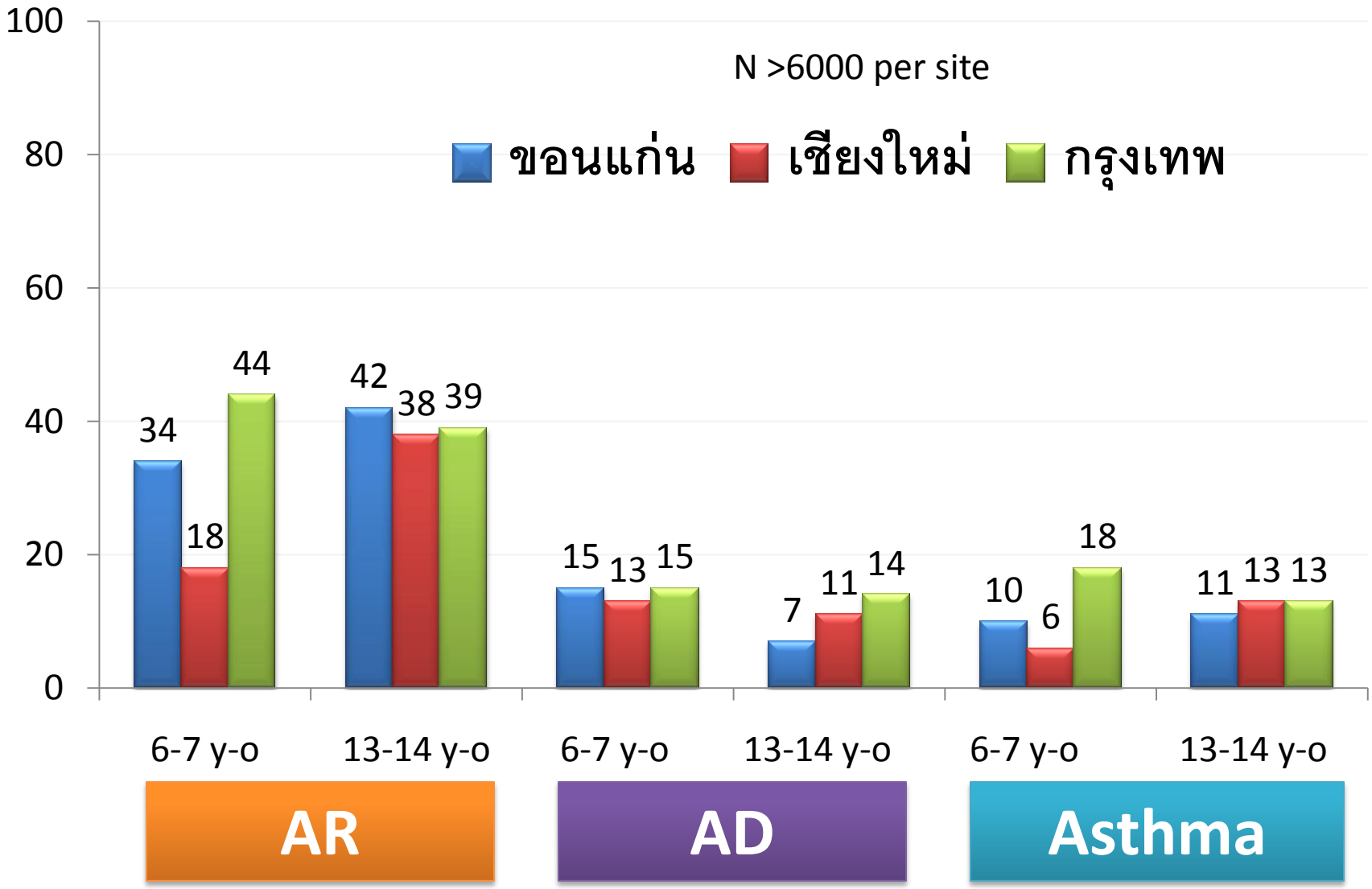
สมาคมโรคภูมิแพ้ โรคหืด และวิทยาภูมิคุ้มกันแห่งประเทศไทย
The Allergy, Asthma, And Immunology Association of Thailand

Pearl and Pitfalls in Treating Allergic Rhinitis

Practical in Diagnosis and Management

Kiat Ruxrungtham
Professor of Medicine
Allergy and Clinical Immunology Division
Department of Medicine
Chulalongkorn University

ISAAC Surveys in Thailand

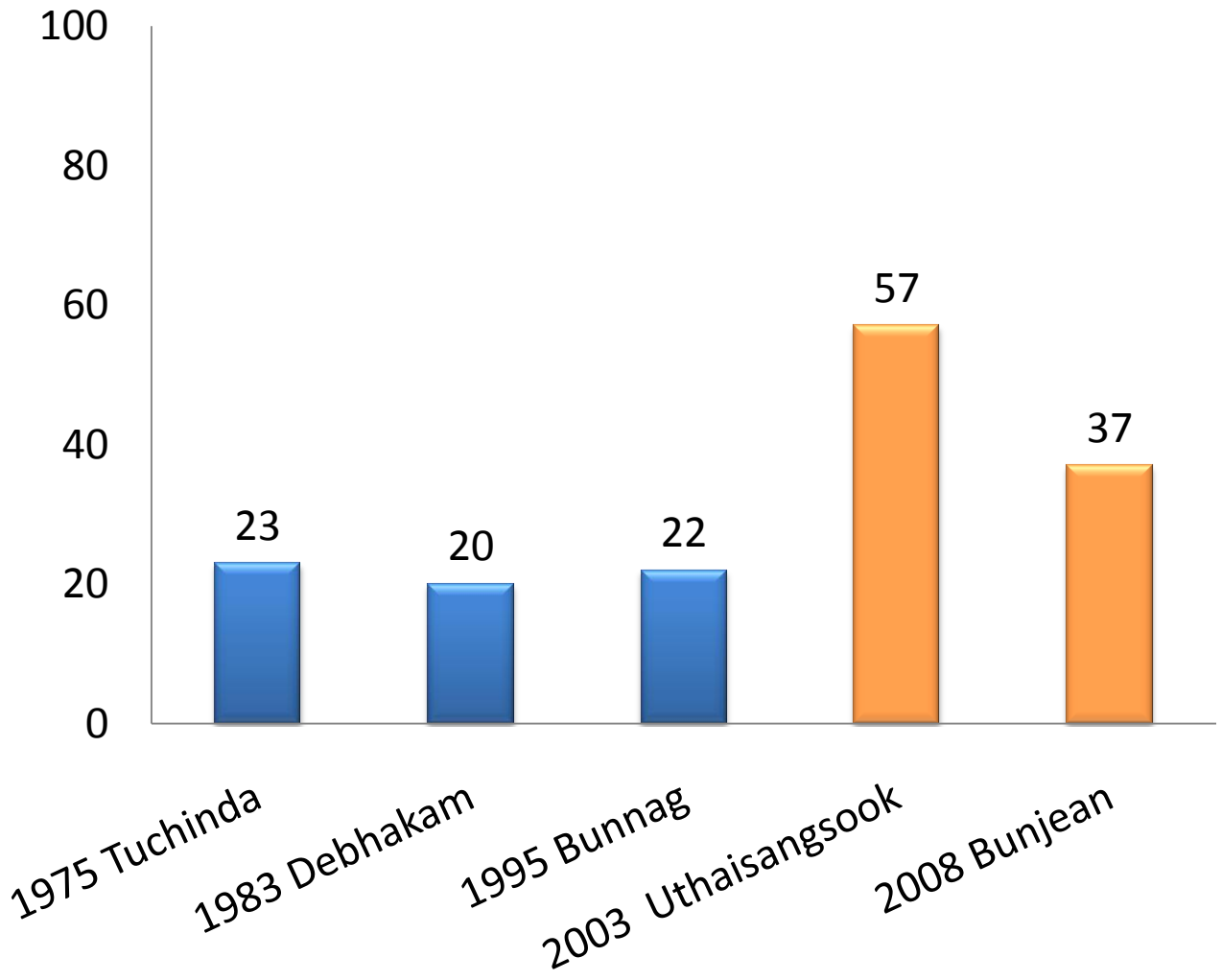


Trakultivakorn M 1999; Vichyanond P 1999; Teeratakulpisarn J 2000

AllergyChula

AllergyChula

Adult Prevalence of Allergic Rhinitis



Pearl and Pitfalls in Dx

Chief complaints

Keys physical findings

From this VDO Clip

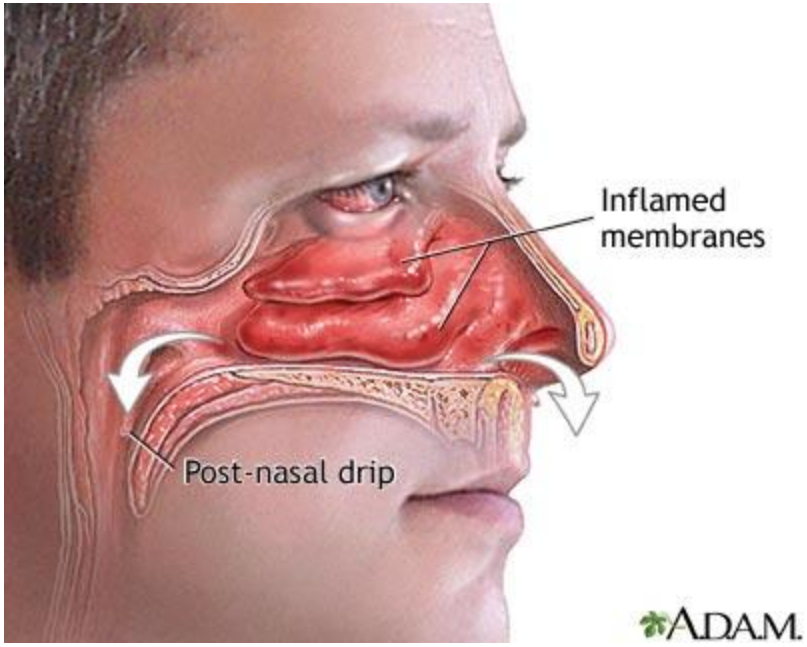
What is your diagnosis?

