過敏氣喘致病機轉

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徐世達醫師

簡介遺傳性過敏病

- 近年來醫學界已經瞭解了**遺傳性過敏病**基本上乃是一種與**多重基因遺傳**有關的**障壁層缺陷**與**過敏免疫反應缺陷**所造成的**障壁層器官慢性過敏性發炎反應**。此炎症反應會因受到各種遺傳的**誘發因素**的激發造成臨床上的過敏發作，而其發作的部位則與其所遺傳到的**各別障壁層器官異常**有密切的關係。

Barrier organ

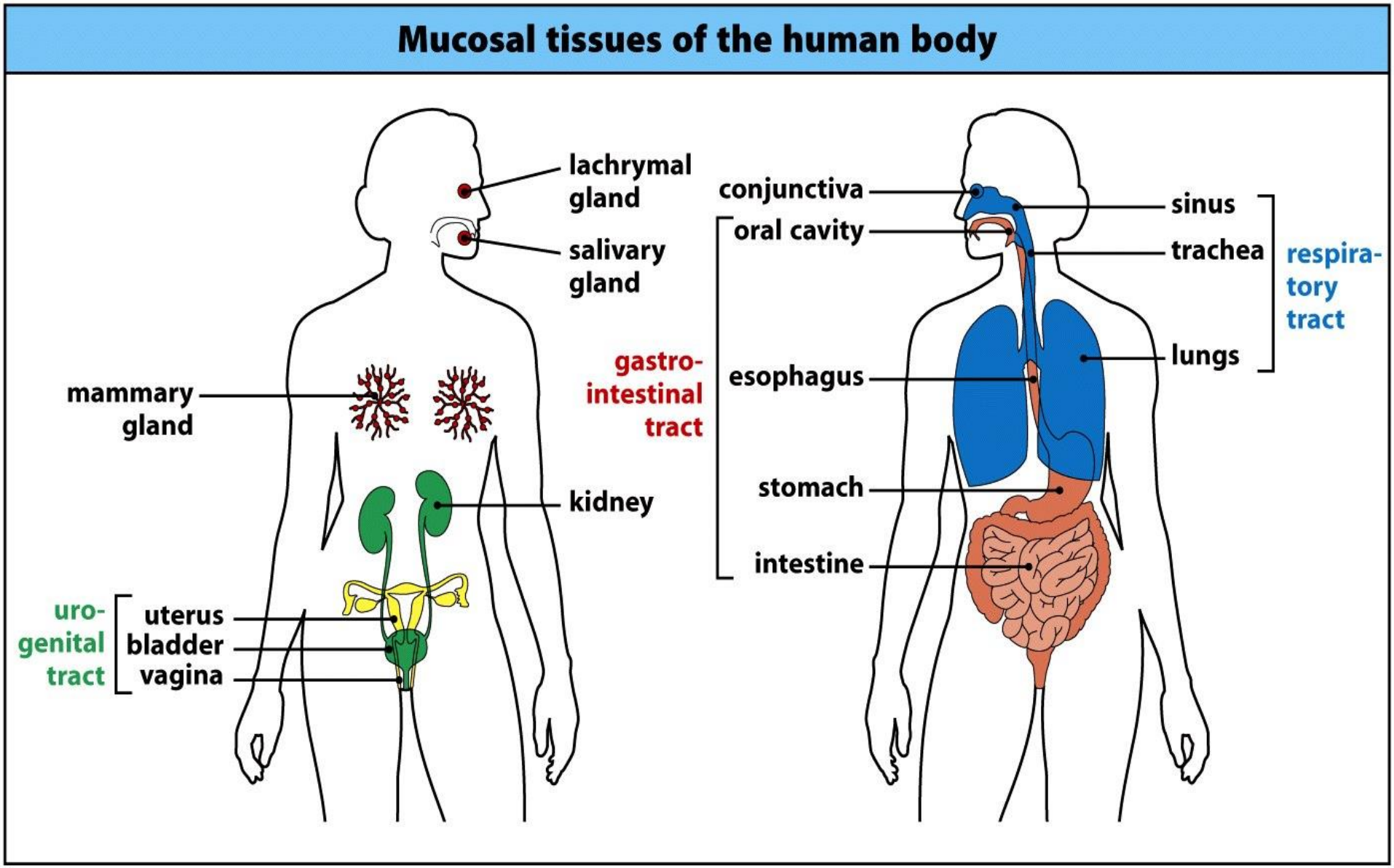


Figure 11-1 Immunobiology, 7ed. (© Garland Science 2008)

簡介遺傳性過敏病

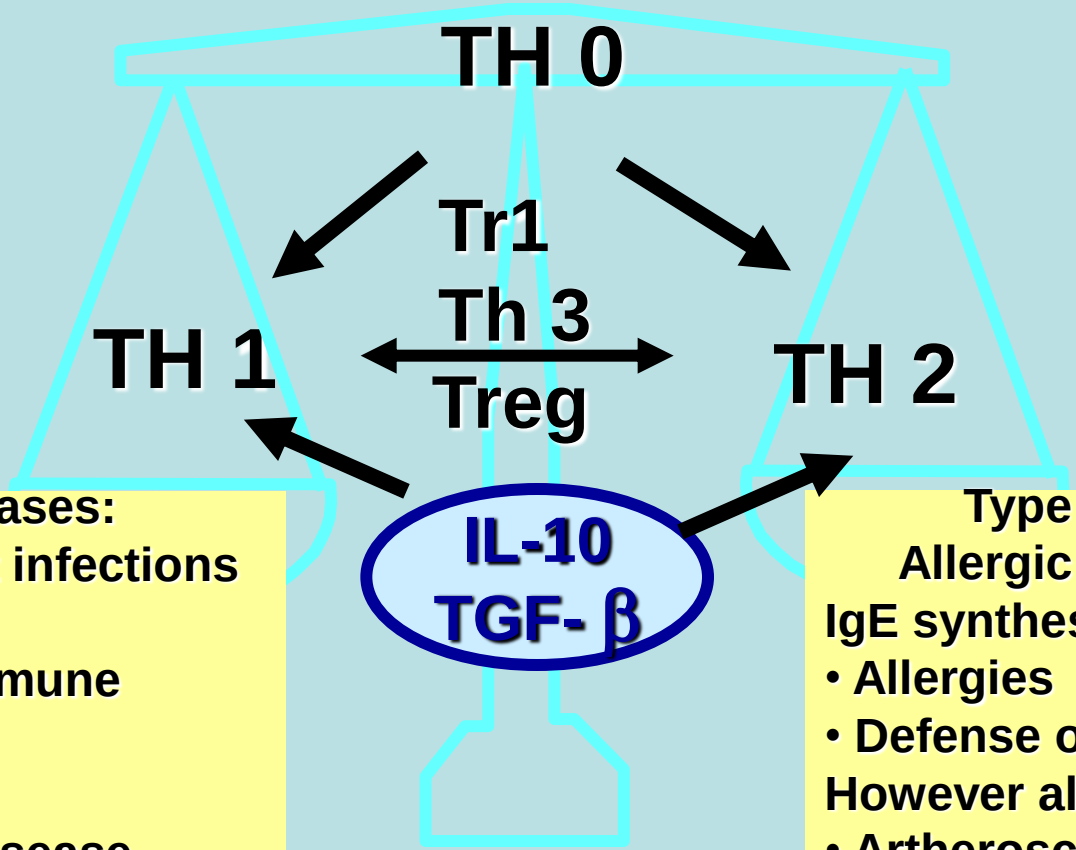
- 當此炎症反應發生於支氣管時我們稱之為氣喘病，發生於鼻腔、眼結膜時稱之為過敏性鼻結膜炎，發生於胃腸時稱之為過敏性胃腸炎，而當其發生於皮膚時我們稱之為異位性皮膚炎。

Allergy or oral tolerance:

人體免疫反應 TH1-TH2 的平衡

Jenmalm M.C., Björkstén B. - PAI 9 (11) : 5-12 (1998) and many others

Immune responses to allergens, pathogens, etc



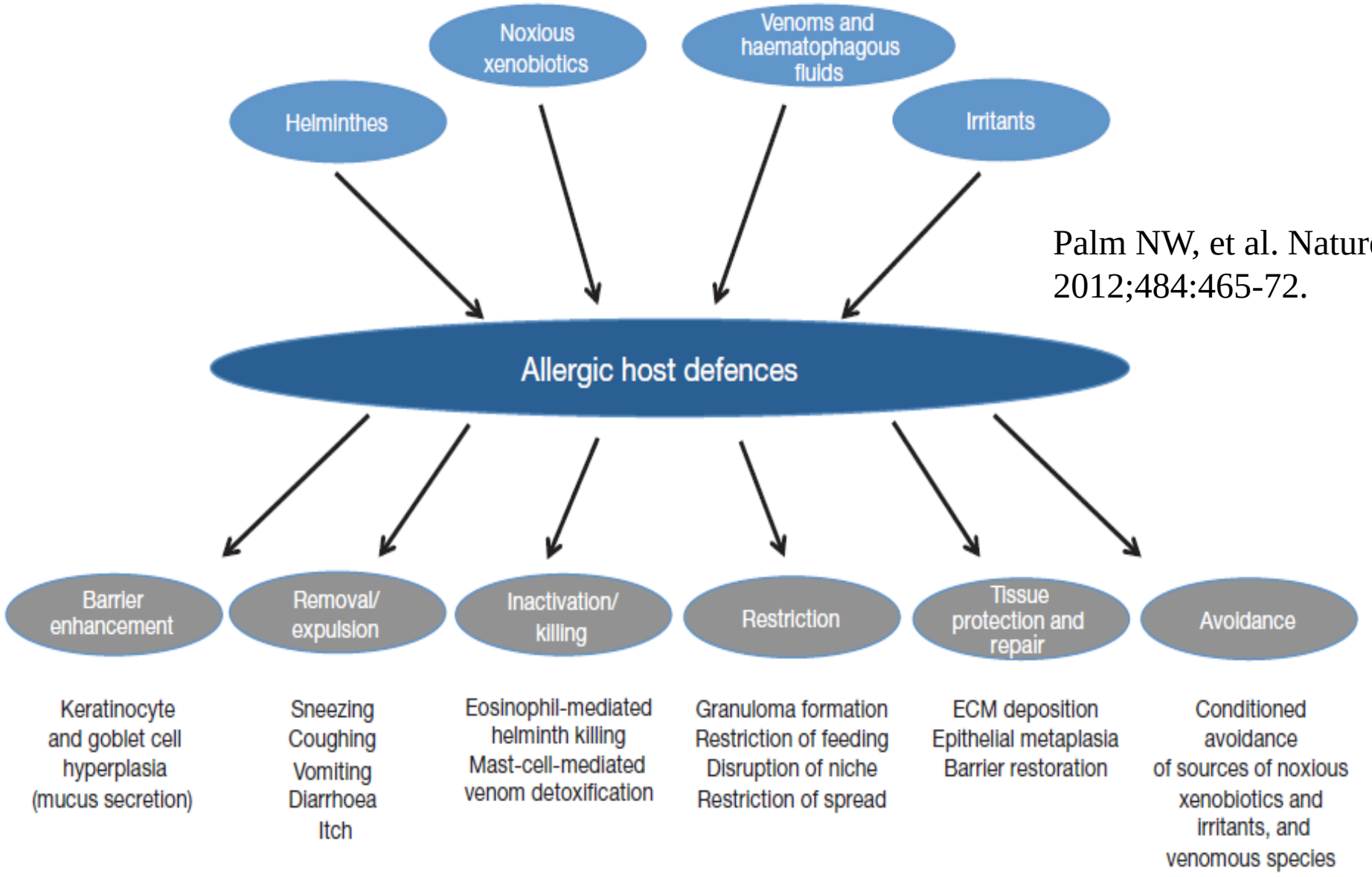
Type I diseases:
- Defense against infections
- Oral tolerance

However: Autoimmune diseases
- Typ I diabetes
- IBD & Crohns disease
- Multiple Sclerosis

Type II diseases:
Allergic host defenses
IgE synthesis and therewith
- Allergies
- Defense of parasites

