

* Allergic Rhinitis

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Definition

“IgE mediated hypersensitivity disease of mucous membranes of nasal airways characterized by sneezing, watery nasal discharge, itching and nasal obstruction” (Durham, 1999)



Prevalence

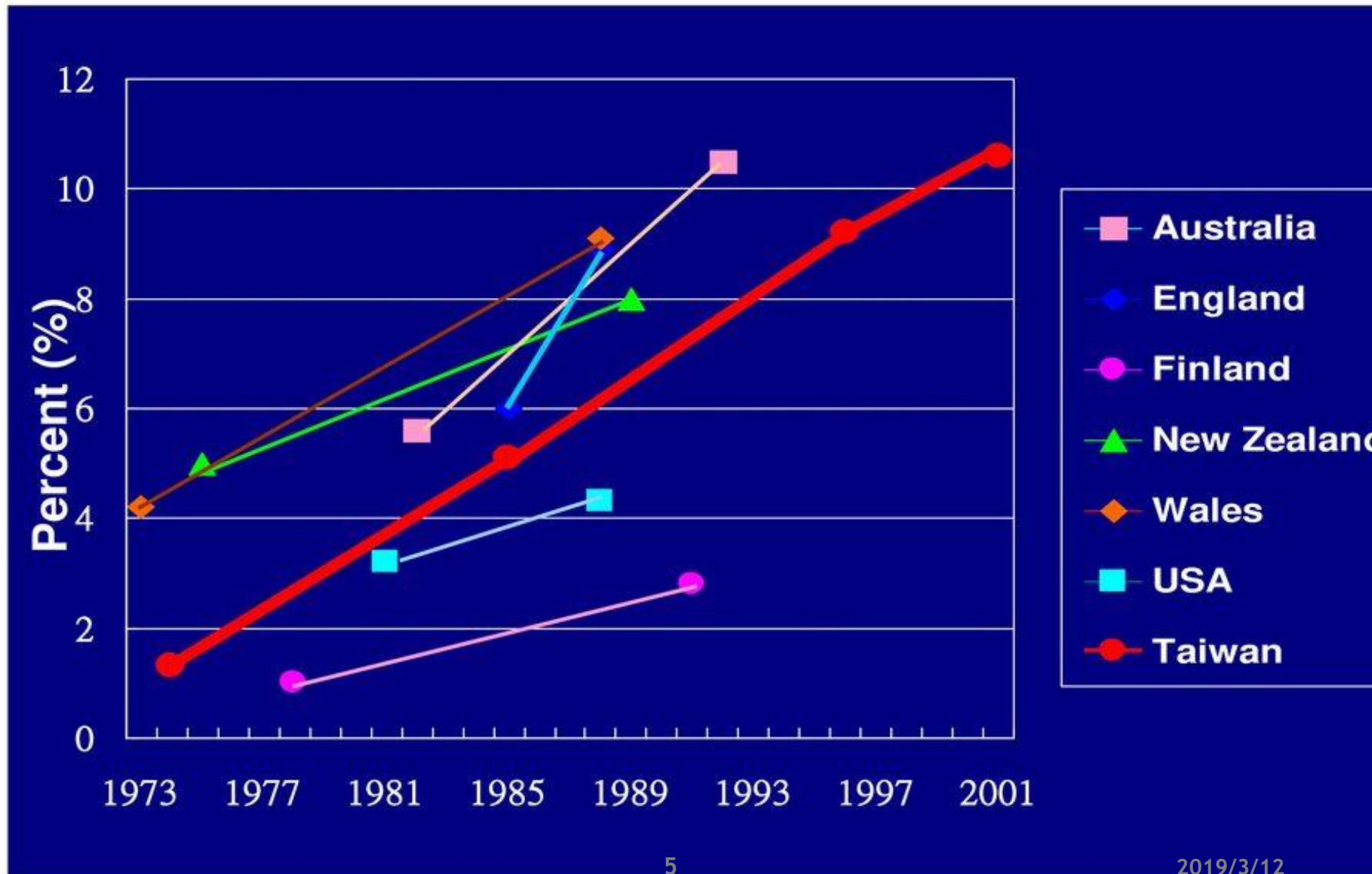
- Global health problem
- Prevalence - 15% and 20% (Nathan et al.,1999)
- Higher in pediatric age group(Wright et al.,1994)
- Approx. 80% develop symptoms before age of 20 (Skoner et al., 2001)



Allergic Rhinitis (AR)

- Clinically definition: a symptomatic disorder of the nose, allergen exposure, IgE-mediated inflammation
- Global health problem (2008)
 - (1) > 10-25 % (600 million) of general population
 - (2) 29.3% were persistent AR in the global study
- Increasing prevalence of allergic rhinitis
 - (1) UK: 12.0 % (1958) → 23.1 % (1970)
 - (2) Taiwan (NTUH, Ped.): 7.8 % (1985) → 33.5 % (1994)
(perennial type: 40%, combined Otitis Media / Paranasal Sinusitis: 33%)
 - (3) Taiwan (北市醫, 北市二萬名小一生): 49.4 % (2008)

Changing prevalence of atopic disease in children



Epidemiologic Study of Atopic Disease in Taiwan

Asthma >> Allergic rhinitis
Hospital-based >> Community-based

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Climate, traffic-related air pollutants and allergic rhinitis prevalence in
middle-school children in Taiwan

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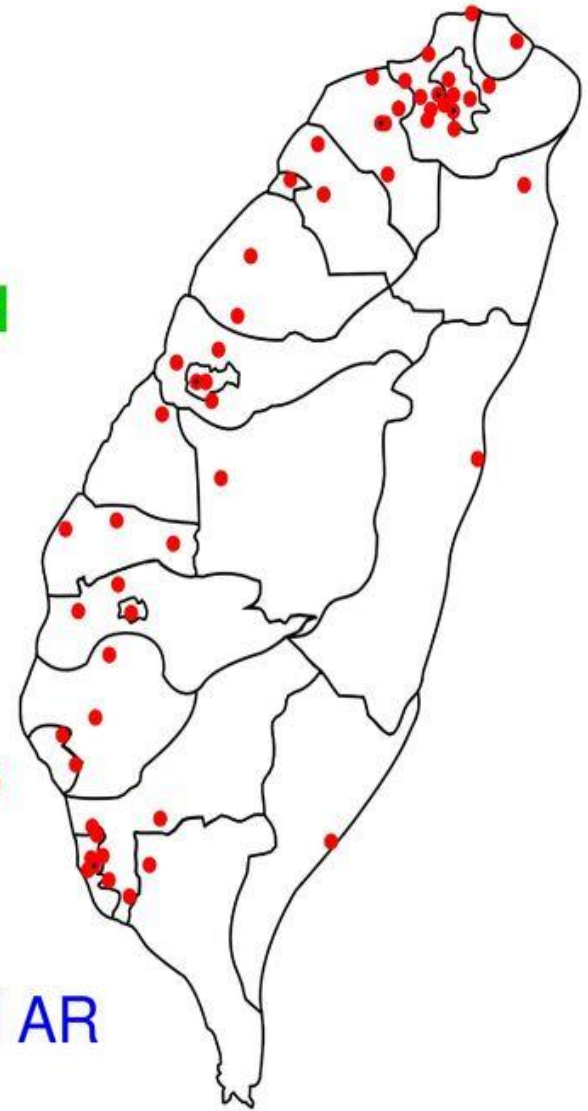
1018031, nationwide survey, 1995-1996

Prevalence of physician-diagnosed AR

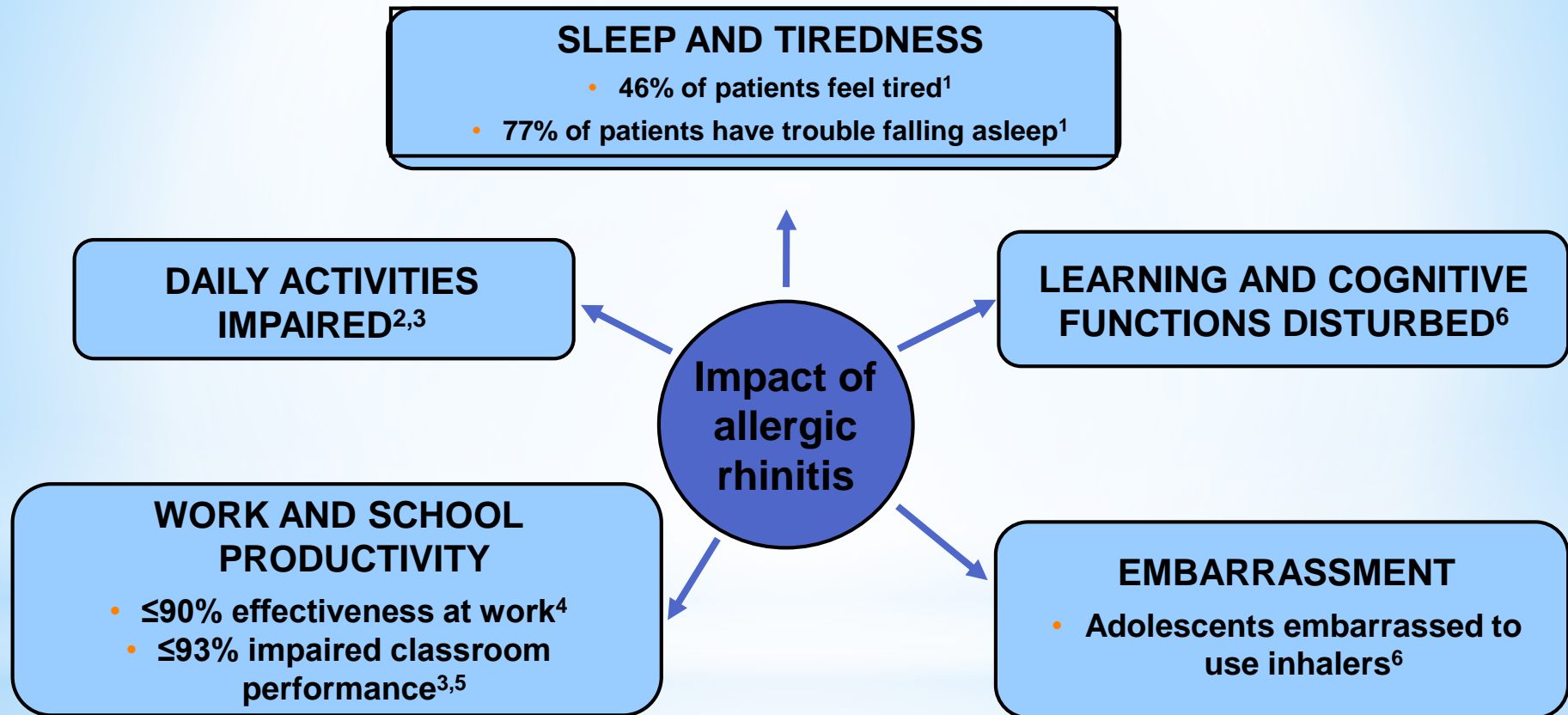
→ M / F = 28.6 % / 19.5%

Prevalence of questionnaire-determined AR

→ M / F = 42.4 % / 34.0% (ISAAC)

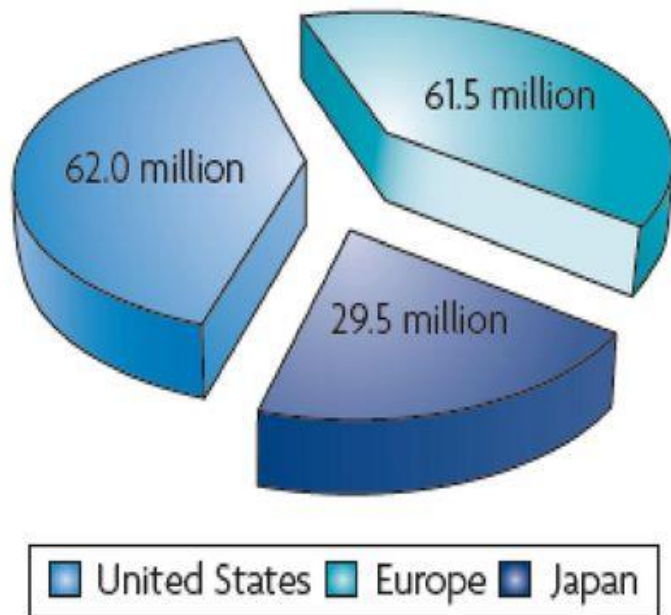


* Impact of allergic rhinitis on patients' daily life



1. Scadding G et al. EAACI 2007, Abstract 1408. 2. Reilly MC et al. *Clin Drug Invest* 1996;11:278–88.
3. Tanner LA et al. *Am J Manag Care* 1999;5(Suppl 4):S235–S247. 4. Blanc PD et al. *J Clin Epidemiol* 2001;54:610–18.
5. Juniper EF et al. *J Allergy Clin Immunol* 1994;93:413–23. 6. Marshall PS, Colon EA. *Ann Allergy* 1993;71:251–8.

a



b

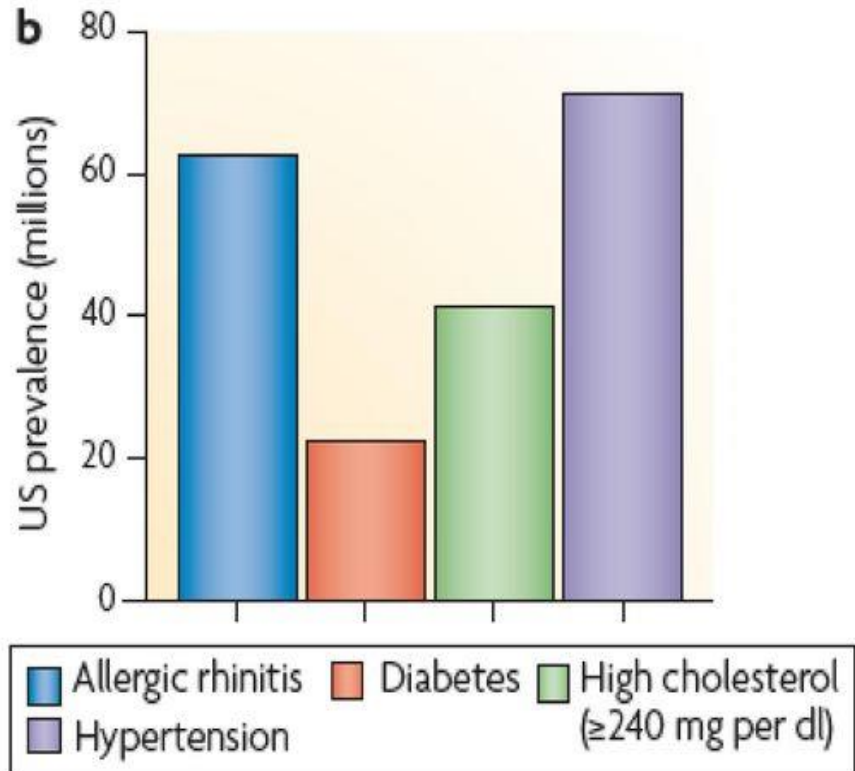
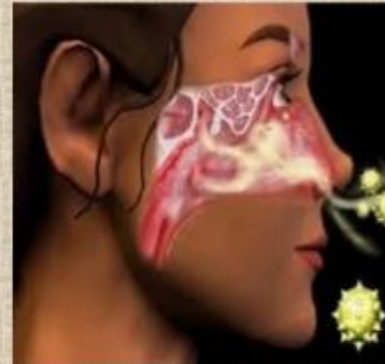


Figure 1 | **The prevalence of allergic rhinitis is comparable to other major chronic diseases.**
a | Global prevalence of allergic rhinitis². **b** | Estimated US prevalence of various chronic conditions¹⁻⁴.

(Clark et al., 2009)

Risk factors

1. Genetic susceptibility:
2. Family history of atopy: e.g. asthma,eczema,hay fever,urticaria
(Genes involved in atopy - loci on 5q,11q and 12q chromosomes)
3. Environmental factors:
 - Pollution-climate interaction
 - **Irritants**
eg. fumes, tobacco smoke, diesel exhaust, mosquito repellents, perfumes, scented sticks, domestic sprays, bleaches
4. Exposure to **allergens**:
 - Seasonal : Pollen, Fungus
 - Perennial: Dust mite, domestic pets, cockroaches



5. Hygiene hypothesis

- Increased exposure to various allergens → immune maturation → help decrease the incidence of allergic diseases and asthma (Svanes C et al., 2003)
- Early environmental exposure to infectious agents, protects against development of atopy (Tulic MK et al., 2003)
- Early nursery attendance also reduces subsequent atopy (Kramer et al., 2003)
- Lack of immune maturation (understimulated immune system) in infancy → allergic responses (Liu A, 2007)



Predisposing factors

- Atopic factor

- 56-74% of asthma associated with A.R.

