF	L/sec	7.95	6.20	78%	5.53	5.83	6.20
Evol	L	---	0.05	0%	0.06	0.04	0.05

Phenotypes of Asthma

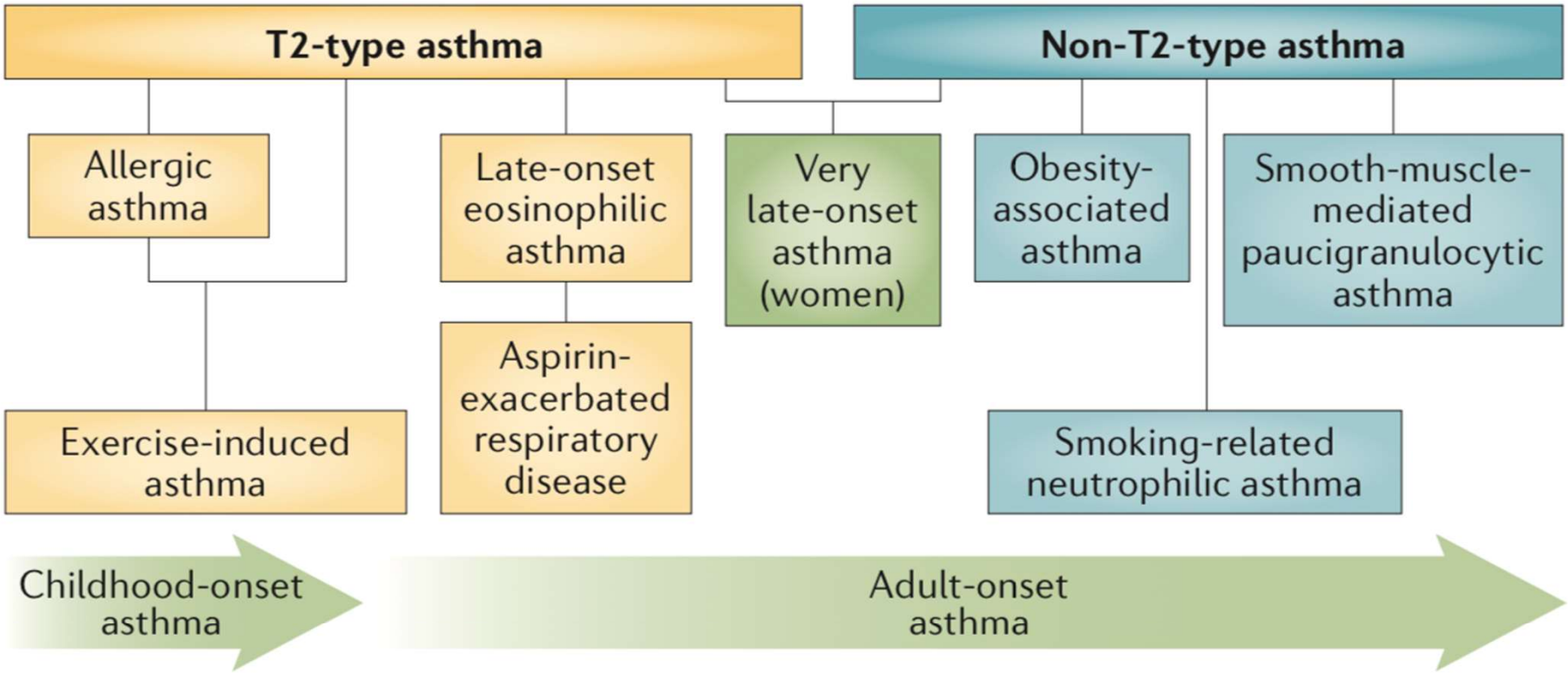
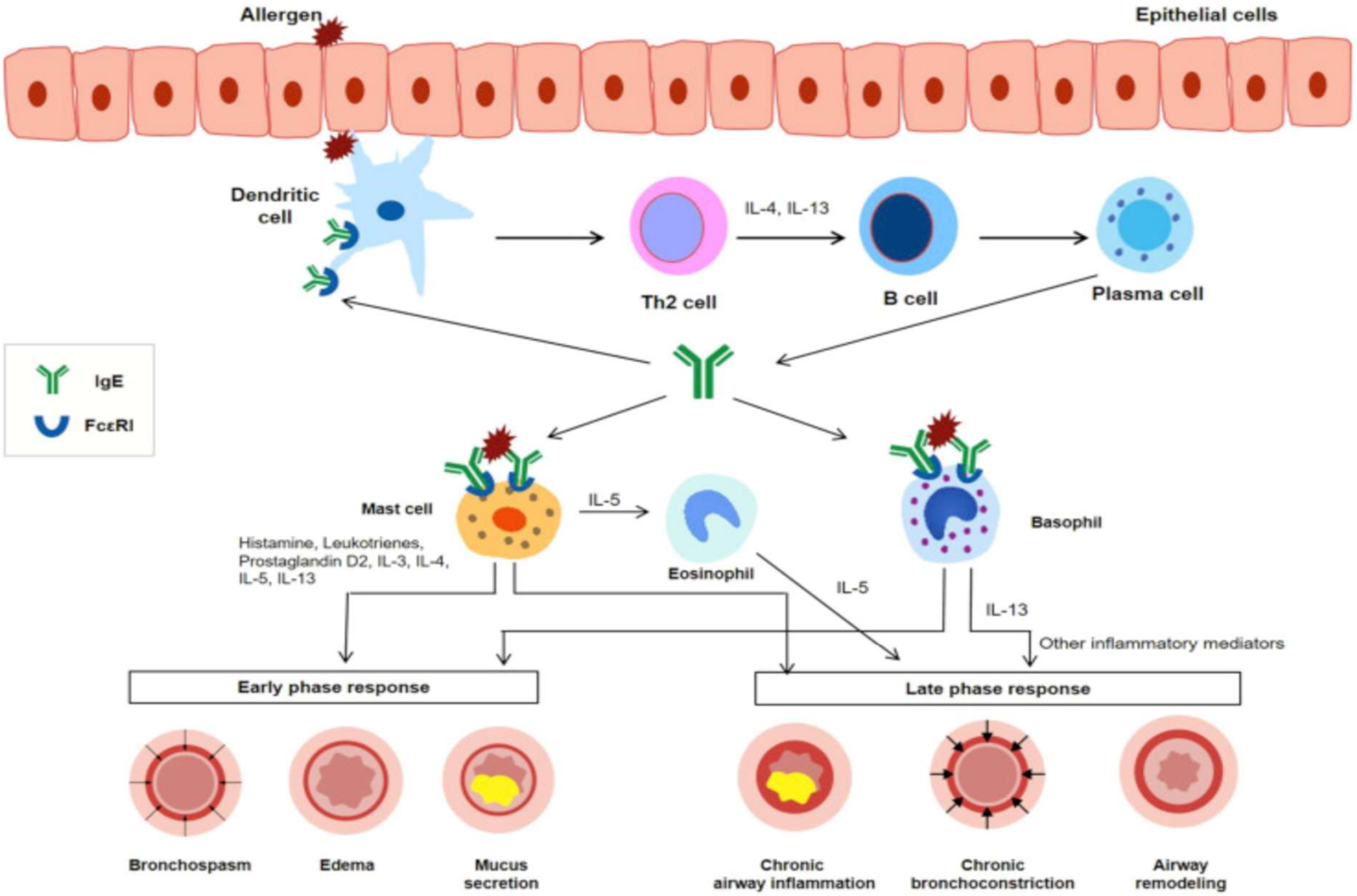


