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Asthma Endotypes

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Disclosures

Marketing Advisory Board for Enzyvant

Primary Investigator for a clinical research trial site with AstraZeneca

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Objectives

Review	Apply	Utilize
Review pediatric and adult asthma endotypes	Apply evaluation approaches based on these endotypes	Utilize endotypes in considering treatment strategies

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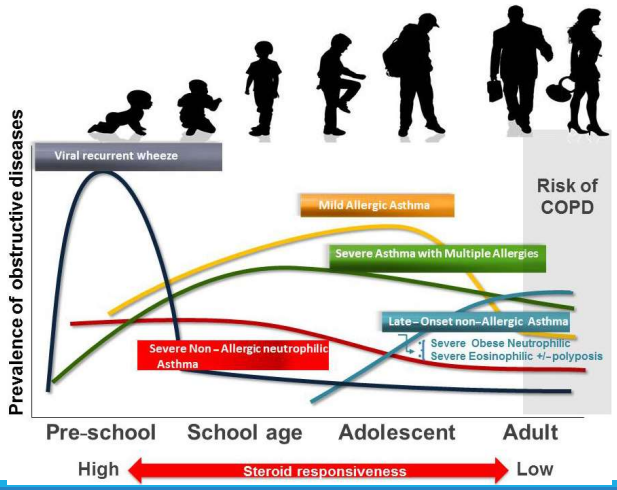
The Spectrum of Asthma

Group of disorders that result in reversible airflow obstruction

Variability
- Age
- Triggers
- Response to therapy



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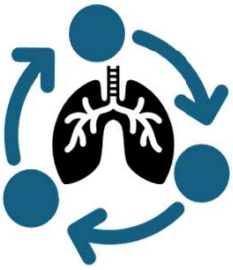
Asthma Endotypes vs Phenotypes



Endotype: Mechanistic pathway

T2 High: Allergic inflammation

T2 Low: Non-allergic inflammation

Phenotype: Clinical presentation

Age

Triggers

Presence of allergic disease

COPD overlap

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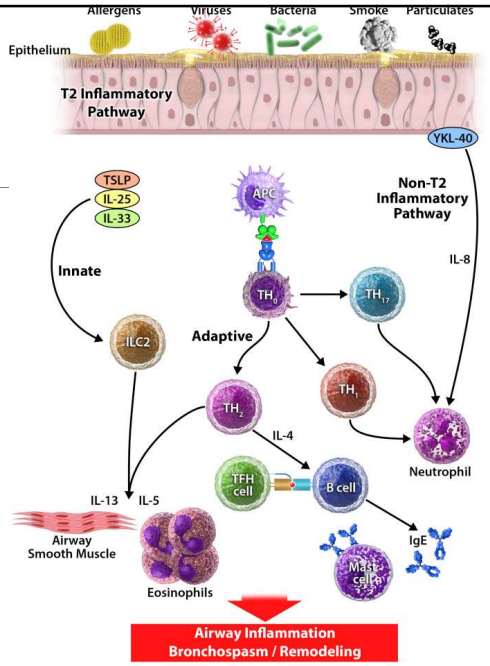
Helper T Cell Polarization

T_H2

- ILC2 and "allergic" cytokines
- Activation of eosinophils, IgE production, and mast cells
- Downstream effects on airway smooth muscle and epithelium

Non-T_H2

- Neutrophils
- Type 3 immunity: T_H17 cells
- T_H1 immunity: IFN-γ
- Systemic inflammation: obesity, metabolic dysfunction