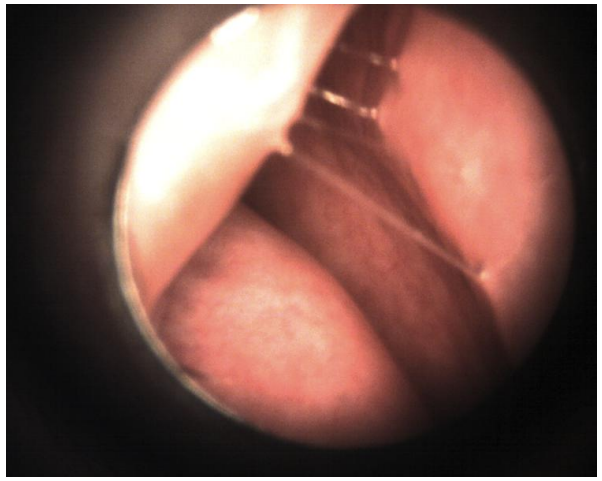
From this VDO Clip

Here is the answer

AR and Upper airway obstruction

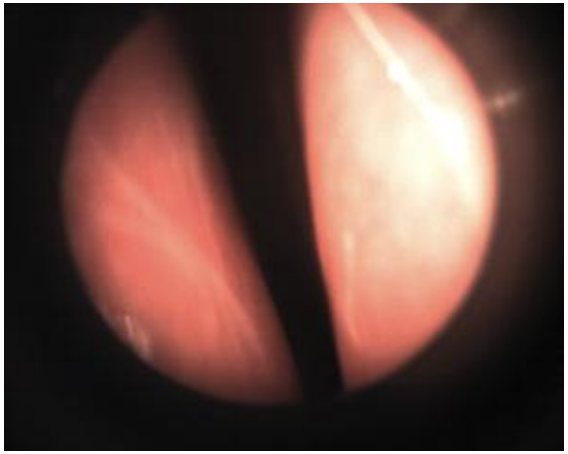
Commonly presented with dyspnea or SOB

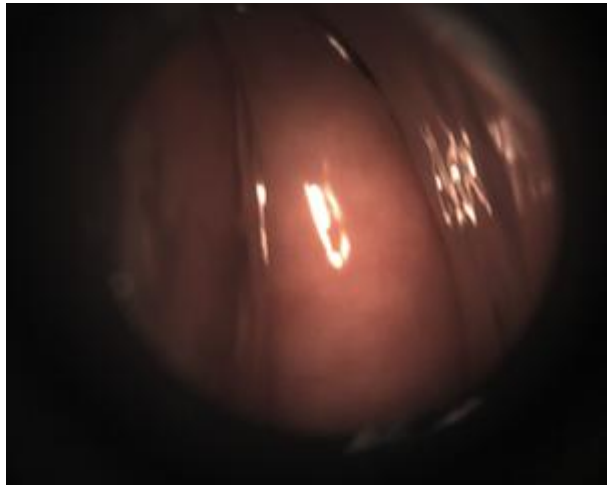




Obstructive

Normal



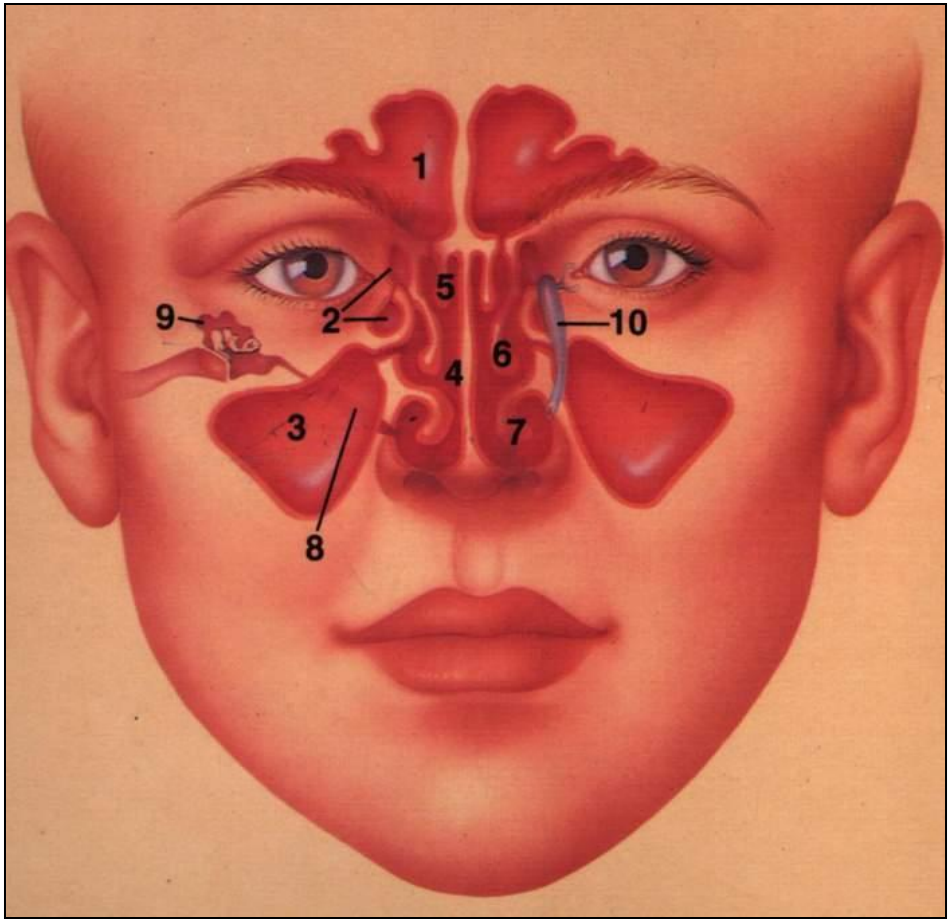


Middle turbinate

Headache and Allergic Rhinitis

AllergyChula

The link of
Noses, Eyes, Ears, and Sinuses



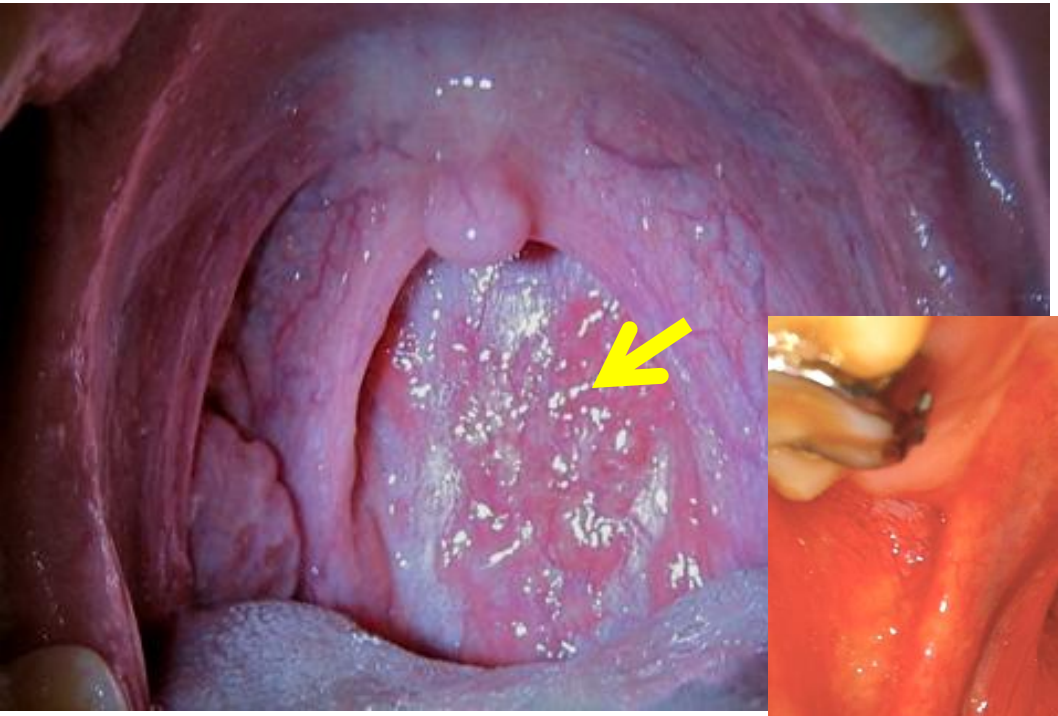
Chronic cough had been treated as asthma and also with various expectorant and cough suppressants, but not improved