However also:
- Artherosclerosis
- Reumatoid athritis

第二型幫助型T細胞(TH2)媒介的過敏免疫防禦反應-寄生蟲、叮咬蟲類、過敏原與刺激物對障壁層器官的防治反應

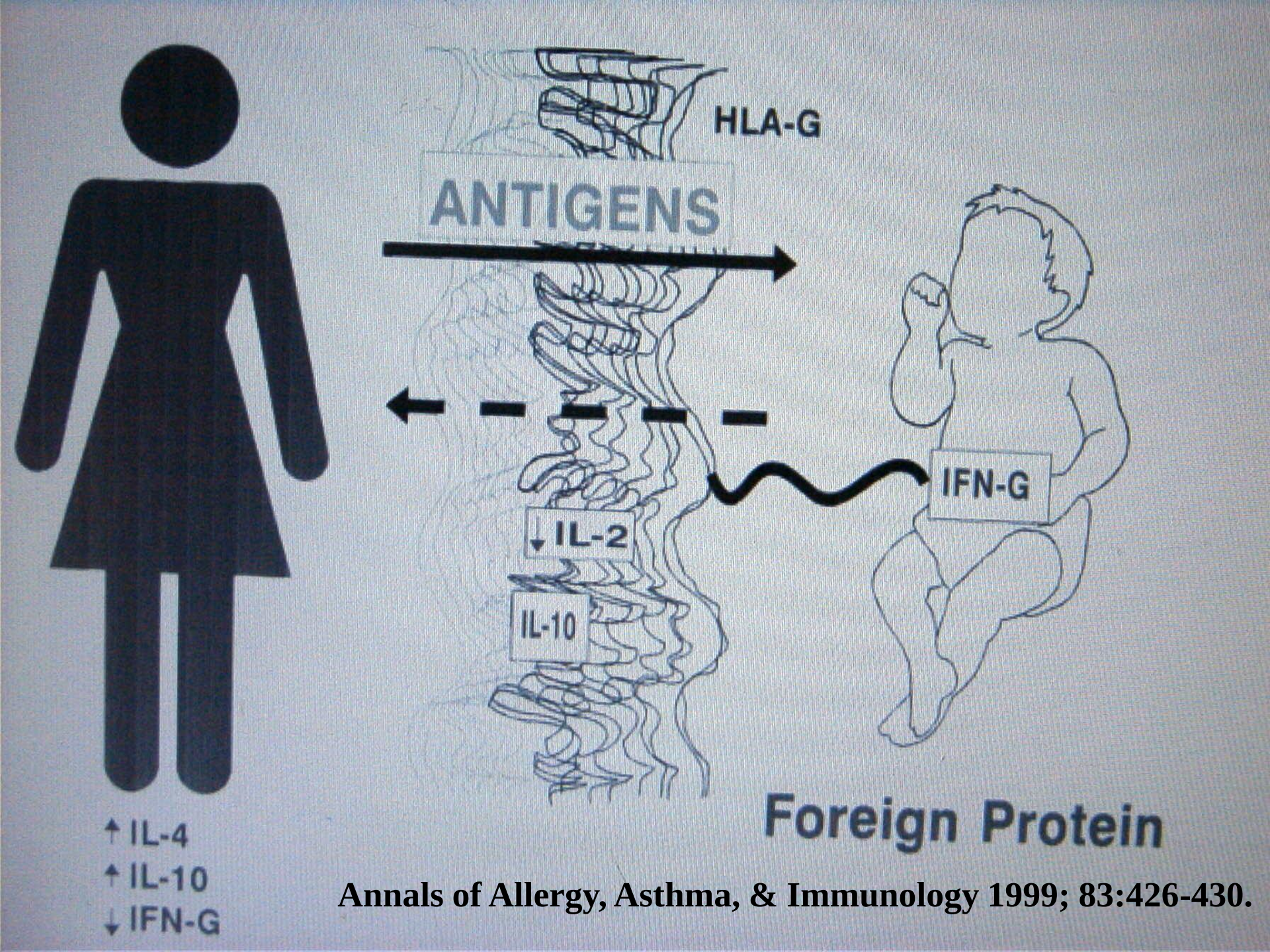


Palm NW, et al. Nature 2012;484:465-72.

異位性體質及第二類幫助型T細胞

- 子宮內:以第二型幫助型T細胞(Th2)為主。懷孕十六週後，胎兒的T細胞可被穿過胎盤的環境過敏原所致敏化。
- 新生兒:出生時以Th2反應為主
  - 正常新生兒: 轉移到偏向第一型幫助型T細胞(Th1)反應
  - 異位性體質: 繼續增強Th2反應

Annals of Allergy, Asthma, & Immunology 1999; 83:426-430.



Annals of Allergy, Asthma, & Immunology 1999; 83:426-430.

影響過敏兒形成的因素

- 過敏母親與多產
- 母親生產年齡
- 剖腹生產與自然生產
- 居家環境過敏原與刺激物濃度(早期餵食, 皮膚保養, 農場, 養貓)
- 維生素 D

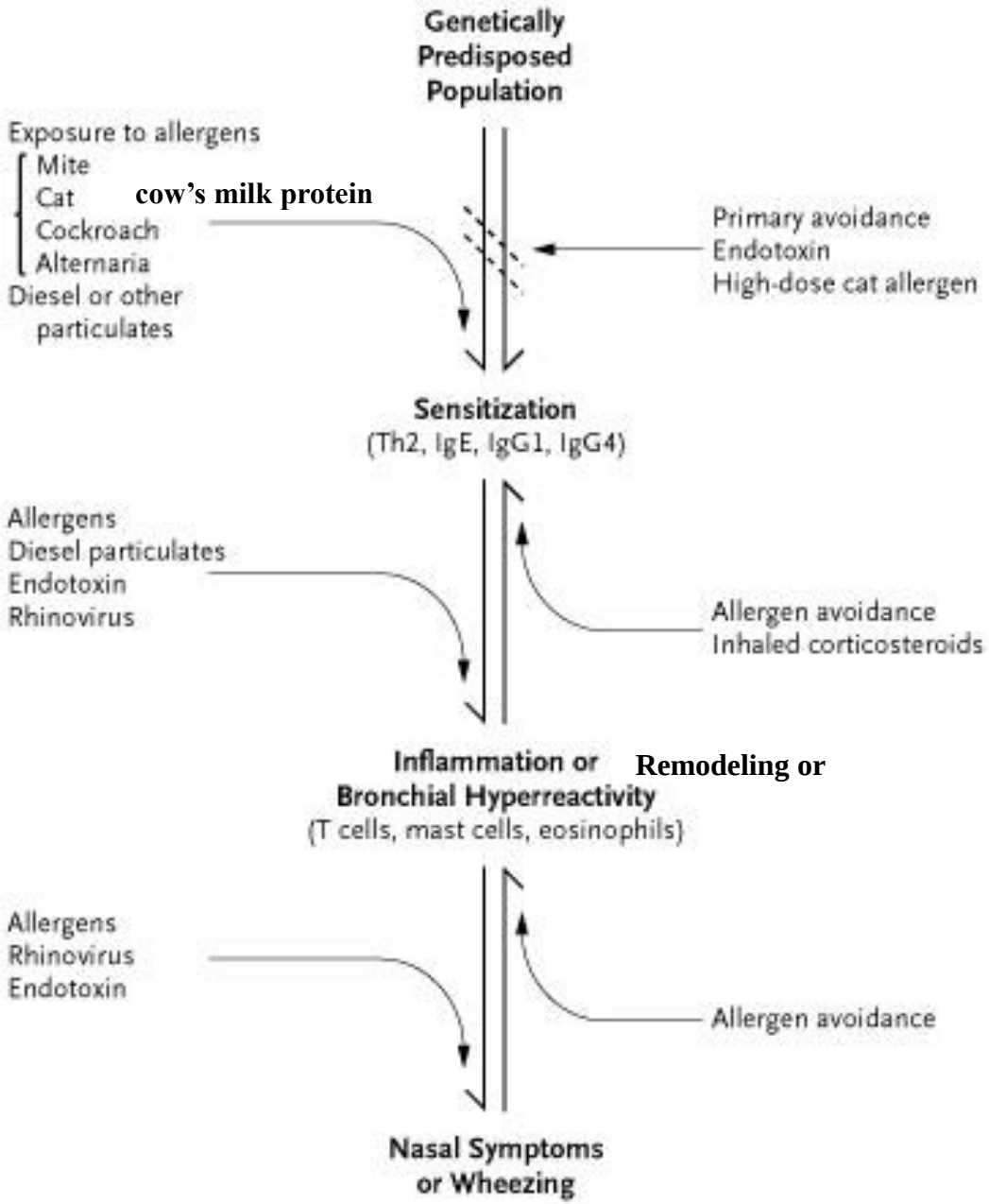
JAMA 2016 Jan 26;315(4):353-61.
JAMA 2016 Jan 26;315(4):362-70.

- 益生菌
- ω-3多元不飽和脂肪酸（ω-3 PUFA）
- 母乳與低過敏食物(水解蛋白配方奶粉)
- β型轉形生長因子(TGF-β)

Pediatr Allergy Immunol. 2014; 25(3): 257–263.
Clinical & Experimental Allergy 2016;1–12.

Pediatr Allergy Immunol 1997;8:134-137
Pediatr Res 2002;52:6-11
Respir Med 2007;101:1431-8
Eur J Pediatr 2010; Feb
Lancet 2001;351:1076-9
AAAI 2008 Dec;101(6):570-9
Am J Clin Dermatol 2008;9:93-103
Am J Respir Crit Care Med 2008;178:124-31
Pediatr Allergy Immunol 2010: 21: 47–59

- NEJM 2016 Dec 29;375(26):2530-9.



NEJM 2003; 349:207-208

過敏病預防的新觀念
一個或以上過敏病患的高敏感家庭

懷孕期

- 1. **母親食物不禁**。除非經**食物激發試驗**證實的過敏食物。
- 2. **減少**室內外**過敏原(包括**塵蟎、蟑螂、黴菌、貓狗有毛寵物等)與**刺激物**(包括PM2.5 、空氣污染物、化學刺激物和香煙等)的接觸。
- 3.懷孕期間可補充**益生菌、ω-3多元不飽和脂肪酸食物**與與**牛奶乳清蛋白萃取精華(乙型轉化生長因子TGF-β2)食品**。

Curr Opin Pediatr 2008;20:682-7

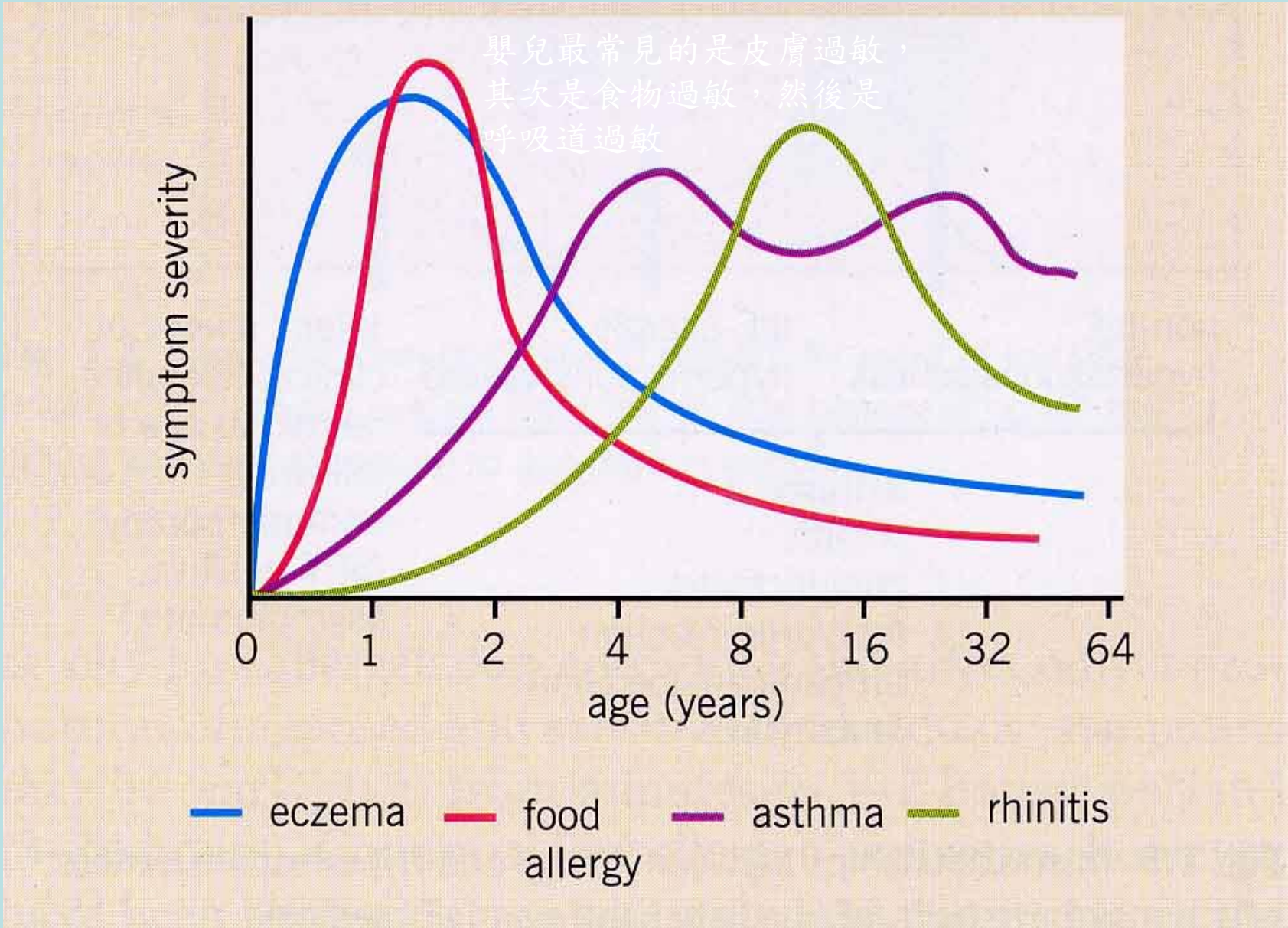
過敏病預防的新觀念
一個或以上過敏病患的高敏感家庭

產後預防或減少過敏病的發生措施

- 餵食**母乳**時，**母親食物不禁**。除非經**食物激發試驗**證實的過敏食物。
- 當**不能餵食母奶**時，建議使用**適度水解蛋白嬰兒奶粉**餵食。可補充**益生菌**、**ω-3多元不飽和脂肪酸食物**與與**牛奶乳清蛋白萃取精華(乙型轉化生長因子TGF-β2)食品**。
- 可于**四至六個月**開始添加**副食品**，但最好**同時哺育母奶**。
- **減少**室內外**過敏原(包括**塵蟎、蟑螂、黴菌、貓狗有毛寵物等)與**刺激物**(包括PM2.5 、空氣污染物、化學刺激物和香煙等)的接觸。

Ped Allergy Immunol 2004;16:4-5, 9-32

過敏進行曲


嬰兒最常見的是皮膚過敏，
其次是食物過敏，然後是
呼吸道過敏
symptom severity
0
1
2
4
8
16
32
64
age (years)
eczema
food allergy
asthma
rhinitis

