SCIT SCRIPTS 101: MAKING YOUR SCRIPTS THE MOST EFFECTIVE

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DISCLOSURES

- No financial or relevant disclosures.

OBJECTIVES

- Identify indications which warrant immunotherapy (IT) consideration
- Understand allergen cross-reactivity and factors which affect allergen potency
- Be able to discuss dosing ranges for perennial and seasonal allergens
- Discuss other IT aspects to achieve "effectiveness"

EFFECTIVENESS

- Is what you are doing achieving the intended outcome or objective

AIT INDICATIONS

- Allergic rhinitis
- Allergic conjunctivitis
- Allergic asthma
- Atopic dermatitis*
- Stinging insect allergy (VIT)

* Mainly focused on dust mite sensitization. Yepes-Nunez JJ et al. J Allergy Clin Immunol. 2023 Jan;151(1):147-158.

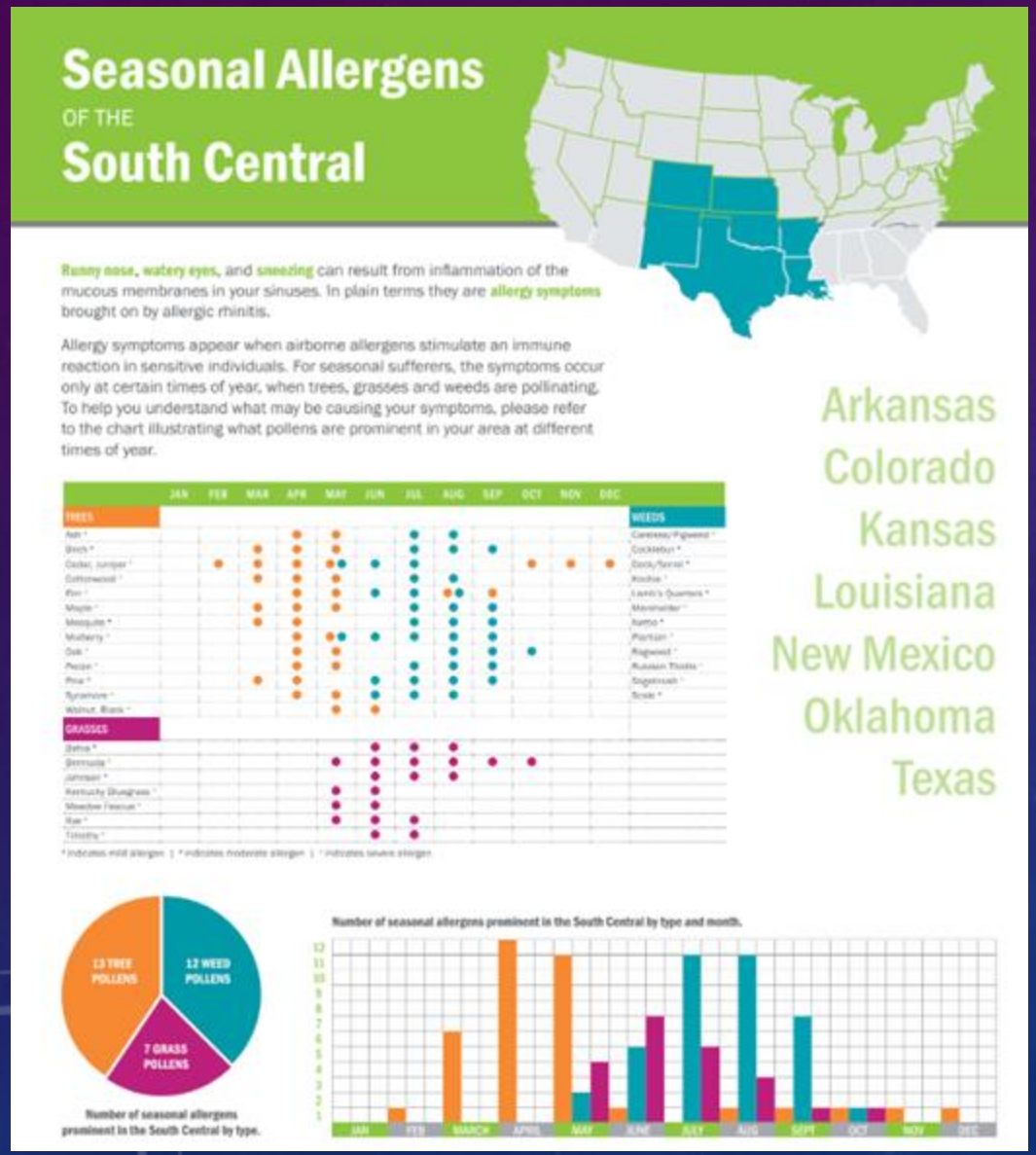
AIT ROUTES

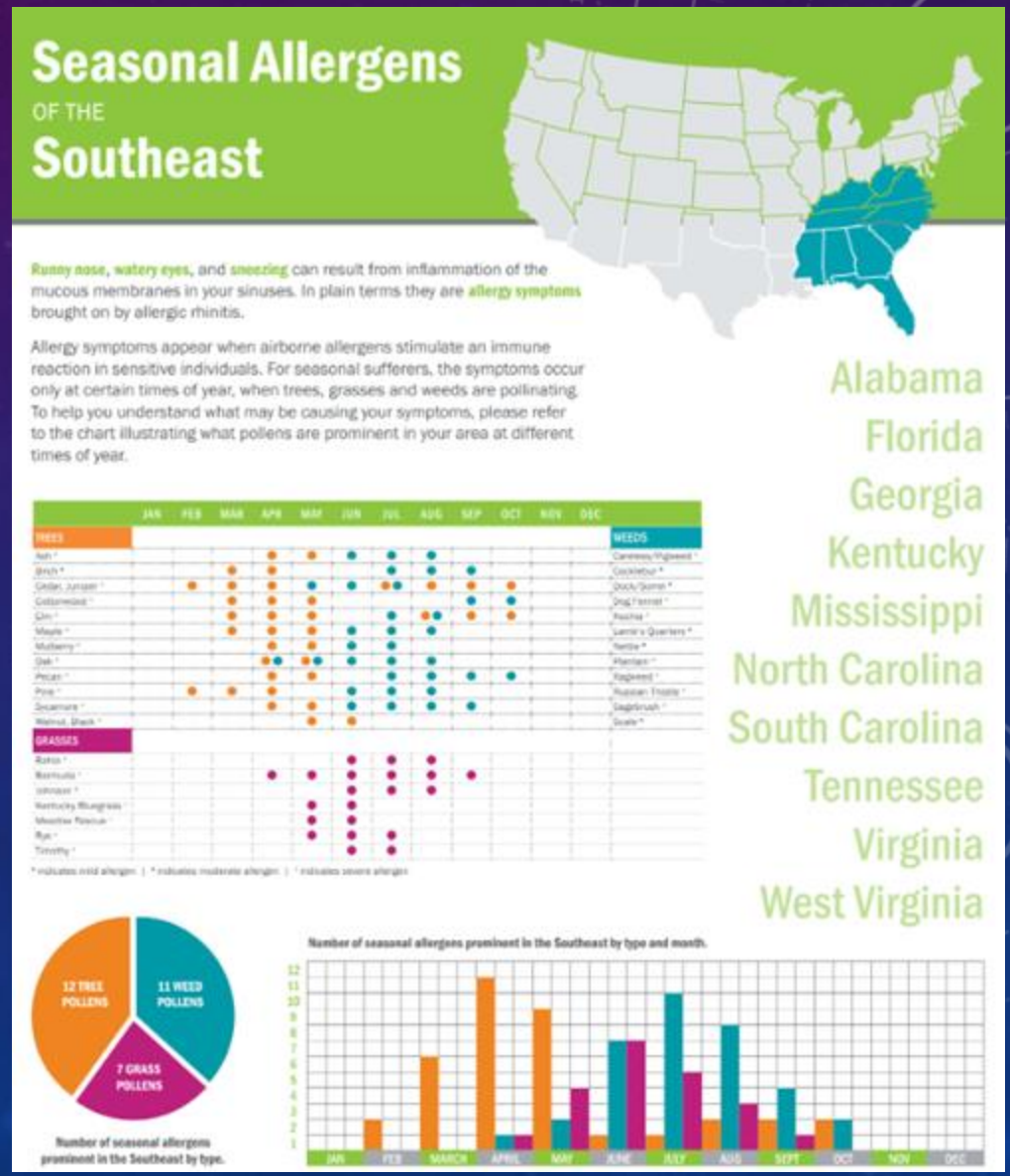
- Subcutaneous immunotherapy (SCIT) - "allergy shots"
- Sublingual immunotherapy (SLIT) - "allergy drops"
- Intralymphatic immunotherapy (ILIT)
- Epicutaneous immunotherapy (EPIT)
- Oral immunotherapy (OIT)