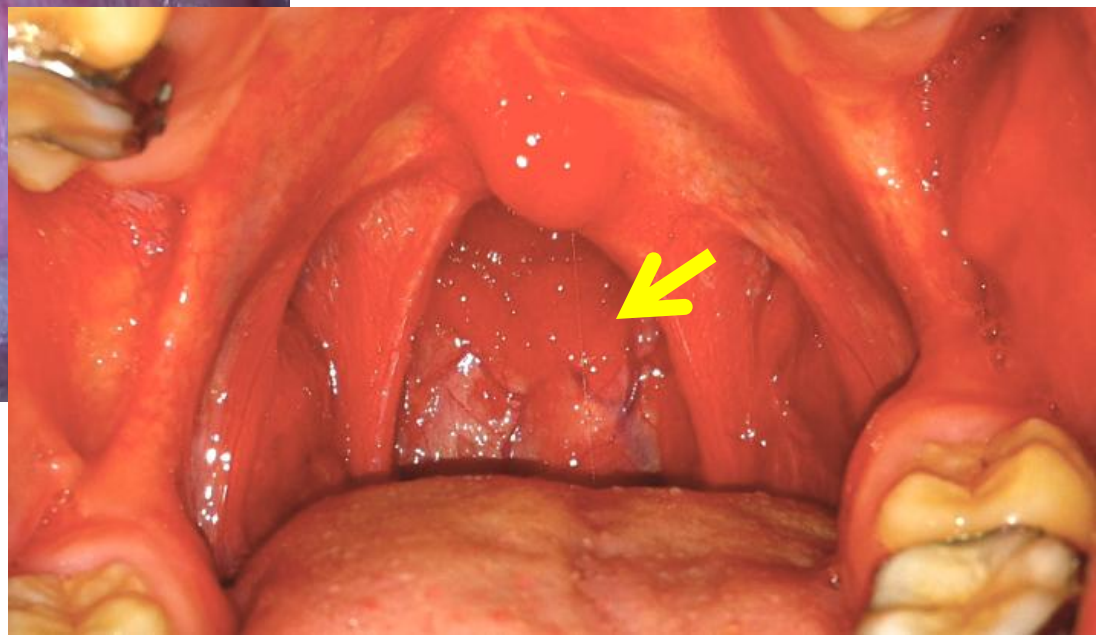
Chronic Paroxysmal Cough
Had been treated as asthma for years

After Topical Nasal Decongestant Treatment

Chronic cough, throat clearing,

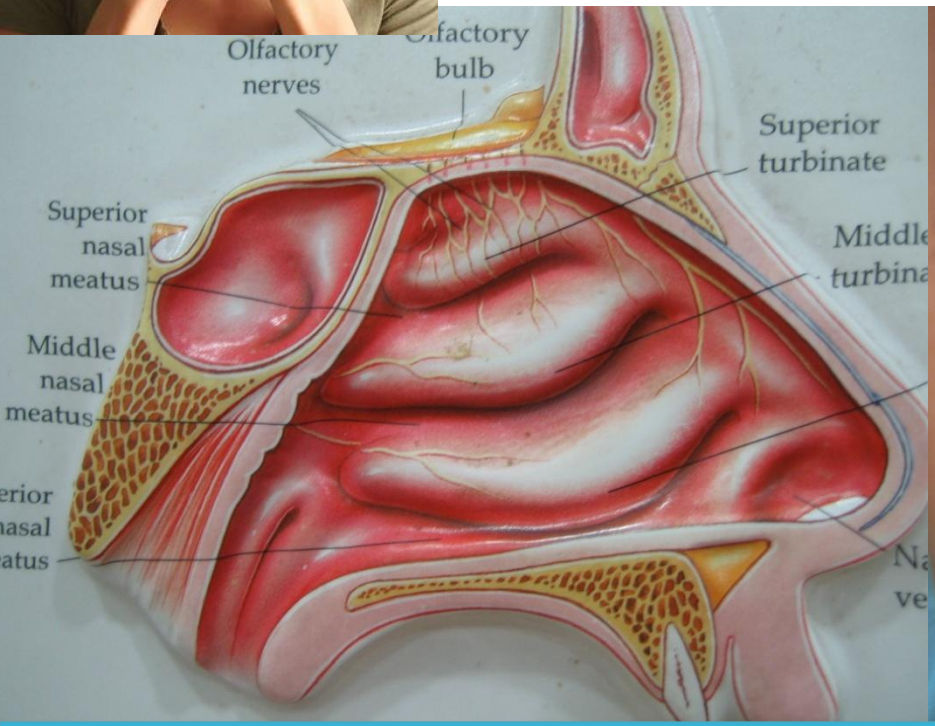
some with symptom of globus hystericus

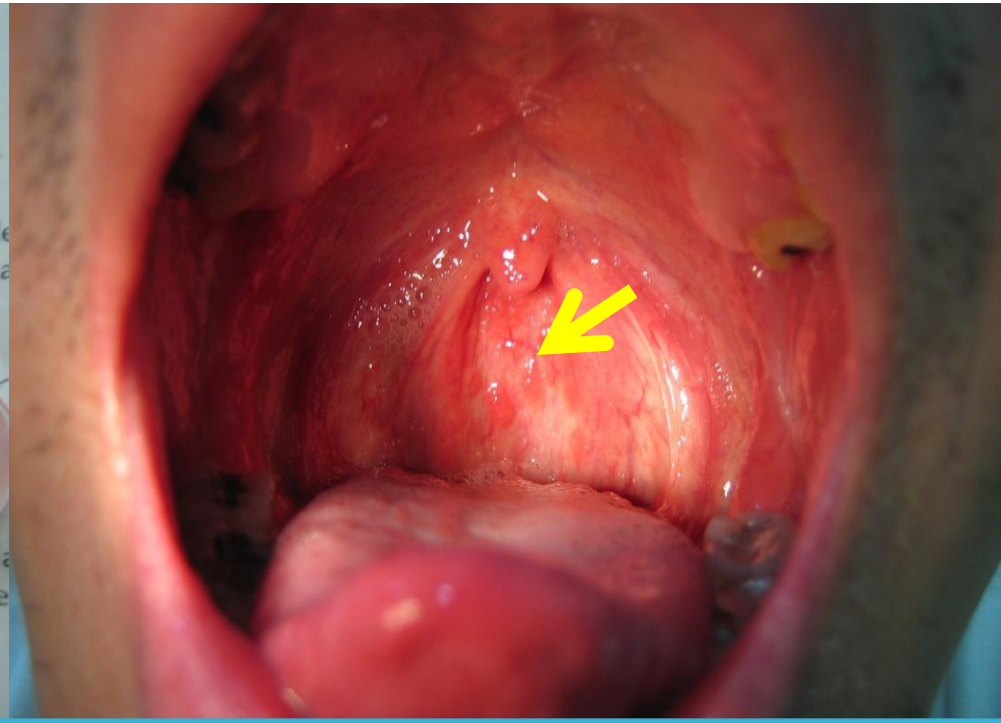




ทำไมภูมิแพ้มีกลิ่นปากแรง
Halitosis

Fetor Oris, Oral Malodor

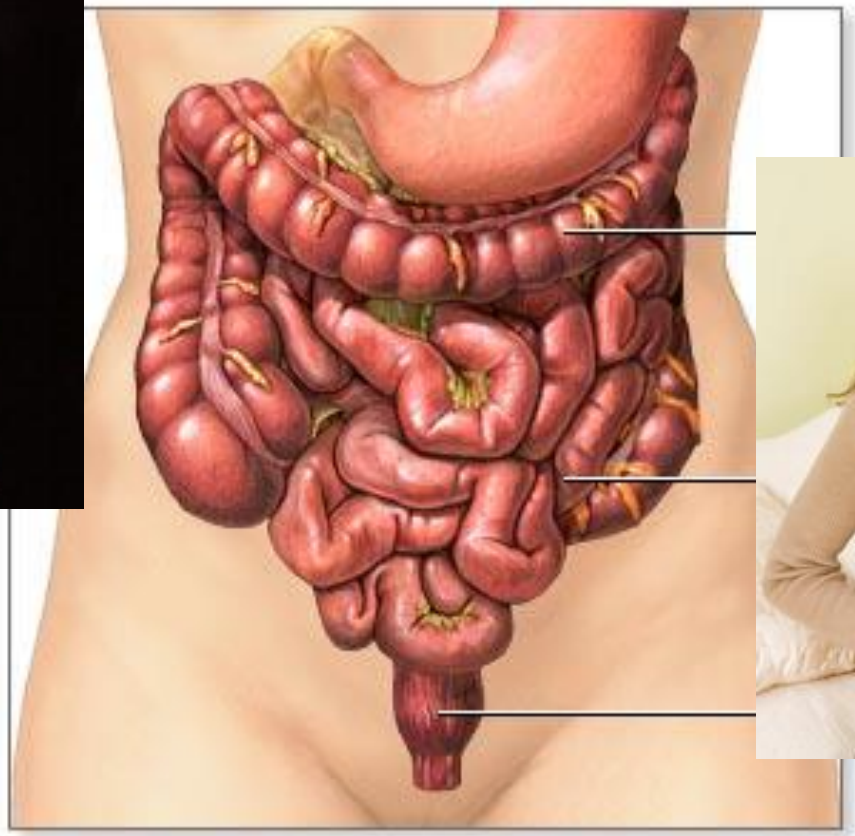




เพราะจมูกบวม ทำให้เมือกระเหยไม่ได้ ติดอยู่หลังคอ ทำให้อาหารมาติดค้างอยู่เนืองๆ จึงเกิดกลิ่นเหม็นจากแบคทีเรีย โดยเฉพาะเวลาทานขนมหวานๆ