Figure 1 | **Selected asthma subphenotypes.** New subphenotypes and associated causal pathways, or endotypes, of asthma are being discovered through the application of non-hierarchical statistical analyses of clinical, physiological and laboratory characteristics. Figure from REF. 163, Nature Publishing Group.

Sly et al. Asthma. *Nature Reviews.* 1(1): 2015. doi:10.1038/nrdp.2015.25

Pathophysiology of Allergic Asthma



Papadopoulos et al. IgE mediated Multimorbidities in Allergic Asthma and the Potential for Omalizumab Therapy. *J Allergy Clin Immunology In Pract.* 7(5): 2019.

Components of a Treatment Plan

- Preventive Strategies
- Medical Therapy
- Immune Modulating Therapy

Preventive Measures: Does it Help Allergic Asthma?

2020 FOCUSED UPDATES TO THE Asthma Management Guidelines

CLINICIAN'S GUIDE

- **Single intervention studies** were NOT associated with improvement in clinical asthma outcomes (i.e. reduction of exacerbations, improved pulmonary function); most strategies showing inconclusive results or no effect.
  - Ex) acaracides, air purifiers, impermeable mattress covers
- **Multicomponent intervention studies** demonstrated improvement in various outcomes, but no specific combination of interventions was identified as more effective than others.
  - High or moderate strength evidence suggests that HEPA vacuums or pest control may be effective in reducing exacerbations and improving QOL.
- For many primary outcomes for both single and multicomponent interventions, the **evidence is inconclusive because of a lack of studies**.
- Further research is to detect clinically meaningful differences in validated and relevant asthma outcomes.

Allergy Prevention Measures: Pollens

Tree pollens: March – June

Grass pollens: May – June

Weeds pollens: August – September

- During pollen season try to maintain bedroom as reduced exposure area
- Keep windows closed, avoid fans, use air conditioning or fans with window filters rather than open windows
- Drive with windows closed

Allergy Prevention Measures: Dust Mites

Dust mites: year-round, especially fall

- To reduce dust mite burden, buy dust mite encasings on pillow and mattress
- Wash sheets in *hot* water weekly
- Minimize carpeting, curtains, stuffed animals in bedroom
- Maintain humidity 25-50%

Allergy Prevention Measures: Animals

Animals: year-round

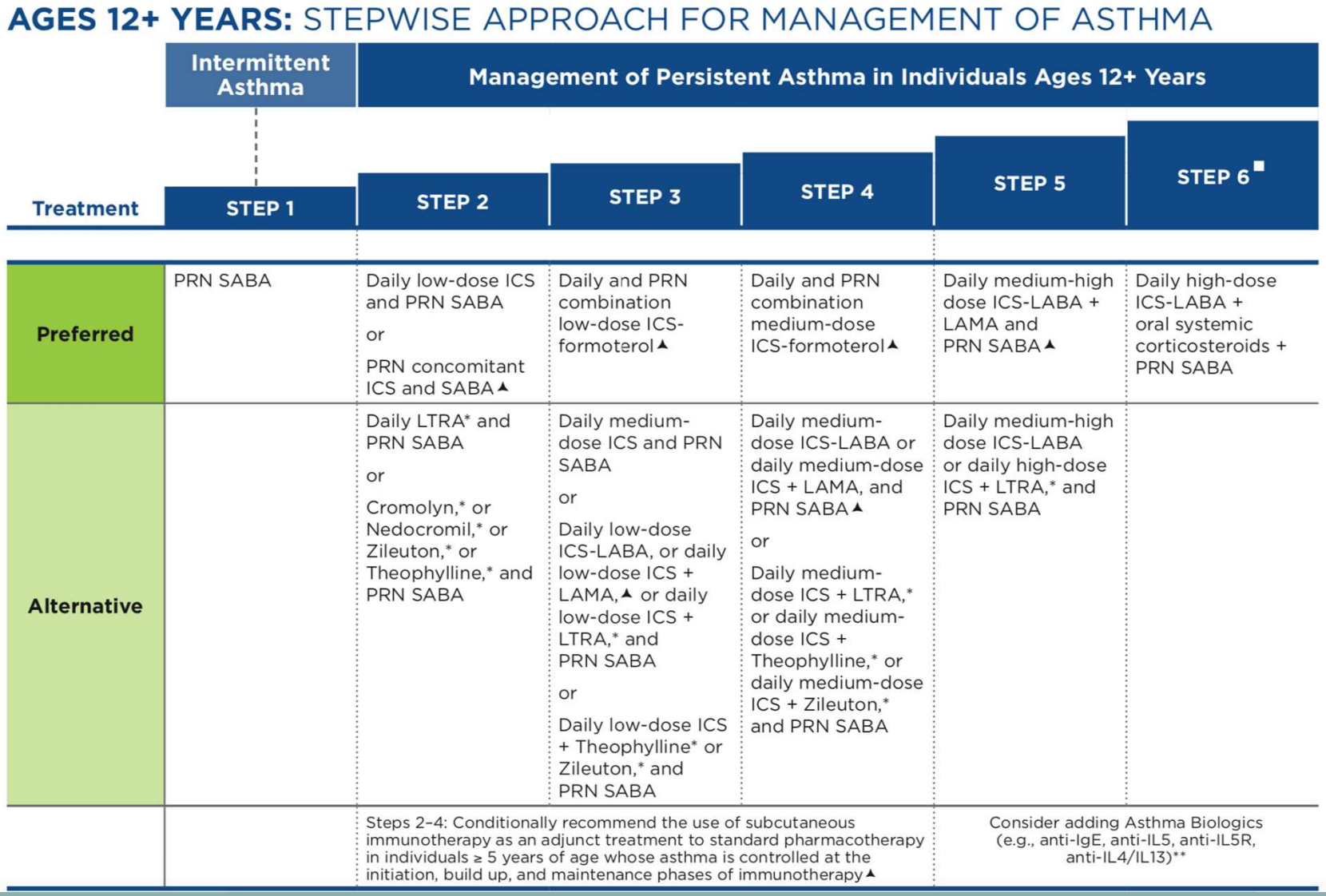
- Eliminating or reducing carpet
- HEPA filter
- Allergy encasings for pillow and mattress, and allergy appropriate vacuum may help
- Keep animal out of bedroom if possible

