ADJUSTING IMMUNOTHERAPY FOR NON-RESPONDERS

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DISCLOSURES

- No financial or relevant disclosures.

OBJECTIVES

- Recognize clinical scenarios which can result in "nonresponsiveness" to SCIT
- Understand variables which can affect immunotherapy effectiveness
- Develop differential diagnosis for chronic rhinitis

A CASE YOU HAVE LIKELY SEEN….

- A 60 year old female presents for follow up stating that she has been on allergy shots for the past 2 years and feels it "is not working."

CMS GUIDELINES

- The duration of all forms of immunotherapy must be individualized. A presumption of failure can be made when, after 12-24 months of therapy, a person does not experience a noticeable decrease of symptoms, an increase in tolerance to the offending allergen, and a reduction in medication usage.

  Treatment will not be reimbursed after a 2-year period when there is no apparent clinical benefit.

https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdId=32553

WHAT TO DEFINE?

- Noticeable change?
- Medication reduction?

"IMPROVEMENT"

- Retrospective review of 1,624 AIT patients with 1,519 matched patients not on AIT
- 30% improvement in CSMS
  - 84% (vs 8%) of SCIT
- 60%+ improvement from baseline
  - 71% (vs 6%) of SCIT

CSMS criteria (0-6)

Symptom scoring

Itchy nose	0–3	
Sneezing	0–3	
Runny nose	0–3	
Blocked nose	0–3	
Conjunctival symptoms	Itchy/red eyes	0–3
	Watery eyes	

- Add up and divide by 6 = daily symptom score (dSS)

PLUS

- Daily medication score (dMS) [0-3]
  - 1 = oral and/or topical H1
  - 2 = INCS and/or H1
  - 3 = OCS +/- INCS +/- H1

Jakalski M et al. Hum Vaccin Immunother. 2019 Jun 21;15(12):2896–2902.

GOOD HISTORY, SUPPORTING TEST RESULTS BUT…

- Failure to treat with adequate allergen dose
- Failure to remove significant allergen exposure
- Exposure to high level of allergen
- Incomplete identification of relevant allergens

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

FAILURE TO TREAT WITH ADEQUATE DOSE

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

- Dust mite: 0.5 -2mL
- Cat 1-4mL
- Dog (depends)
- Bermuda 0.3 -1.5mL
- Timothy 0.1-0.4mL
- Non-standardized pollens 0.5mL

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

FAILURE TO REMOVE SIGNIFICANT ALLERGEN EXPOSURE

- Dust mite
  - Washing sheets, impermeable covers, stuffed animals in the dryer, air filtration units
    - Dust mite levels decrease but no effect on symptoms, peak flows, or eczema
- Cat dander
  - Removal from home
  - Washing – different techniques but airborne Fel d 1 returned in 1 week
    - Similar issues with reduced allergen detected but lack of clinical improvement
- Obtaining a "hypoallergenic" cat or dog
  - Similar levels of Can f 1 or Fel d 1. Found in all locations. Allergen levels significantly vary even within individual breeds

Aroyave WD et al. Ann Allergy Asthma Immunol 2015; 19(1): 237-248.

EXPOSURE TO A HIGH LEVEL OF ALLERGEN

- Mowing the grass
  - 8-fold increase in grass pollen during mowing
- Summary effect estimate for a 10 grains/m³ increase in pollen exposure showed on average a 2% increase in the risk of any allergic or asthmatic symptom (mainly upper airway)

TABLE I. The NAB scale for interpreting pollen and spore levels

Mold	Grass	Trees	Weeds
0, Absent	0, Absent	0, Absent	0, Absent
1-6499, Low	1-4, Low	1-14, Low	1-9, Low
6500-12,999, Moderate	5-19, Moderate	15-89, Moderate	10-49, Moderate
13,000-49,999, High	20-199, High	90-1499, High	50-499, High
>50,000, Very high	>200, Very high	>1500, Very high	>500, Very high

Kernerman SM et al. J Allergy Clin Immunol 1992; 90(1): 131-133.