SENSITIZATION ≠ CLINICALLY RELEVANT

- Clinical history
- Allergy testing
  - Skin prick testing
  - Intradermal testing
  - sIgE
  - Nasal provocation
  - Exposure chambers
- Geographic relevance

GEOGRAPHIC RELEVANCY





ALLERGEN TYPES

Standardized	Non-standardized
House dust mite (HDM)	Trees
Cat dander	Most weeds
Bermuda, kentucky blue, rye, timothy	Johnson grass, bahia
Short ragweed	Dog dander

- Dog dander
  - dog AP
  - dog UHF
- Molds
  - Outdoor (alternaria, cladosporium)
  - Indoor (aspergillus, penicillium)
- Non-standardized extracts are based on dry weight (w/v)
- Significant variation in # of allergens, relative potency, etc.

WRITING SCIT PRESCRIPTIONS

- Ideal dose of each allergen
- Cross-reactivity
- Interactions which can lead to extract degradation
- Stationary vs mobile population
- Ultimately up to the prescriber's discretion

PROBABLE EFFECTIVE DOSE (PED)

TABLE IX. Probable effective dose range for standardized and nonstandardized US- licensed allergen extracts

Allergenic extract	Labeled potency or concentration	Probable effective dose range	Range of estimated major allergen content in US-licensed extracts
Dust mites: *D farinae* and *D pteronyssinus*	3,000, 5,000, 10,000, and 30,000 AU/mL	500-2,000 AU	10,000 AU/mL 20-160 μg/mL Der p 1, Der f 1* 2-180 μg/mL Der p 2, Der f 2* 78-206 μg/mL Der p 1, Der f 1† 13-147 μg/mL Der p 2, Der f 2†
Cat hair	5,000 and 10,000 BAU/mL	1,000-4,000 BAU	10,000 BAU/mL 20-50 μg/mL Fel d 1*‡ 30-100 μg/mL cat albumin§
Cat pelt	5,000-10,000 BAU/mL	1,000-4,000 BAU	10,000 BAU/mL 20-50 μg/mL Fel d 1*‡ 400-2,000 μg/mL cat albumin§
Grass, standardized	100,000 BAU/mL	1,000-4,000 BAU	100,000 BAU/mL 425-1,100 μg/mL Phl p 5* 506-2,346 μg/mL group 1‖
Bermuda	10,000 BAU/mL	300-1,500 BAU	10,000 BAU/mL 141-422 Cyn d 1 μg/mL*
Short ragweed	1:10, 1:20 wt/vol, 100,000 AU/mL	6-12 μg of Amb a 1 or 1,000-4,000 AU	1:10 wt/vol 300 μg/mL Amb a 1‡ Concentration of Amb a 1 is on the label of wt/vol extracts
Nonstandardized AP Dog	1:100 wt/vol	15 μg of Can f 1	80-400 μg/mL Can f 1† 10-20 μg/mL dog albumin¶
Nonstandardized extract, dog	1:10 and 1:20 wt/vol	15 μg of Can f 1	0.5 to 10 μg/mL Can f 1† <12-1,500 μg/mL dog albumin¶
Nonstandardized extracts: pollen	1:10 to 1:40 wt/vol or 10,000-40,000 PNU/mL	0.5 mL of 1:100 or 1:200 wt/vol	NA
Nonstandardized extracts: mold/fungi, cockroach	1:10 to 1:40 wt/vol or 10,000-40,000 PNU/mL	Highest tolerated dose	NA
Hymenoptera venom	100 μg/mL single venom 300 μg/mL in mixed vespid extract	50-200 μg of each venom	100-300 μg/mL of venom protein
Imported fire ant	1:10 to 1:20 wt/vol whole-body extract	0.5 mL of a 1:100 wt/vol to 0.5 mL of a 1:10 wt/vol extract	NA