遺傳性過敏病的兩大類型

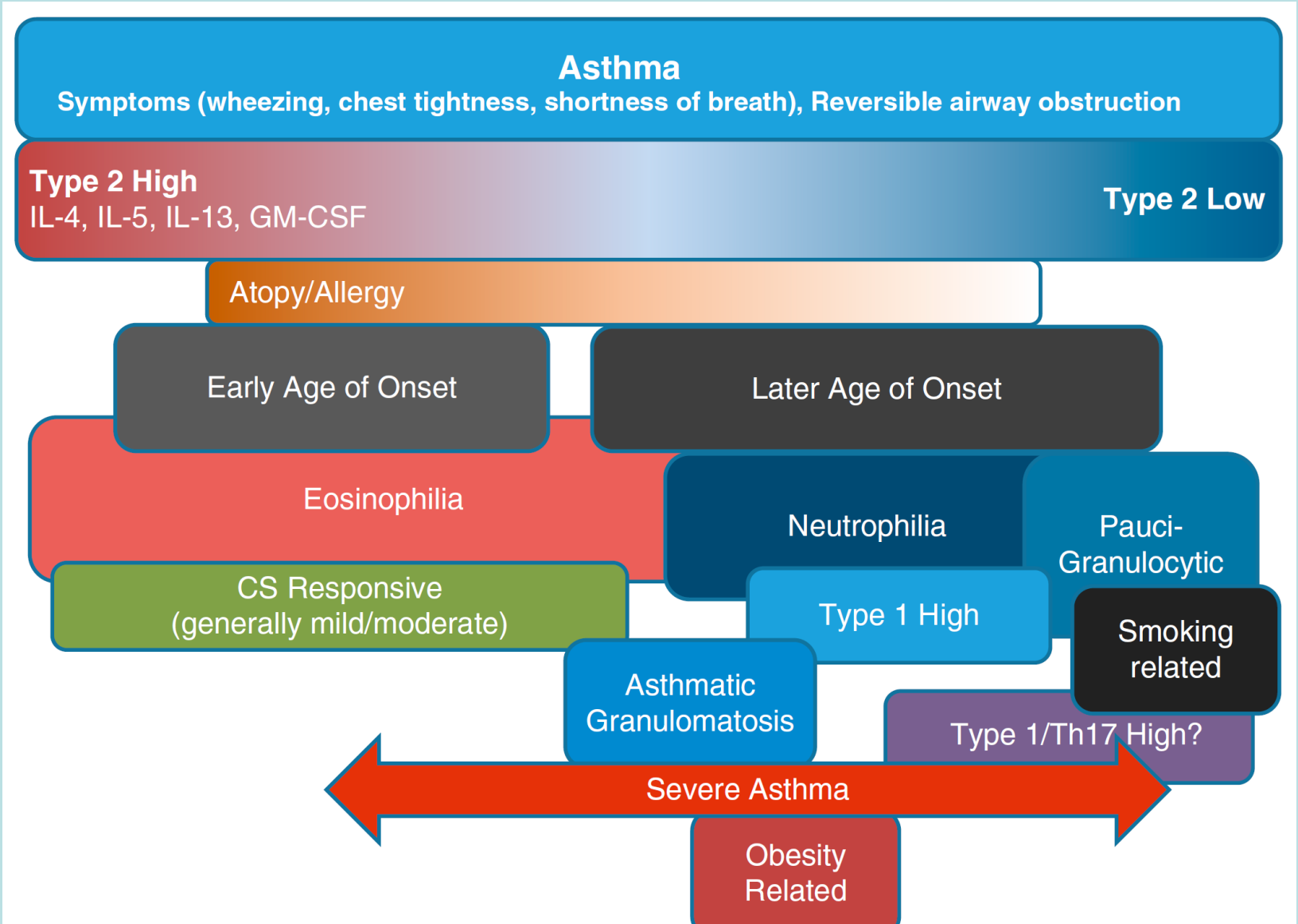
- **外因性** :佔70-90%；**IgE**總量上升

  對環境中**過敏原**和/或過敏原以外的對身體有害物質包括微生物成份產生致敏反應

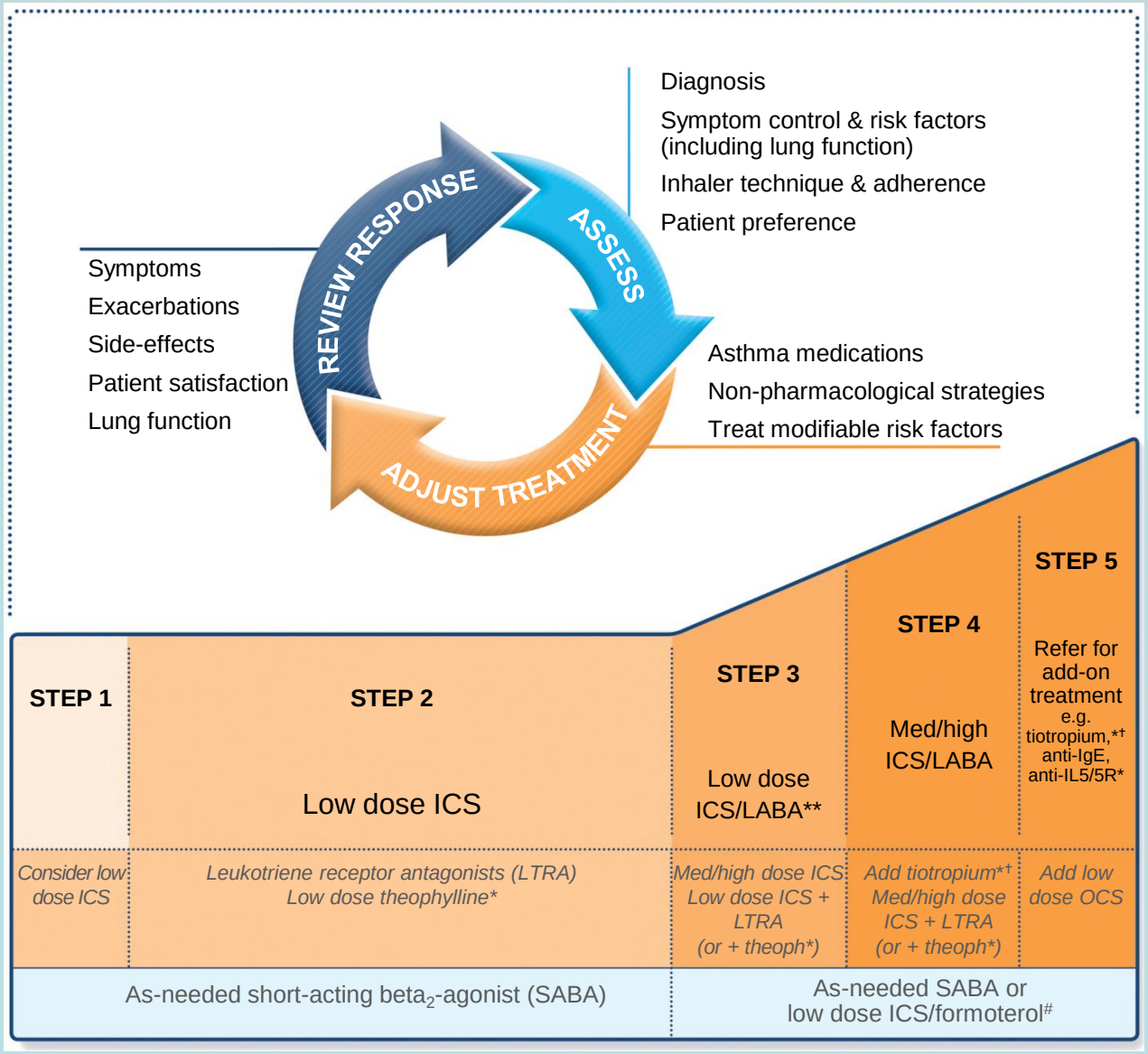
- **內因性** : 佔 10-30% ；**IgE總量沒有上升**

  只對環境中的**過敏原以外**的對身體**有害物質**包括微生物成份產生致敏反應

An example of current asthma phenotypes as they relate to inflammatory type (type-2 high or low) and other variables



Stepwise management - pharmacotherapy

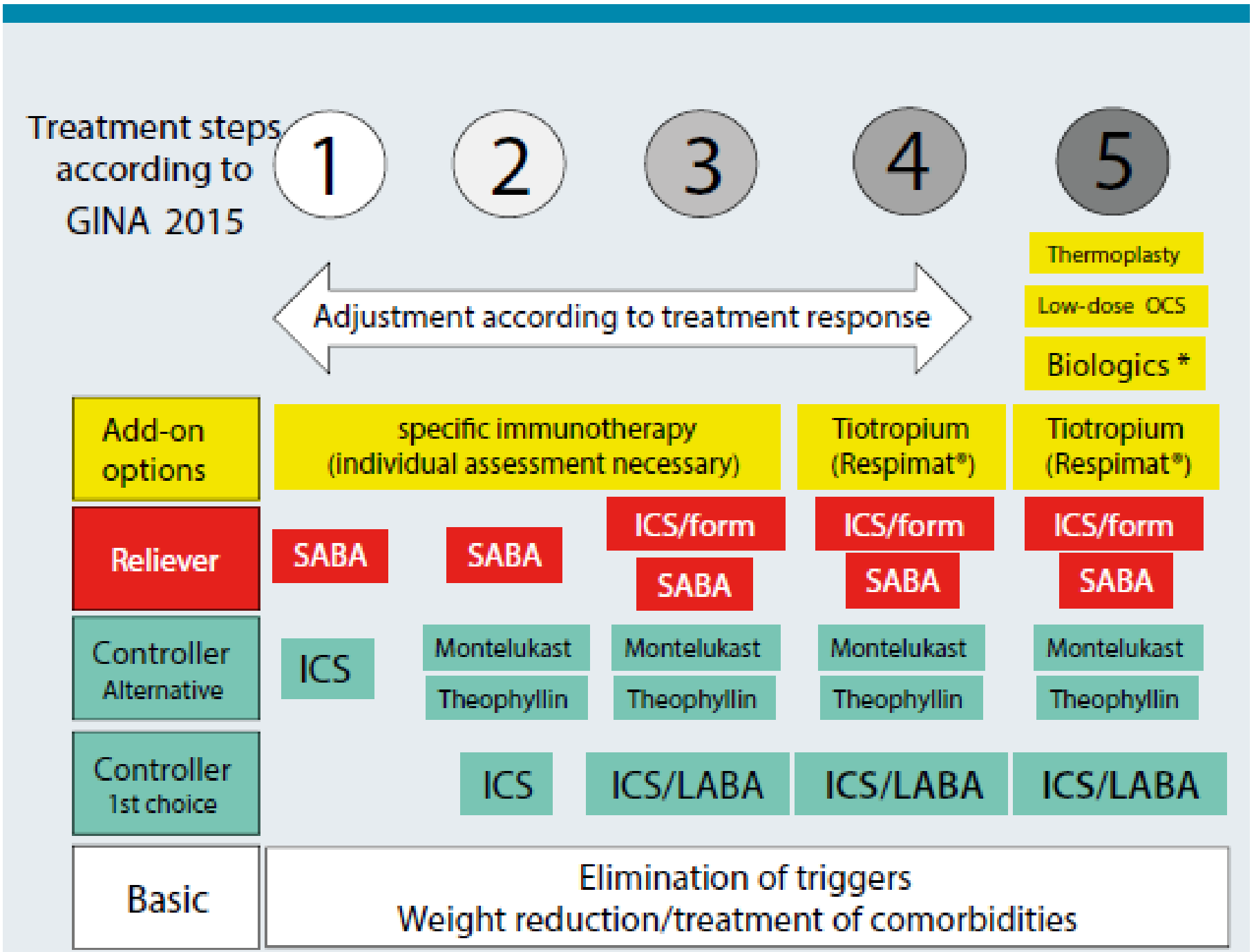


*Not for children <12 years

**For children 6-11 years, the preferred Step 3 treatment is medium dose ICS

#For patients prescribed BDP/formoterol or BUD/formoterol maintenance and reliever therapy

† Tiotropium by mist inhaler is an add-on treatment for patients ≥12 years with a history of exacerbations


Treatment steps according to GINA 2015
1
2
3
4
5
Thermoplasty
Low-dose OCS
Biologics *
Adjustment according to treatment response
Add-on options
specific immunotherapy (individual assessment necessary)
Tiotropium (Respimat®)
Tiotropium (Respimat®)
Reliever
SABA
SABA
ICS/form
SABA
ICS/form
SABA
ICS/form
SABA
Controller Alternative
ICS
Montelukast
Theophyllin
Montelukast
Theophyllin
Montelukast
Theophyllin
Montelukast
Theophyllin
Controller 1st choice
ICS
ICS/LABA
ICS/LABA
ICS/LABA
Basic
Elimination of triggers
Weight reduction/treatment of comorbidities

Assess and treat severe asthma phenotypes *cont'd*

Continue to optimize management as in section **3** (including inhaler technique, adherence, comorbidities)

6b Consider *add-on biologic Type 2* targeted treatments

- Consider add-on Type 2-targeted biologic for patients with exacerbations or poor symptom control on high dose ICS-LABA, who:
  - have eosinophilic or allergic biomarkers, or
  - need maintenance OCS
- Consider **local payer eligibility criteria** and **predictors of response** when choosing between available therapies
- Also consider cost, dosing frequency, route (SC or IV), patient preference

Which biologic is appropriate to start first?

Anti-IgE

*Is the patient eligible for **anti-IgE** for severe allergic asthma?*

- Sensitization on skin prick testing or specific IgE
- Total serum IgE and weight within dosage range
- Exacerbations in last year

What factors may predict good asthma response to anti-IgE?

- Blood eosinophils ≥260/µl ++
- FeNO ≥20 ppb +
- Allergen-driven symptoms +
- Childhood-onset asthma +

no / *no*

Anti-IL5 / Anti-IL5R

*Is the patient eligible for **anti-IL5 / anti-IL5R** for severe eosinophilic asthma?*

- Exacerbations in last year
- Blood eosinophils ≥300/µl

What factors may predict good asthma response to anti-IL5/5R?

- Higher blood eosinophils +++
- More exacerbations in previous year +++
- Adult-onset of asthma ++
- Nasal polyposis ++

no / *no*

Anti-IL4R

*Is the patient eligible for **anti-IL4R***

… for severe eosinophilic asthma?

- Exacerbations in last year
- Blood eosinophils ≥150/µl or FeNO ≥25 ppb

… or because of need for maintenance OCS?