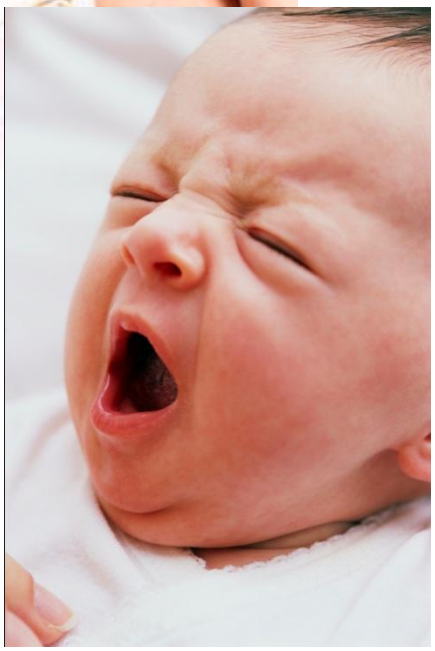
ภูมิแพ้จมูก กับ ปัญหาท้องอืด ท้องเฟ้อ

อาการคล้ายโรคกระเพาะแต่ทานยาไม่ได้ผล



Aerophagia and flatulency

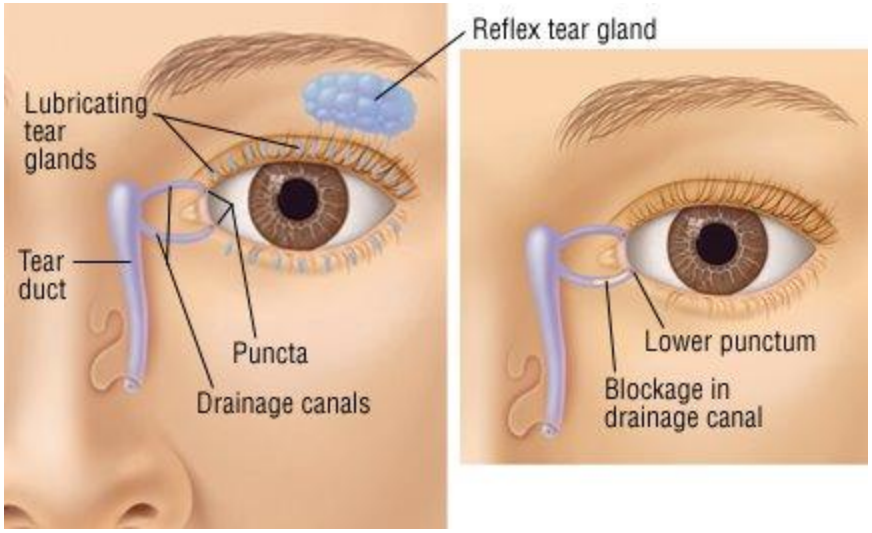
Sleepiness, Fatigability
Severe AR affects the QoS

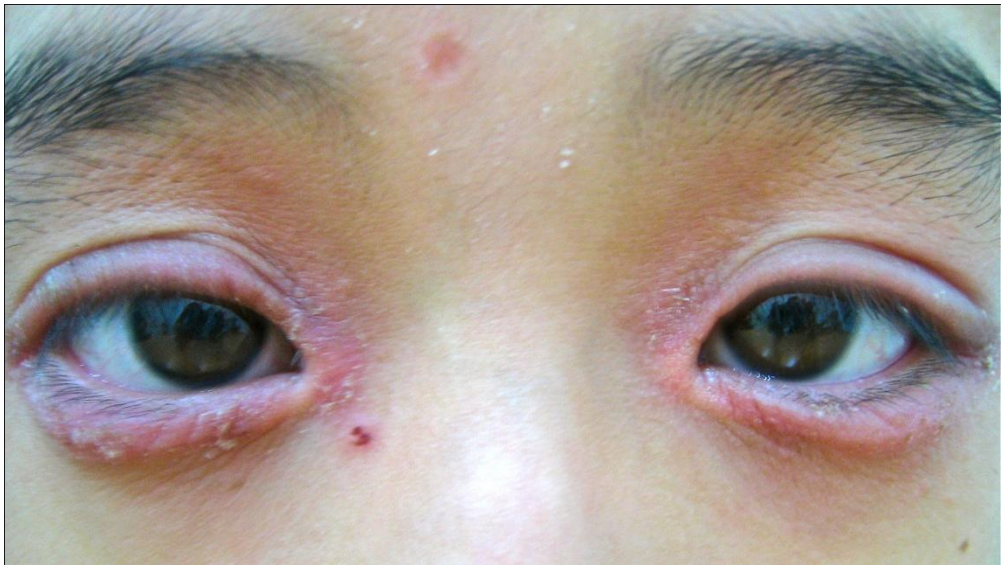


Cheilitis and AR

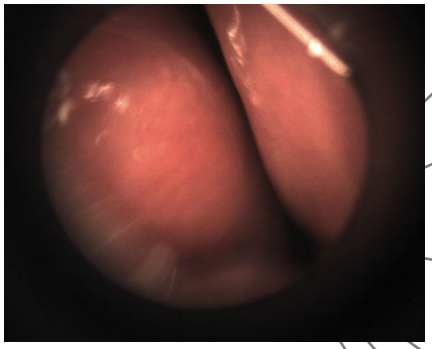
secondary to chronic mouth breathing and lip licking