Cox L et al. Allergen immunotherapy: A third practice parameter update. J Allergy Clin Immunol. 2011; 127(1): S1-S55.

DUST MITE

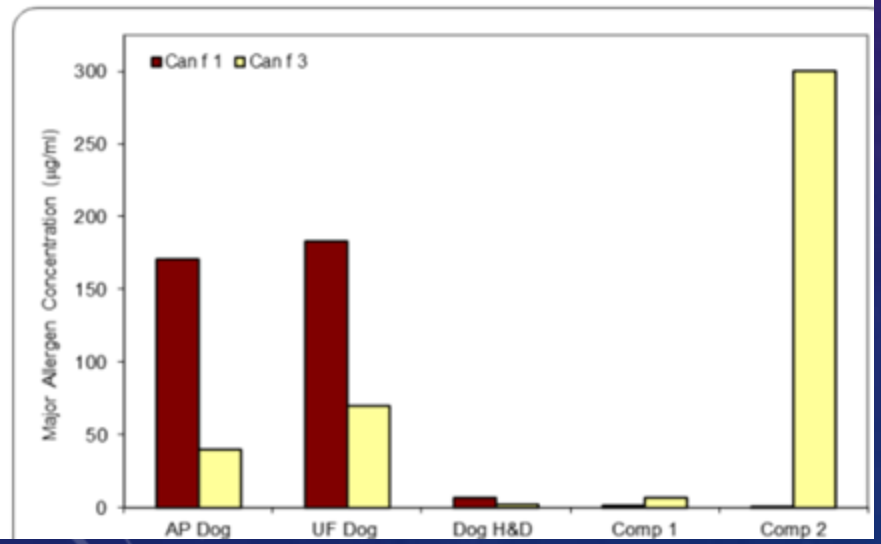
- Goal: 500-2,000 AU for maintenance dose
- Supplied at 10,000 AU/mL
- If the 1:1 v/v 5mL maintenance vial contains 1 mL of a 10,000 AU/mL dust mite extract
  - Maintenance vial has 10,000 AU
    - Administer a 0.5mL dose of a 5mL vial is 1/10th of the contents
    - 1/10th of 10,000 AU is 1,000 AU per 0.5 mL dose of the maintenance vial
- If you add 0.2mL of dust mite for maintenance vial then it will have 2,000 AU in vial. A 0.5mL dose of this vial will contain 200 AU per dose.

DOG DANDER

Sample	Can f 1 (µg/ml)	Can f 3 (µg/ml)
AP Dog Hair & Dander (1:100 w/v)	171	40
UF Dog Hair & Dander (1:650 w/v)	183	70
Dog Hair & Dander (1:10 w/v)	5-10	2
Competitor 1 (Dog Hair & Dander, 1:10 w/v)	2	5-10
Competitor 2 (Dog Epithelia, 1:20 w/v)	< 1	300

Figure 3: Chart of Allergen Concentrations

Values taken from Table 3.