- 17-19% of A.R. associated with asthma

“one airway, one disease”

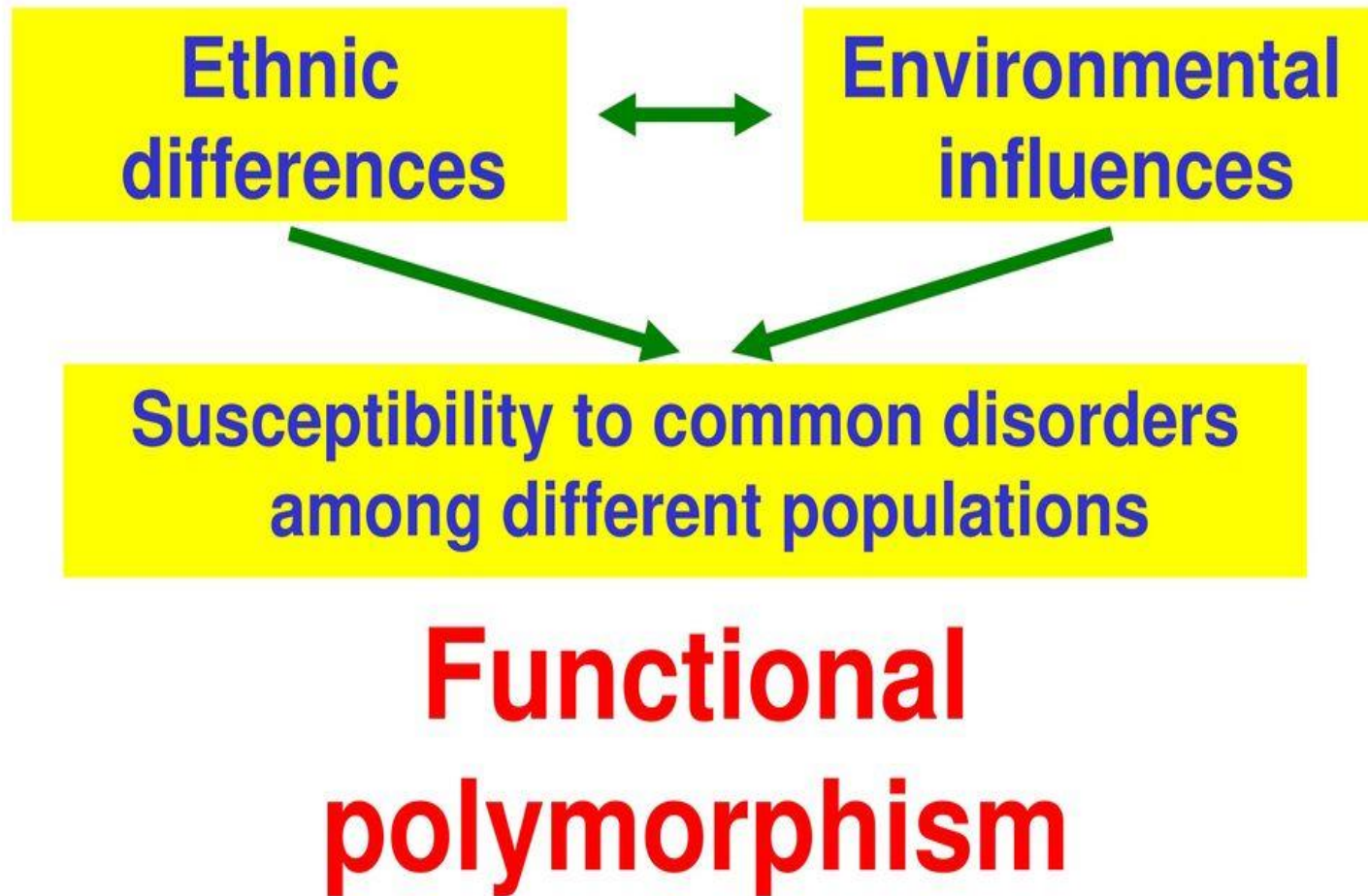
- Two parents(+): 47% risk

- Possible genes on chromosomes 5q, 11q

- Early exposure of aeroallergen

- Higher risk if born just before pollen season

Uncertainty still exits on the way !!!



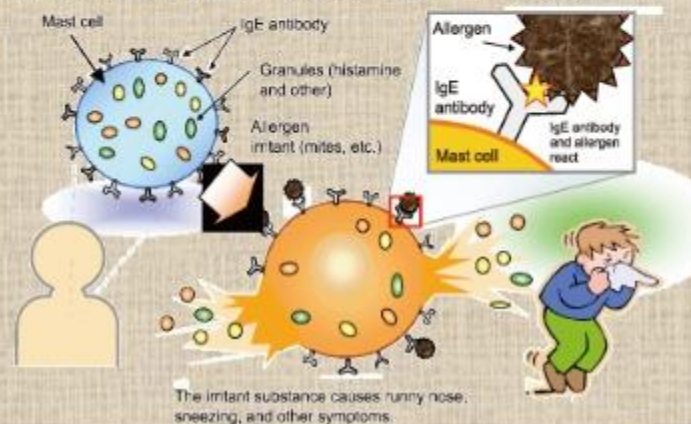
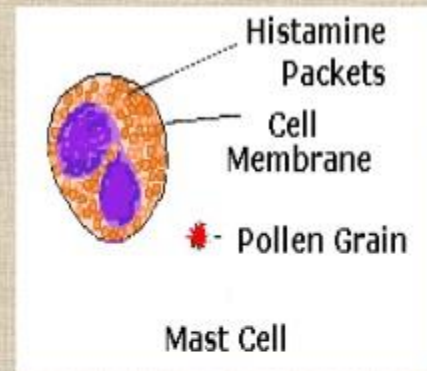
Pathogenesis

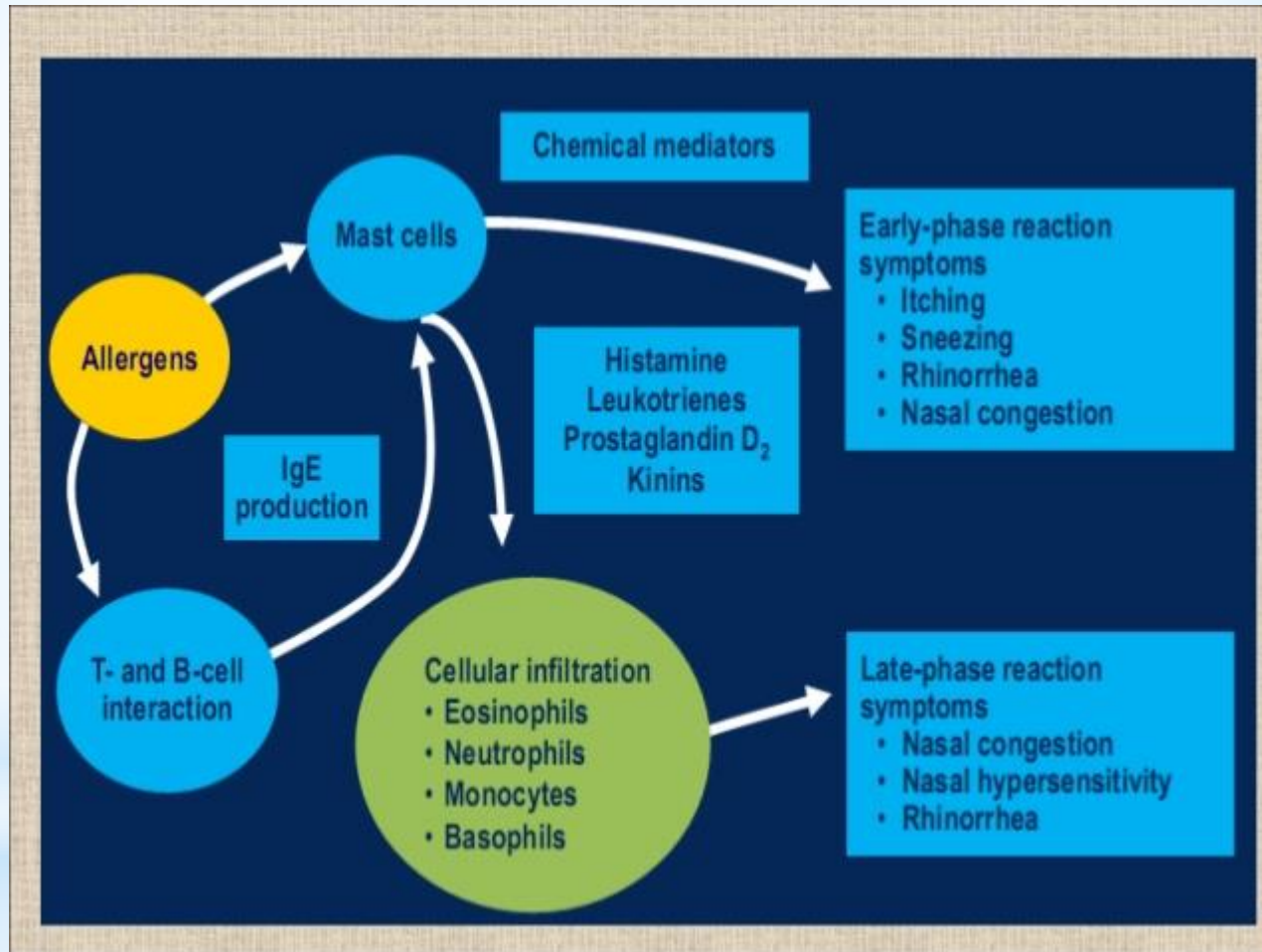
- Sensitization & Priming to specific antigen:

Inhaled allergen produces specific IgE antibody which gets attached to mast cells

- Subsequent exposure to same antigen:

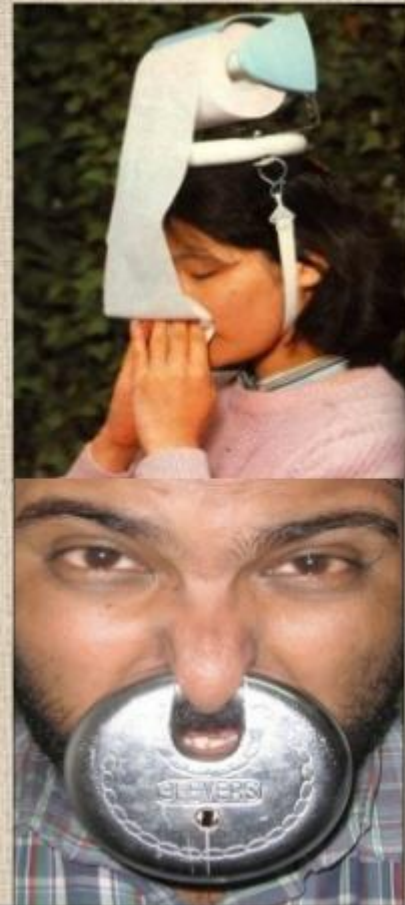
Allergen combines with specific IgE antibody → degranulation of mast cells → chemical mediators released





Acute or early phase response

- Occurs 5–30 min after antigen exposure
- Release of inflammatory mediators
- Increased nasal gland secretion → **runny nose**
- Mucosal edema & Vasodilation → **nose block**
- Nerve irritation → **sneezing & itching**



Late or delayed phase response

- Occurs 2-8 hours after antigen exposure
- Infiltration by inflammatory cells
(eosinophils, neutrophils, basophils, monocytes & CD4+ T lymphocytes)
- Edema, congestion & thick nasal secretion
- Sneezing & itching decreases



Symptoms

1. Running

2. Blocking

3. Sneezing

4. Itching



Signs

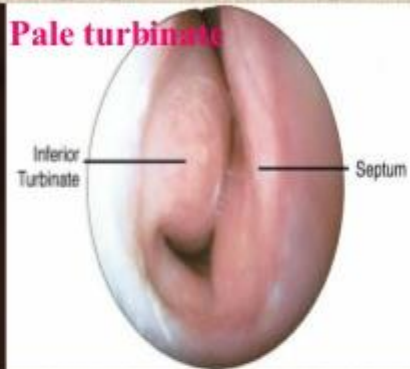
The allergic salute



Nasal crease



Pale turbinate



Face:

- Bunny nose-frequent twitching of face
- Dennie-Morgan creases (in lower eyelid skin)
- Allergic shiners (dark discoloration below lower eyelids)

Eye: Conjunctiva is congested, increased lacrimation

Ear: Aural fullness(ET dysfunction)

Throat: Chronic pharyngitis, laryngitis



Types of allergic rhinitis

- **Seasonal allergic rhinitis:**

Nasal discharge and conjunctivitis (more common)

- **Perennial allergic rhinitis:**

Nasal blockage (more common), Hyposmia

Less sneezing/nasal discharge /eye symptoms



Inducing factors

Allergens

- **Aeroallergens**

Indoor → mites, domestic animals, insects, plant origin

Outdoor → pollens, molds

- **Occupational rhinitis** (less documented than occupational asthma)
- **Latex allergy** (patients, health professionals)

Pollutants

- **Indoor air pollution:** indoor gas pollutants (tobacco)
- **urban-type pollution:** automobile origin, O_3 , NO_x , SO_2

Medication (eg. Aspirin, ACE inhibitor)



Seasonal allergic rhinitis

- **Pollen:**

Spring (March-June) = Tree pollen

Summer (May-August) = Grass

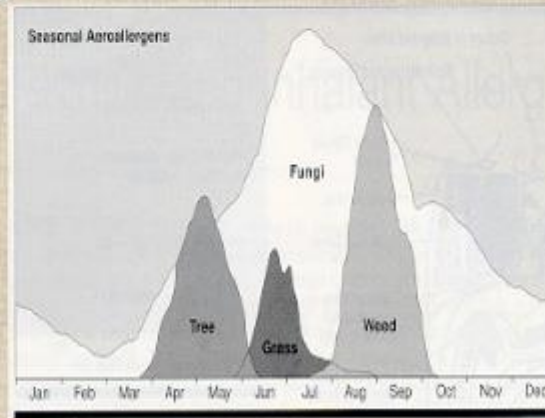
Fall (August-October) = Weeds

- **Mold:**

Spores in outdoors have seasonal variation (reduced in winter, increased in summer/fall due to humidity)

- **House dust mites:**

Generally “perennial” allergen, but increased in damp autumn months



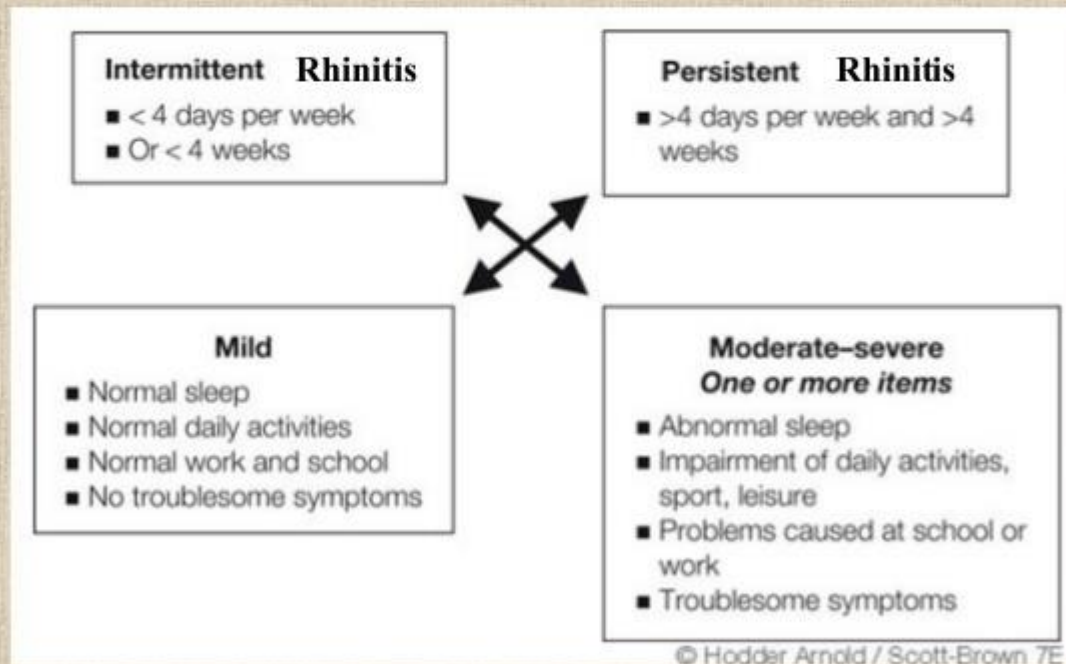
Perennial allergic rhinitis

- **Fungi/mold:**
Exposure peaks accompany activities such as harvesting & cutting grass
- **Pet dander** (cats, dogs):
up to 4 months after pet removal
- **House dust mites:**
Live in bedding & carpets
- **Cockroaches:**
Respiratory allergy
Important allergen

ALLERGENS



ARIA classification= Allergic Rhinitis & its Impact on Asthma



Diagnosis

1. History

2. Physical exam

3. Allergy diagnosis

(I) Skin prick test (SPT)

(II) Blood tests for allergy: Total IgE, Specific IgE

(III) Nasal allergen challenge test



Skin Prick test

Advantages:

1. Cheap
2. Immediate result
3. Sensitive

Contraindications:

1. Patients on antihistamines
2. Severe eczema
3. Previous anaphylaxis
4. Dermographism



(III) Nasal allergen challenge (nasal provocation) test

- **Indication:**

- +ve history & -ive SPT

- **Subjective** –symptom scores, VAS
- **Objective** –sneeze count, nasal inspiratory peak flow , rhinomanometry , acoustic rhinometry , spirometry,pulmonary peak flow