What factors may predict good asthma response to anti-IL4R?

- Higher blood eosinophils +++
- Higher FeNO +++

Anti-IL4R may also be used to treat

- Moderate/severe atopic dermatitis
- Nasal polyposis

Eligible for none?

Return to section **6a**

Choose one if eligible; trial for at least 4 months and assess response

Good asthma response?

yes → Good response to T2-targeted therapy

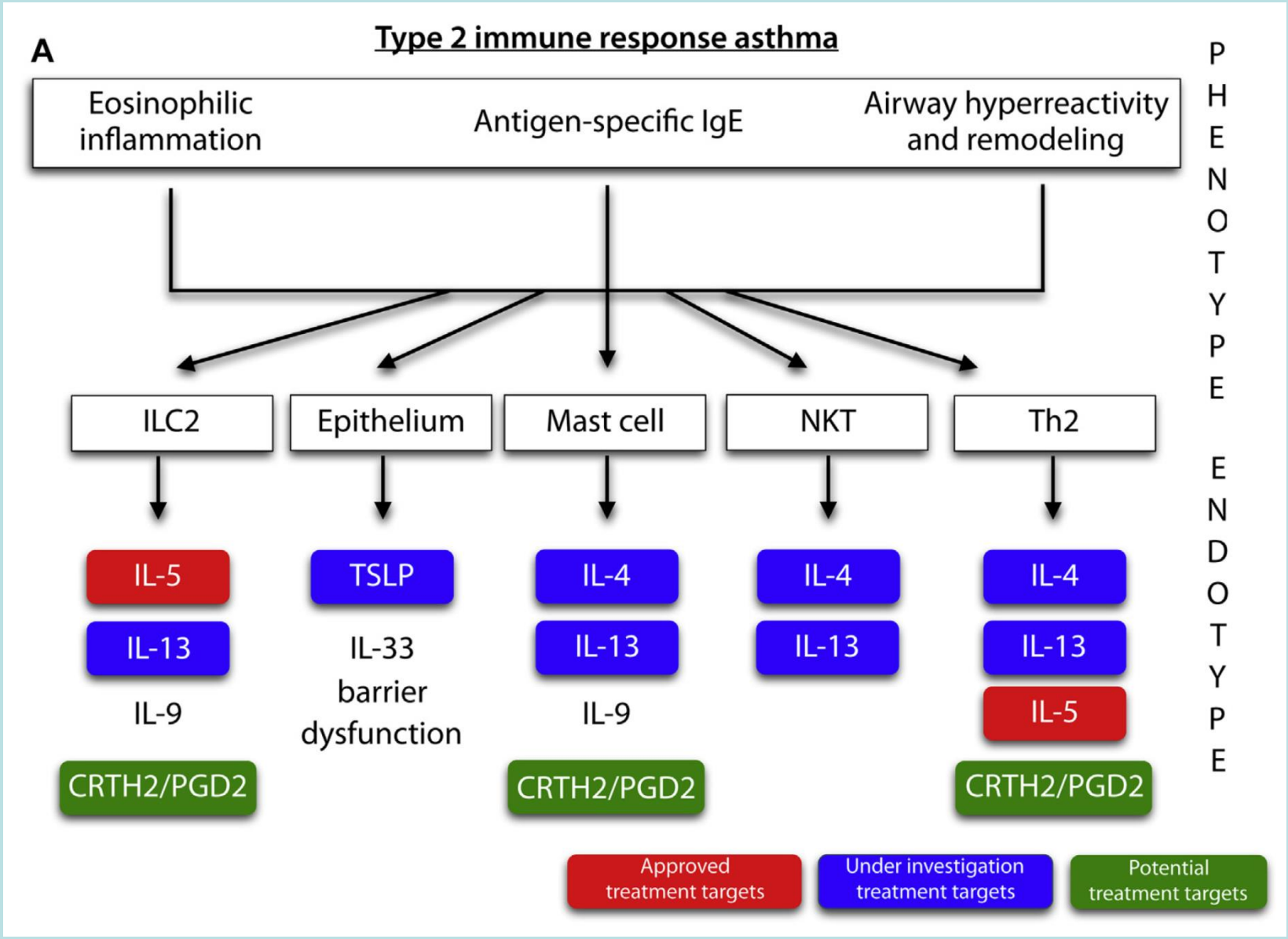
unclear → Extend trial to 6-12 months

no → **STOP add-on**

Consider switching to a different Type 2-targeted therapy, if eligible

no → Little/no response to T2-targeted therapy

Overview of the type 2 immune response in asthmatic patients



RCTs of Interventions Reducing Airway Smooth Muscle Mass in Asthma

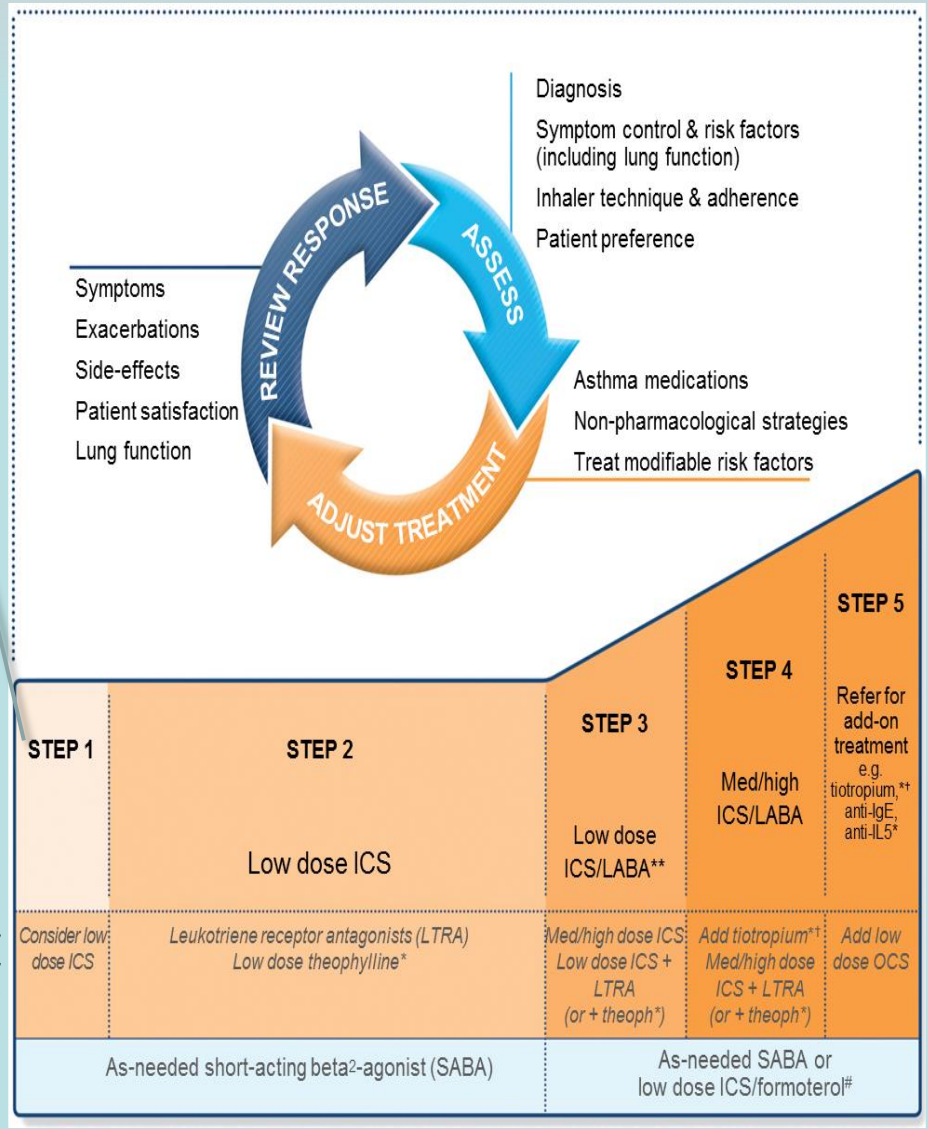
	Bronchoscopy Study	ASM reported	Intervention ASM ↓	Intervention ASM ↓ versus placebo
Corticosteroids	Yes	Yes	No	Unknown
Anti-IgE	Yes	No	Not Reported	Not Reported
Thermoplasty	Yes	Yes	**Yes**	Unknown
Gollopamil	Yes	Yes	Yes	No
Anti-IL5 (Mepolizumab)	Yes	Yes	No	No
Anti-IL5R (Benralizumab)	Yes	No	Not reported	Not reported
Anti IL13 (Lebrikizumab)	Ongoing?			
Anti IL13 (Tralokinumab)	Yes	No	No	No
Anti-IL4Rα (Dupilumab)	Ongoing?			
Anti-DP2	**Yes**	**Yes**	**Yes**	**Yes**

Berair R et al. *Drugs* 2014;74:1345-1369; Chernyavsky et al. *Eur Respir J* 2018; 515:1701680; Haldar et al. *N Engl J Med* 2009;360:973-984; Girodet et al. *Am J Respir Crit Care Med*. 2016;193:627-33; Russell et al. *Lancet Resp Med* 2018;6:499-510; Saunders et al. *Sci Trans Med* 2019;11:eaao6451.

GINA 2018 – main treatment figure

Step 1 treatment is for patients with symptoms <twice/month and no risk factors for exacerbations

Previously, no controller was recommended for Step 1, i.e. SABA-only treatment was 'preferred'



*Not for children <12 years

**For children 6-11 years, the preferred Step 3 treatment is medium dose ICS

#For patients prescribed BDP/formoterol or BUD/formoterol maintenance and reliever therapy

† Tiotropium by mist inhaler is an add-on treatment for patients ≥12 years with a history of exacerbations

Assessment of risk factors for poor asthma outcomes

Risk factors for exacerbations include:

- Uncontrolled asthma symptoms

Additional risk factors, even if the patient has few symptoms:

- High SABA use (≥3 canisters/year)
- Having ≥1 exacerbation in last 12 months
- Low FEV_1; higher bronchodilator reversibility
- Incorrect inhaler technique and/or poor adherence
- Smoking
- Obesity, chronic rhinosinusitis, pregnancy, blood eosinophilia
- Elevated FeNO in adults with allergic asthma taking ICS
- Ever intubated for asthma

Risk factors for fixed airflow limitation include:

- No ICS treatment, smoking, occupational exposure, mucus hypersecretion, blood eosinophilia; pre-term birth, low birth weight

Risk factors for medication side-effects include:

- Frequent oral steroids, high dose/potent ICS, P450 inhibitors

Initial controller treatment for adults, adolescents and children 6–11 years

- Start controller treatment early **GINA 2018**
  - For best outcomes, initiate controller treatment as early as possible after making the diagnosis of asthma
- Indications for regular low-dose ICS - any of:
  - **Asthma symptoms more than twice a month**
  - **Waking** due to asthma **more than once a month**
  - Any asthma symptoms plus **any risk factors** for exacerbations
  - **i.e. most asthma patients, to reduce risk of flare-ups**
- Consider starting at a higher step if:
  - Troublesome asthma symptoms on most days
  - Waking from asthma once or more a week, especially if any risk factors for exacerbations
- If initial asthma presentation is with an **exacerbation**:
  - Give a **short course of oral steroids** and **start regular controller treatment** (e.g. high dose ICS or medium dose ICS/LABA, then step down)

GINA 2018, Box 3-4 (1/2)

Background to changes in 2019 – the risks of ‘mild’ asthma

- Patients with apparently **mild asthma** are at risk of **serious adverse events**
  - 30–37% of adults with **acute asthma**
  - 16% of patients with **near-fatal asthma**
  - 15–20% of adults **dying** of asthma

  had **symptoms less than weekly** in **previous 3 months** *(Dusser, Allergy 2007)*
- Exacerbation **triggers** are variable (**viruses, pollens, pollution, poor adherence**)
- **Inhaled SABA** has been first-line treatment for asthma for 50 years
  - This dates from an era when asthma was thought to be a disease of bronchoconstriction
  - Patient satisfaction with, and reliance on, **SABA** treatment is reinforced by its **rapid relief** of symptoms, its prominence in **ED and hospital** management of exacerbations, and **low cost**
  - Patients commonly believe that ***“My reliever gives me control over my asthma”***, so they often don’t see the need for additional treatment

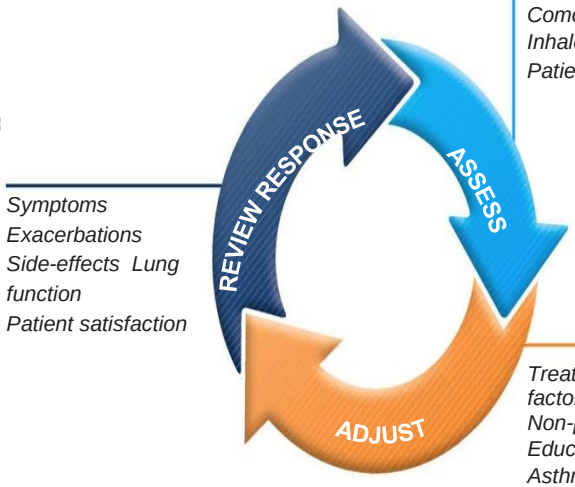
Background to changes in 2019 – the risks of SABA-only treatment

- Regular or frequent use of **SABA** is associated with adverse effects
  - **β-receptor downregulation, decreased bronchoprotection, rebound hyperresponsiveness, decreased bronchodilator response** *(Hancox, Respir Med 2000)*
  - **Increased allergic response**, and **increased eosinophilic airway inflammation** *(Aldridge, AJRCCM 2000)*
- Higher use of SABA is associated with adverse clinical outcomes
  - Dispensing of **≥3 canisters per year** (average 1.7 puffs/day) is associated with higher **risk of emergency** department presentations *(Stanford, AAAI 2012)*
  - Dispensing of **≥12 canisters per year** is associated with higher **risk of death** *(Suissa, AJRCCM 1994)*