- Goal: 15 ug protein for maintenance dose
- 1mL of 1:10w/v - 10ug
- 10ug in 5mL vial that you added 1mL
- Giving a 0.5mL maintenance dose = 1/10th of the 5mL vial = 1/10th of 10ug = 1ug protein/dose

https://www.hsally.com/wp-content/uploads/2022/10/UF-Dog-Technical-Report-Final-June-2021.pdf

PROTEOLYTIC ACTIVITY

- Mold
- Cockroach
- Dust mite can be mixed with pollen and pet dander without deleterious effects

Allergenic Extract	Protease-containing Extracts: Insects	Fungi	Mites	Comments
Insects	∅	⊕	⊕	Whole-body insect extracts contain very high protease levels; susceptible to endogenous proteases unless stored in 50% glycerin
Fungi	⊕	⊕	⊕	Fungal extracts do not appear to be adversely affected by proteases;
Mites	∅	∅	⊕	Mite allergens resistant to insect and fungal proteases if stored in ≥ 10% glycerin.
Pollens	⊗	⊗	⊕	Pollen extracts susceptible to insect and fungal proteases; compatible with mite extracts when stored in ≥ 10% glycerin.
Cat hair/epithelia	⊕	⊕	⊕	Fel d 1 in cat extract is highly resistant to fungal and insect proteases
Dog hair/epithelia	⊕	∅	⊕	Dog allergens susceptible to most fungal extracts, but more stable when mixed with insect extracts.

Esch RE. Allergen immunotherpy What can and cannot be mixed? J Allergy Clin Immunol 2008; 659-660.

CROSS REACTIVITY

- One study demonstrated up to 25% of US-made allergen extracts could be reduced by 50% if cross-reactivity was considered

Allergen	Cross-reactive
Cedar	Cypress
Ash	Olive, privet
Cottonwood	Willow
Timothy	Rye, orchard, Kentucky blue
Oak	beech
Birch	alder

* timothy, Johnson, and Bermuda account for almost all US grasses

Esch RE. Allergen immunotherapy What can and cannot be mixed? J Allergy Clin Immunol 2008; 659-660.