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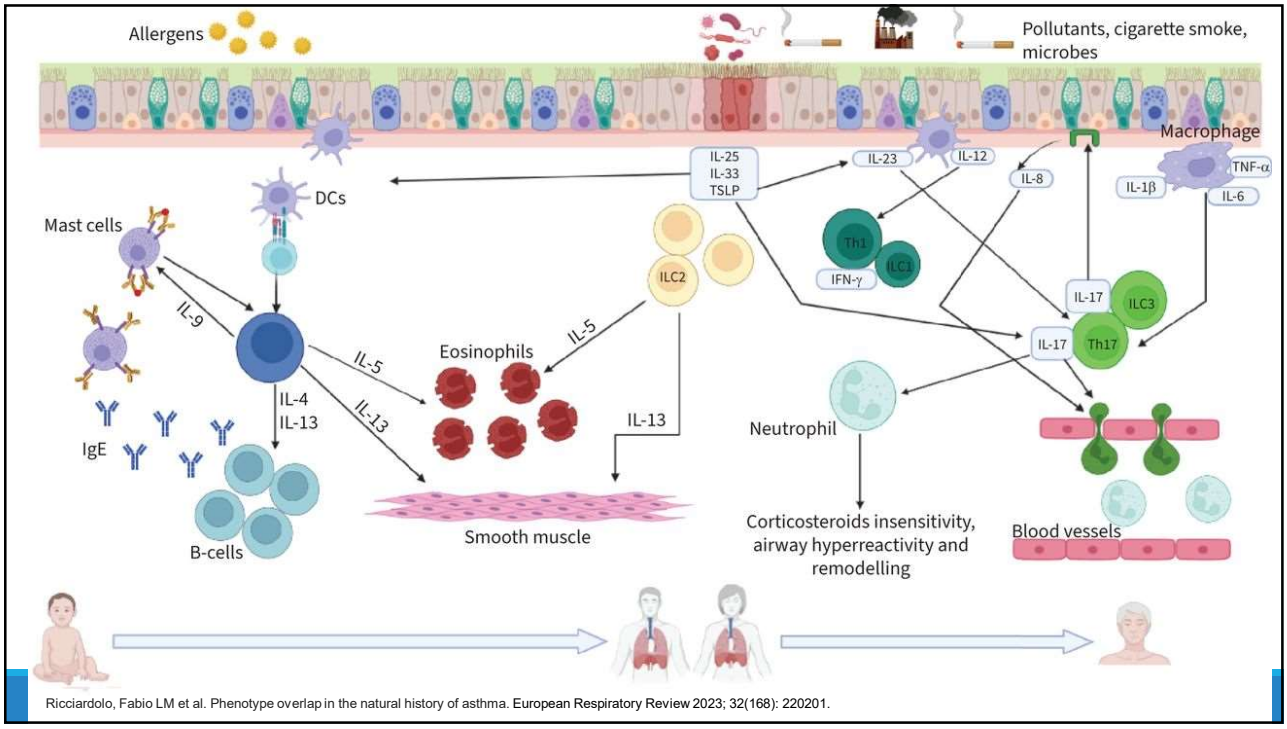

Ricciardolo, Fabio LM et al. Phenotype overlap in the natural history of asthma. European Respiratory Review 2023; 32(168): 220201.

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Clinical Evaluation Based on Endotype

T2 HIGH: ALLERGIC

Peripheral eosinophilia

Elevated serum IgE

Positive environmental allergy testing (skin prick, specific IgE)

Elevated FeNO

Sputum and BAL eosinophilia

T2 LOW: NON-ALLERGIC

Absence of T2 high markers

Peripheral neutrophilia

Sputum and BAL neutrophilia

Elevated BMI

Smoking status

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Treatment Approaches Based on Endotype

T2 HIGH

Guidelines-based asthma therapy

Environmental control of allergic disease

Biologic therapy targeting the allergic pathway

Allergen immunotherapy

T2 LOW

Evaluation and treatment of co-morbidities
- OSA
- GERD
- Obesity
- Smoking cessation

Tiotropium

Macrolides

Limited biologic therapies

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Table I. Common features of T2-"high" vs T2-"low" asthma