Box 3-5A

Adults & adolescents 12+ years

Personalized asthma management:
Assess, Adjust, Review response



Confirmation of diagnosis if necessary
Symptom control & modifiable risk factors (including lung function)
Comorbidities
Inhaler technique & adherence
Patient goals

Symptoms
Exacerbations
Side-effects Lung function
Patient satisfaction

Treatment of modifiable risk factors & comorbidities
Non-pharmacological strategies
Education & skills training
Asthma medications

Asthma medication options:
Adjust treatment up and down for individual patient needs

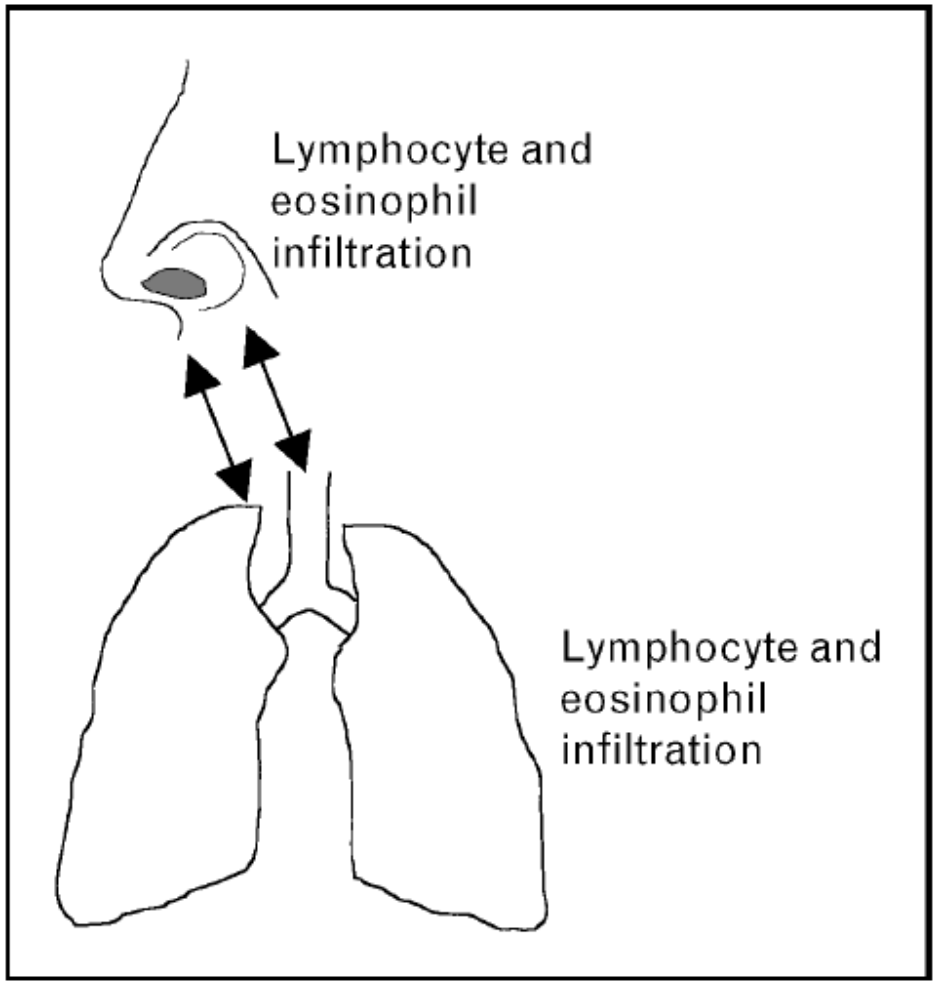
	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms	As-needed low dose ICS-formoterol *	Daily low dose inhaled corticosteroid (ICS), or as-needed low dose ICS-formoterol *	Low dose ICS-LABA	Medium dose ICS-LABA	High dose ICS-LABA Refer for phenotypic assessment ± add-on therapy, e.g.tiotropium, anti-IgE, anti-IL5/5R, anti-IL4R
Other controller options	*Low dose ICS taken whenever SABA is taken †*	*Leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken †*	*Medium dose ICS, or low dose ICS+LTRA #*	*High dose ICS, add-on tiotropium, or add-on LTRA #*	*Add low dose OCS, but consider side-effects*
PREFERRED RELIEVER	As-needed low dose ICS-formoterol *		As-needed low dose ICS-formoterol ‡		
Other reliever option	*As-needed short-acting β_2 -agonist (SABA)*				

* Off-label; data only with budesonide-formoterol (bud-form)
† Off-label; separate or combination ICS and SABA inhalers

‡ Low-dose ICS-form is the reliever for patients prescribed bud-form or BDP-form maintenance and reliever therapy
# Consider adding HDM SLIT for sensitized patients with allergic rhinitis and FEV >70% predicted

Functional relationship between upper and lower airway

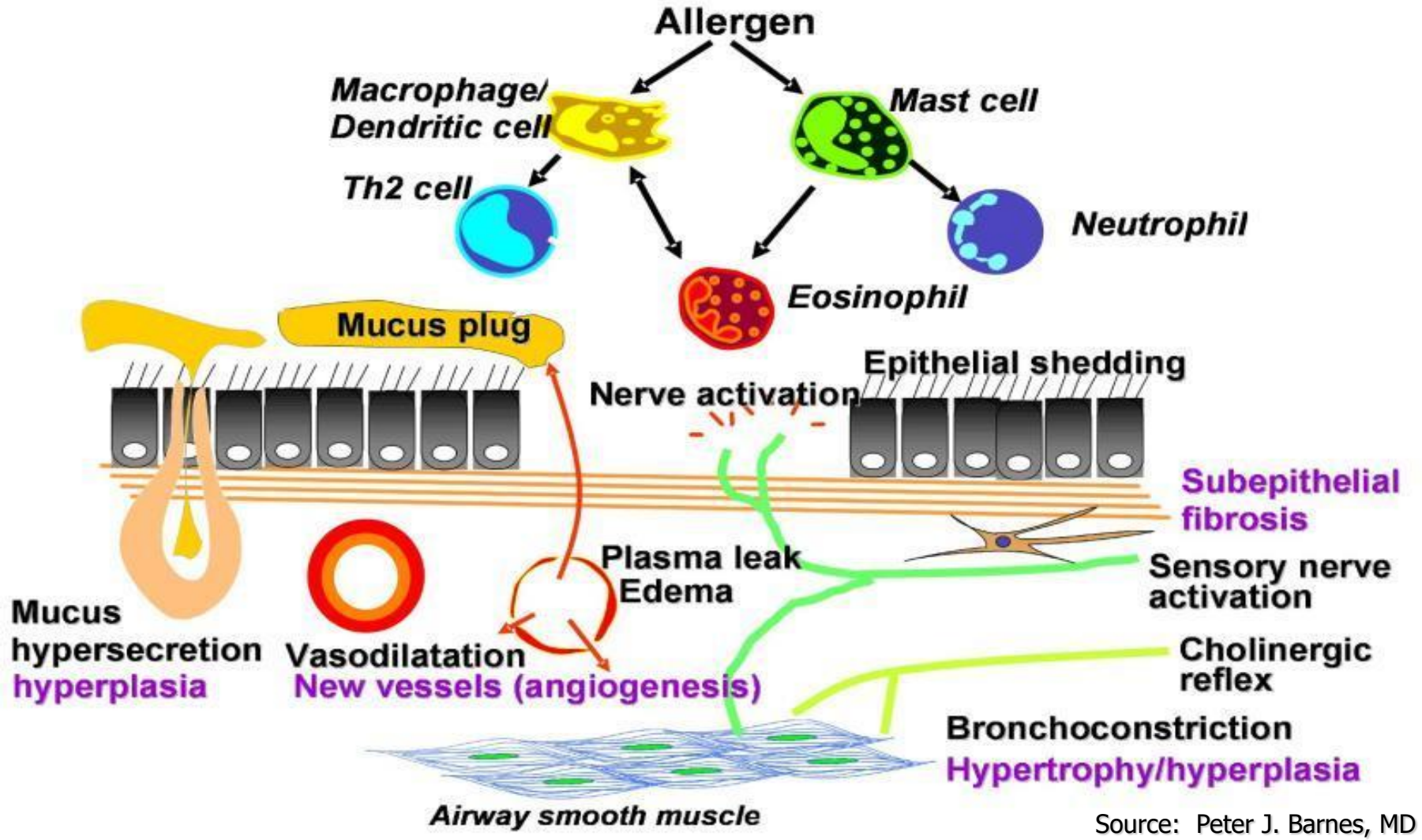
United airway disease
VS
One airway, one disease



Dixon AE. Current Opinion in Pulmonary Medicine 2009, 15:19–24

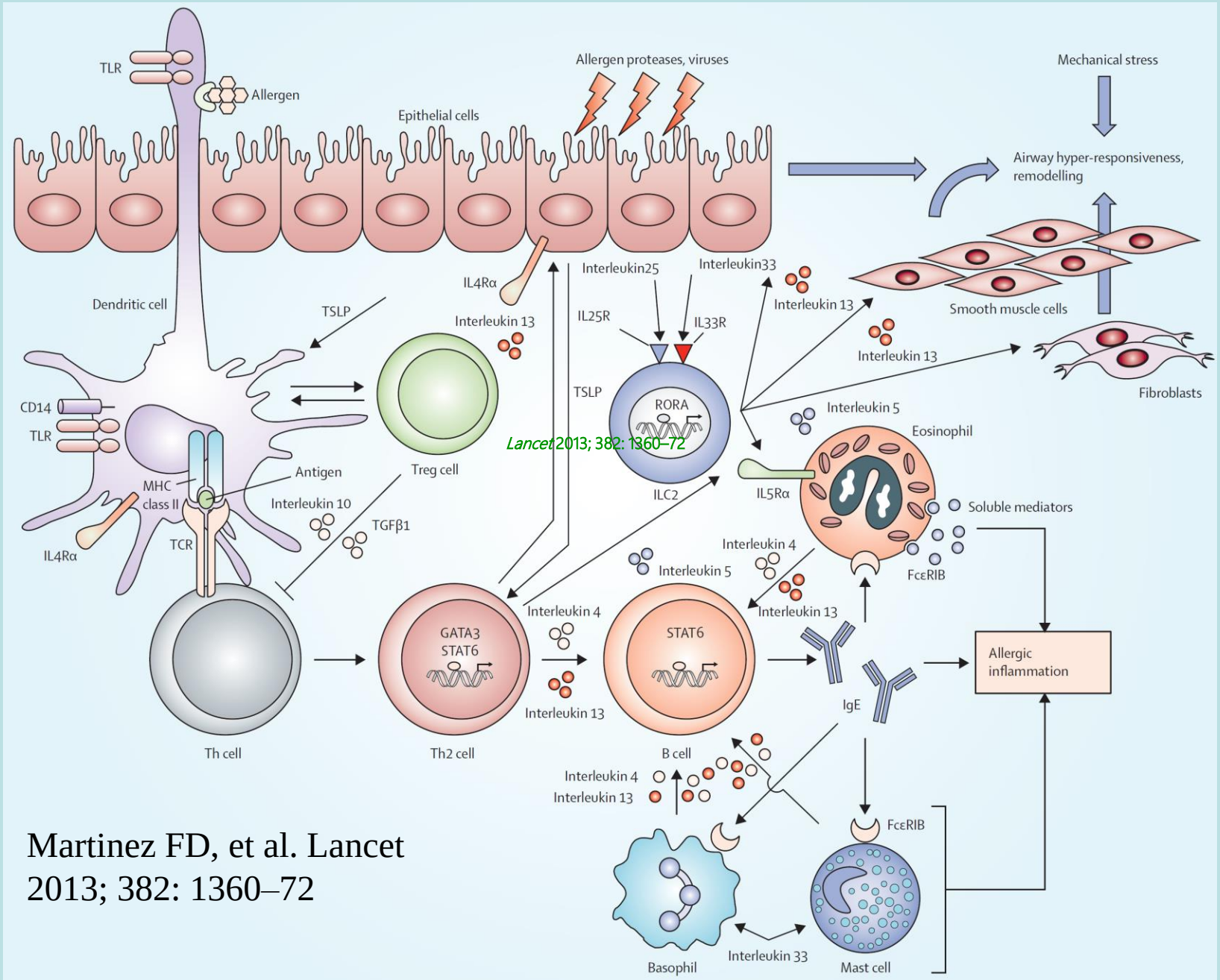
Inflammation in the nose, sinuses and lungs is characterized by similar inflammatory profile, and disease severity in nose and sinuses parallels that in the lungs of asthmatics.