Itching Eyes and Atopic Dermatitis





Symptoms of Chronic Nasal Blockade

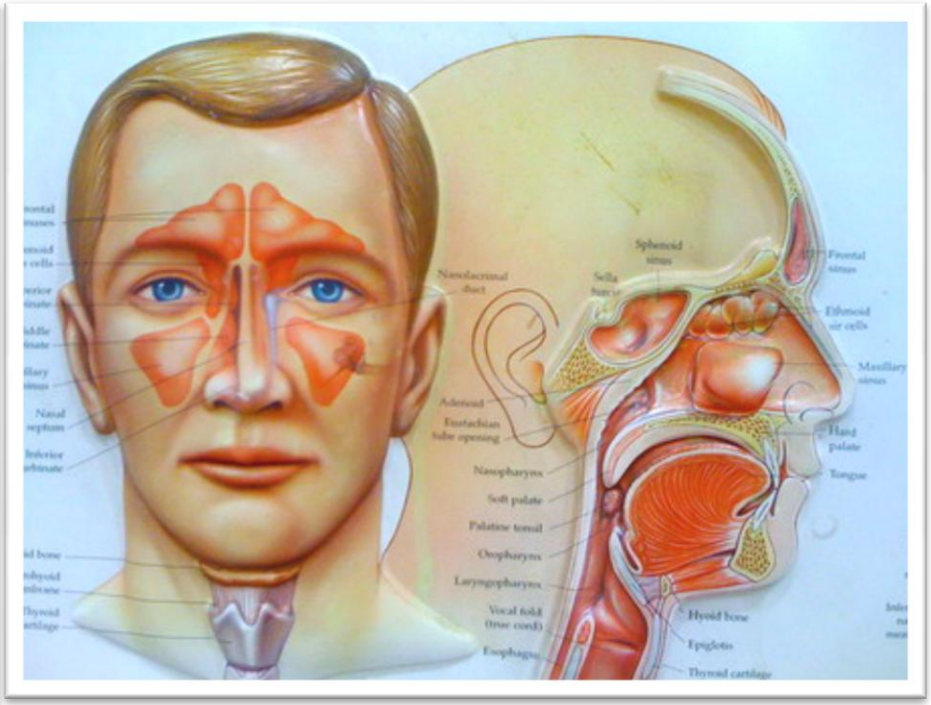


Most patients may not aware of such obstruction

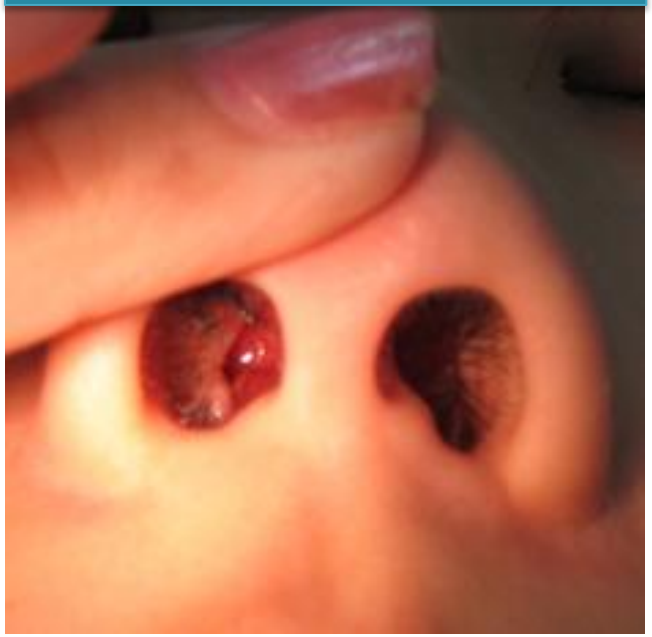
- **Chronic Cough** — Postnasal drip, +/- BHR
- **Chronic Headache** — Paranasal sinsuses obstruction
- **Throat clearing S/S** — Postnasal drip
- **Difficulty in Breathing** — Severe obstruction, Mouth breathing, Dry mouth, stomatitis, Aggravating asthma
- **Vertigo** — ET dysfucntion
- **Snoring or problem in sleeping**