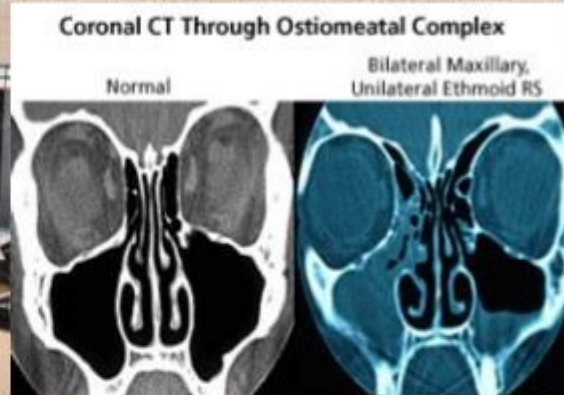
Disadvantages

1. Time consuming
2. Difficult
3. Excessive lab facilities
4. Trained staff
5. Resuscitation equipment

Nasal endoscopy



CT scan-Nose and PNS

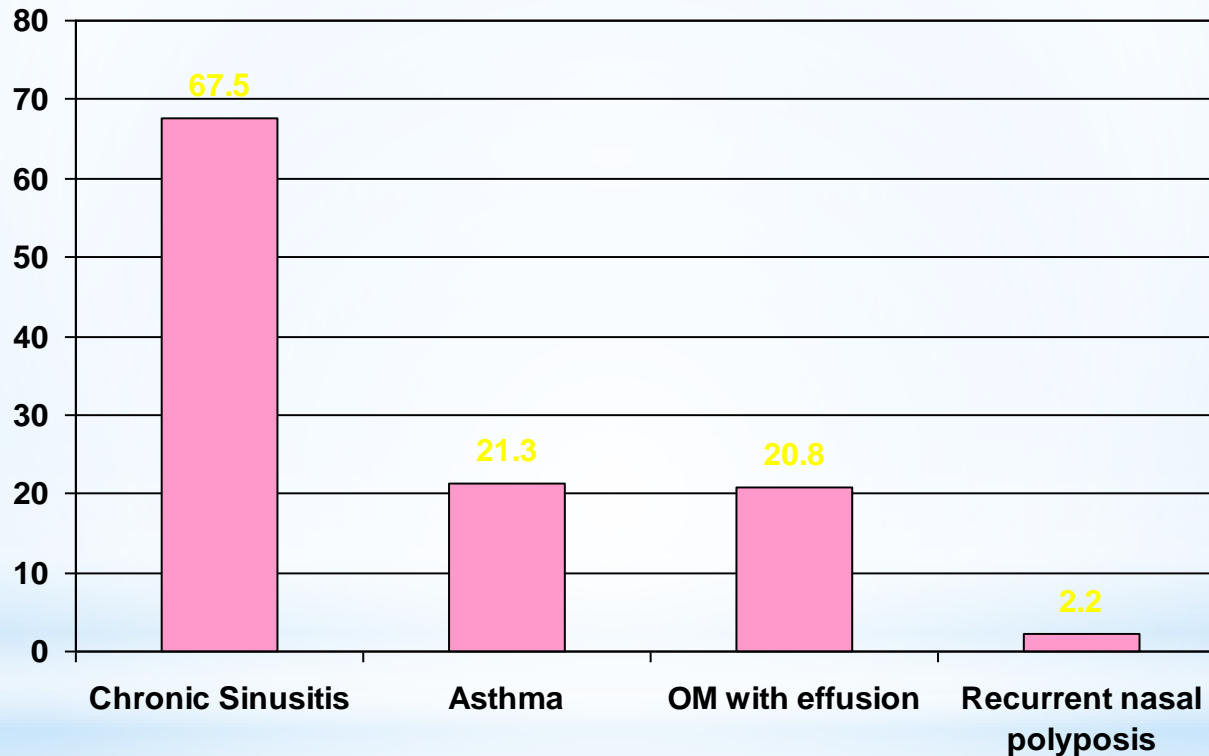


Complications (Co-morbidities)



Allergic Rhinitis and Co-morbidities

How Common are the co-morbidities?



Proportion of Allergic Rhinitis patients who also have
selected co-morbid disorders

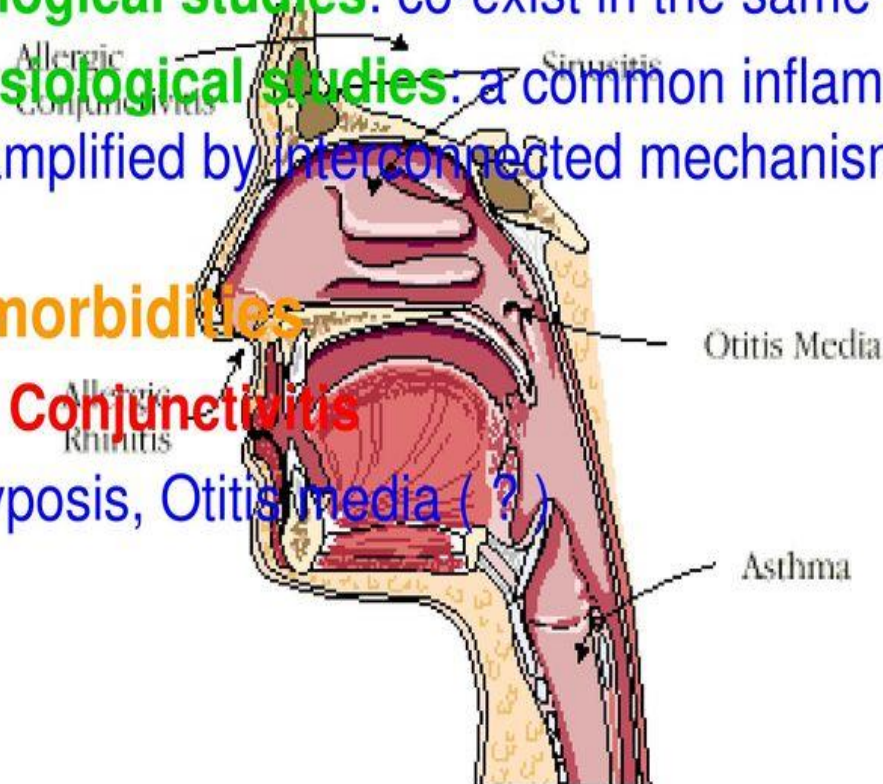
Co-morbidities

Asthma Allergic inflammation does not limit itself to the nasal airway

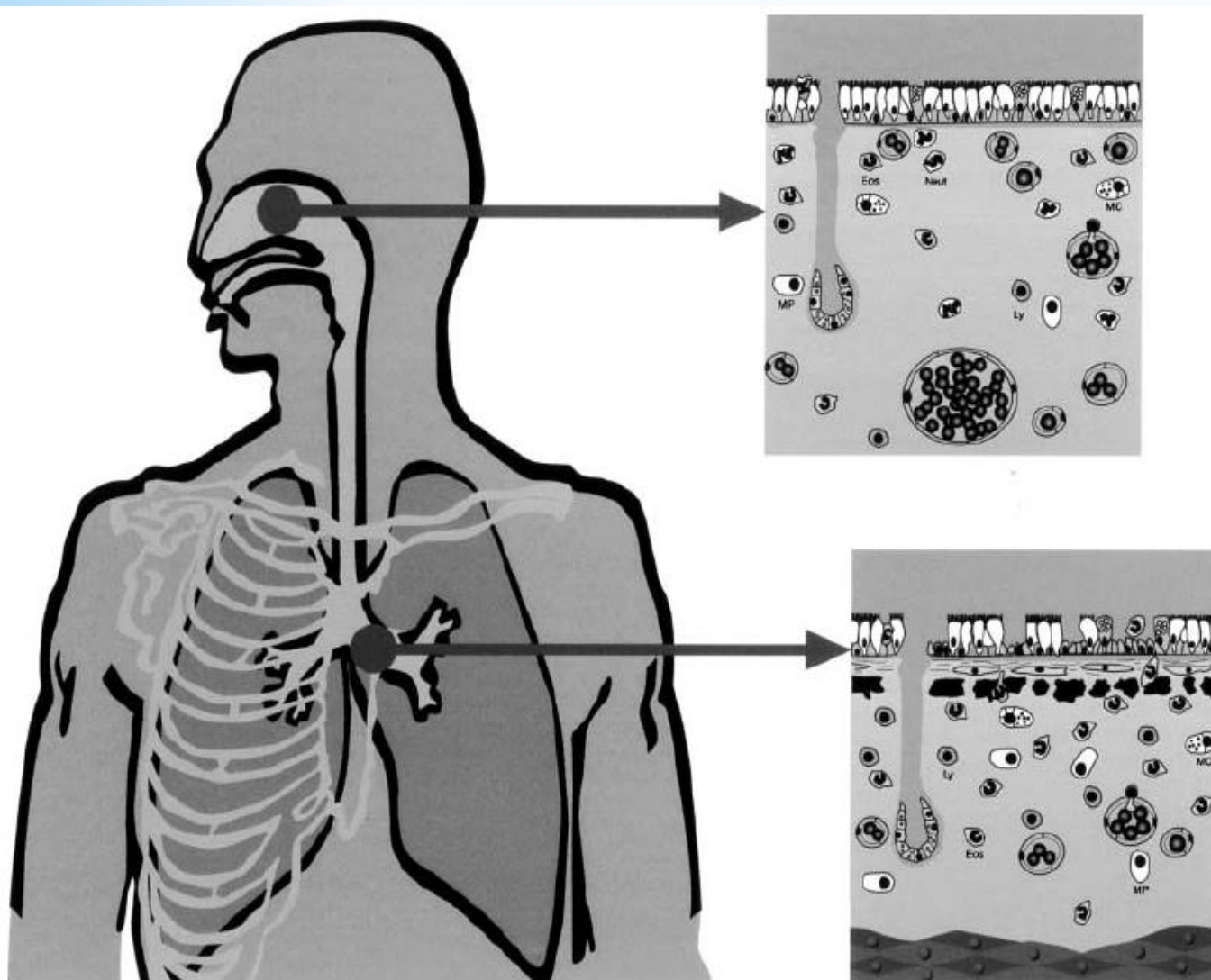
- **Epidemiological studies:** co-exist in the same patients
- **Pathophysiological studies:** a common inflammatory process, amplified by interconnected mechanisms

Other co-morbidities

- **Sinusitis, Conjunctivitis**
- Nasal polyposis, Otitis media (?)

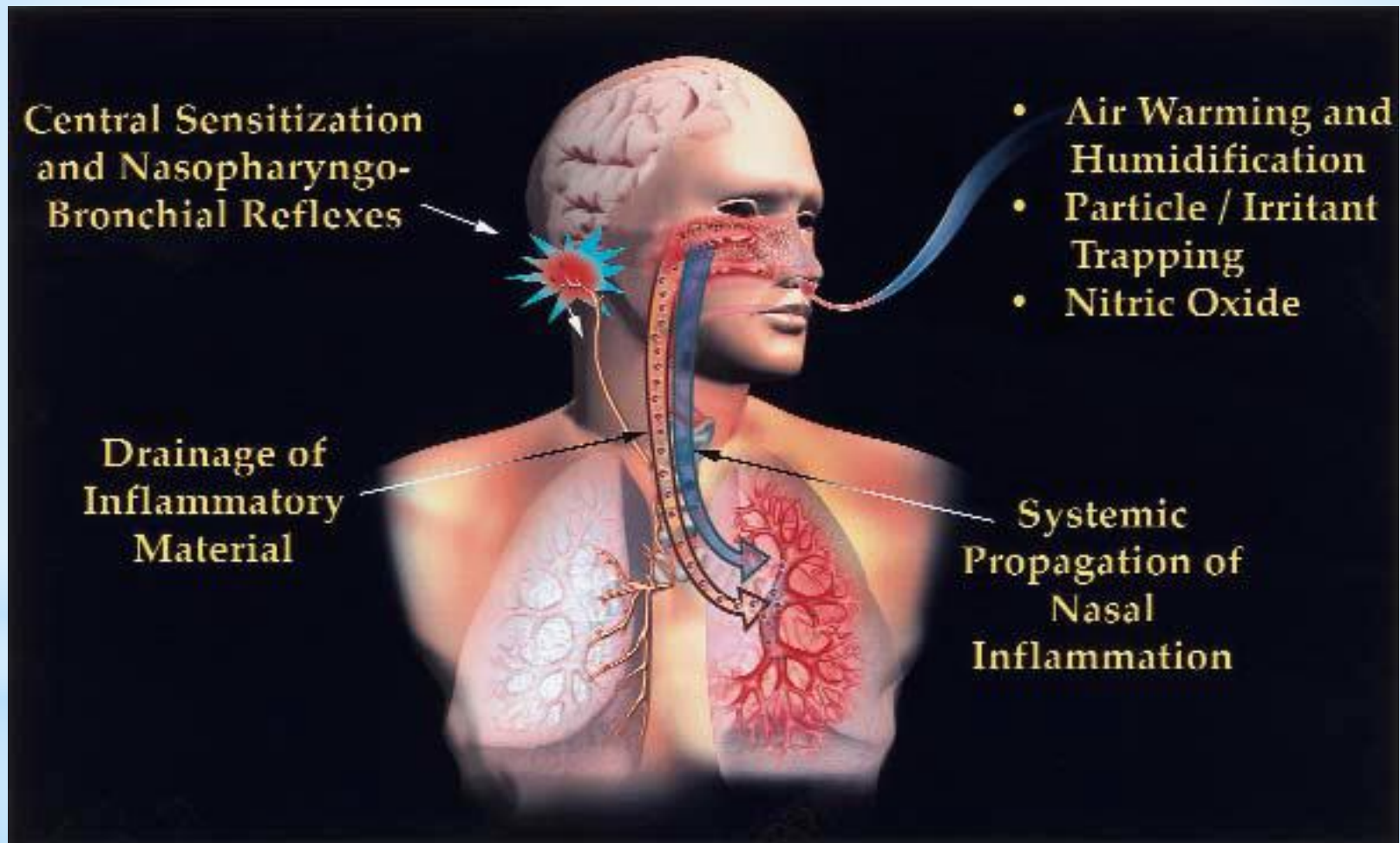


* Links between rhinitis and asthma



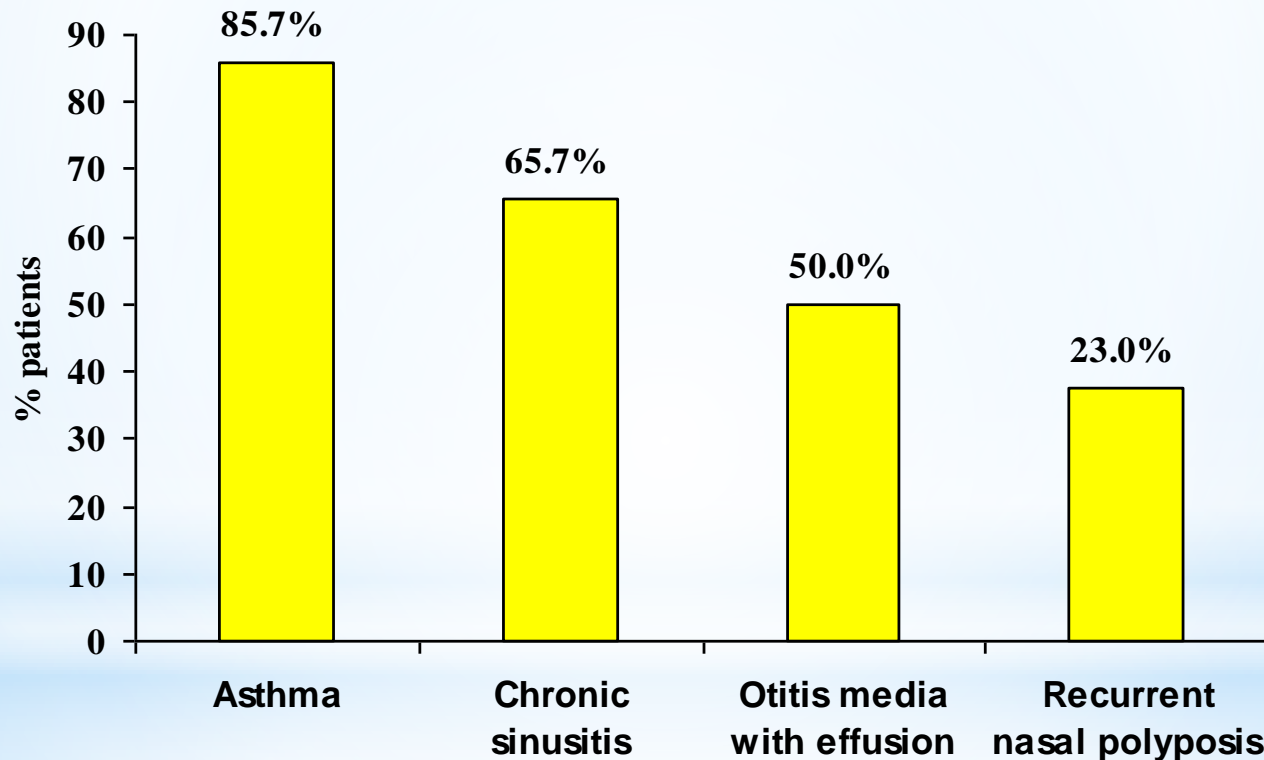
presence of Ig E
providing an adaptor
molecule between the
offending allergen and
inflammatory cell
activation and mediator
release