氣喘致病機轉– 發炎反應



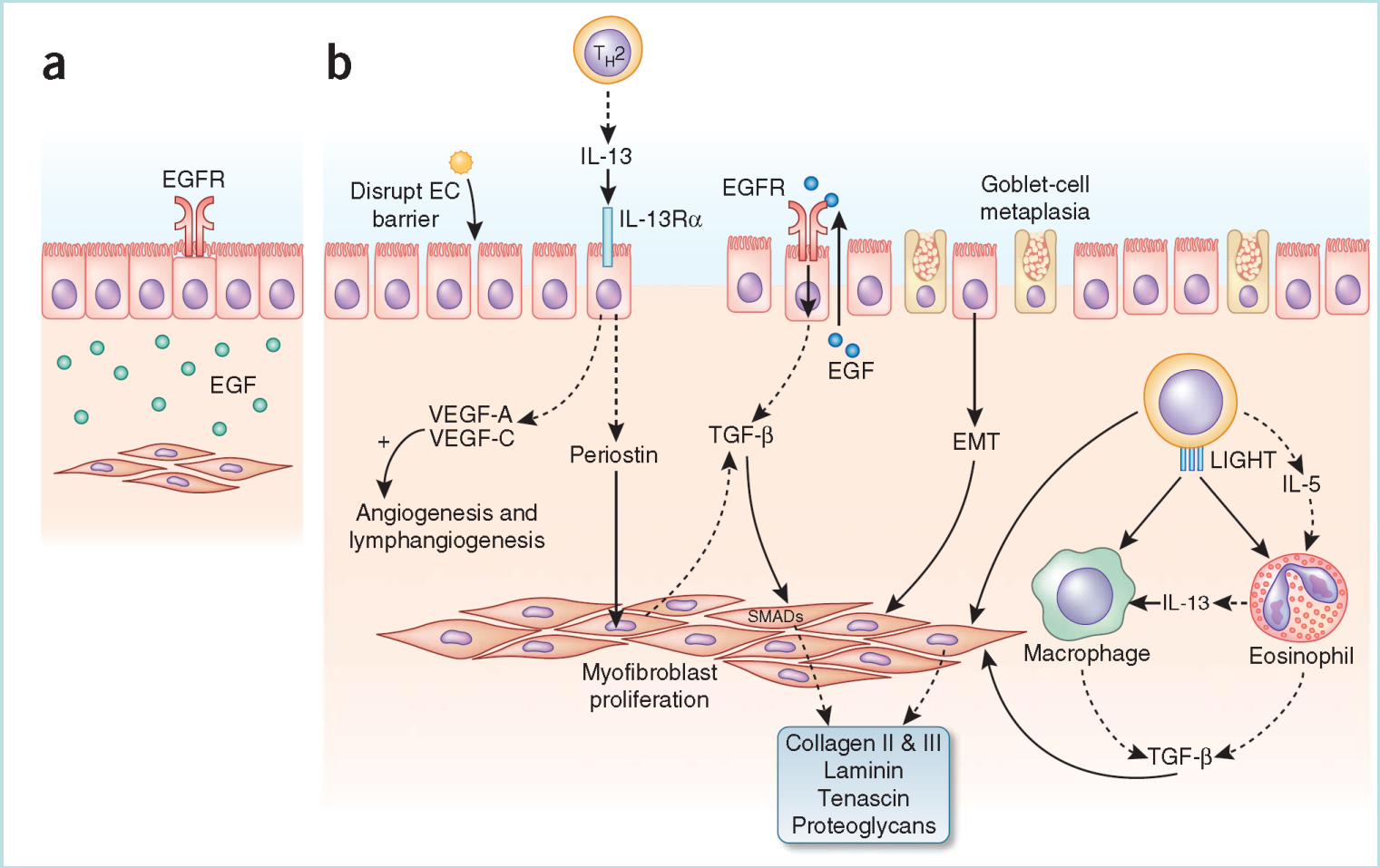
Source: Peter J. Barnes, MD

Major immune pathways involved in asthma pathogenesis

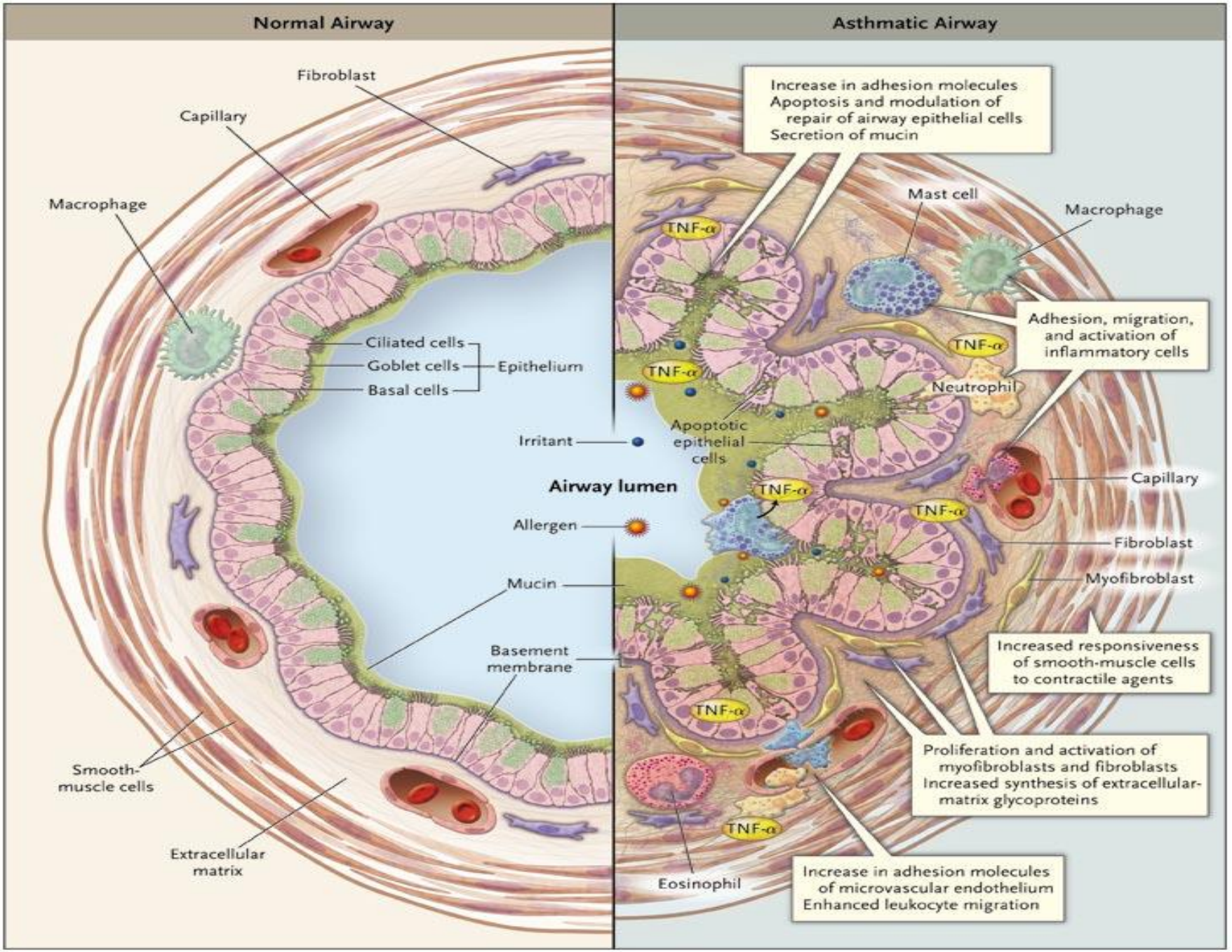


Martinez FD, et al. Lancet 2013; 382: 1360–72

Airway remodeling in the epithelial mesenchymal trophic unit



Lambrecht BN, et al, Nature Medicine 2012


Normal Airway
Asthmatic Airway
Fibroblast
Capillary
Macrophage
Ciliated cells
Goblet cells
Basal cells
Epithelium
Irritant
Airway lumen
Allergen
Mucin
Basement membrane
Smooth-muscle cells
Extracellular matrix
Increase in adhesion molecules
Apoptosis and modulation of repair of airway epithelial cells
Secretion of mucin
Mast cell
Macrophage
TNF-α
Adhesion, migration, and activation of inflammatory cells
Neutrophil
Apoptotic epithelial cells
Capillary
Fibroblast
Myofibroblast
Increased responsiveness of smooth-muscle cells to contractile agents
Proliferation and activation of myofibroblasts and fibroblasts
Increased synthesis of extracellular-matrix glycoproteins
Eosinophil
Increase in adhesion molecules of microvascular endothelium
Enhanced leukocyte migration

環境中有那些物質容易造成空氣污染

- 環境中會造成**空氣污染**的物質，包括**室內與室外的吸入型過敏原與空氣污染物**。環境中會造成空氣污染的室內外的吸入型過敏原與空氣污染物的過度增加，不但會造成免疫力正常的健康民眾容易產生呼吸系統疾病，對於免疫力偏差的呼吸道過敏病人所造成的傷害，會遠大於正常人。
- 居家的**環境污染影響健康**最嚴重的確定因素主要包括**抽煙與二手煙**、居家鄰近**交通頻繁的大馬路**、居家環境潮濕且有**黴菌**滋生以及家中有**塵蟎**及確定會過敏的**寵物**過敏原。

Indoor pollutions

Common sources of indoor pollution in the home environment	
Allergenic source	Main allergens
Cats	Der p 1
Dogs	Can f 1
Horse	Ecu cx
Rats/mice	Mus m 1, Rat n 1
House dust mites (HDM)	Der p 1, Der f 1, Der m 1
Tropical storage mite (*Bloomia tropicalis*)	Blo t
Cockroaches	Per a 1, Bla g 1
Mould (e.g. *Penicillium sp. Cladosporium sp, Alternaria sp.*)	various allergens
Pot plants (e.g. *Ficus benjamina, Yucca elephantipes, Dieffenbachia picta* and *Euphorbia pulcherrima*)	various allergens
Other indoor factors	Type of emissions
New building materials	formaldehyde, various VOC
New chip board	formaldehyde
Environmental tobacco smoke (ETS)	nicotin, aldehydes, particles, VOC
Biomass and wood combustion	aldehydes, particles, VOC
Low ventilation flow (poor ventilation)	Increased levels of all pollutants
Building dampness	aldehydes, VOC, microbial VOC (MVOC), mycotoxins, endotoxin, mould, bacteria, microbial compounds

過敏體質者避免接觸一些特定過敏原的方法

過敏原	避免接觸的方法
寵物	遷移寵物和清掃房屋，尤其是地毯和墊子的表面 鼓勵學校禁止寵物進入
塵蟎	每1至2週以熱水清洗一次寢具和衣服 每週一次，把填充玩具放進冷凍庫中 使用不通透的套子罩住床墊、枕頭和被褥 使用除濕機
蟑螂	清掃房屋 使用專業的除蟲方法 使用不通透的套子罩住床墊和枕頭
黴菌	使用稀釋的漂白水清洗發黴的表面 使用除濕機 修補滲漏處 不要放置地毯 使用高效能的HEPA空氣濾淨機

誘發過敏性體質發作的因素

- 在臺灣，家**塵蟎**是家中最主要的過敏原。它會導致多種過敏性疾病，例如**氣喘、過敏性鼻炎、過敏性結膜炎、蕁麻疹與異位性皮膚炎**等。

誘發過敏性體質發作的因素

- 在臺灣地區，**環保署**曾委託**臺灣大學昆蟲系徐爾烈教授**進行蟎相調查，結果發現臺灣地區75%住家充斥著**塵蟎**，室內**每公克灰塵**隱藏著**平均兩千隻以上**甚至有的高達一萬隻以上的塵蟎，遠高於誘發過敏氣喘所需要的**每公克灰塵一百**至一千隻以上**塵蟎**的濃度。而臺灣地區居家室內總蟎數分佈以地毯最多，其次爲**棉被、床墊、枕頭、地板、及沙發**。

居家有那些物質容易造成空氣污染

- 目前我們已知的主要的**室內空氣污染物**成份包括**懸浮微粒**(PM, particulate matter)、**一氧化氮**、**二氧化氮**、**一氧化碳**、**二氧化碳**、**二氧化硫**、**甲醛**(formaldehyde)、和**生物性內毒素**，這些污染物的產生來源可歸納如下列方式：

1. 用**天然氣或液化丙烷煮飯**，可產生細懸浮微粒(包括PM2.5)、二氧化碳、一氧化碳、二氧化硫、二氧化氮、以及一氧化氮。

居家有那些物質容易造成空氣污染

2. 用**木柴、煤油或煤煮飯**可產生一氧化碳、氮氧化合物、二氧化硫和懸浮微粒。
3. 用瓦斯、木柴、煤和煤油以及壁爐**取暖**者可產生一氧化碳、二氧化碳、一氧化氮、氮氧化合物以及懸浮微粒(包括顆粒性油煙)。
4. 使用含有揮發性有機物**甲醛**的泡沫充填物、粘膠、防火板、壓縮板、合板、地毯隔板以及編織物的**裝璜材料**，以及使用**油漆**或其他可釋放**異氰**的材質。

居家有那些物質容易造成空氣污染

5. 其他刺激氣體如家用**噴霧劑**、**揮發性有機化合物**(如**芳香劑**、**清潔劑**、**烹調油**等)和其他空氣污染物。
6. **抽煙與二手煙**可產生大量而複雜的混合氣體、蒸氣、和懸浮微粒(包括PM2.5），是最常見的室內刺激物的來源，菸草的煙霧中已鑑定出4,500種以上的化合物和污染物，其中包括可吸入性懸浮微粒、多環氫碳化合物、一氧化碳、二氧化碳、一氧化氮、尼古丁和丙烯醛(acrolein)等。
7. **室內空氣汙染**源約有**28%是來自室外**空氣污染。