Allergy Prevention Measures: Molds

Molds: year-round, especially fall

- Remove obvious mold
- Minimize humidity / leaks
- Maintain humidity 25-50%

Medical Therapy Options for Asthma



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		Steps 2–4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherapy in individuals ≥ 5 years of age whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy▲			Consider adding Asthma Biologics (e.g., anti-IgE, anti-IL5, anti-IL5R, anti-IL4/IL13)**	

Medical Therapy Options

- Allergic Rhinitis (seasonal or perennial):
  - 1) Nasal Steroid, 1 – 2 sprays in each nostril 1-2x daily
    - Rhinocort (budesonide) is unscented and first line in pregnancy
  - 2) Nasal antihistamine (Azelastine), 1 - 2 sprays 1-2x daily
    - Can be used as primary treatment for SAR
    - Can be used in conjunction with Flonase for severe SAR or PAR
  - 3) Antihistamines, 1 – 2x daily
    - Cetirizine 10 mg or Loratadine 10 mg or Fexofenadine 180 mg
      - Allegra is the least sedating of the antihistamine medications
      - Decongestant formulations should NOT be used long-term

Medical Therapy Options

- 4) Montelukast
  - FDA Black box warning due to concern for neuropsychiatric side effects
  - Sansing-Foster et al. Risk of Psychiatric Adverse Events Among Montelukast Users. *J Allergy Clin Immunol In Pract.*. 9(1): Jan 2021.
    - Study Objective: To determine whether there are associations of depressive disorders, self-harm, and suicide with use of montelukast compared with inhaled corticosteroid (ICS) use.
    - Conclusion: *"When compared with use of ICS, we did not find associations between montelukast use and hospitalizations for depression or self-harm events. Our findings should be interpreted considering the study's limitations. Psychiatric comorbidity was common, and most PAEs occurred in patients with a past psychiatric history."*

Allergen Immunotherapy: Does it Help Allergic Asthma?

2020 FOCUSED UPDATES TO THE Asthma Management Guidelines

CLINICIAN'S GUIDE

- Subcutaneous immunotherapy (SCIT) reduces the use of long-term control medications.
- SCIT improves quality of life, reduces the use of quick-relief medications, reduces the need for systemic corticosteroids, and improves FEV1.
- Insufficient evidence regarding the effect of SCIT on asthma symptoms and health care utilization.
- Local and systemic allergic reactions are frequent but infrequently required a change in treatment.