* Mechanisms through which the nasal airways might interact with the lower airways



*Common allergic rhinitis co-morbidities

Patients (%) with selected conditions + co-morbid AR



AR is a common co-morbidity in patients with other upper respiratory tract conditions

- Nasal symptoms -noted 80% of asthmatics
- Adults-Asthma present in 22.5% of adults with AR, Vs 7.2% in general population (Laynaert, 1999)
- Children-Ratio of asthmatics with AR to asthmatics without AR is even higher (Wright et al.,1996)
- Effective treatment of allergic rhinitis reduces development of subsequent asthma (Ragab et al., 2006)



Differential diagnosis

1. Vasomotor rhinitis (Intrinsic rhinitis/NANIPER)

2. Sinonasal polyposis

3. Rhinitis medicamentosa

4. Hormonal rhinitis

(Pregnancy, Hypothyroidism, OCP use)

5. CSF leak



Take a moment to consider
differential diagnosis

Management of allergic rhinitis

1. Environmental control measures (Avoidance of allergens)
2. Patient education
3. Nasal douching
4. Medical therapy
5. Immunotherapy
6. Surgery



General advice

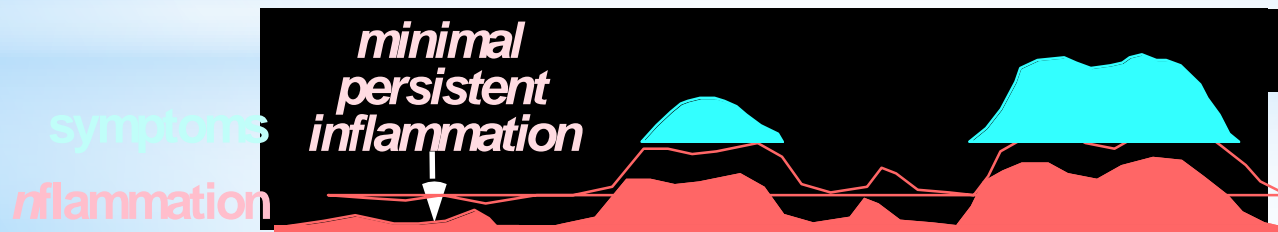
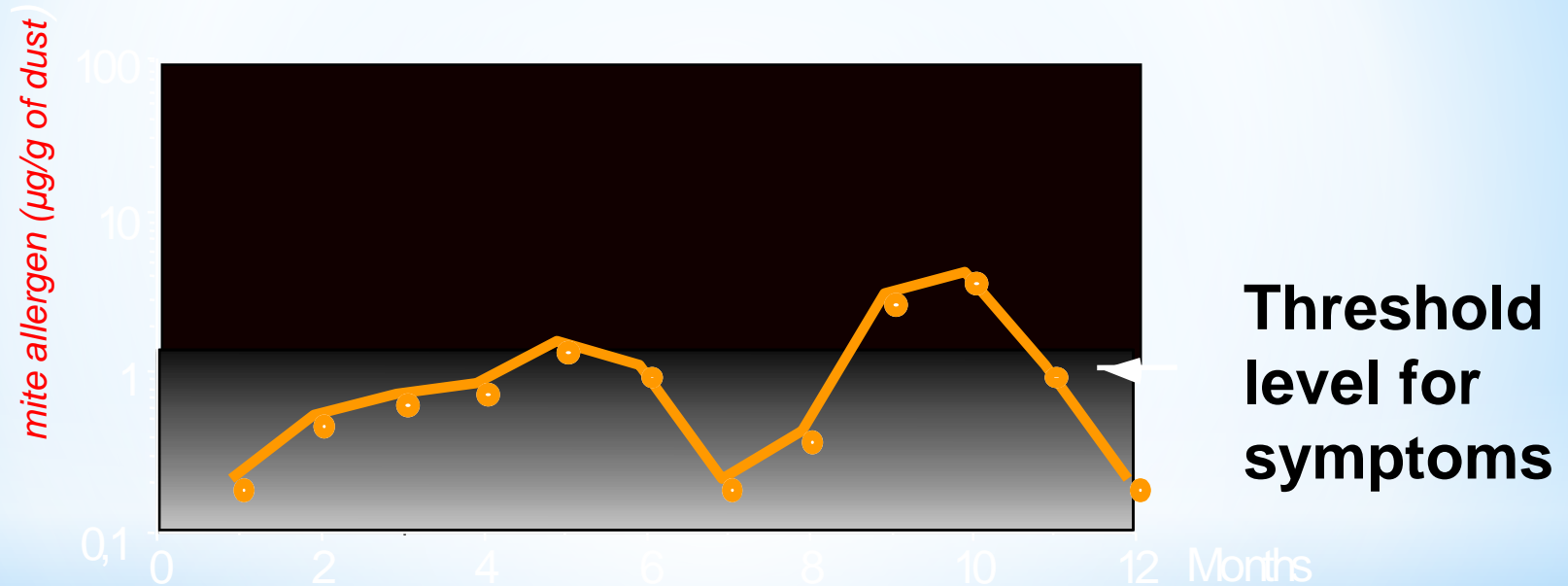
- Avoid **irritants**: smoke, dust, vehicular & other atmospheric pollutants,
- Physical factors – extreme changes in temperature → can produce symptoms like allergic rhinitis but are non-IgE mediated responses
- Avoid foods & drugs to which you are allergic
- Avoid occupational irritants or change profession





Concept of "minimal persistent inflammation"

Mechanisms of house dust mite induced rhinit



(I) Avoidance of allergens

- Best treatment method
- Not always practical
- **Indoor allergens:** Removing allergen from the indoor environment should be a primary strategy for the management and treatment of allergic disease
- **Outdoor allergens:**

Avoidance of indoor allergens



Avoidance of animal allergen

- Remove pet animals (cats, dogs) from bedroom
- Wash the pet weekly



Measures to avoid house dust mite

- Mattress covers
- Covers for pillows & bedding
- Vacuuming
- Regulation of ventilation & humidity at home
- Liquid nitrogen
- Acaricides
- Protein denaturing agents- Tannic acid



Pollen avoidance measures

- Avoid walking in open grassy spaces during hot, dry days
- Keep windows closed
- Wear facemask & sunglasses when moving out



(II) Patient education

Educate patients on environmental control measures, which involve both the avoidance of known allergens (substances to which the patient has IgE-mediated hypersensitivity) & the avoidance of nonspecific, or irritant, triggers



(III) Nasal douching

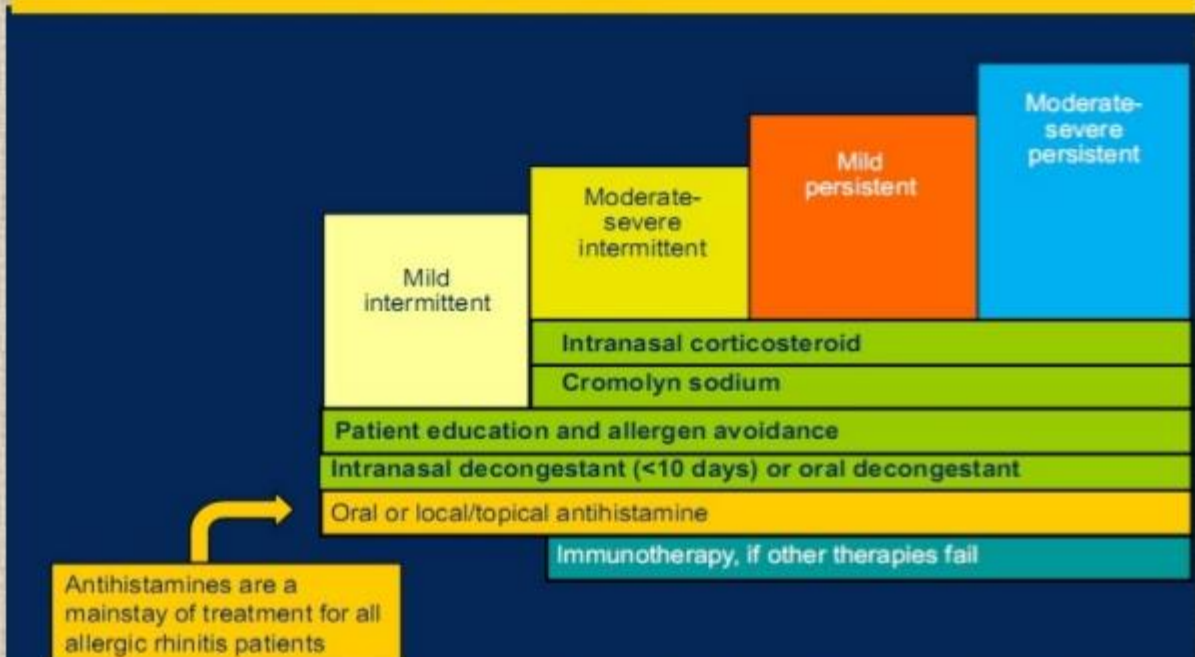
- Saline irrigation
- Improves quality of life



Neti Pot: Home remedy to clean nasal passages

(IV) Medical therapy

Step-Care Treatment of Allergic Rhinitis



Adapted from Bousquet J, et al. *J Allergy Clin Immunol*. 2001;108(suppl 5):S147-S334.

Practicing Clinician

過敏性鼻炎的診斷

(病史±皮膚過敏原測試或血清特異性IgE檢查)

避免接觸過敏原

間歇性症狀

持續症狀

輕度

不一定按順序選擇

- 口服H1抗組織胺
- 鼻內H1抗組織胺
- 有/或去充血劑

中/重度

輕度

不一定按順序選擇

- 口服H1抗組織胺
- 鼻內H1抗組織胺
- 有/或去充血劑
- 鼻內類固醇
- 鼻內咽達永樂

對持續性鼻炎患者
2-4週覆檢

失敗：升階治療
改善：持續治療一個月

中/重度

鼻內類固醇 2-4週後覆檢

改善

降階並繼續
治療一個月
以上

失敗

審視診斷是否正確
審視藥物順從性並詢問
是否有感染或其他原因

增加鼻內
類固醇劑量

鼻癢/噴嚏加用
H1抗組織胺

鼻涕加
ipratropium

鼻塞加用去充
血劑或口服類
固醇(短期)

1. Antihistamines:

Topical: Azelastine

Systemic: Cetirizine, Levocetirizine, Fexofenadine, Loratadine, Desloratadine

2. Nasal Decongestants:

Topical: Oxymetazoline, Xylometazoline

Systemic: Phenylephrine, Pseudoephedrine

3. Mast cell stabilizers: Sodium cromoglycate nasal drop

4. Anticholinergics: Ipratropium bromide nasal spray

5. Corticosteroids:

Topical: Beclomethasone, Budesonide, Mometasone, Fluticasone

Systemic: Prednisolone

6. Leukotriene receptor antagonists: Montelukast, Zafirlukast



Steroid

- Most effective treatment for Allergic rhinitis(AR)
 - Topical:** Nasal spray or nasal drop
 - Systemic:** Oral, extremely effective
- Reduces inflammation & consequent hyperreactivity→reduce nasal symptoms, eye symptoms, improve smell sense
- Topical steroid when combined with antihistamines→ reduces risk of asthma exacerbation and hospitalization by 50% or more (Adams et al., 2002, Crystal peters et al., 2002)
- Fluticasone and mometasone have low systemic bioavailability→lower risk



Effect of Histamine

H1 receptor

- Upregulated in allergic rhinitis
- On Endothelium
 - ↑ Vascular permeability
 - Vasodilatation
- On Nociceptive nerve
 - Itch
 - Systemic reflex: sneezing
 - Parasympathetic reflex: glandular exocytosis

Antihistamines

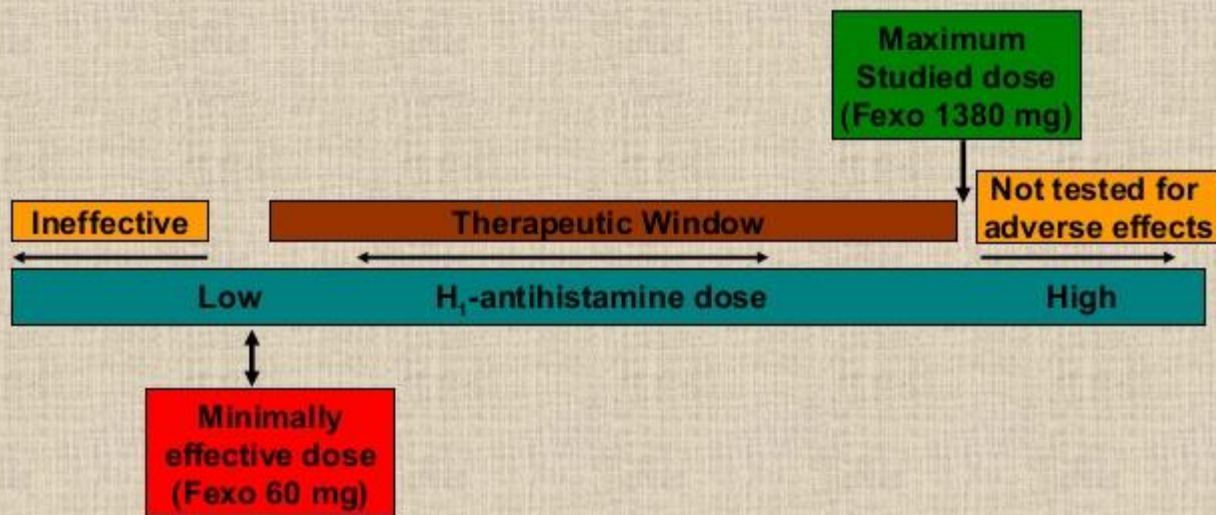
- Adverse effects of first generation antihistamines



“First-generation oral H₁-antihistamines are not recommended when second-generation ones are available, due to safety concerns”

(Allergy. 2008 Apr;63 Suppl 86:8-160)

Significance of wide therapeutic window (fexofenadine)



Howarth PH. Advanced Studies in Medicine. 2004;4(7A):S508-512

Decongestants

- Topical vasoconstrictor:
 - imidazoline (eg, oxymetazoline)
- systemic (oral) vasoconstrictor
 - Phenylephrine
 - Pseudoephedrine.
- Monotherapy with vasoconstrictors has limited role
- Oral decongestants + Antihistamine → all cardinal symptoms of allergic rhinitis targeted



Mast cell stabilizer

- Sodium cromoglycate inhibits degranulation of sensitized mast cells
- 2% Nasal drop: Use 3 to 4 times daily → limits compliance
- Poorly absorbed systemically → excellent safety record
- Used before the onset of symptoms
- Can be used in younger children < 2 years of age



Ipratropium Bromide

- Useful against nasal discharge
- Occasionally helpful in pts with AR who do not respond to topical steroid (Dockhom et al., 1999)

Antilukotrienes

- Zafirlukast performed no better than placebo - seasonal allergic rhinitis (Pullerits T et al., 1999)
- Montelukast clinical efficacy seasonal Allergic rhinitis (Chervinsky P et al., 2004)
- Montelukast + loratadine -superior reducing day time nasal symptoms in seasonal Allergic rhinitis. (Meltzer EO et al., 2000)
- Montelukast + ebastine- better symptomatic control in allergic rhinitis.
- Montelukast -less effective than Intranasal steroid (Ratner PH et al., 2003)
- Leukotriene antagonist (Montelukast) doesn't appear more effective than nonsedating antihistamines (Fexofenadine) (Wilson AM et al., 2004)

(V) Immunotherapy

- Repeated administration of allergen extract induce state of immunological tolerance
- Render an allergy patient less symptomatic when exposed to the offending antigen
- **Desensitization or Hyposensitization:**
because complete elimination of the allergic reaction is seldom achieved
- Subcutaneous injection or sublingual route



Side effects of Immunotherapy

- Local reactions - trivial
- Systemic reactions-10%-up dosing phase
- Occasionally – severe systemic reactions-general urticaria , severe asthma or anaphylaxis