Allergic Shiners

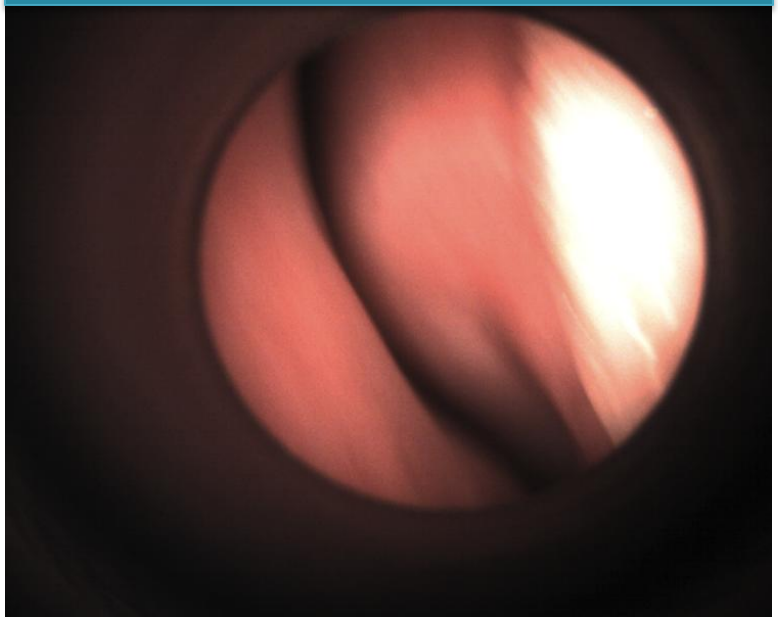
การตรวจโรคภูมิแพ้

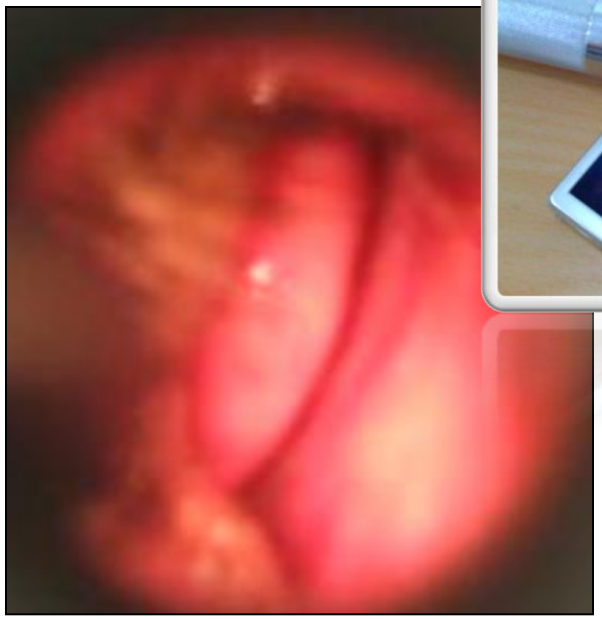


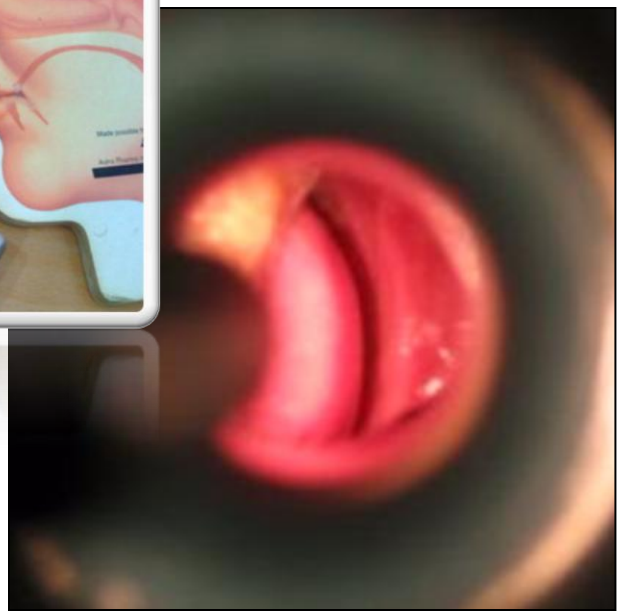
ตรวจส่องจมูก ข้างขวาบวมปิดรู

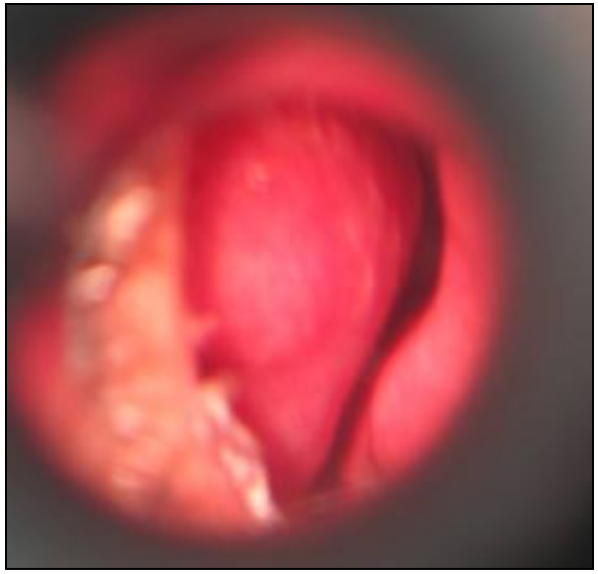


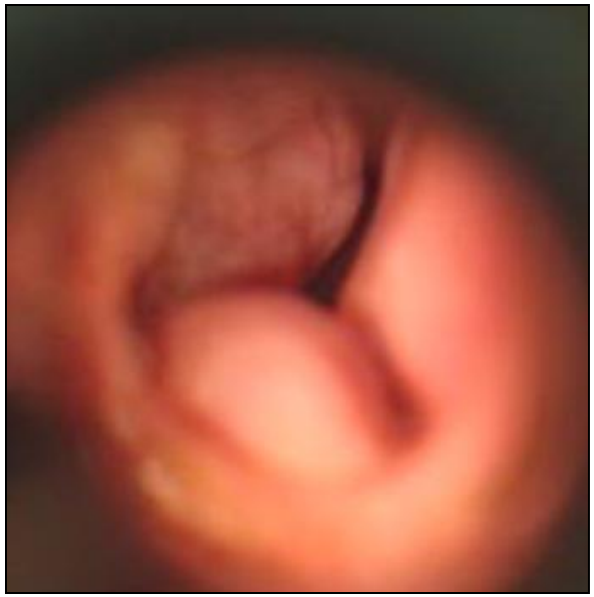
ส่องกล้องจมูกด้านซ้าย บวมปิดสนิท



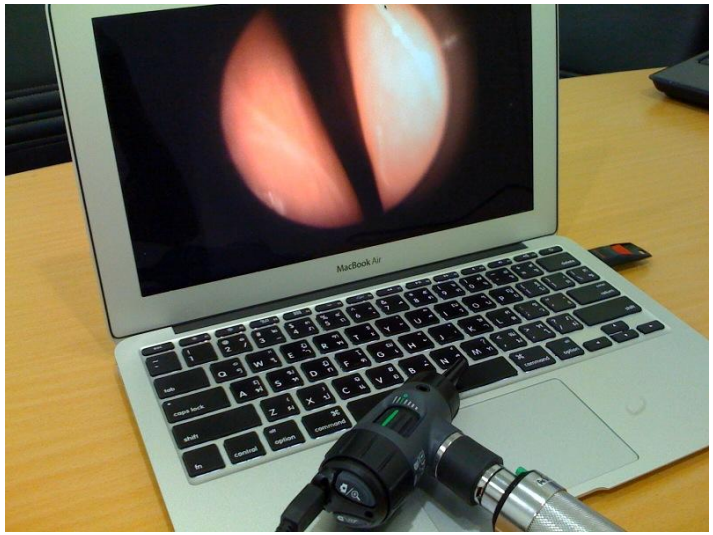


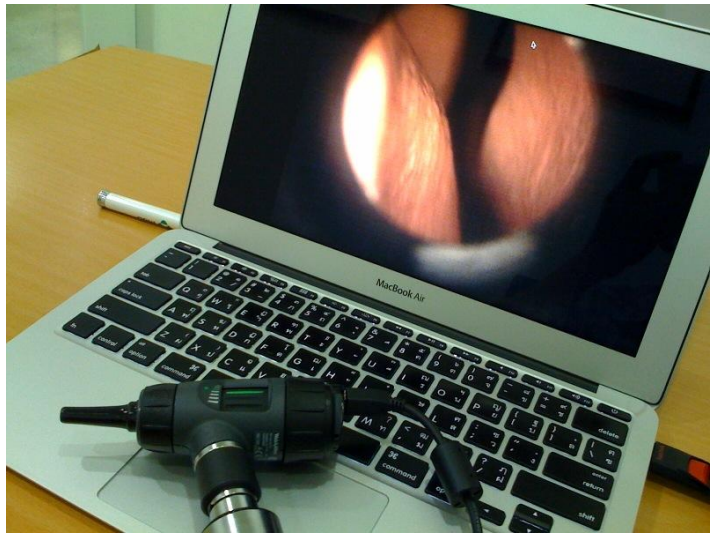






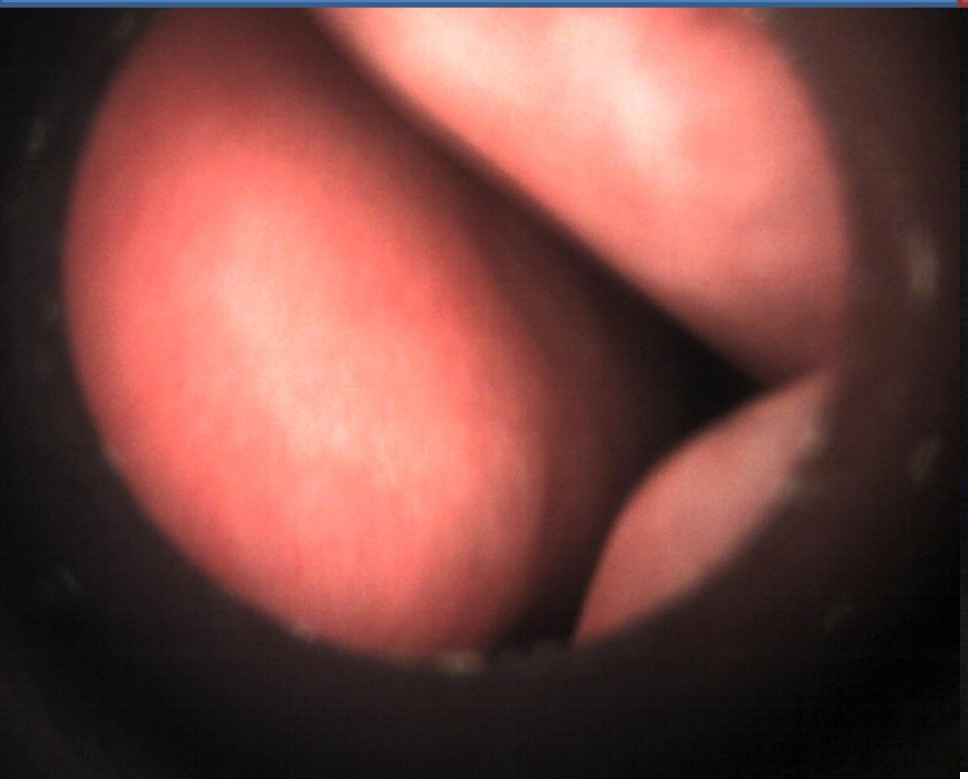
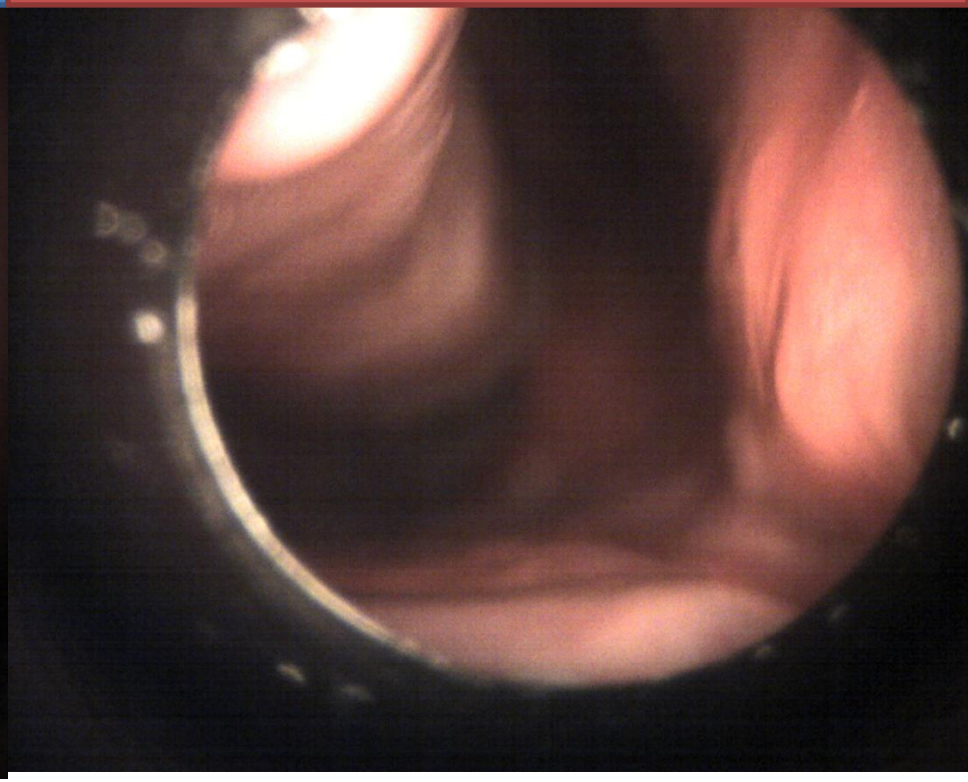
Digital Nasoscopy



