

Type 2 low asthma diagnostic and management challenges

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 (Asthma, Bronchiectasis, COPD)



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Disclosures

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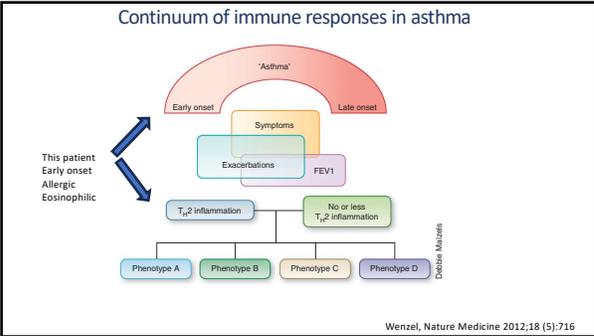
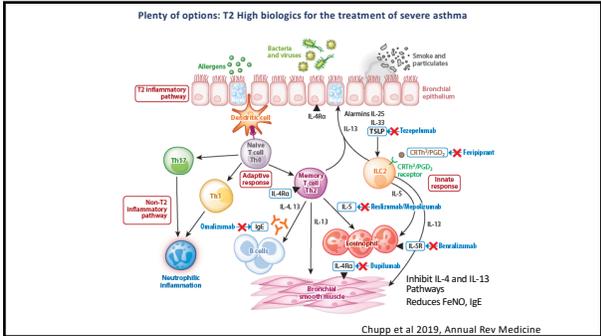
Case 1- History

- HPI:** 18 y.o. male- asthma/allergies since birth. Asthma was moderately severe on prednisone every few years- used ICS/LABA for control
- ~12 months prior asthma symptoms increased. Multiple exacerbations required prednisone. Continued at 20mg a day for control. Tapering from this dose increased symptoms. In ER 3x last year.
- Developed a red, itchy, nodular rash that resolved when on prednisone. Rash was located on his hands, feet, and thighs. Biopsy of the rash- allergic reaction, no vasculitis.
- Medications:** FF/V/U 200 daily, montelukast 10 mg, Loratidine 10 mg, pred 20mg, albuterol
- Social Hx:** Used to vape nicotine, quit ~1 year ago. Has gained 50lbs on prednisone. Works as a car mechanic. Lives with his mother, dog in the home that he is allergic to. Hobbies are cars, motorcycles.
- ROS:** negative for other symptoms to suggest EGPA. No nasal polyps

Case 1- Exam/labs (2024)

- FeNO:** 25 ppb
- Bloodwork:** IgE 720 IU/L
 Eos 780 cells/ul- on prednisone, rechecked.
 ANCA negative (MPO/PR3)
 ABPA titers neg,
 ANA Neg,
 Flow cytometry negative, PDGF mutation neg
- Allergy tests:** Molds negative, grasses +2, dog/cat +3, trees +3, dust mite +4, cockroach +1, trees +2
- Radiology:** PA/Lat CXR and HRCT unremarkable
- PFT:** Mild obstructive physiology with reversibility (FEV1 80%)

Phenotyping indicates this patient is both Allergic and Eosinophilic



Case 2- History

- HPI:** 64 yo male presents for an opinion regarding severe uncontrolled asthma. He thinks he may have had undiagnosed asthma as a child. Had protracted URI with coughing. No hx of allergies. First diagnosed with asthma in his 20s when he had SOB and chest tightness. Given albuterol and stopped smoking. Would have flares requiring prednisone 2x per year. Started Symbicort at some point which helped but still flared and got OCS 2x per year. Flares are protracted. Montelukast didn't help.
- PMH:** GERD, controlled on PPI, deviated septum on CT scan, CAD, HTN, Afib OSA on CPAP
- Medications:** Symbicort 160, 2p BID, tiotropium, and albuterol PRN, Flonase, Zetia, PPI, Eliquis
- Social Hx:** Smoked from age 16 to 25 yo, 1/2 PPD, Runs PR firm, home with HVAC, area rugs, no pets.
- Family Hx:** Father had COPD

Case 2- PE/Labs

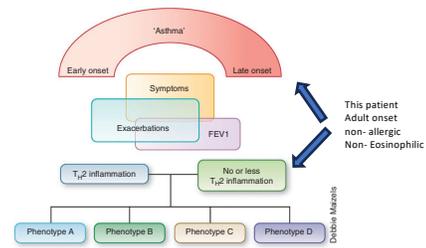
- PE:** Good air entry. Clear with no wheezing. ACT score 13
- Bloodwork:** IgE 100 IU/ml, Eos 70 cells/ml. (past results- 70, 30, 30, 60 cells/ul over the last 3 years) ANCA negative Normal total IgG and subclasses
- Allergy tests:** Immunocap and SPT negative
- Radiology:** PA/Lat CXR, HRCT - unremarkable

	FVC	FEV1	FEV1/FVC	FENO	TLC	RV	DLco
08/3/21	113%	79%	0.69	7ppb	118%	72%	115%

Evaluation of patients with asthma

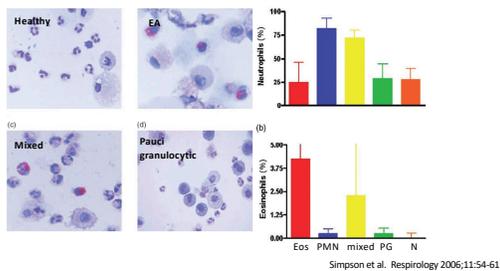
- Confirm the diagnosis
- Rule out asthma mimics/alternative Dx
VCD, IgG deficiency, bronchiectasis, GERD, A1AT, heart disease, Tracheobronchomalacia etc.
- Optimize standard treatments- adherence, etc
- Phenotype the patient
- Consider phenotype specific therapy