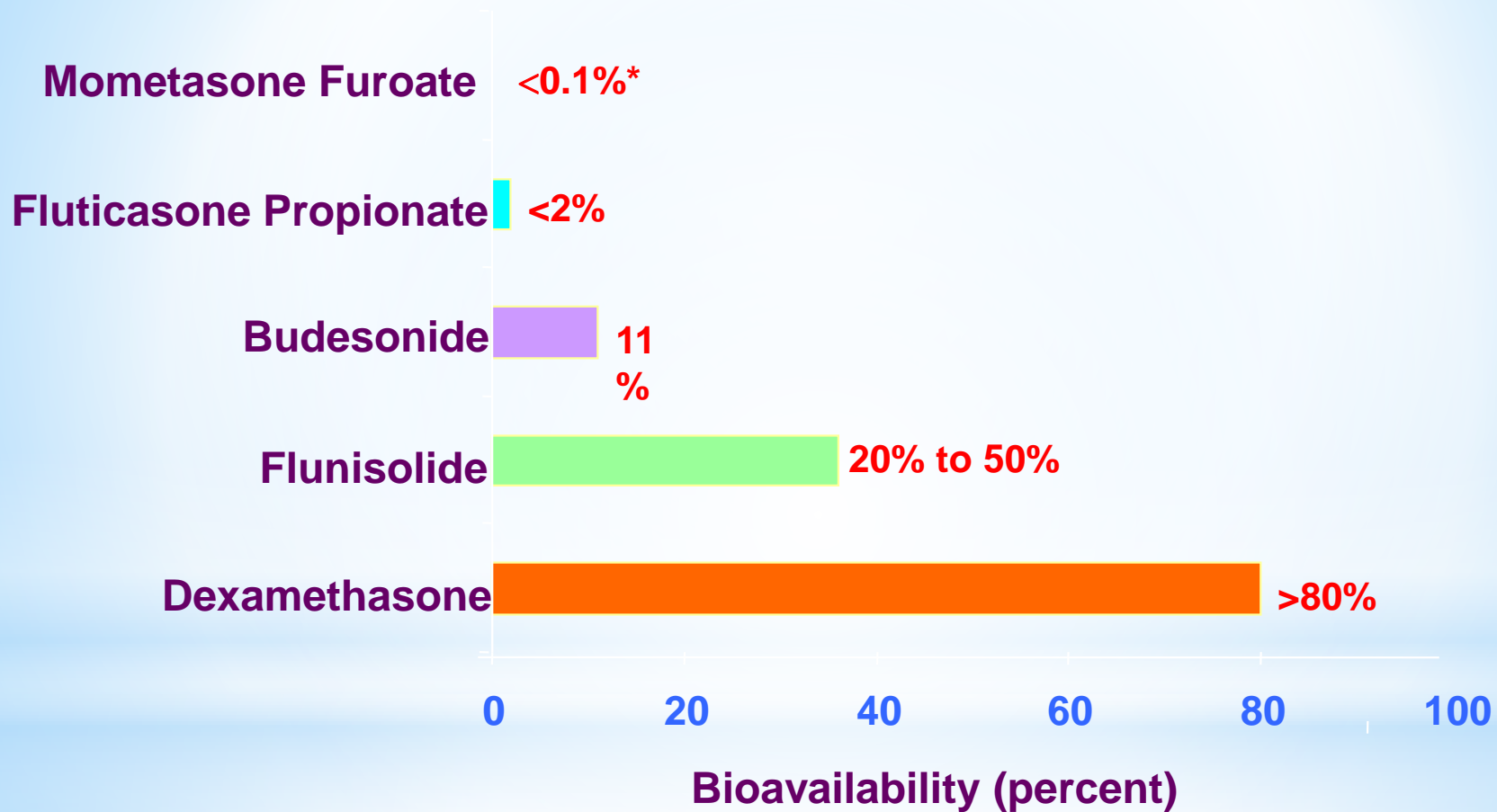
常見鼻炎藥物

通稱	類固醇鼻噴劑		口服 / 肌注類固醇	
商品名	Beclomethasone (Beclomet) Budesonide (Pulmicort) Flunisolide	Fluticasone (Flixonase) Mometasone (Nasonex) Triamcinolone (Nasacort)	Dexamethasone Hydrocortisone Methyprednisolone Prednisolone	Prednisone Triamcinolone Betamethasone Deflazacort
作用機轉	<ul style="list-style-type: none"> 降低鼻腔敏感性 有效減低鼻腔炎性反應 (↓Th2 cell, dendritic cell, mucosal mast cell & eosinophil)		<ul style="list-style-type: none"> 降低鼻腔敏感性 有效減低鼻腔炎性反應 	
副作用	<ul style="list-style-type: none"> 些許的局部副作用：刺激感、鼻乾燥 全身性副作用很少 少數類固醇鼻噴劑可能影響兒童骨骼生長 (mometasone, fluticasone除外) 		<ul style="list-style-type: none"> 全身性副作用常見，尤其是肌注藥物 注射處的藥物沉積，可至局部組織萎縮 	
建議	<ul style="list-style-type: none"> 最有效的藥物治療方式 對鼻充血有效 會影響嗅覺 在6 ~ 12小時後可見效果 最大效果是在數天之後 		<ul style="list-style-type: none"> 如果可能的話，應使用類固醇鼻噴劑取代口服或肌注類藥物 然而，短期內的口服類固醇有助於嚴重症狀的改善 (Prednisolone 5-25 mg/ day within 2 wk) 	

鼻內類固醇鼻噴劑的藥物動力學比較

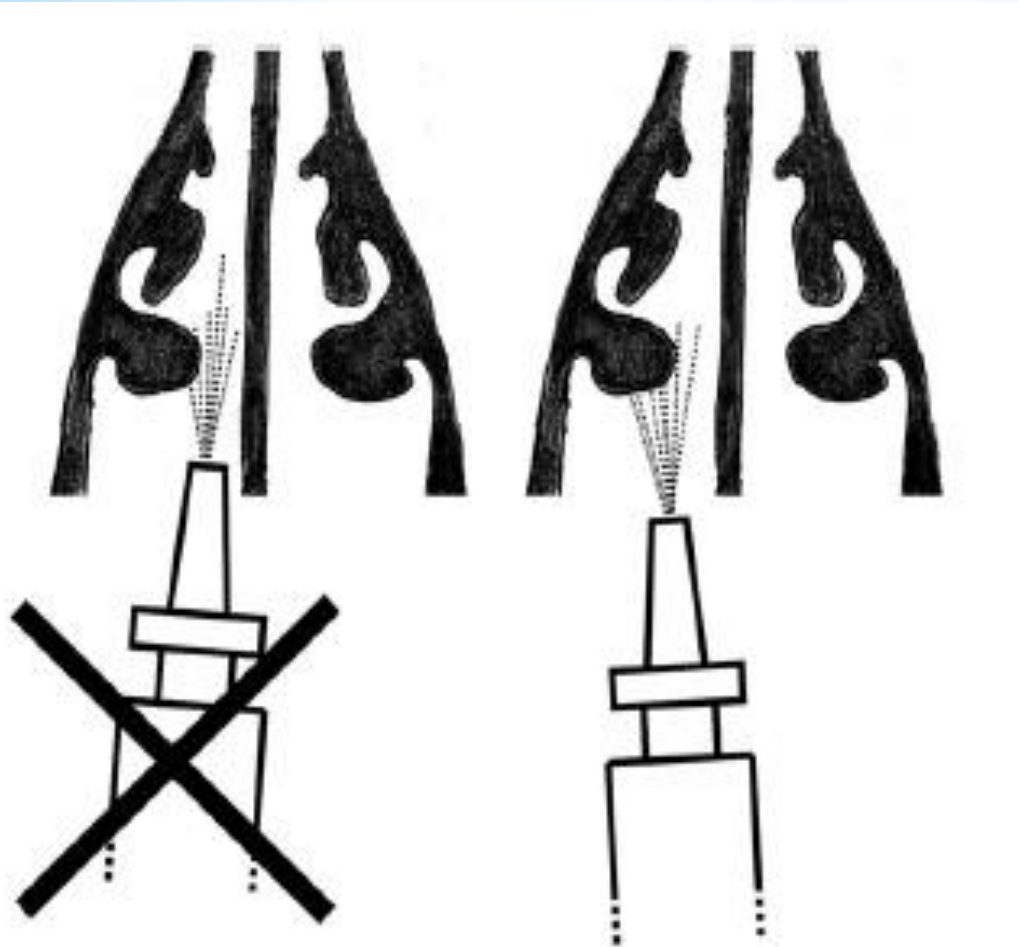
化學名	商品名	Systemic bioavailability (%)	Systemic clearance (1/hr)	Onset of action (day)
Beclomethasone dipropionate	Beclomet	17	230	3
Budesonide	Pulmicort	11	84	1
Flunisolide	Nasarel	20-50	58	4-7
Fluticasone propionate	Flixonase	<2	69	0.5
Mometasone Furoate	Nasonex	<0.1	-	0.5
Triamcinolone acetonide	Nasacort	23	37	1

* Intranasal Steroids: Systemic Bioavailability



*1. Brannan et al. *J Allergy Clin Immunol.* 1996;97(pt 3):198; 2. Beconase® PI. At: <http://www.rxlist.com>; 3. Rhinocort® PI. At: http://www.az-air.com/phy_prod/rhinocort_prescribing_information.asp; 4. Flonase® PI. At: <http://www.flonase.com>; 5. NASONEX® PI. At: <http://www.nasonex.com>.

* 正確噴鼻式類固醇使用方法



- 噴鼻式類固醇使用方向須**朝向同側耳朵上方**。噴嘴須要於鼻腔口不可深入鼻腔且須向外噴向鼻甲黏膜。

第二代口服H1型抗組織胺的藥物動力學

	Azelastine	Cetirizine	Fexofenadine	Loratadine
Time to peak concentration (hr)	4-6	1	2.6	1.3
Onset of action (hr)	0.5-3.5	<1	1	1-3
Time to peak effect (hr)	4	4-8	2-3	8-12
Half-life (hr)	22-36	7-10	14.4	8.4
Duration-single dose (hr)	10-12	24	12-24	24-48
Elimination pathway	Hepatic	Renal	Renal / Feces	Hepatic
Active metabolites	Yes	No	No	Yes
Drowsiness & somnolence (drug / placebo)	11.5% / 5%	13.7% / 6.3%	1.3% / 0.9%	8% / 6%

Leukotrienes receptor antagonist

- **Cysteinyl leukotrienes**
 - ↑vascular permeability
 - ↑vasodilatation
 - ↑mucosal swelling
 - ↑nasal secretion
- **Montelukast** (Singulair), **Zafirlukast** (Accolate)
 - Monotherapy: less effective
 - Additive efficacy with antihistamine
 - Particularly important for “rhinitis + asthma”

Effect of Therapies on Rhinitis symptoms

Table 2. Characteristics of pharmacologic treatments

Characteristic	Oral antihist.	Nasal antihist.	Nasal steroids	Nasal decong.	Ipratropium bromide (anti-cholinergics)	Nasal cromone (disodium cromoglycate)
Rhinorrhoea	++	++	+++	0	++	+
Sneezing	++	++	+++	0	0	+
Itching	++	++	+++	0	0	+
Blockage	+	+	+++	++++	0	+
Eye symptoms	++	0	++	0	0	0
Onset of action	1 h	15 min	12 h	5–15 min	15–30 min	Variable
Duration	12–24 h	6–12 h	12–48 h	3–6 h	4–12 h	2–6 h

+ Marginal effect; ++++ substantial effect (under natural exposure conditions).

(Allergy, 2000)

How to Select Medications

- Medications have no long-lasting effect
→ **maintenance treatment** required for persistent disease
- **Intranasal corticosteroids** are the first-line therapy for moderate-severe disease; effective against ocular symptoms
- Alternative therapy (e.g. **herbalism, acupuncture**) for the treatment of rhinitis
- **Intramuscular / Intranasal injection of steroids** is not usually recommended (systemic, blindness)

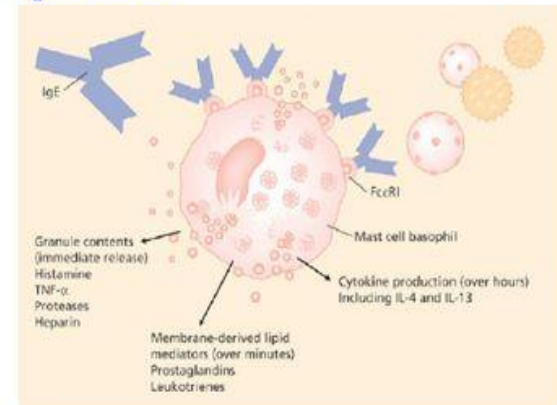
Anti-IgE treatment

- **Omalizumab**

- A humanized kappa IgG1 antibody
- Binds to free IgE at the FcεRI binding site
- Prevent interaction with FcεRI receptors (mast cell, basophil)

- **Effect**

- Rapid decrease of free IgE
- Down-regulation of FcεRI receptors



Surgical intervention

(only for nasal obstruction)

- **Indication**

- Drug-resistant inferior turbinate hypertrophy
- Nasal septal deviation with functional relevance
- Secondary chronic sinusitis

- **Modality**

- Turbinate surgery: cautery, laser, radiofrequency
- Septomeatoplasty
- Functional Endoscope Sinus Surgery

Treatment of Concomitant Rhinitis and Asthma

- **Glucocorticosteroids & Antileukotrienes**
→ Effective for both diseases
- **H1-antihistamines: Important for “Rhinitis”**
“Asthma”
- **Optimal management of rhinitis may improve coexisting asthma**

Pediatric Aspects

- Intermittent allergic rhinitis is **unusual before 2 y/o**
Allergic rhinitis is **most prevalent during school age years**
- Symptoms can impair cognitive functioning and school performance (**sedating oral H1-antihistamines**)
- Oral & intra-muscular **steroids** should be avoided

HOW CHILDREN USED TO SPEND THEIR TIME



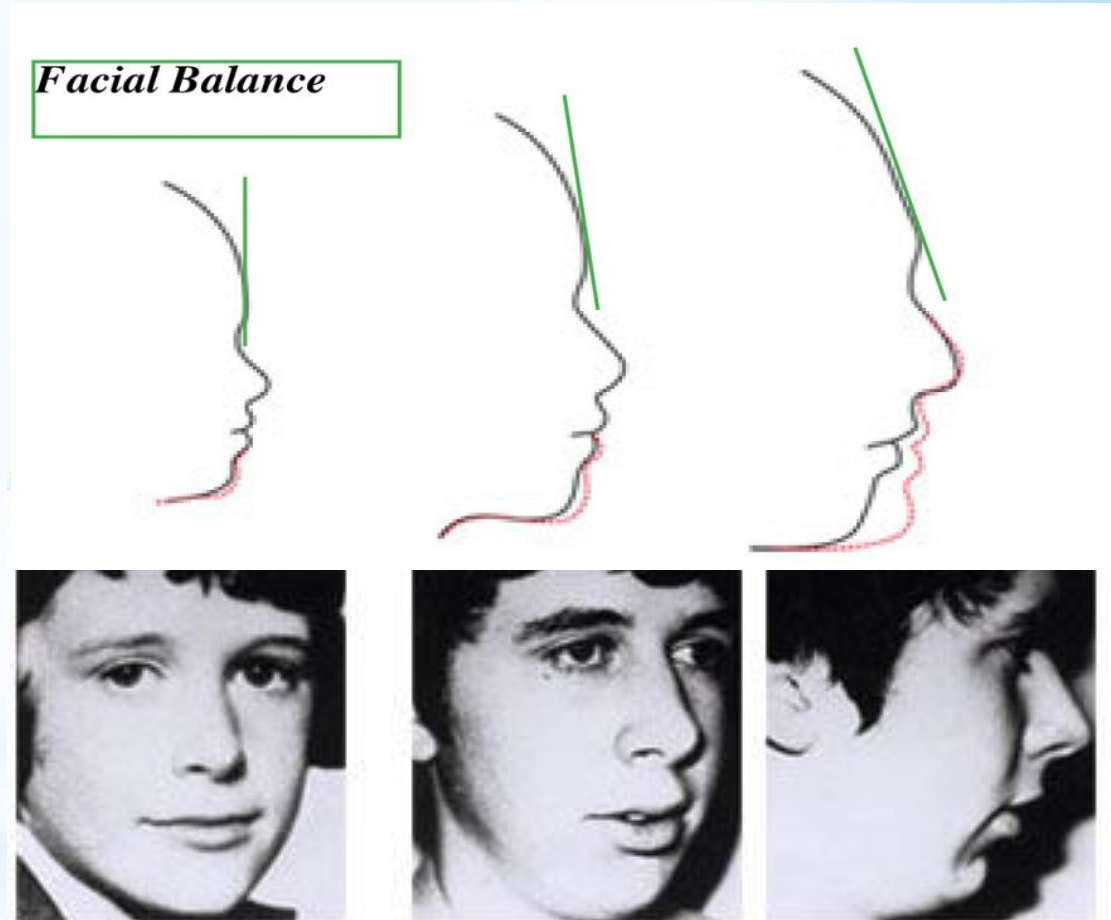
90's



NOW!!!!!!

* Dento-facial abnormalities in AR

- * Mouth breathing
- * Long face syndrome (adenoid face)
- * Dental malocclusion
- * Halitosis、thirsty
- * Gingivitis、periodontitis
- * Dental caries



Vázquez-Nava F. Arch Dis Child. 2006;91:836-40

Special Considerations

Pregnancy

- **Nasal obstruction aggravated** by the pregnancy itself
- **Caution** for any medication during pregnancy

Ageing

- **Allergy** is less common
- **Atrophic rhinitis** is common and difficult to control
- **Phentolamine, Methyldopa, ACEI** can cause rhinitis
- **Decongestants & Anti-cholinergics & some Anti-histamine** may cause urinary retention in BPH patients
- **Sedative** drugs may have greater side effects

*Phentolamine: α -adrenergic antagonist *Methyldopa: adrenergic anti-HTN medication *ACEI: for HTN, CHF

過敏性鼻炎治療藥物的FDA懷孕危險分級

分級	分級描述	說明	過敏性鼻炎治療藥物
A	動物實驗及完整的人類研究無致畸胎性	無危險性	-
B	動物實驗無致畸胎性，但無完整的人類研究；動物實驗有致畸胎性，但完整的人類研究排除致畸胎性	無危險證據	Budesonide , Cetirizine, Cromoglycate, Dexchlorpheniramine, Diphenhydramine, Ipratropium, Loratadine, Nedocromil, Pseudoephedrine
C	動物實驗有致畸胎性或無動物實驗資料，亦無無完整的人類研究；但藥物的好處超過其可能的危險性	不能排除危險性	其他的corticosteroids, Azelastine, Brompheniramine, Fexofenadine, Hydroxyzine,, 其他的充血解除劑
D	完整的人類研究具致畸胎性，但於某些狀況下，藥物的好處超過其危險性	有危險證據	-
X	完整的人類研究顯示增加致畸胎性，且危險性遠超過藥物的好處	使用禁忌	-

Table 3 ABRS Diagnosis Requires the Presence of at Least 2 Major Symptoms*

	Major Symptom
P	Facial P ain/pressure/fullness
O	Nasal O bstuction
D	Nasal purulence/discolored postnasal D ischarge
S	Hyposmia/anosmia (S mell)

*At least 1 symptom must be nasal obstruction or nasal purulence/discolored postnasal discharge. Thus, a diagnosis requires at least 2 PODS, one of which must be O or D.