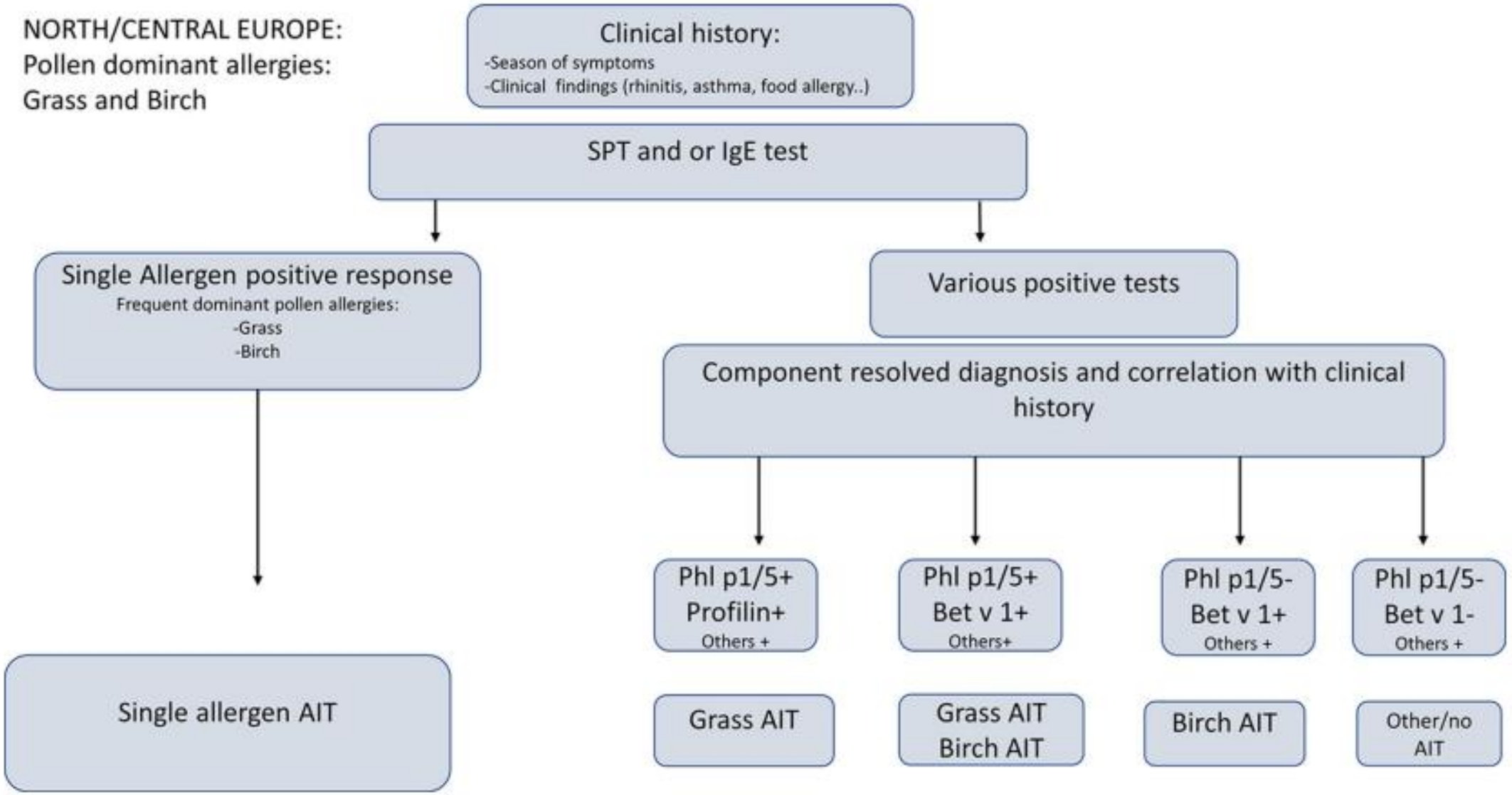


Figure 10 Suggested algorithm for areas with high exposure to grasses and birch pollen

SYSTEMIC REACTIONS

Table 3 Summary of Identified Risk Factors for Patients with Systemic Reactions to SCIT

Risk factor	Number of patients
1. First injection from a new serum vial	4
2. Seasonal exacerbation of allergic disease	4
3. History of previous systemic reactions to SCIT	3
4. Sub-optimally controlled asthma	2
5. Omission of pre-medication	1
6. Exercise 1 h prior to injection	1
7. ACE-Inhibitor and NSAID usage coinciding with injection	1
8. Intramuscular administration	1

ACE Angiotensin converting enzyme, *NSAID* Nonsteroidal anti-inflammatory drug, *SCIT* Subcutaneous immunotherapy

My observations
Any Asthma (4-fold)
Faster protocols (cluster, rush)
Too much grass
Too much cat
Wrong patient
Buildup >> maintenance
Buildup during pollen season

Aue et al. Systemic reactions to subcutaneous allergen immunotherapy: real-world cause and effect modelling Allergy Asthma Clin Immunol (2021) 17:65.

OTHER ASPECTS OF "EFFECTIVENESS"

- Counseling on the different SCIT "phases"
- Safety
  - Mandatory wait time
  - Risk for systemic reaction
- Reaching the desired maintenance dose
- Reassessment
  - Combined symptoms and medication score (CSMS) (0-6)
- Trial off SCIT
- Biomarkers for long-term success (i.e., "cured")
- Minimizing systemic reactions

OTHER ASPECTS OF "EFFECTIVENESS"