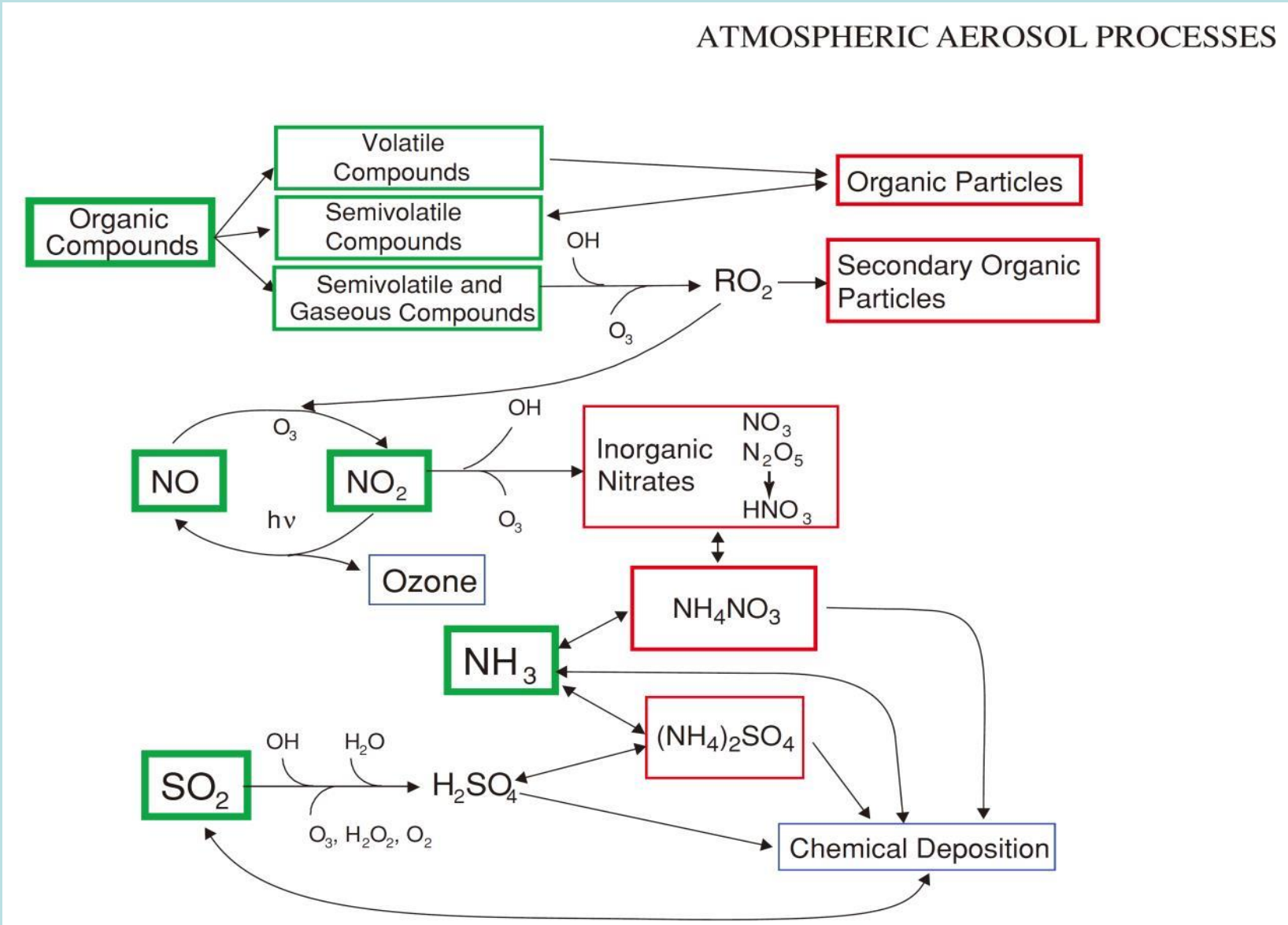
室外有那些物質容易造成空氣污染

- **室外空氣污染**(目前歸類為**第一級致癌物**與**肺癌**有關)的型式主要可分為：**工業煙霧**(二氧化硫顆粒複合物)和**光化煙霧**(臭氧和氮氧化合物)以及**懸浮微粒**，在某些地區可混合存在(所謂的霾害)。空氣污染物的程度多寡乃受天候條件和當地的地理特徵影響。
- **室外懸浮微粒**(目前也被歸類為**第一級致癌物**與肺癌有關)包括**人為**(如來自車輛、工廠、焚化爐之廢氣、香煙等)及**自然環境**(如森林火災所造成的霾害或大陸的沙塵暴及工廠汽車汙染的霾害等)的影響。
- **汽機車**，特別是柴油車所排放的廢氣最為可怕，因為它所產生的超細懸浮微粒體積最小，而且**柴油車**所噴發的**超細懸浮微粒**是一般汽車的**100倍**，因此引發人體呼吸道疾病及癌症的可能性也就越大。

細懸浮微粒(PM2.5)生成機制

- **細懸浮微粒**(PM2.5)，係指懸浮在空氣中氣動粒徑小於2.5μm以下的粒子。
- PM2.5懸浮微粒來源可分為**自然界產出**及**人類行為產出**等二種。自然界產生源包含火山爆發、地殼岩石等，人類行為則以燃燒為主，如石化燃料及工業排放、移動源廢氣等燃燒行為。
- **PM2.5包含許多化學性物質**， 其中經**光化反應**後，常見形成組成有**原生性有機碳、衍生性有機碳、元素碳、硫酸鹽、硝酸鹽、及其他離子性物質**，反應生成機制相當複雜，如下圖所示。

細懸浮微粒(PM2.5)生成機制



細懸浮微粒(PM2.5)如何影響敏感脆弱族群

細懸浮微粒(PM2.5)對人體呼吸系統主要有三種影響：

- 對**主支氣管**產生危害，造成纖毛麻痺、支氣管粘膜過度分泌、粘液腺增生，引起可逆性痙攣，抑制深呼吸，並漫延至小支氣管道。
- 粒徑較小之微粒對**末稍細支氣管**有強烈之影響，且低濃度的微粒即可造成明顯的反應，並可能形成慢性支氣管炎、細支氣管擴張、肺水腫或支氣管纖維化等症狀。
- 粒徑1μm以下之微粒特別容易到達細**肺泡組織**，促使肺部之巨噬細胞明顯增加，形成肺氣腫並破壞肺泡。

細懸浮微粒(PM2.5)如何影響敏感脆弱族群

- 細懸浮微粒(PM2.5)會入侵身體，深入到**肺泡**，甚至沉入肺泡的**微血管**中，可以自由穿透人體的細胞組織，藉由**血液循環**，跑遍全身各處。對於**全身**都會有影響，特別是**心、肝、肺、腎及大腦**。
- 對於**呼吸道**的影響，主要的症狀有咳嗽、呼吸困難等，不但會降低肺功能、促發氣喘、引起慢性氣管炎，還可能增加呼吸疾病的住院率及死亡率以及**老人和孩童**的慢性呼吸系統疾病的危險性。
- 兒童**中耳炎**的反覆發作，嚴重的話會導致**兒童聽力受損**。
- 對於**心臟**方面，它會造成**心跳速率不規律**，以及心跳該快不快、該慢不慢的心跳速度變異性降低，這些都可能會引發**心肌梗塞**等心臟病風險。會降低左心室的功能，也可能造成**心臟衰竭**等嚴重的心臟病。會造成**冠狀動脈疾病**。會影響**自主神經**系統的恆定性。

細懸浮微粒(PM2.5)如何影響敏感脆弱族群

- 可能會造成**早產**、**流產**的機率增加及**新生兒死亡**。
- 會使孩童**學習**及語文**記憶**能力下降，達平均3.4%。
- 會引起主**動脈粥狀硬化**。
- **中風**病人的死亡率和他死前2小時所接觸的空氣微粒污染程度有關。
- 會造成神經退化性疾病，如阿茲海默症（**老年痴呆症**）。
- 會引起精神官能症(尤其是**憂鬱症**)。
- **第二型糖尿病**、**肥胖症**、**死亡率**。
- PM10每增加10微克，**肺腺癌**增加51%；PM2.5每增加5微克肺腺癌增加55%。肝炎、**肝癌**(PM2.5)。**胃癌**(PM2.5)。**膀胱癌**(PM10；PM2.5)。**卵巢癌**(PM2.5)。
- 如果空氣中的懸浮微粒中含有**金屬成份**，有可能會引發及加成**肺癌**的產生。

如何避免空氣對人體的危害

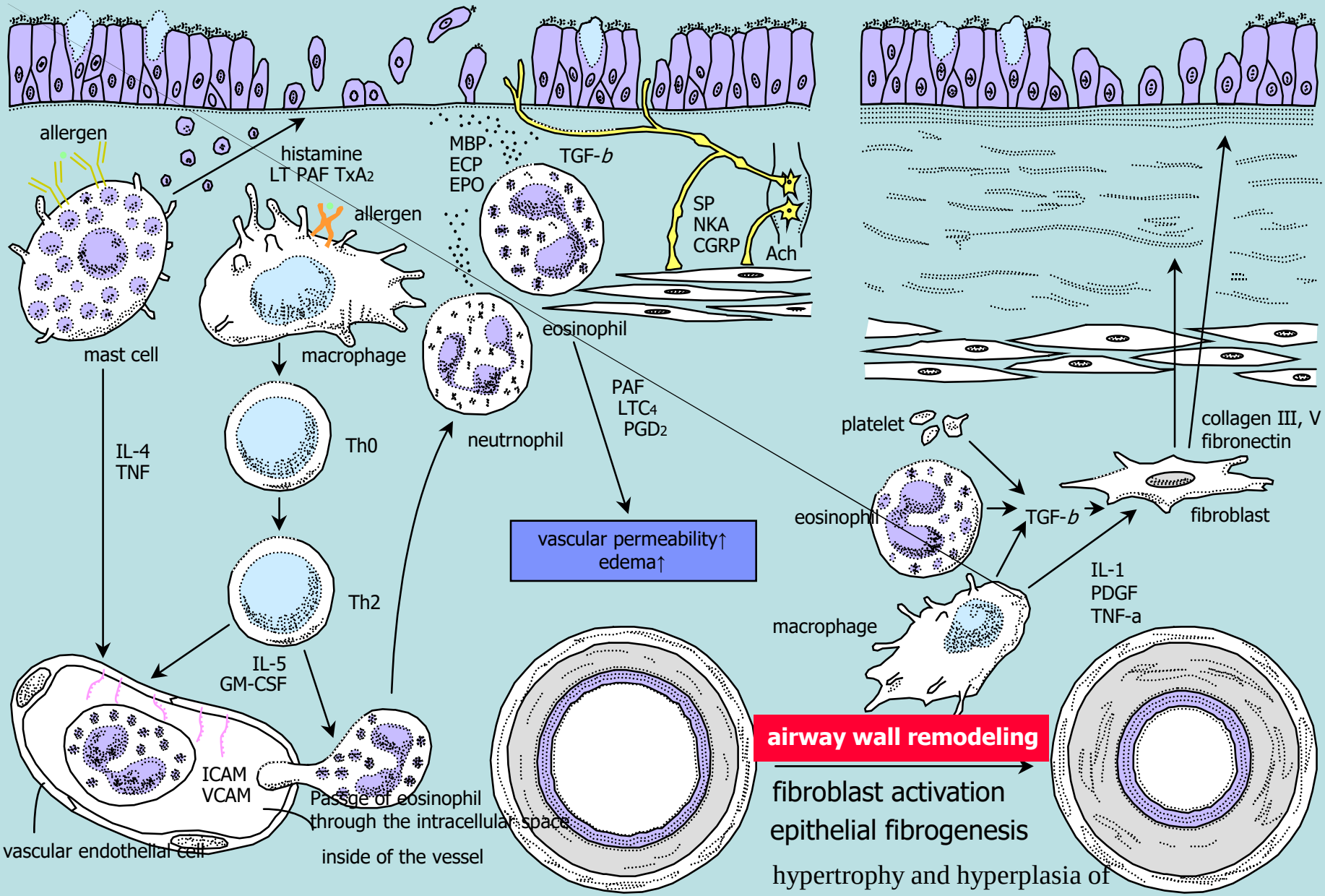
- 由於**空氣汙染**暴增大量懸浮微粒(尤其是PM2.5)，造成空氣品質惡化，因此患有呼吸道疾病或心血管疾病之民眾，尤其是**老年人或小孩**，在此期間應該遵守下列原則：
- 盡量**避免出門**，**緊閉門窗**，居家使用**空調**，可使用具高效能粒子空氣過濾（high-efficiency particulate air filter；**HEPA**）系統的**空氣濾淨機**。
- **如需外出**，則應帶上**口罩、護目鏡、穿著長袖衣物與長褲**以隔離髒空氣，避免直接之接觸。**回家後儘速清潔**衣物與身體。戴**隱形眼鏡**者因可能會刺激眼睛我們建議暫時**不帶**。
- **氣喘患者**或呼吸道敏感族群外出須攜帶**急救藥物**。年紀大的氣喘患者如要外出，尤其是出外晨間運動，最好還須要有**家人陪伴**以防萬一。