Consider ABRS when viral URTI persists beyond 10 days or worsens after 5 to 7 days with similar symptoms [22]. Bacterial etiology should be suspected if sinus symptoms persist for more than 7 days without improvement [20].

Desrosiers et al. Allergy, Asthma & Clinical Immunology 2011, 7:2

- * Diagnosis is based on **history and physical examination**:
- * • Sinus aspirates or routine nasal culture are not recommended
- * • Radiological imaging is not required for uncomplicated ABRS.
- * **Topical INCS** can be useful as **sole therapy of mild-to-moderate ARS**.

Desrosiers et al. Allergy, Asthma & Clinical Immunology 2011, 7:2



For Angelline

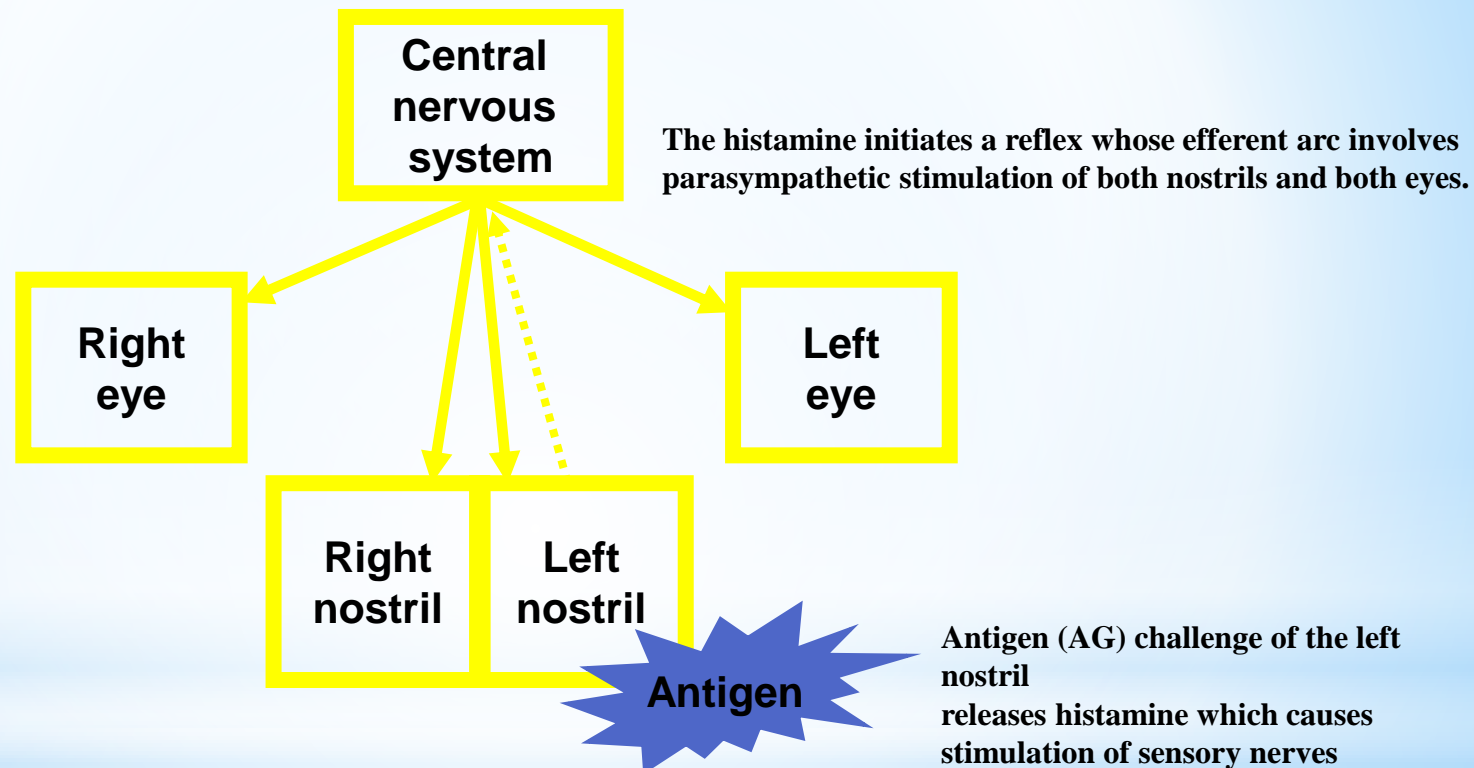
*Ocular allergy

Winnie Yang MD
Taipei City Hospital

* Possible mechanisms of co-eXISTENCE of ALLERGIC CONJUNCTIVITIS WITH ALLERGIC Rhinitis

- * In addition to direct contact, undefined mechanism for allergic ocular symptoms without direct contact of allergen with the conjunctiva
- * Possible mechanisms:
 - * Mediator release from the nose inducing an immune response by the conjunctiva or upregulating circulating cells
 - * Pooling of mediators due to nasal lacrimal duct congestion
 - * Neural reflex; nasal-conjunctival reflex
 - * Reflux of allergen up the nasolacrimal duct to the conjunctiva resulting in a direct immune response

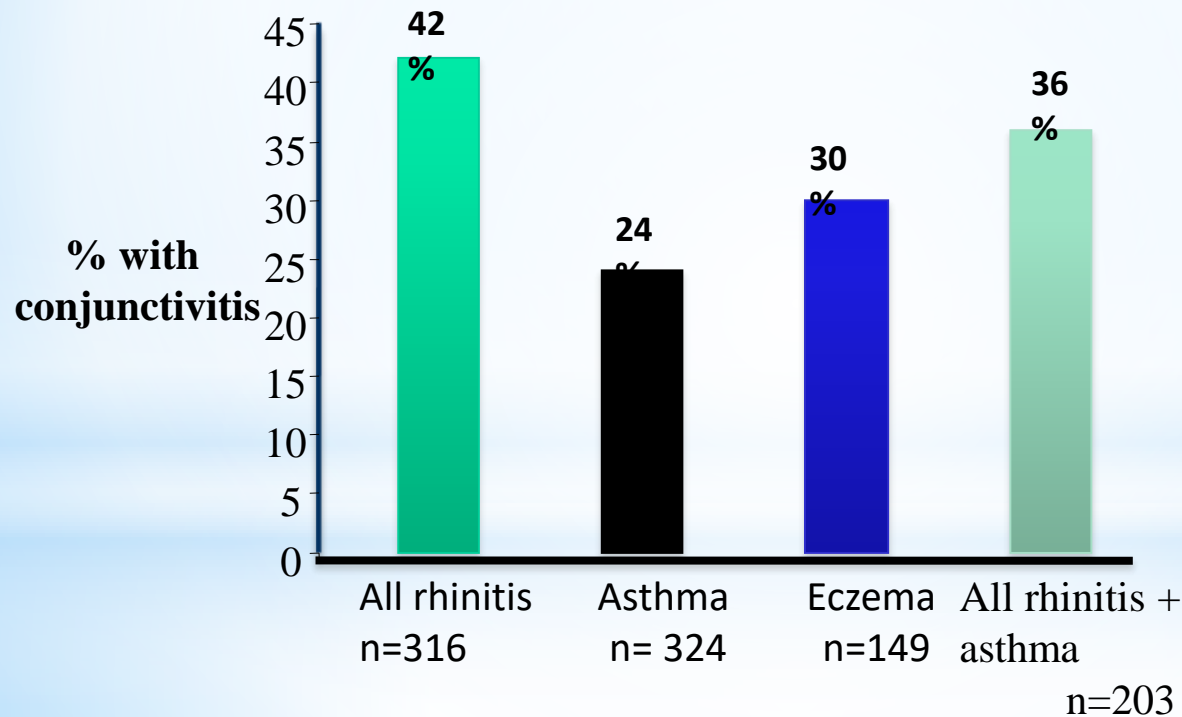
*Naso-ocular reflexe



Antigen (AG) challenge of the left nostril releases histamine which causes stimulation of sensory nerves

Ocular symptoms arise from naso–ocular reflex

* Co-existence of Allergic Conjunctivitis with other Allergic Diseases



- * 1) Allergic conjunctivitis (AC):
 - * Acute allergic conjunctivitis:
 - Seasonal or hay fever.
 - Toxic- induced (induced by acute contact with irritant, drugs, preservatives, etc).
 - * Chronic allergic conjunctivitis:
 - Perennial.
 - Toxic-induced (long standing).
- * 2) Contact dermatoblepharitis.
- * 3) Vernal keratoconjunctivitis (VKC)
- * 4) Giant papillary conjunctivitis (GPC)
- * 5) Atopic keratoconjunctivitis (AKC)
- * 6) Atopic blepharoconjunctivitis (ABC).

* Clinical classifications:

- * Acute and chronic diseases have in common:
 - * 1) sensitization to environmental allergens.
 - * 2) Ig E mast cells activation with subsequent mediator cascade.
 - * 3) conjunctival inflammation with prevalence of eosinphils.
 - * 4) the presence of lymphocytes with a Th2 profile of cytokines production .

*Sensitization

- * . The cytokines released by Th2 cells (IL3,IL4,IL5,IL6,IL13,GM-CSF) stimulate B cell IgE production and inhibit development of Th1 mediated delayed type hypersensitivity reactions .
- * B cells which recognize the same allergen that induce Th2 differentiation, in present of appropriate signals such as IL4,IL6 and IL13 undergo heavy chain switching to produce IgE.

*Sensitization

- * Is the commonest and one of the mildest forms of allergic conjunctivitis. It accounts for 25%-50% of all cases of ocular allergy.
- * SAC is often associated by rhinitis and even sinusitis.
- * 70% of patients provide either a personal or familial allergic history.
- * SAC can develop suddenly when patient comes in contact with an appropriate antigen, such as pollens, grasses, or trees.

* Seasonal allergic conjunctivitis

*Symptoms:

- * Itching.
- * Watery discharge.
- * Rhinitis.
- * Sinusitis.



*Signs:

- * Not always present.
- * Lid swelling.
- * Ptosis.
- * Conj hyperemia.
- * Chemosis (=/- dellen).
- * Papillary reaction.
- * Follicular reaction.

*SAC

*Diagnosis:

- *Clinically.
- *Family history.
- *Conj scrapings for eosinophils.
- *Tear level of IgE, serum tear.
- *Radioallergosorbent test measures specific IgE levels for a specific antigens.
- *Mast cells activity by measuring tryptase and histamine levels in tear film.



*Treatment:

*Avoidance of allergen:

- * Limit outdoor activities.
- * Use air conditioning or air filter system.
- * Drive car with windows closed.
- * Use protective eyegear when outdoor.

*Washing allergen.

*Antihistamines.

*Mast cell stabilizers.

*NSAIDs.

*Steroids.

*Immunotherapy.



- * Usually triggered by external non- airborne antigens such as drugs, contact lens solution, irritants, and preservatives.
- * Type I mediated.
- * Symptoms are similar to SAC but no seasonal component.
 - * Itching, tearing, eyelid erythema and swelling, and conjunctival redness and chemosis. Typically occur within minutes after application of an allergen.
 - * Bactriacin..cephalosporins..sulfacetamide..tetracycline
 - * Atropine...homatropine.
 - * Epinephrine..pilocarpine..apraclonidine.
 - * Antiviral agents.
 - * Thimerosal..chlorhexidine...bezalkonium chlo

* Acute allergic toxic induced conjunctivitis

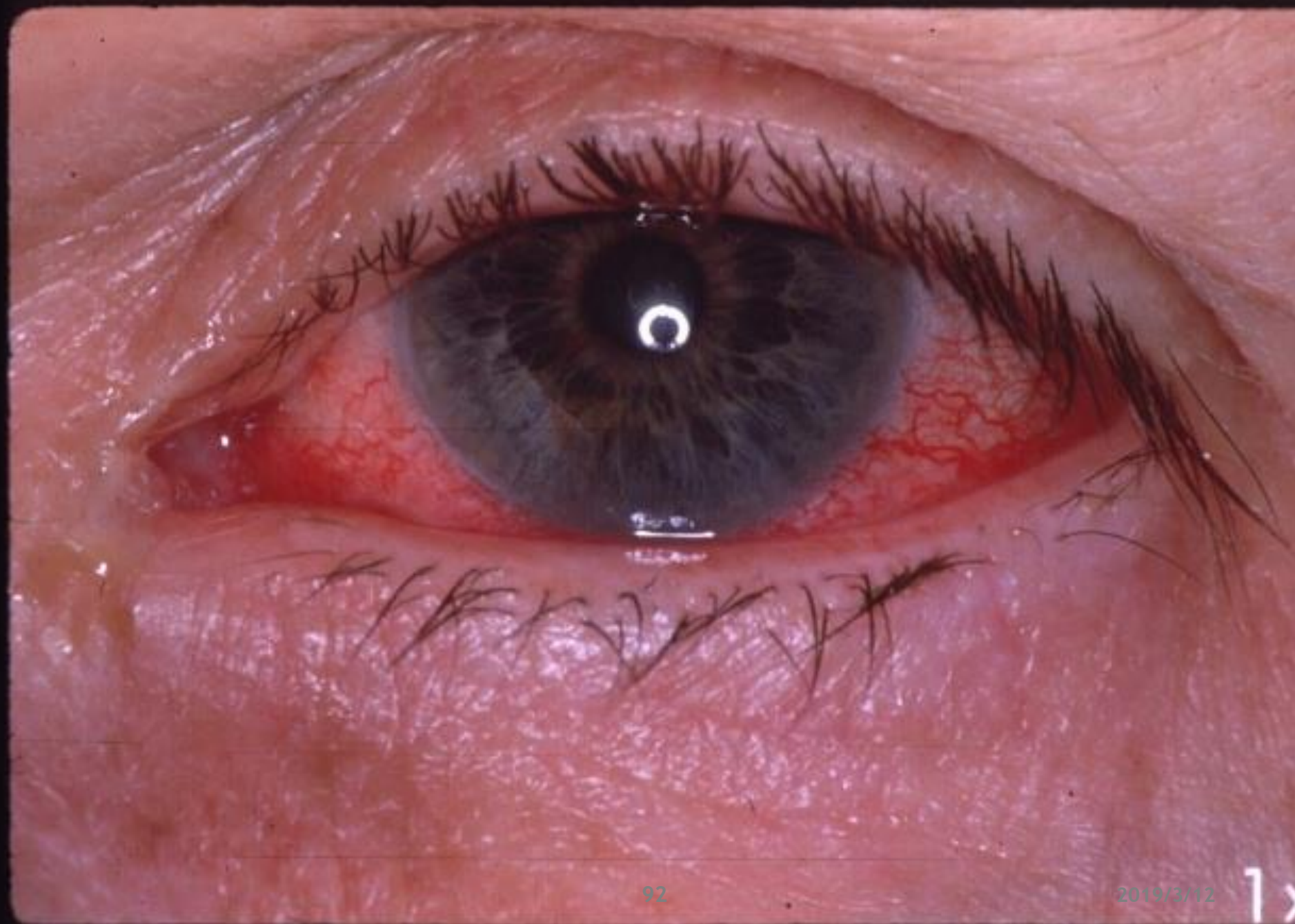
*Diagnosis:

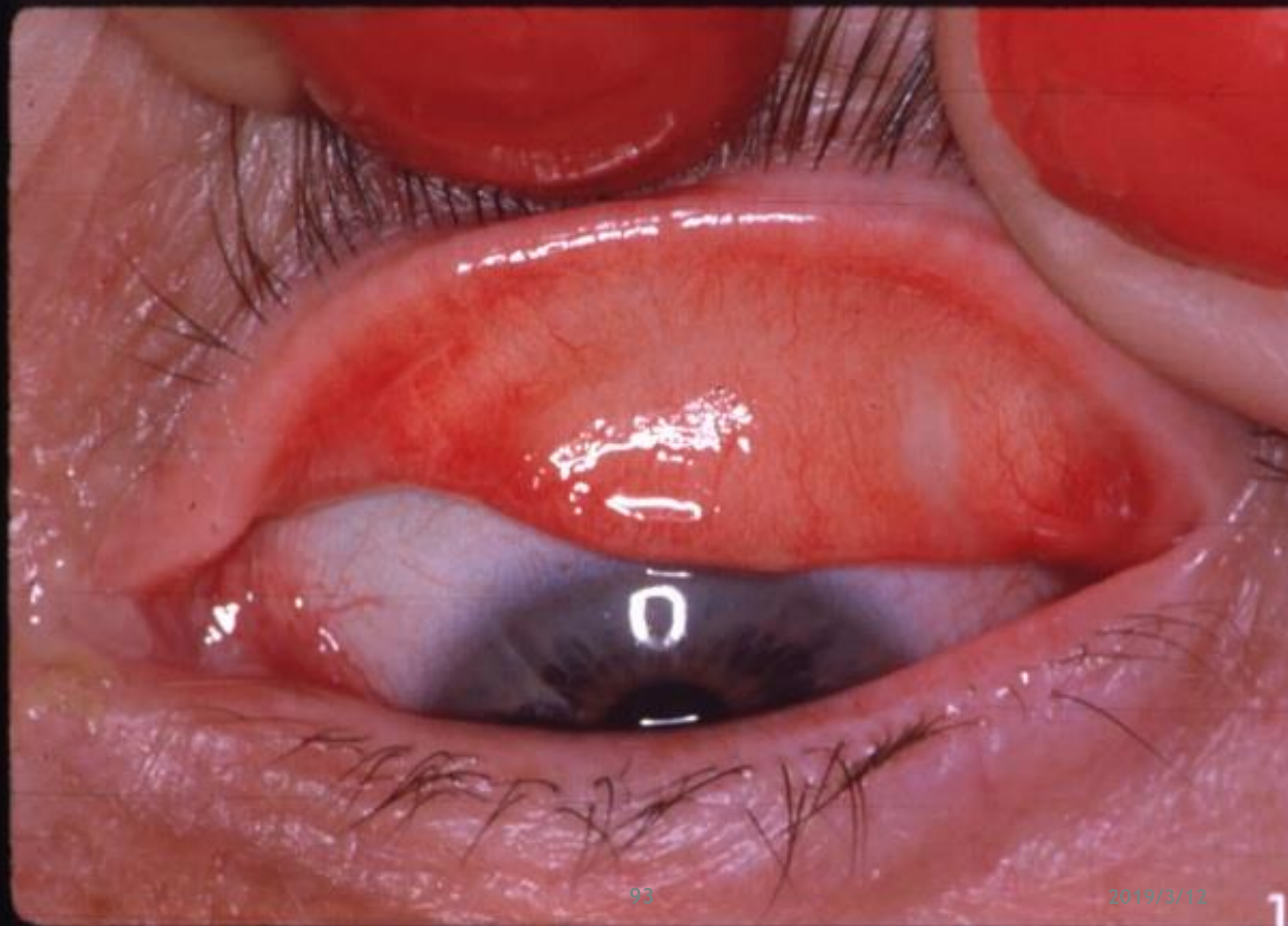
- * Clinical presentation.
- * Offending agents.
- * Conj scrapings.