Current Concept: continuum of immune responses in asthma



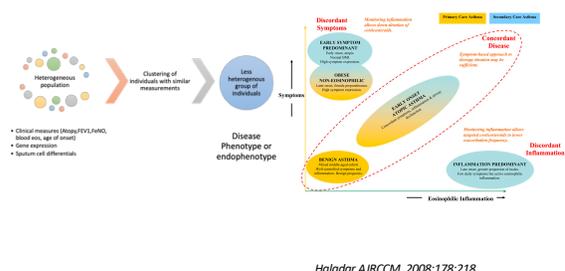
Wenzel, Nature Medicine 2012;18 (5):716

Sputum phenotypes of asthma

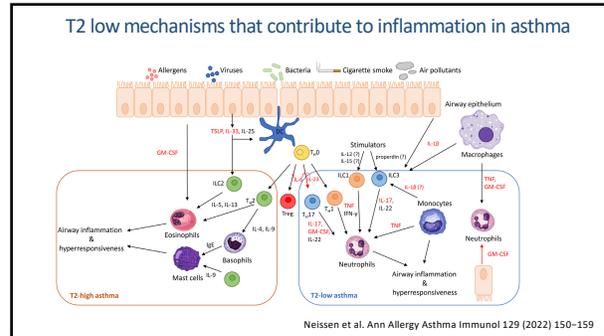
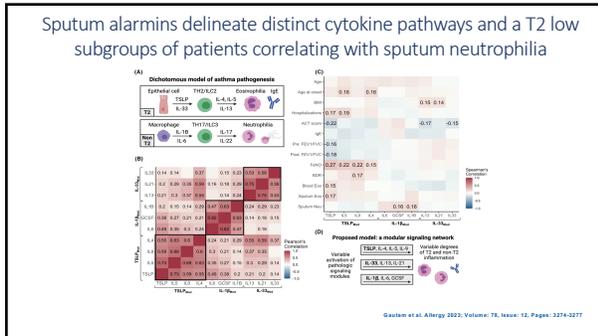
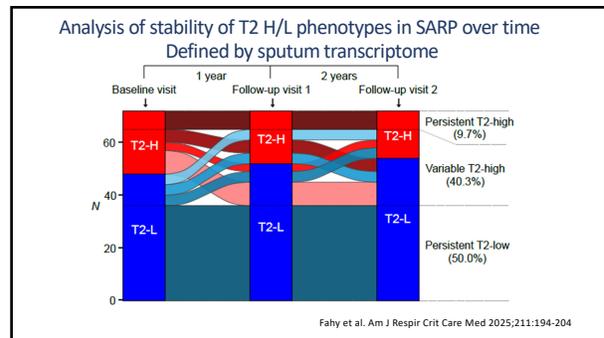
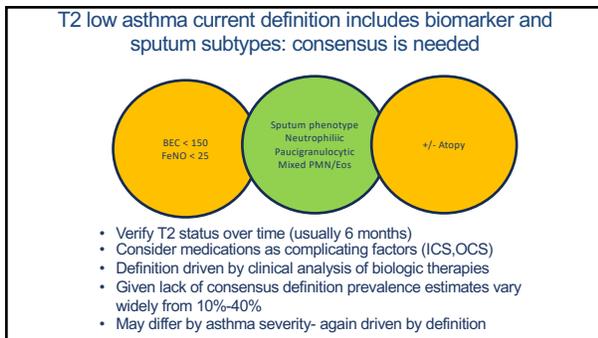
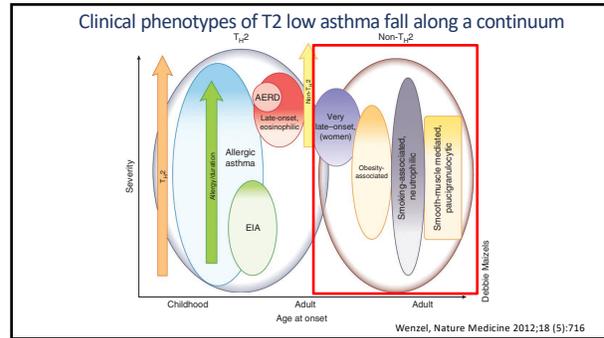
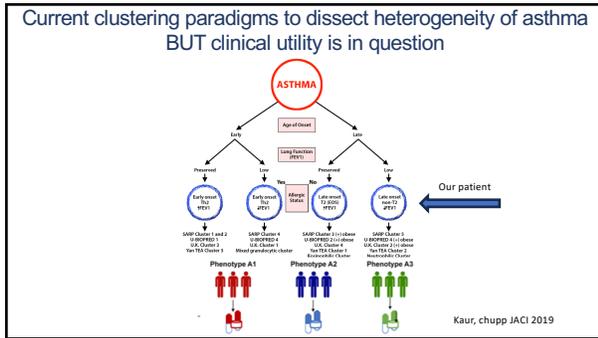


Simpson et al. Respirology 2006;11:54-61

Early cluster analysis of patients with asthmatics



Haladaj AJRCCM. 2008;178:218



Conclusion

- T2 low asthma remains a poorly defined entity but for practical purposes is includes patients that have FeNO < 25, BEC <150, and non-allergic (my opinion).
- Significant evidence exists that non-T2 pathways contribute to inflammation in asthma and maybe the primary driver in some patients
- Patients with T2 low asthma clinical phenotypes exist (adult onset, sputum neutrophils, pauci-cellular, obesity)
- There maybe specific molecular features active in some patients such as IL-1beta IL-33
- Treatment options are limited but at this point include biologic therapies (Tezepelumab) or macrolide therapy.

Thank You!
Time for discussion