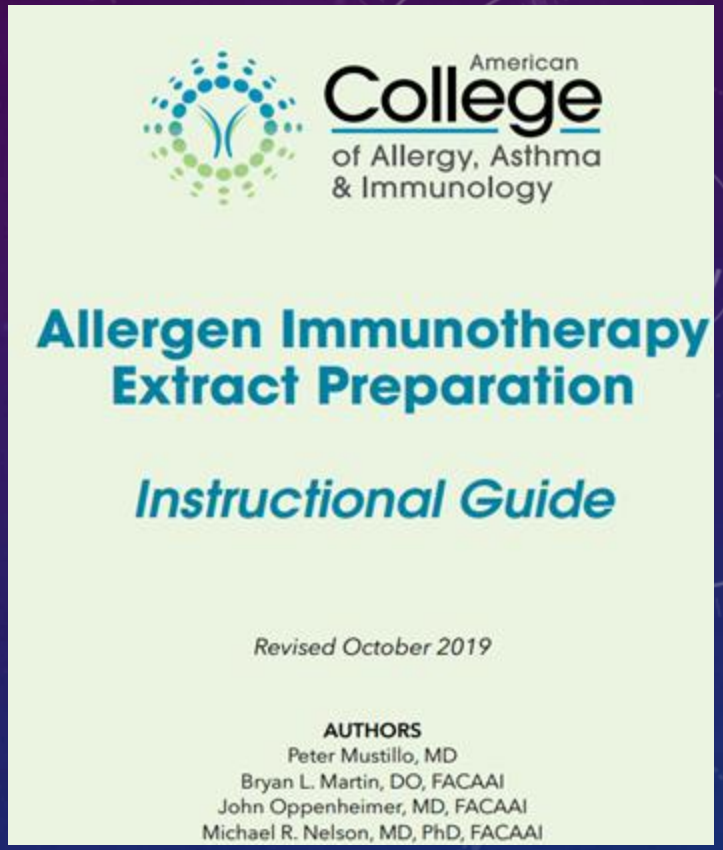
- SCIT duration
  - Relapse in 62% treated for HDM <35 months vs. 48% treated > 36 months
- Communication
- History of noncompliance

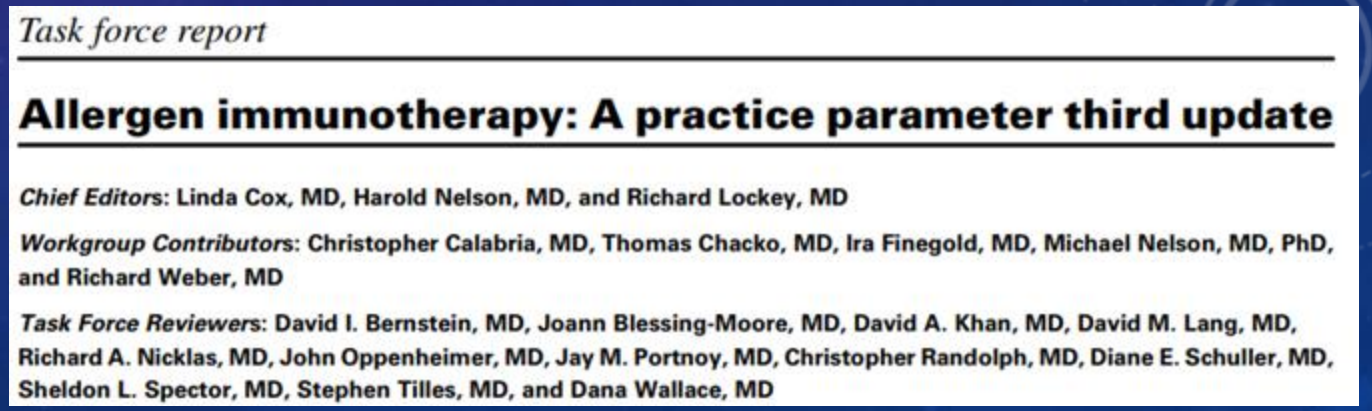
MY TYPICAL SCIT PRESCRIPTION

- T/G/W vial (0.2-0.5mL per allergen)
- Pet dander (if needed) 1-2 mL of cat and/or dog
- Dust mite/mold vial
  - 1-2mL of dust mite
  - 0.2-0.5mL of each mold (focused on more mL of relevant molds)