氣道變形

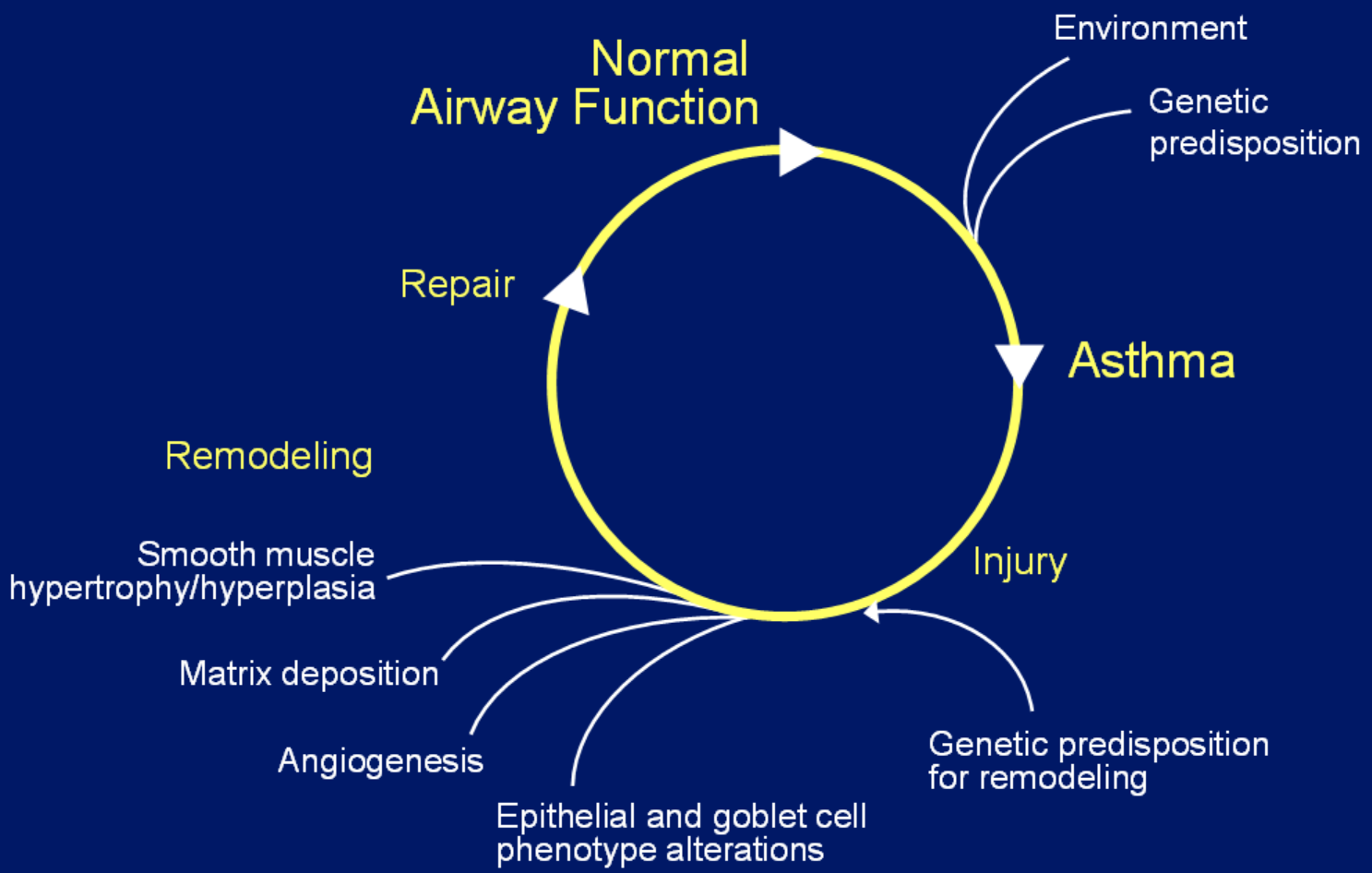
氣道變形

- **氣道變形**所引起的**結構變化**包括有**平滑肌**細胞的增生，**黏液腺體**的肥大，皮下組織的**纖維化**，**血管生成**，**神經**密度和**細胞外基質**的改變。
- 每一位氣喘病患的氣道變形皆不盡相同，其造成的結果亦是多樣化。
- 近年來的研究發現建議：要**避免孩童氣道變形**，逐漸喪失肺功能，過敏免疫學專科醫師需要於**五歲以前**找出氣喘病童並加以治療。

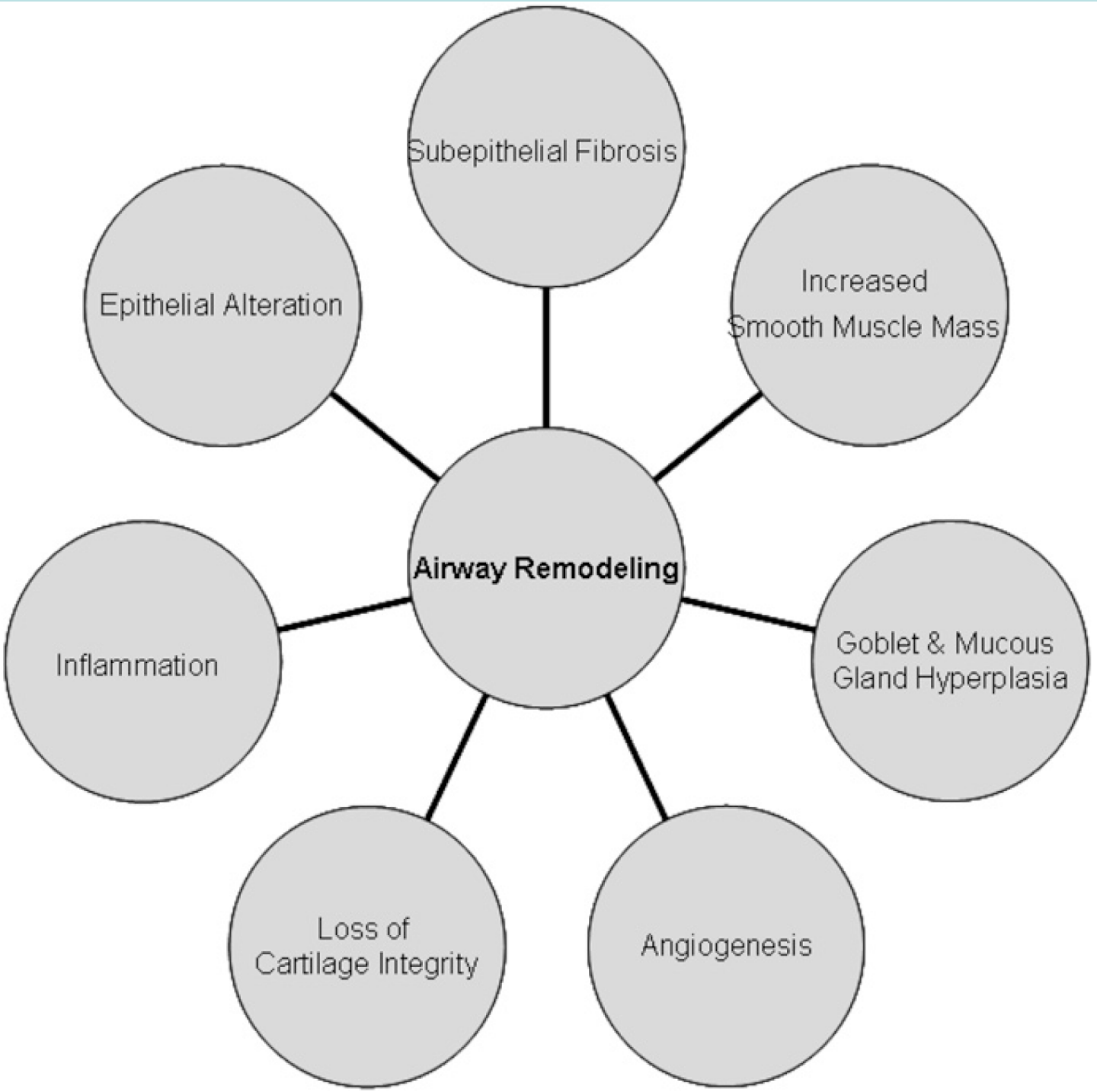
Airway Inflammation and Remodeling



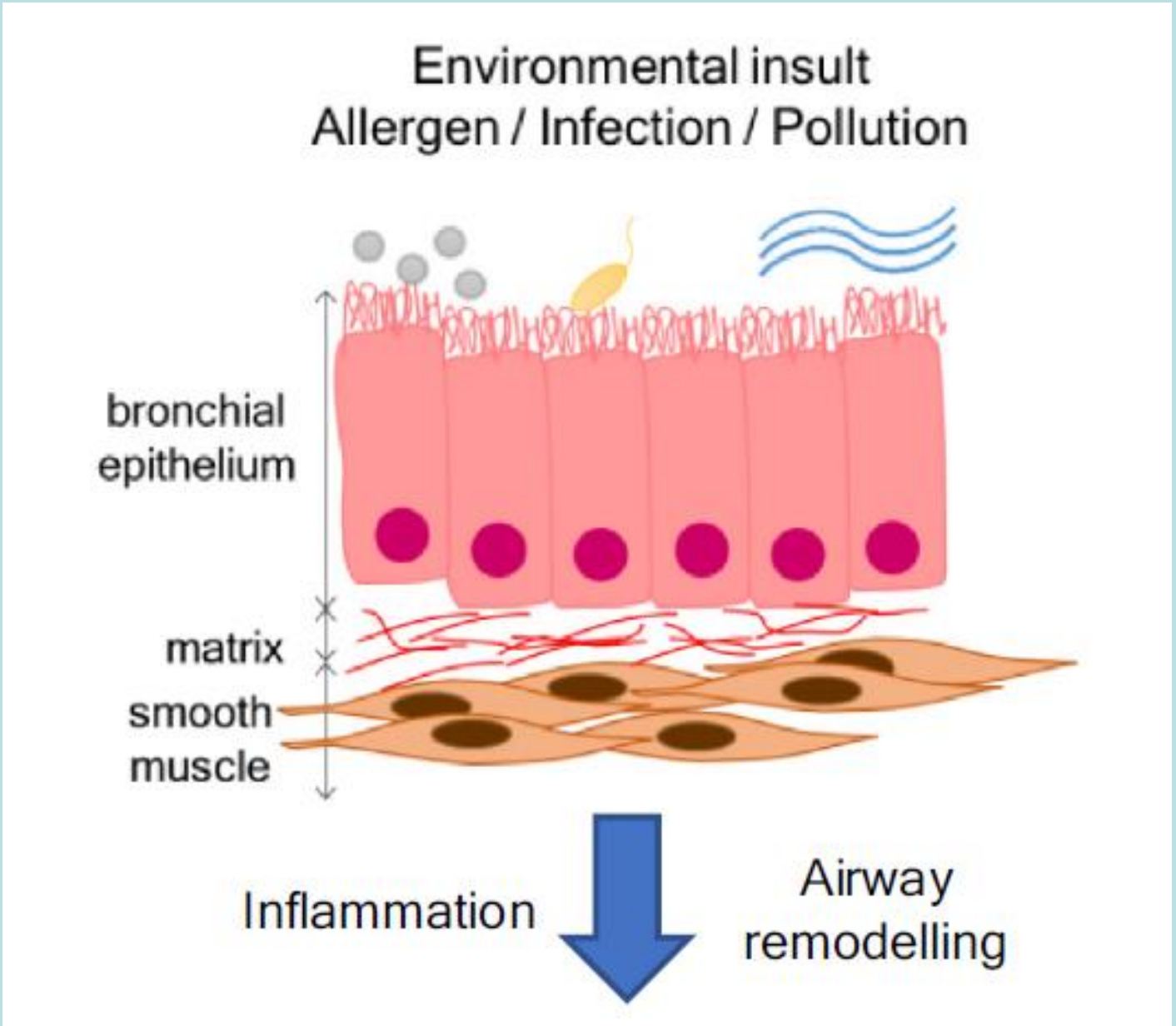
Possible Factors Contributing to Airway Remodeling



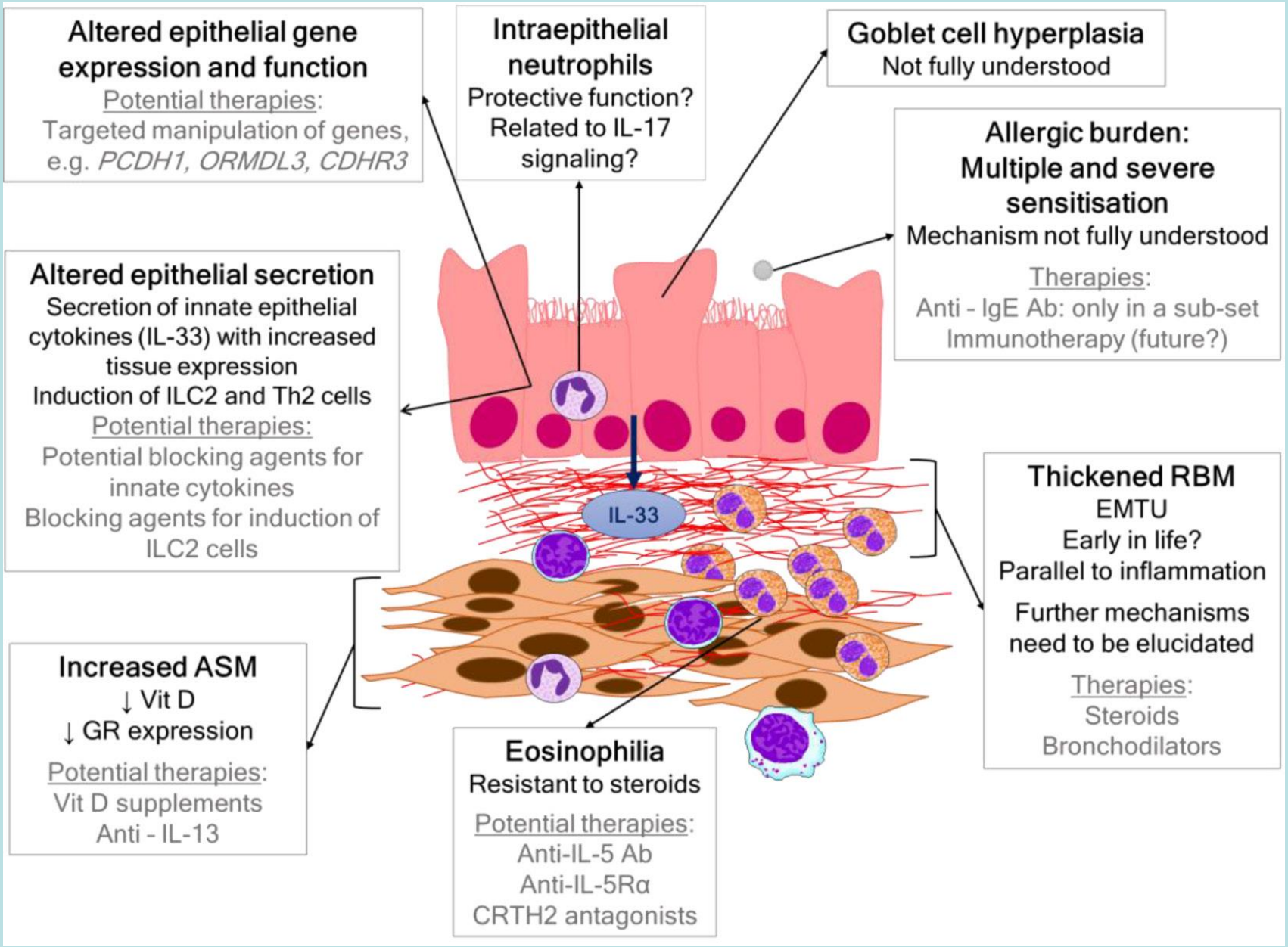
Main characteristics of airway remodeling



Scheme showing airway wall features, mechanisms, and current and/or potential therapies in pediatric severe asthma



Scheme showing airway wall features, mechanisms, and current and/or potential therapies in pediatric severe asthma



感謝您的聆聽

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