Allergen Immunotherapy

- IT may prevent additional sensitizations and reduce chance of developing asthma, alter natural history of the disorder and reduce use pharmacotherapy.
- Injection immunotherapy (allergy shots) can contain multiple allergens.
- Sublingual immunotherapy: grass (Grastek, approved age 5-65), ragweed (Ragwitek, approved age 18-65), dust mite (Odactra, approved age 18-65).

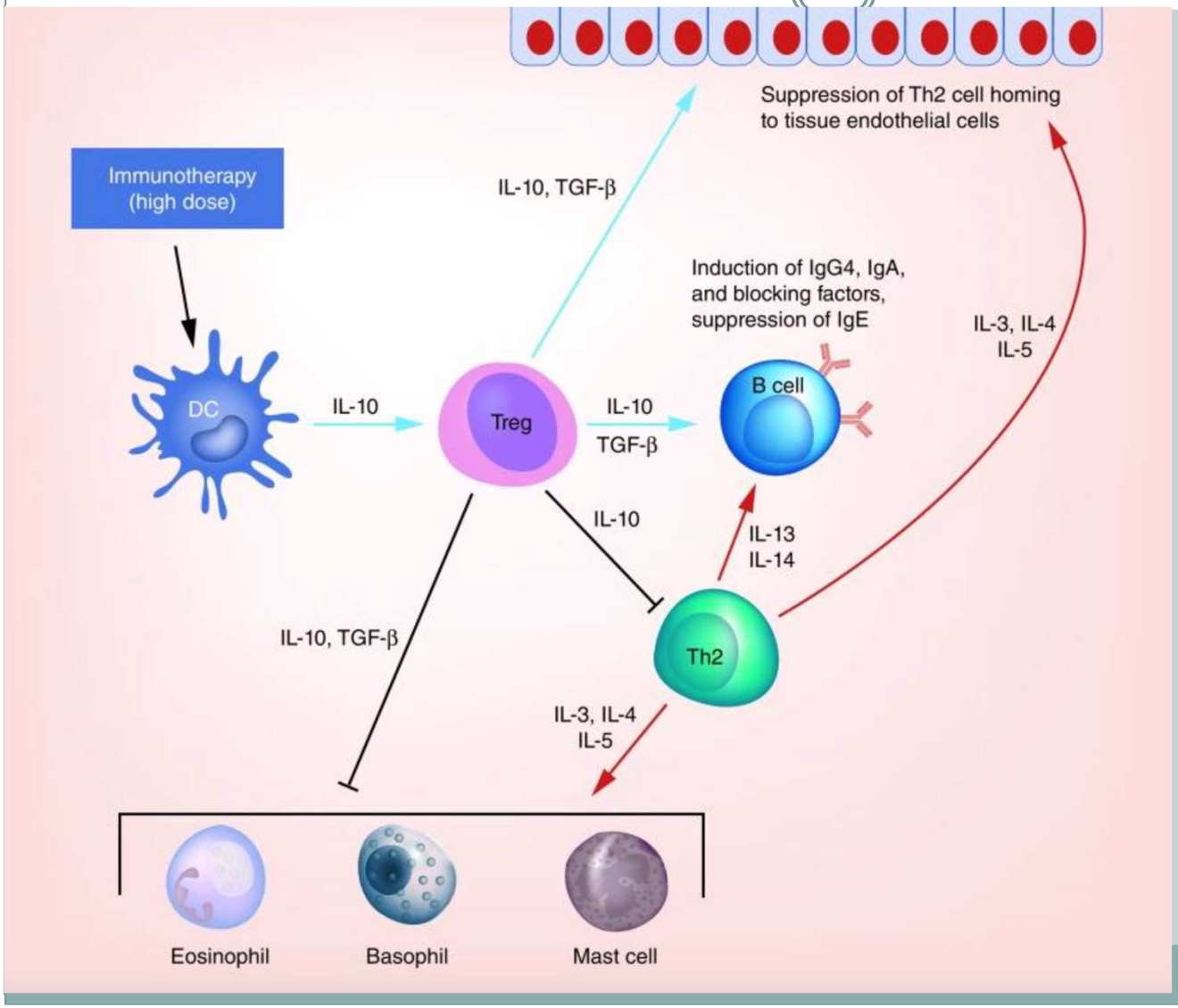
Allergen Immunotherapy

- Long-lasting effects of SCIT and SLIT are maintained at least 7–12 years after discontinuation of treatment
- 2010 Cochrane review of SCIT for asthma assessed the impact of SCIT on bronchial hyper-responsiveness (BHR) with data from 19 studies that reported allergen specific BHR and 18 studies that reported nonspecific BHR
  - While there was an overall reduction in nonspecific BHR after SCIT and treated patients were significantly less likely to develop increased nonspecific BHR, SCIT introduced significant reductions in allergen specific BHR
- Steroid-sparing effect of IT has been demonstrated in multiple studies
  - A 2010 RCT reported a steroid-sparing effect with mite allergoid SCIT in children with mite-induced allergic asthma. The mean daily dose of fluticasone propionate in the treatment group 2 years post-SCIT dropped to 151.1 µg, compared with 330.3 µg at baseline

Allergen Immunotherapy

- Indications:
  - Allergic rhinitis
  - Allergic conjunctivitis
  - Allergic atopic dermatitis
  - Allergic asthma
- Schedule:
  - Build-up: once or twice weekly injections for 3-6 months (24 shots total)
  - Maintenance: once weekly injections for 4-5 years
- Clinical Outcomes:
  - Expect clinical improvement within 6 mo – 1 year of initiation
  - If no improvement after 2 years, stop the course early

How does immunotherapy work?



- Balance between Th2 cells and Treg cells is crucial for the development or suppression of allergic inflammation
- **Decrease in mast cell and basophil reactivity**