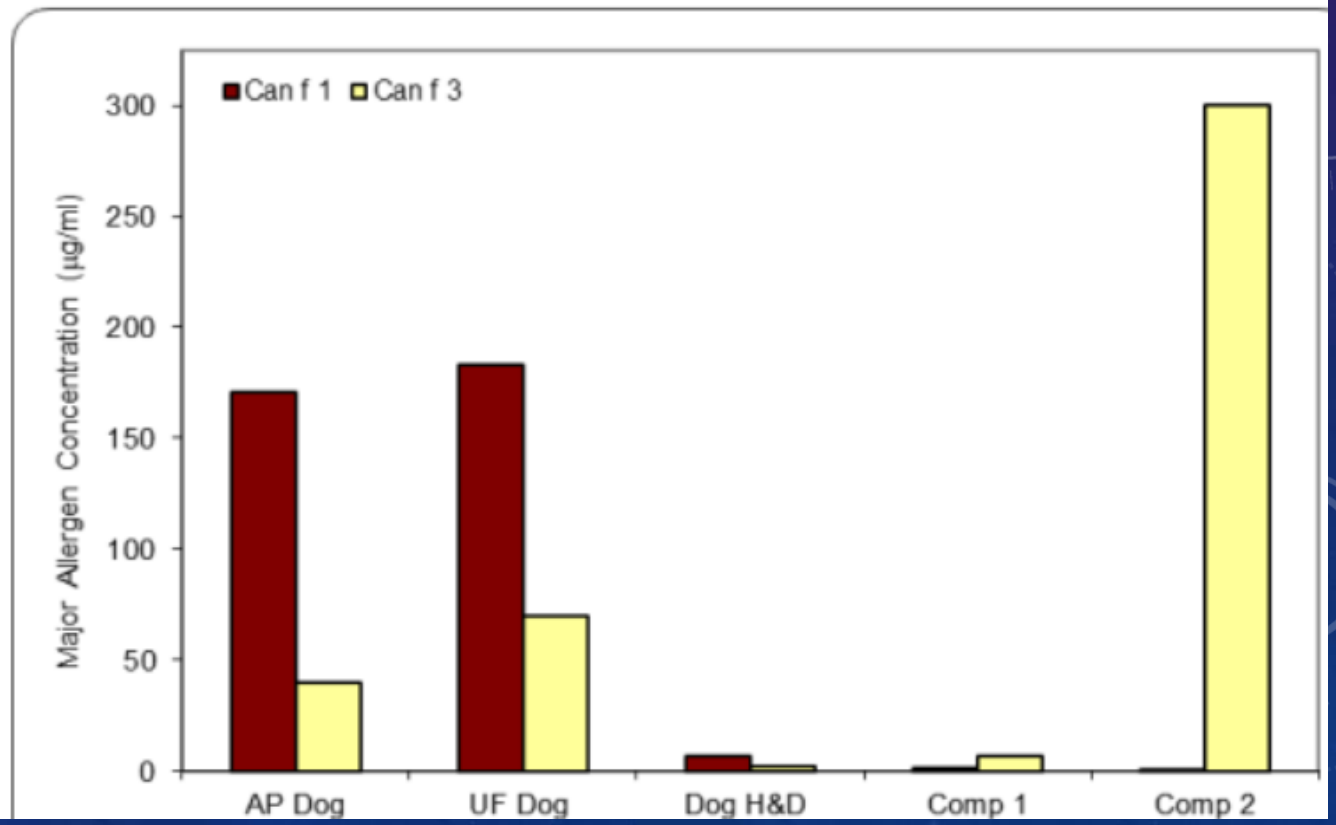
Kirinoja et al. BMK Open 2020;10:e029069. doi:10.1136/bmjopen-2019-029069

INCOMPLETE IDENTIFICATION OF THE ALLERGEN

- Skin testing techniques
- Interfering medications
  - Mirtazapine
  - Quetiapine
  - TCAs
- Dog dander
- "honeymoon phase"