*Treatment:

- * Discontinue the offending agents.
- * Tears..
- * Cold compresses.
- * Antihistamines..
- * NSAIDs..
- * Steroid

*Acute allergic toxic
induced conjunctivitis







* Perennial allergic conjunctivitis

- * Symptoms persist throughout the year, with seasonal variation in up to 87% of patients.
- * The clinical signs and symptoms are similar to SAC, but more persistent.
- * Allergens could be house dust mites, animals, etc..
- * Type I mediated.

*Treatment:

- * Avoidance of allergen:
 - * Cover for mattress and pillows.
 - * Washing bedding regularly.
 - * Reduce humidity.
 - * Vacuum and damp dust.
 - * Eliminate animals from house.
- * Washing allergen.
- * Antihistamines.
- * Mast cell stabilizers.
- * NSAIDs.
- * Steroids.
- * Immunotherapy

- * Reaction that may begin 24-72 hours following instillation of topical medication.
- * Patients are often sensitized by previous exposure to the offending drugs or preservatives.
- * Acute eczema with erythema, leatherlike thickening, and scaling of the eyelid.
- * Lower eyelid ectropion, and hyperpigmentation.
- * Papillary conjunctivitis and mucoid discharge may develop.

* Contact dermatoblepharitis

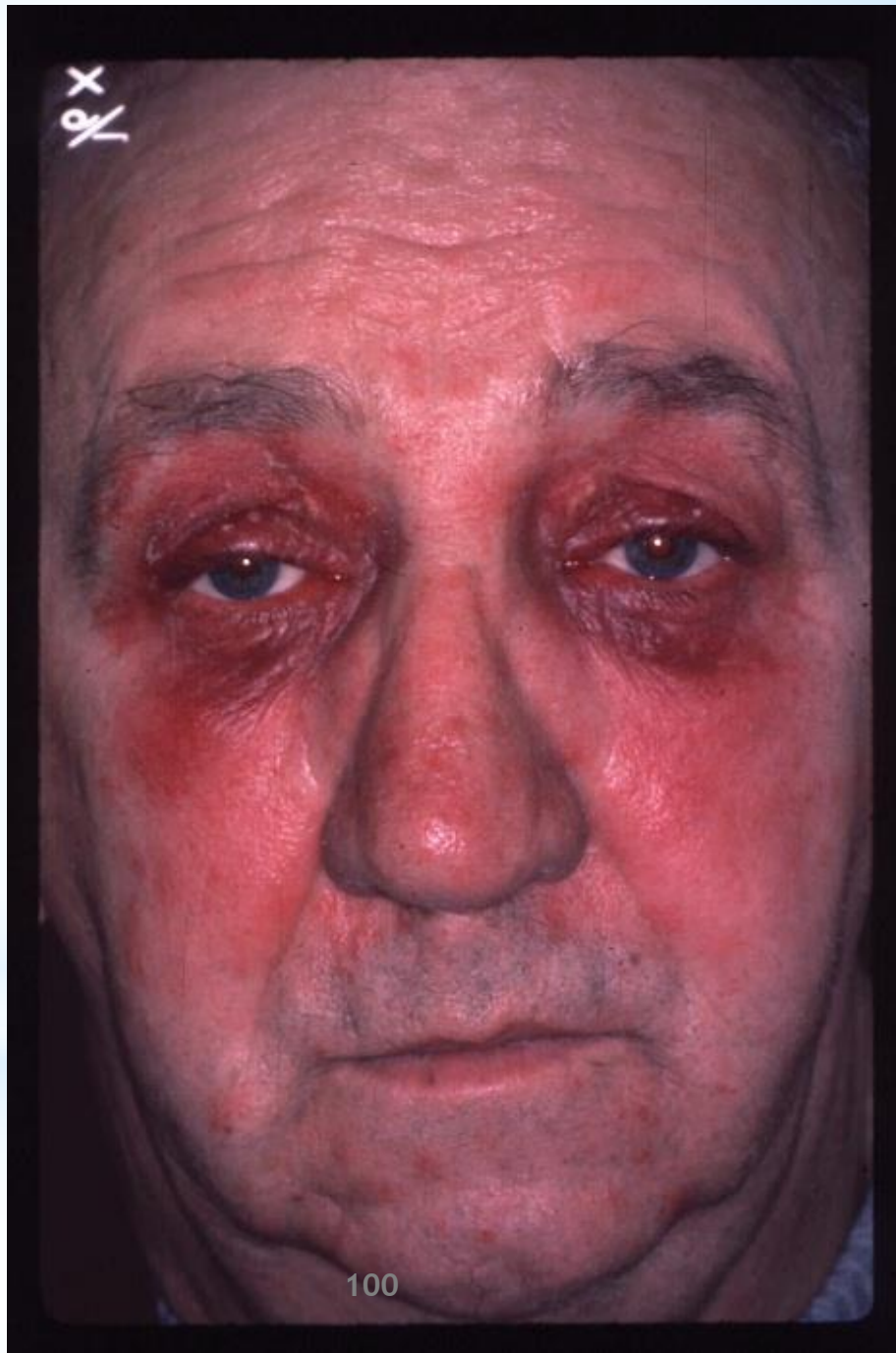
- * Medications commonly associated with these symptoms:
 - * Atropine..homatropine.
 - * Neomycine..gentamycine..tobramycine.
 - * Idoxuridine..trifluridine.
 - * Thimerosal.
- * Type IV reaction.

* Contact
dermatoblepharitis

*Treatment:

- * Allergen withdrawal.
- * In severe cases...brief course of topical steroids applied to the eyelids and periorcular skin may speed resolution.

*Contact
dermatoblepharitis



2019/3/12

*Epidemiology:

- * Rarely appear in patients younger than 3 or older than 25 years of age.
- * M:F is 2:1.
- * The disease usually lasts 4 to 10 years and resolved after puberty, but also can still be present and even worsened in some adult patients.
- * Occurs more frequently in the Mediterranean area, central Africa, India, and South America.
- * It also occur in cooler climates, such as Great Britain and other northern European countries, which is possibly as a consequences of migratory movements of the susceptible population.
- * Association with atopy is 15 to 60%.

- *VKC is usually bilateral, although monocular forms and asymmetric symptoms do occur.
- *Three clinical forms can be observed : tarsal, limbal (more common in African and Asian patients), and mixed tarsal/limbal.
- *In majority of the cases, the disease is seasonal, lasting from the beginning of spring until fall. Nevertheless, perennial cases have been observed, especially in warm subtropical or desert climates.

*Symptoms:

- * Itching.
- * Tearing.
- * Mucus secretion.
- * Photophobia.
- * Pain.
- * Blepharospasm.
- * Decreased visual acuity.

*Signs:

- *Papillary reaction.
- *Conjunctival redness and edema
- *GPC.
- *Limbal gelatinous infiltrate.
- *Trantas dots.
- *Mucus discharge.
- *Pseudoptosis.
- *Tarsal conjunctival fibrosis.

- *Diagnostic approaches:

- *Clinically.

- *Specific IgE maybe assayed in serum and tears.

- *CBC for eosinophilia.

- *Conj scraping and tear cytology:

- *Eosinophils.

- *Basophils.

- *Neutrophils.

- *Tears tryptase level .

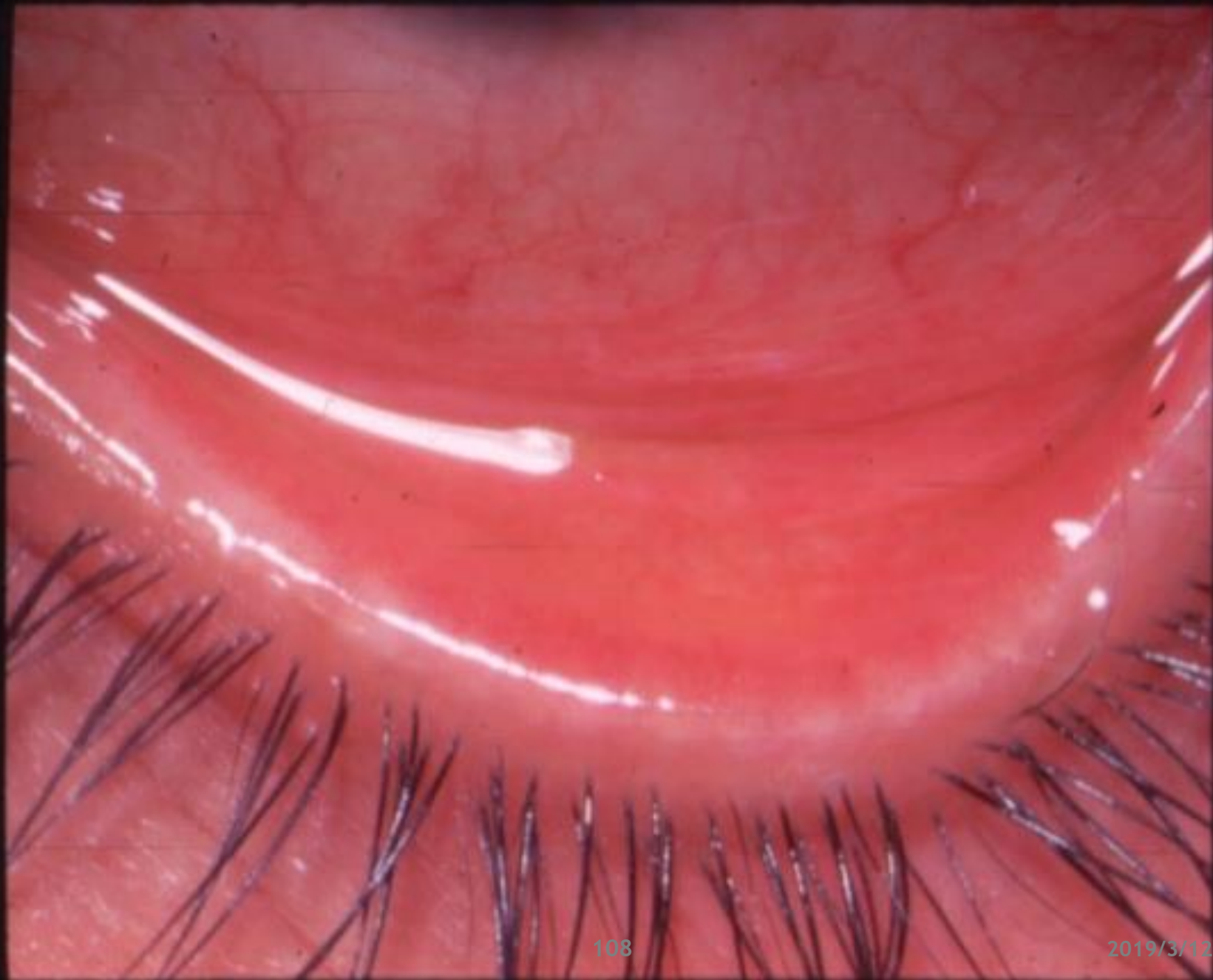


- *Pathogenesis:

- *Type I hypersensitivity.
 - *Type IV hypersensitivity.

*Therapy:

- * Preventive measures:
 - * Change of climate.
 - * Avoid exposure to nonspecific triggering factors such as sun, wind, and salt water.
- * **Mucolytic agents 10% Acetylcysteine**
- * Tears/vasoconstrictors/ cold compresses.
- * Mast cells stabilizers:
 - * Should be used continuously throughout the season.
- * Antihistamines.
- * NSAIDS: either locally or systemically.
- * Steroids. Short pulses, topical/ tarsal injection.
- * Cyclosporine.



- * Atopy is hereditary condition that manifests in ocular diseases, skin abnormalities, and respiratory tract dysfunction.
- * Atopy occurs in 5 to 20% of the general population.
- * The term AKC is misleading, although ocular surface disease is most prominent, the disease usually involve the lid also.



*Epidemiology:

- * AKC occur in up to 25% of patients with atopic dermatitis.
- * A review of family history frequently reveals the presence of other diseases such as asthma, hay fever, and urticaria.
- * AKC occurs more frequently in men.
- * Typically begin in the late teens or early twenties, and they persist until the fourth or fifth decade of life.
- * The peak incidence occurs between the ages of 30 and 50 years.



- * Clinical signs of the disease generally improve with age and may totally regress.
- * Patients with severe cases don't follow this trend.
- * AKC is often worse in the winter, but it usually has a perennial pattern of occurrence.

- * Clinical features:
 - * Symptoms:
 - * Bilateral itching
 - * Tearing
 - * Watery discharge
 - * Burning
 - * Photophobia
 - * Blurred vision.

*Signs:

*Lid:

- * Thickening of the eyelid margins (tylosis)
- * Eyelid swelling.
- * Scaly, indurated, and wrinkled appearance of the periocular skin
- * With profound swelling, a dennie-morgan folds or Dennie line is seen.
- * Chronic inflammation can give upper lid ptosis.
- * Fissures can occur at the lateral canthus owing to excessive skin rubbing.
- * An absence of lateral eyebrows, or Hertoghe's sign can be seen in severe form.
- * Marginal belpharitis caused by staphylococcal infection is common.

*Management:

- * Tears.
- * Vasoconstrictors.
- * Cold compresses
- * Antihistamines
- * NSAID.
- * Mast cell stabilizers.
- * Steroid.
- * Cyclosporine.
- * Antibiotics.
- * Surgical: lid procedures/ PKP.



Ocular allergy treatment approach

- * Elimination of allergen.
- * Eliminate eye rubbing.
- * Cool compresses/ tears/ vasoconstrictors.
- * Antihistamines for acute attack.
- * Mast cell stabilizer as prophylactic.
- * NSAIDs for acute attack
- * Steroid mainly for AKC/ VKC / GPC in short pulses..
- * Cyclosporine in VKC / AKC.
- * Immunotherapy.

*Drug therapy

- * Vasoconstrictors.
- * Antihistamines.
- * Mast cell stabilizers.
- * NSAIDs.
- * Steroids.
- * Cyclosporine.

Topical antihistamine/vasoconstrictorw	Vascon-A.Naphcon-A. AK-Con-A.Opcon-A.
Topical antihistamine	Livostin. Emadine. Alocril Patanol. Alamast Optivar Zaditor.
Systemic antihistamine	Claritin .Allegra. Benadryl .
Mast cell stabilizers	Opticrom Crolom Alamast Alocril Alomide Patanol Zaditor Optivar
Antihistamine+Mast cell stabilizer+ NSAID	Alamast Alocril Optivar Zaditor
NSAIDs	Acular Voltaren Ocufen Aspirin
Steroids	FML inflammase mild/forte Pred mild/forte vexol Alrex Lotemax
Cyclosporine	

*Antihistamines

*Systemic antihistamines:

- * Rarely prescribed by ophthalmologist.
- * Useful in patients with rhinitis.
- * Peak action within 1 to 2 hours.
- * Last 4 to 6 hours.
 - * Claritin (loratadine) 10 mg daily.\$26.99
 - * Allegra (fexofentadine) 60 mg twice daily.\$21.19
 - * Benadryl (diphenhydramine).
 - * Zytrec (cetirizine). \$1/pill

*Antihistamines

*Side effect:

*Topical:

- * Irritation.
- * PEE due to preservatives.
- * Dry eye symptoms.
- * Vasoconstrictors should be used with caution in patient with narrow angle/ HTN/ CVD/ arrhythmias.