- Antigen-specific T_{reg} and B_{reg} increases during both natural allergen exposure and IT; secrete IL-10, essential for the **induction of T-cell tolerance**
- Successful IT results in a **diminished late-phase response**, which involves the recruitment, activation and persistence of eosinophils and T cells at sites of allergen exposure

Allergist's Plan

- Prevention:
  - Keep animals out of bedroom, wash sheets weekly in hot water, allergen encasings for mattress / pillows, HEPA filter in bedroom
- Medical Therapy:
  - Continue Symbicort 80 mcg 2 puffs BID with PFT reassessment in 1 month
  - Start Flonase 2 sprays in each nostril at night followed by Astelin 2 sprays in each nostril at night
- Immune Modulating Therapy:
  - Start allergen immunotherapy for pollens, dust mite, animals

References

- Abramson et al. Injection allergen immunotherapy for asthma. *Cochrane Database Syst Rev. 8:CD001186*. 2010.
- Burks et al. Update on allergy immunotherapy: American Academy of Allergy, Asthma; Immunology/European Academy of Allergy and Clinical Immunology/PRACTALL consensus report. *J Allergy Clin Immunol*. 131(5): 2013.
- Madonini et al. Steroid-sparing effects with allergen-specific immunotherapy in children with asthma: a randomized controlled trial. *J Allergy Clin Immunol*. 126(5):942-9: 2010.
- Papadopoulos et al. IgE mediated Multimorbidities in Allergic Asthma and the Potential for Omalizumab Therapy. *J Allergy Clin Immunol In Pract.* 7(5): 2019.
- Robinson et al. Comparative Effectiveness Review 196: The Role of Immunotherapy in the Treatment of Asthma. *AHRQ Publication* No. 17(18)-EHC029-EF: 2018.
- Umscheid et al. Comparative Effectiveness Review 201: Effectiveness of Indoor Allergen Reduction in Management of Asthma. *AHRQ Publication* No. 18-EHC002-EF: 2018
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UVM CME/CEU

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Who to Contact with Questions:

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