Figure 3: Chart of Allergen Concentrations

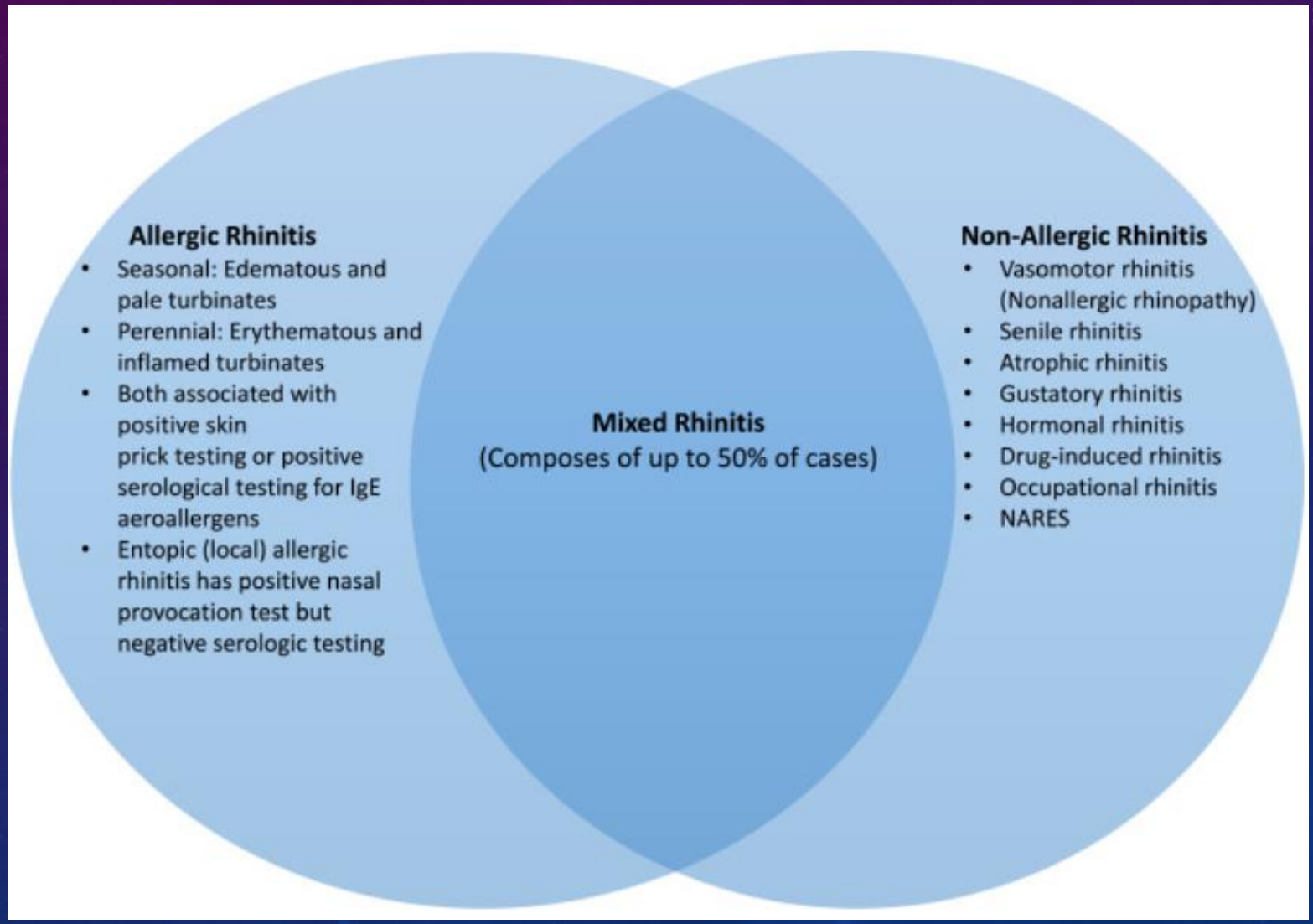
Values taken from Table 3.



BACK TO THE CASE

- Why else might a patient "not respond?"