*Antihistamines

- *Systemic:
 - * Sedation.
 - * Dizziness.
 - * Fatigue.
 - * Nausea.
 - * Vomiting.
 - * Diarrhea.
 - * Constipation.
 - * Dry eye.

*NSAIDs

*Topical:

- * Acular (Allergan), (ketorolac tromethamine 0.5%). \$50.15
- * Voltaren (CIBA), (diclofenac sodium 0.1%)
- * Ocufer (Allergan), (flurbiprofen sodium 0.03%)

*All act by:

- * Block the cyclo-oxygenase pathway, limiting production of prostaglandins and thromboxanes.
- * Analgesic.

*S/E:

- * PEE.
- * Persistent epithelial defect.
- * Stromal infiltration.
- * Ulceration.
- * Thinning.
- * Perforation.

*NSAIDs

*Systemic NSAIDs:

*Aspirin:

- * 1g /day for 6 weeks found to be useful in treating VKC.

*Steroids(topical)

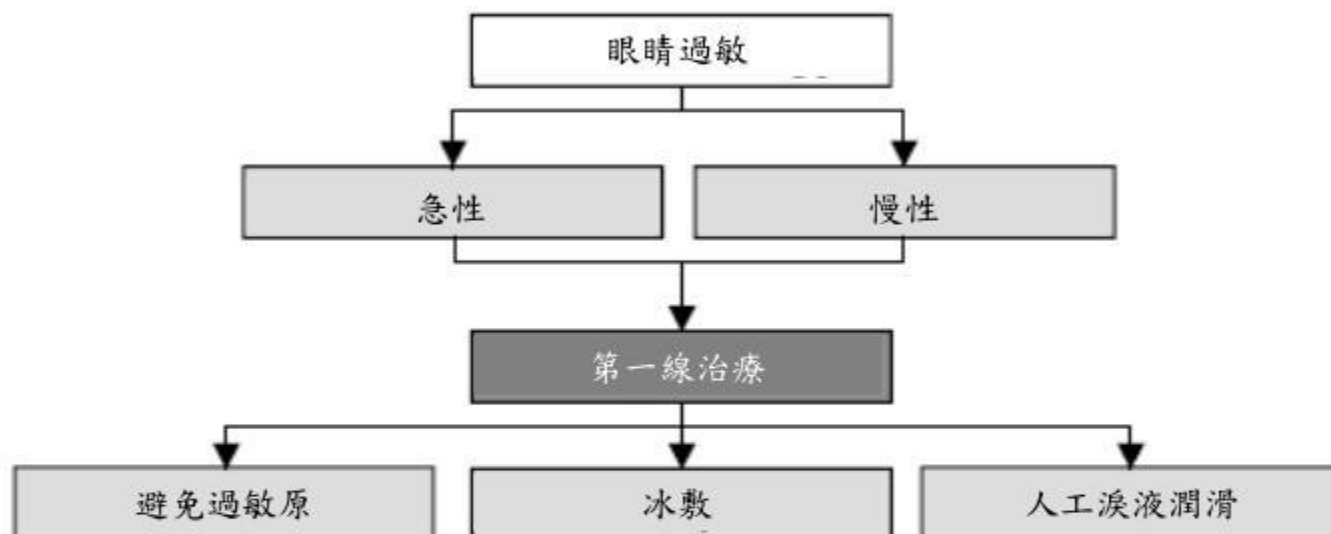
- * **FML** (Allergan), (fluorometholone 0.1%).\$ 35.74
- * **FML-F** (Allergan), (fluorometholone 0.25%).
- * **Vexol** (Alcon), (rimexolone 1%). \$52.01
- * **Pred Mild** (Allergan), (prednisolone acetate 0.12%).\$ 29
- * **Pred Forte** (Allergan), (prednisolone acetate 1%),\$ 54
- * **Ophtho-Tate** (Kenral), (prednisone acetate 1%). \$ 18
- * **Inflamase Mild** (CIBA), (prednisone phosphate 1/8%).
\$ 30
- * **Inflamase Forte** (CIBA), (prednisone phosphate 1%).
\$ 28
- * **Alrex** (Bausch and Lomb), (loteprednol etabonate 0.2%). US \$38.09.
- * **Lotemax** (Bausch and Lomb) ,(loteprednol etabonate 0.5%). US \$33.69.
- * **S/E:**
 - * Ocular discomfort.
 - * Delayed epithelial healing.
 - * HSV flare up.
 - * Increase IOP.
 - * PSCC.
 - * Ptosis
 - * Mydriasis.

*Steroids

- *Local injection.
 - *VKC.
 - *AKC.
- *Oral.
 - *For severe cases as in AKC.

*Cyclosporine

- Cyclosporine (cyclosporine A, CsA) is a selective immunosuppressant that inhibits IL2 and T-cell activation. It also has an inhibitory effect on eosinophils activation.
- Topical CsA 2% was effective as steroid sparing drug in severe VKC and AKC.
- Its effect is usually transient.
 - * S/E:
 - Intense stinging.
 - Keratitis.
- Systemic CsA has been used in patients with AKC.



移除過敏原來源，換工作地點

各式急慢性過敏性結膜炎皆適用。可緩解癢，覆蓋在眼上5到10分鐘，眼藥冷藏後使用也有類似效果

可提供舒適感，稀釋過敏原與濕潤眼睛改善屏障功能。晚上可用藥膏來保持眼睛濕潤



應該轉介眼科醫師的情形

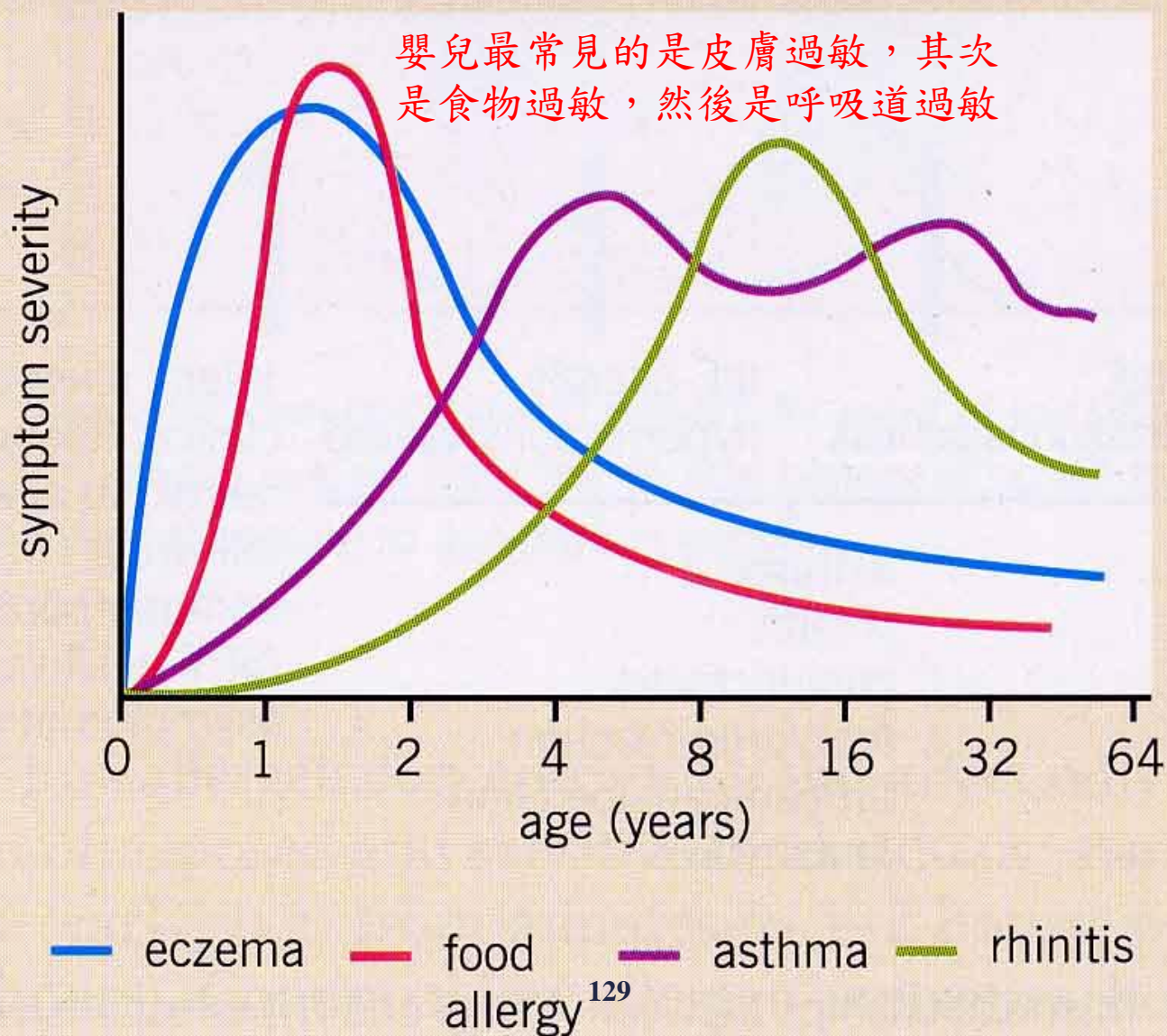
- 不規則或不正常瞳孔變化
- 角膜不透明
- 眼球內發炎
- 眼睛無法轉動
- 病人抱怨有深部眼球痛或視力下降
- 有全身性過敏疾病
- 懷疑有春季型結膜炎或異位性角結膜炎的病人
- 懷疑有巨乳突結膜炎的病人，確定過敏來源與處置
- 已治療但症狀仍持續之病人

* Atopic Dermatitis

* Winnie Yang MD
Taipei City Hospital



過敏進行曲







- * A chronic inflammatory skin disease associated with cutaneous hyperreactivity to environmental triggers
- * influenced by bacterial factors, particularly *Staphylococcus aureus*
- * *S. aureus* colonization on the skin of patients is approximately 90%-100%
- * Up to 65% produces exotoxins with superantigenic properties
- * Predates the development of asthma and/or allergic rhinoconjunctivitis

- * Unclear, Multifactorial
- * prevalence is rising in the industrialized countries
- * Staphylococcus aureus
- * Genetic and pre- and perinatal influences
(Black and Asian race/ethnicity, male gender, higher gestational age at birth, and maternal history of atopy)

Protective effect is established independently early in life

Food allergens (<5y) and aeroallergens (7-12y)

* **Pathogenesis**

High IgE and early sensitization (1 yr)

Decrease INF- γ in intractable AD

Product of interactions between susceptibility genes, the environment, defective skin barrier function, and immunologic responses

skin development is not complete at birth

 **Pathogenesis**

- * Stratum corneum, keratinocytes, immune cells, and nerve fibers are in close proximity to one another and induce itch.
- * Impaired barrier function associated with the itch-scratch cycle further augments this vicious cycle
- * Drives downstream inflammation and allows unrestricted antigen access

* Skin barrier function

* complications

Eczema herpeticum

usually primary HSV infection



Bacterial infection

S aureus colonization : >90%

β -hemolytic group A *Streptococcus*

eczematous and bullous lesions on the palms and soles



- * SA and GAS (3-6y, 53%) were isolated from all body sites
- * Enteric G(-) and bacteroides were often in buttock and leg
- * Antibacterials and topical corticosteroids therapy produces a more rapid decrease in SA colonization but not clinical improvement of dermatitis
- * An exacerbation factor, cause of relapse or worsening of AD
- * Often coexisted with beta-hemolytic streptococci (50%). (CNSA?)

Skin of patients with AD has increased avidity for binding to SA and deficient to generate antimicrobial peptides

- * Food allergens play a major role in the exacerbation and maintenance of eczematous lesion
- * Cow's milk, hen egg, wheat and soy--- infants
- * Nuts, fruit , vegetable--- adolescents
- * Food specific T cells--- adult
- * RAST (sp 42%-64%), SPT (44%-53%), APT (69%-92%) are poor reliability

* The Impact of Food & Aeroallergens in AD

- * A diary for food consumption
- * Specific IgE to milk, egg, fish and peanut—95% predictive positive value

2/3 intolerant to food proteins have NO evidence of IgE sensitization to relevant food protein

* The Impact of Food & Aeroallergens in AD

Food allergy is regarded as IgE mediated
BUT some children with food allergy IgE
hypersensitivity cannot be proven.

Wheat--- often non-IgE-sensitized

Hen's egg--- often in sensitized group

*The Impact of Food & Aeroallergens in AD

- * Allergens applied epicutaneously can influence the systemic allergic response
- * Children with AD and positive skin test have more severe asthma
- * Epicutaneous exposure to Ag in AD enhance the development of asthma
- * Systemic immune activation in AD is supported by increased Th2 cells, eosinophils, macrophages, and IgE.

* The Impact of Food & Aeroallergens in AD

- *Patients with AD present aeroallergen-specific T-cell responses associated with worsening of symptoms when exposed to specific aeroallergens
- *Exposure to high conc. of mite in early infancy may develop AD during the first 3 years of life.
Allergy. 2004 Aug;59 Suppl 78:53-60

- * Aeroallergens induce a positive APT in about 50% of patients with AD

J Allergy Clin Immunol. 2000

may;105(5):1008-16

- * Damage of the skin barrier function enhance epicutaneous sensitization to aeroallergens J

Allergy Clin Immunol. 1999 Dec;104(6):1280-4

- * Dust mite (42.8-65%) and cockroach (25.7-35.9%) were the commonest allergens

Thorax. 1994 Dec;49(12):1205-10

- * Avoid exposure of food and aeroallergens
 - * Only pure amino acid mixtures are considered to be nonallergenic (hypoallergenic formula— extensively or partially)
 - * Exclusive breastfeeding for 4-6 months
 - * BF is not a risk for developing AD, it is protective when compared with conventional cow's milk
- Allergy. 2004 Aug;59 Suppl 78:45-52.**
- * Avoidance of allergenic foods during pregnancy or the use of hydrolyzed or soy formula does not prevent eczema
 - * Delayed introduction of solids may decrease

*Treatment

- * Systemic antibacterials in combination with topical corticosteroid--- large areas
- * Topical abx plus topical corticosteroid--- small area
- * Gentian violet not only reduces SA dramatically, but also reduces the severity of the eczema
Dermatology. 1999;199(3):231-6

*Treatment

*

Cyclosporin A (CsA):

2.5-5 mg/Kg orally X 8wks, improved clinical symptoms in children suffering from severe AD

Pediatr Allergy Immunol. 2003

Feb;14(1):559

2.8mg/Kg/D X 6mo, rapid relief but NOT long-lasting and relapse (3mo)

*

Vitamin B(12) cream:

an effective scavenger of nitric oxide, a new therapeutic approach

NO synthase inhibitor, N omega-nitro-L-arginine, led to a clear decrease in pruritus and erythema in atopic dermatitis.

Br J Dermatol. 2004

May;150(5):977-83.

***Treatment**

Tarcolimus & Pimercrolimus:

1. Inhibit proinflammatory cytokine production in cutaneous lymphocytes
2. reduced expression of the high-affinity IgE receptor FcepsilonRI, a reduced stimulatory capacity of lesional DCs, but not DC apoptosis

J Allergy Clin Immunol

2004 Jul;114(1):137-43

3. Reduces all steroid-induced effects
4. Did not increase the risk of skin infection
5. Herpes infection (face and neck), 2.8% to 4.7%

J Dermatol 2004 Apr;31(4):277-

83

*Treatment

6. Used when topical corticosteroid (TCS) fail and in patient ≥ 2 yrs
7. Whether it is effective after topical TCS failure
8. No more effective than a class II TCS
9. Burning and pruritus at the site of application (5%)

 **Treatment**

10. Severely skin infection and skin cancer maybe the serious side effect
11. Drugs interaction
12. No reason to use Tacrolimus, at least pending studies showing it is effective after TCS failure

 **Treatment**

- * Conventional therapy with hydrocortisone and emollients alone is as effective as WWT for moderately severe, AD

Clin Exp Dermatol. 2004 Jul;29(4):348-53

- * 1/10 diluted 0.1% mometasone furate oint. Plus 1/10 diluted 0.005% fluticasone propionate oint. followed with WWT are improving refractory AD

Pediatr Dermatol. 2001 Jul-Aug;18(4):343-8

* Wet wraps therapy(WWT)

- * More convincing for prevention than treatment
- * Reduced cumulative prevalence of eczema but not atopy

* Probiotics for atopic dermatitis

***65% improving**
mild cases >50% exacerbation
moderate cases 77-91% --- life- long
affected
18%- 40% spontaneously recover

***prognosis**

積極保濕

患者角質層的脂質和天然保濕因子不足
皮膚保濕能力就會不佳
做好保濕是治療關鍵！



避免過敏原暴露

空氣以及食物的過敏原
是否為惡化因子尚有爭論
但減少接觸還是有好處

避免刺激物質接觸

異位性體質對於產生過敏性接觸性



知易行難

(ARIA update)