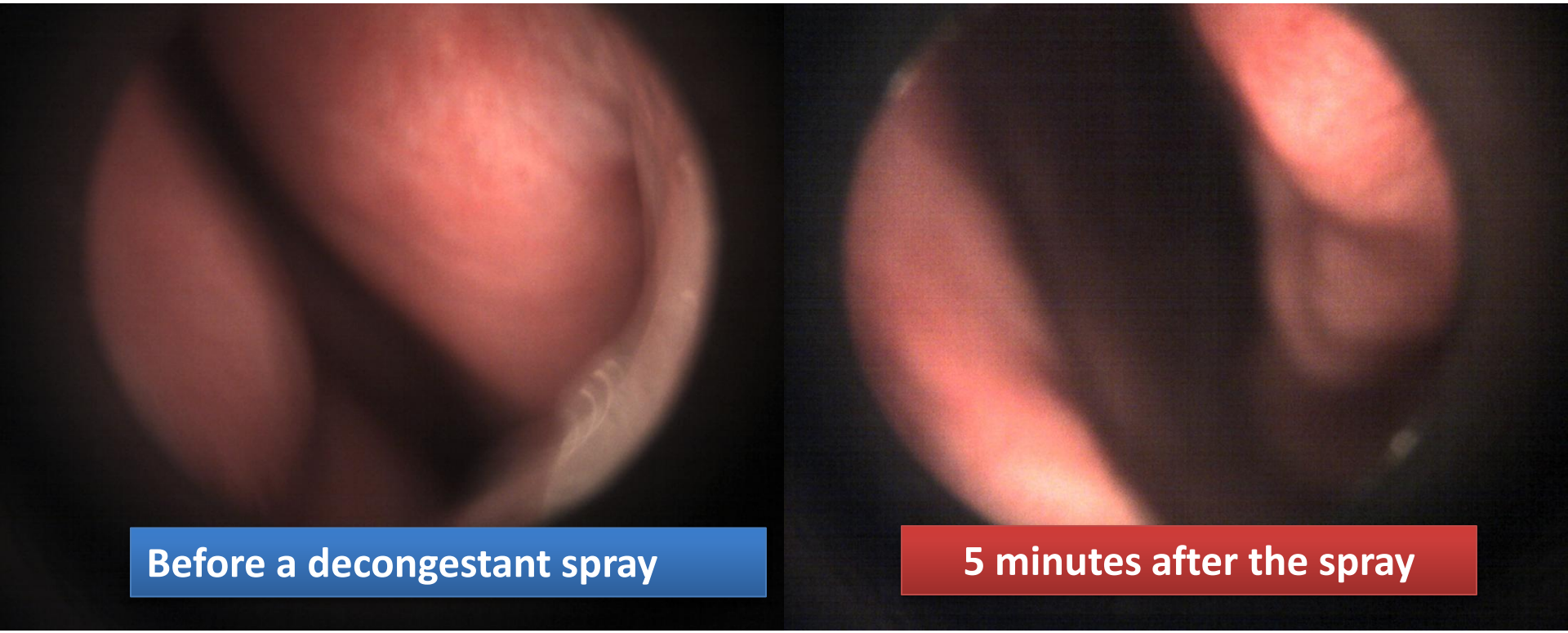


การตรวจแบบง่ายว่าจมูกตันหรือไม่
Nasal Patency Test

Nasal Decongestion: Pre and Post

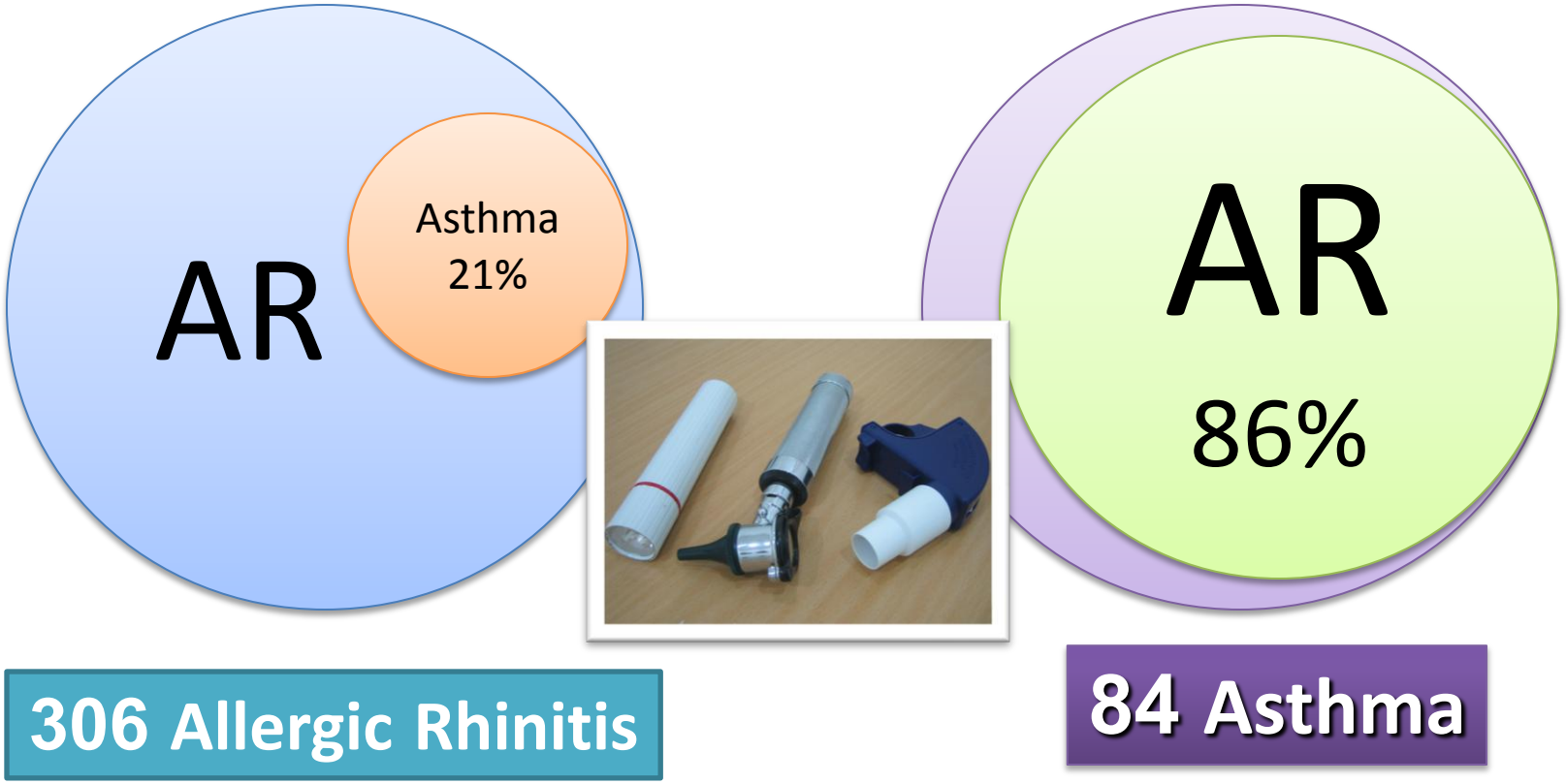
Before a decongestant spray	5 minutes after the spray
	

Nasal Decongestion: Pre and Post



Co-existence of Asthma and AR

23-Years Follow-up Study of
Former Brown University Students (N=738)