NONALLERGIC RHINITIS

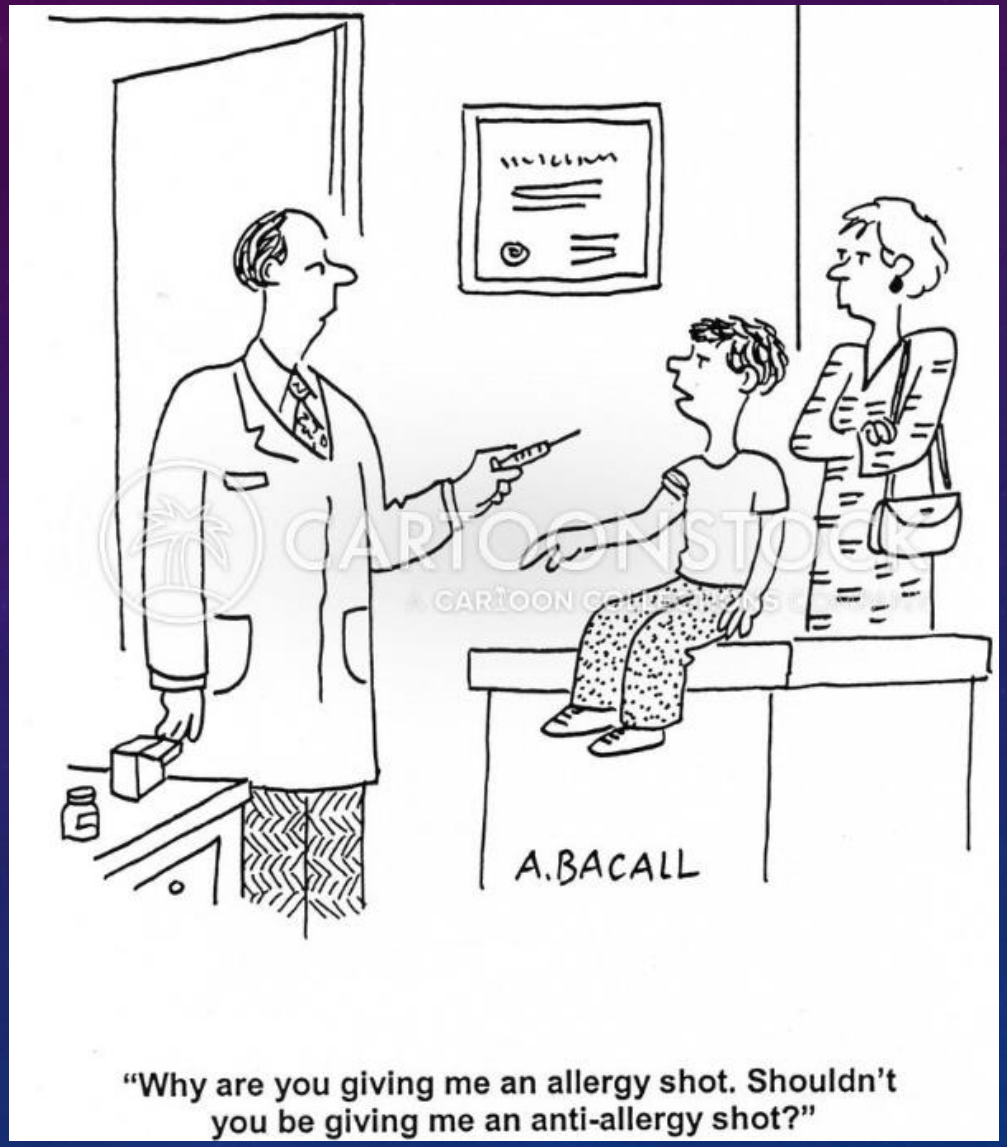


Rackerby N et al. Ann Allergy Asthma Immunol 2025; 135(1): 15-22.

MORE DIFFERENTIAL DIAGNOSIS (OR CO-MORBID/CO-EXISTING DISORDERS)

- Physiologic "nasal cycle"
- Anatomical issues (turbinate hypertrophy, anterior nasal valve collapse, severe septal deviation)
- Underlying recurrent or chronic sinusitis
- Nasal polyps
- Rhinitis medicamentosa
- Hypothyroidism (rhinitis in elderly)
- CSF rhinorrhea, primary headache disorders
- Patients attributing other medical issues as a cause of "allergies"
  - Vocal tic
  - GERD/LPR

QUESTIONS?



https://www.cartoonstock.com/cartoon?searchID=CS176115