Feature	T2-"high"	T2-"low"
Age of onset	Earlier onset	Later onset
Symptoms	May be significant	May be significant
Life-threatening exacerbations	More exacerbations	Fewer exacerbations
Obesity/metabolic dysfunction	May be present	Often present
Lung function	More obstruction	Less obstruction
Short-acting bronchodilator response	More responsive	Less responsive
Allergic sensitization	Present	Absent
Exhaled nitric oxide	Normal to elevated	Low to normal
Airway eosinophilia	Present	Absent
Airway neutrophilia	May be present	May be present
Medication requirements	More responsive to corticosteroids	Less responsive to corticosteroids

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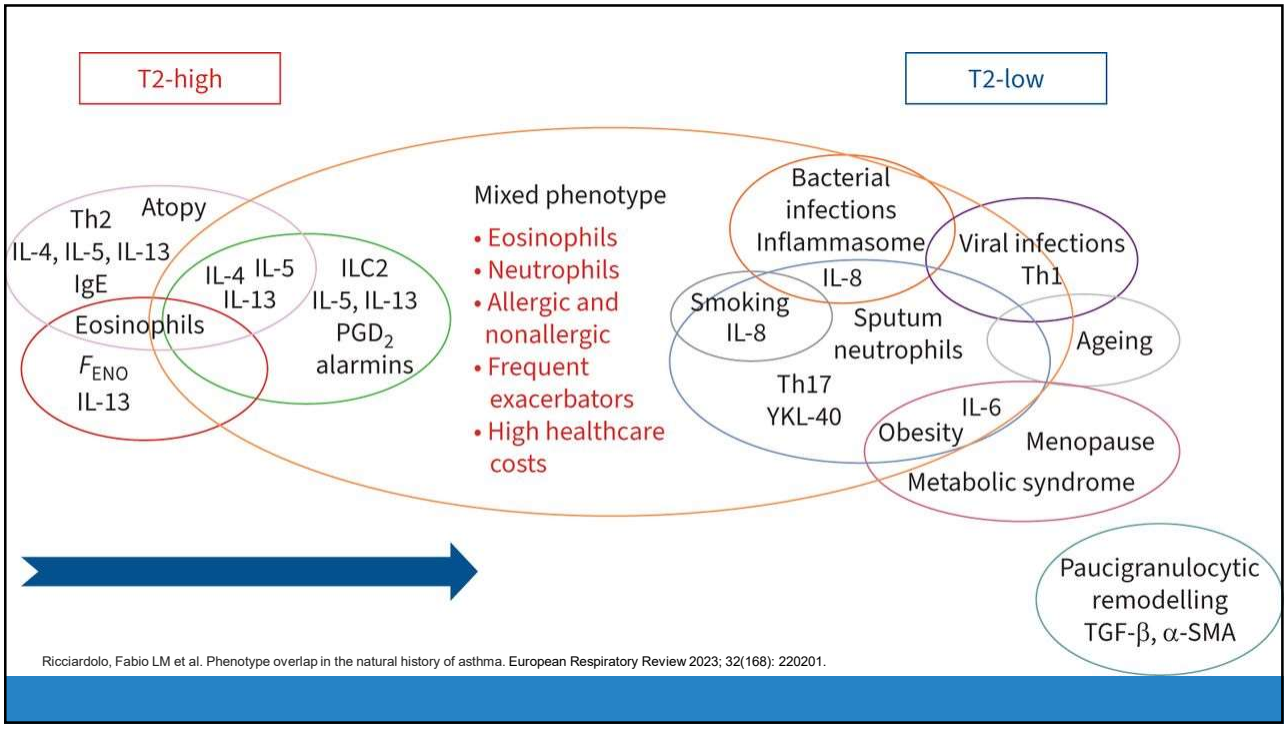

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Future Directions

Cytokine profiling

Biomarkers: periostin, EPX,

Increased utilization of bronchoalveolar lavage

Microbiome evaluation and manipulation

Obesity management

Genetic testing

Biologic therapies

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