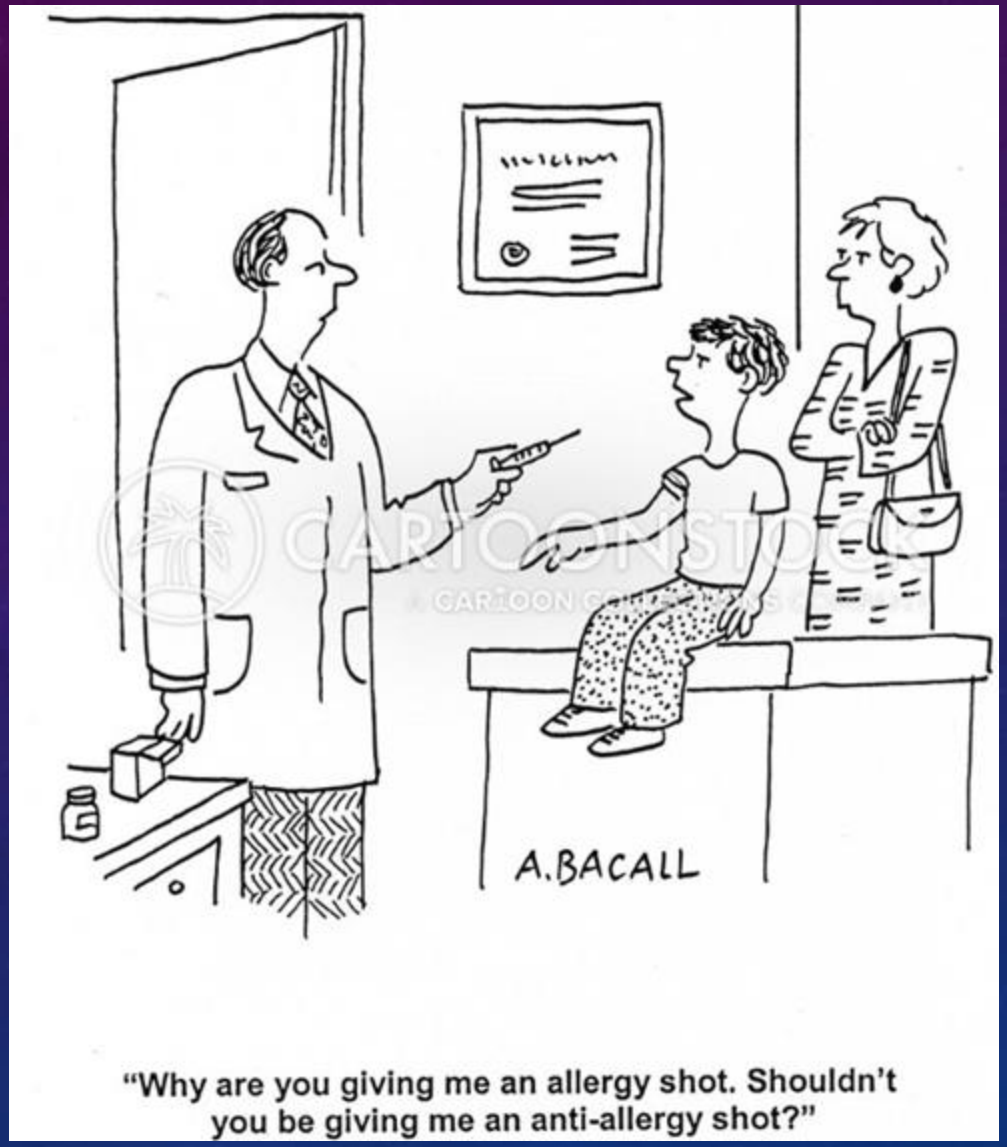
REFERENCES

- ACAAI Allergen immunotherapy extract preparation. Instructional Guide. 2019.
- https://www.youtube.com/watch?v=P-w-CKLcPbo (1/2023)
- Allergen Immunotherapy: A practice paramter third update. J Allergy Clin Immunol 2011; 127(1): S1-S55.





QUESTIONS?



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