Greisner WA et al Allergy Asthma Proc 1998; 19:185-8

Skin Prick Tests

HDM

70%

Cockroach

50 %

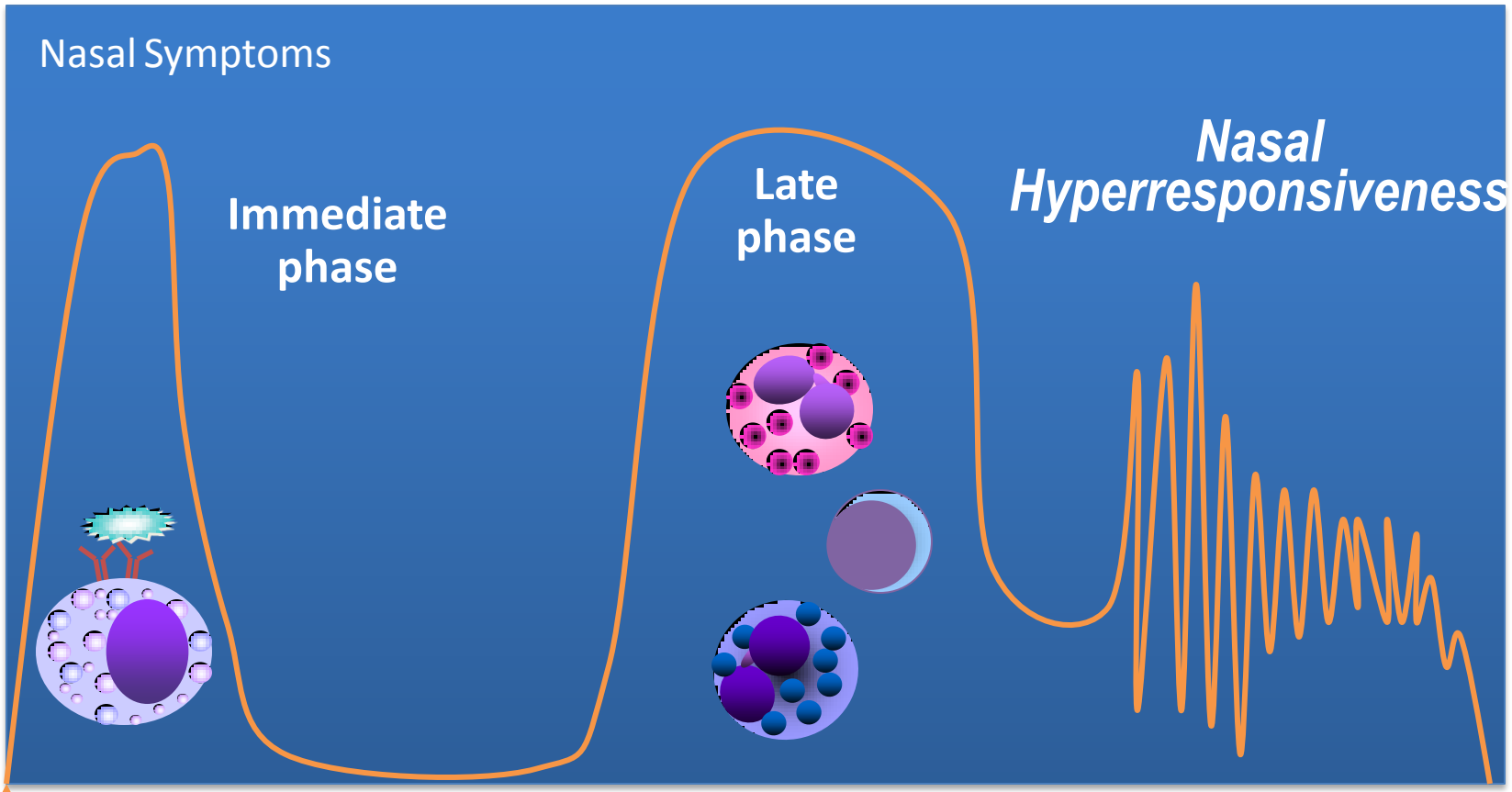
Cat

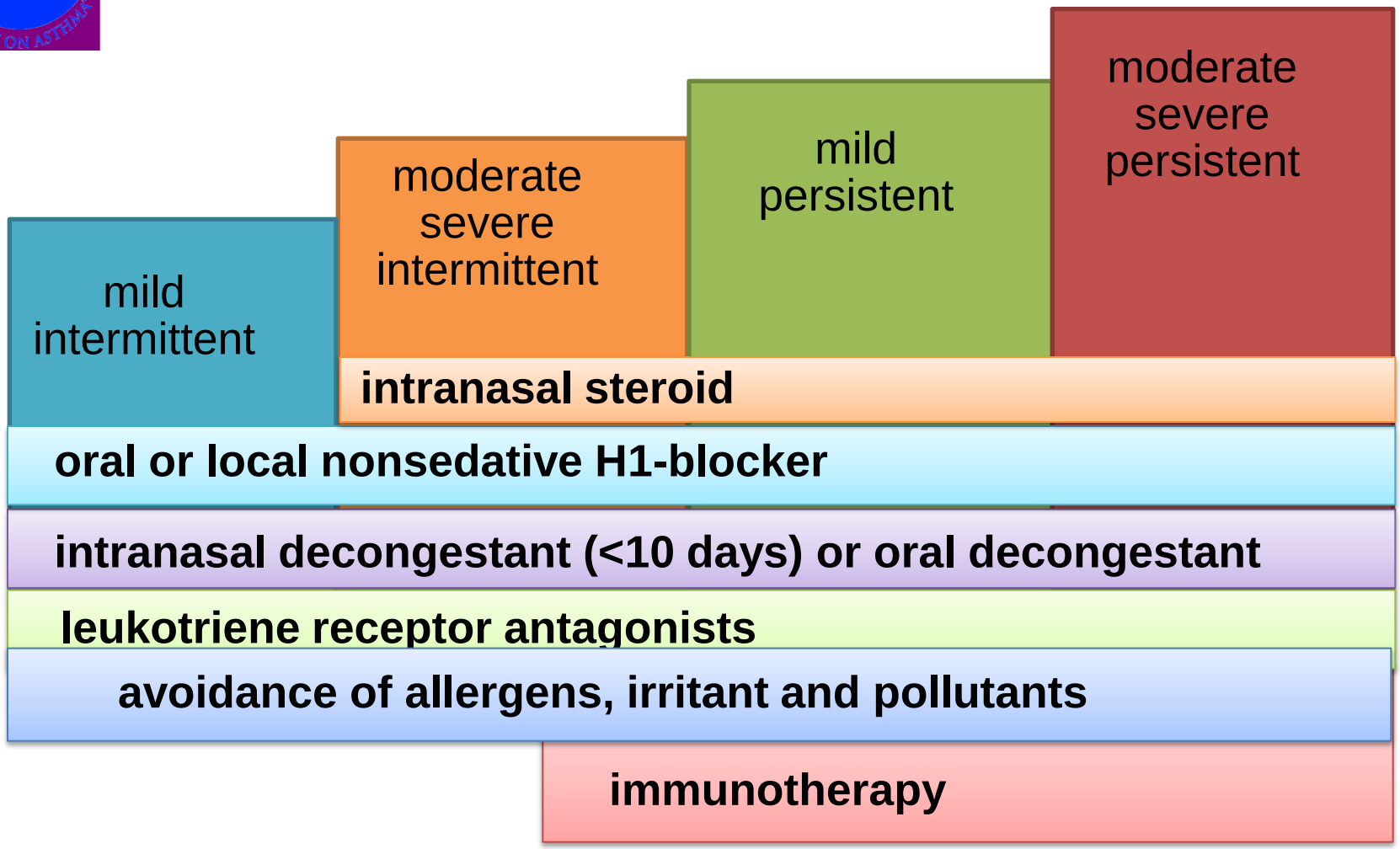
30%

AllergyChula

Allergic Rhinitis

Events After Allergen Exposure





Modified from Bousquet J et al. J Allergy Clin Immunol. 2001;108:S147.

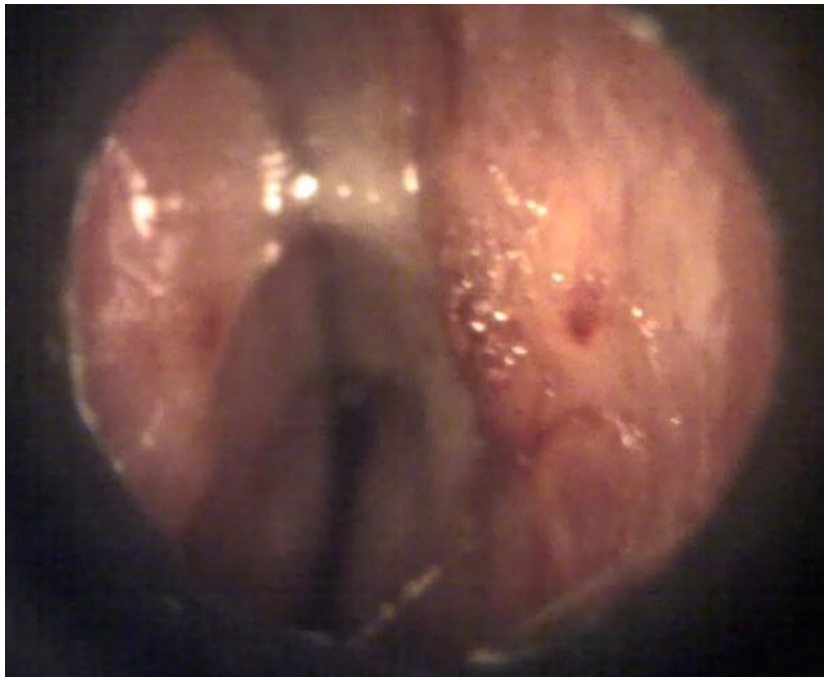
การรักษา โรคภูมิแพ้จมูก

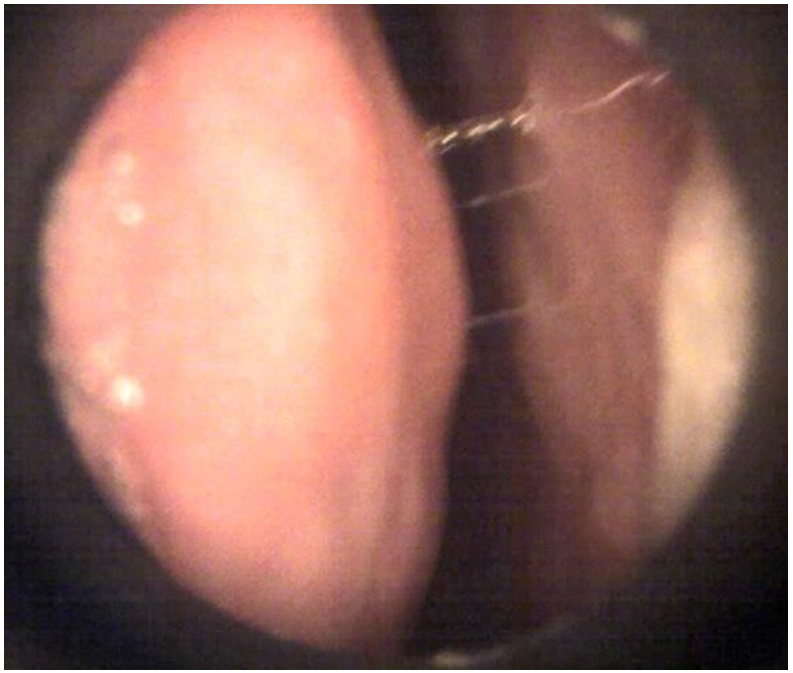
หลักในการรักษามี 4 ขั้นตอน

1. **กำจัดและหลีกเลี่ยงสารก่อภูมิแพ้และสารระคายเคืองต่าง ๆ**
2. **การรักษาด้วยยาเพื่อควบคุมอาการ** เช่น ยาแก้แพ้ชนิดกิน หรือยาพ่นจมูก โดยให้แพทย์หรือเภสัชกรแนะนำ
3. **การฉีดวัคซีนภูมิแพ้** เป็นการรักษาโดยฉีดสารก่อภูมิแพ้ที่เป็นสาเหตุ (วัคซีนภูมิแพ้) โดยค่อยๆ เพิ่มจำนวน เพื่อให้สร้างภูมิต้านทานต่อสิ่งที่แพ้ วิธีนี้มักจะใช้สำหรับผู้ป่วยที่มีอาการมาก
4. **การรักษาโดยการผ่าตัด** เพื่อลดขนาดเยื่อจมูกที่บวมมากๆ หรือแก้ผนังจมูกคด หรือเป็นไซนัสอักเสบเรื้อรัง

Nasal washing

Does it help in AR?





Pre-hypertonic saline wash

Post-hypertonic saline wash

Chulalongkorn DBPC Comparison Study

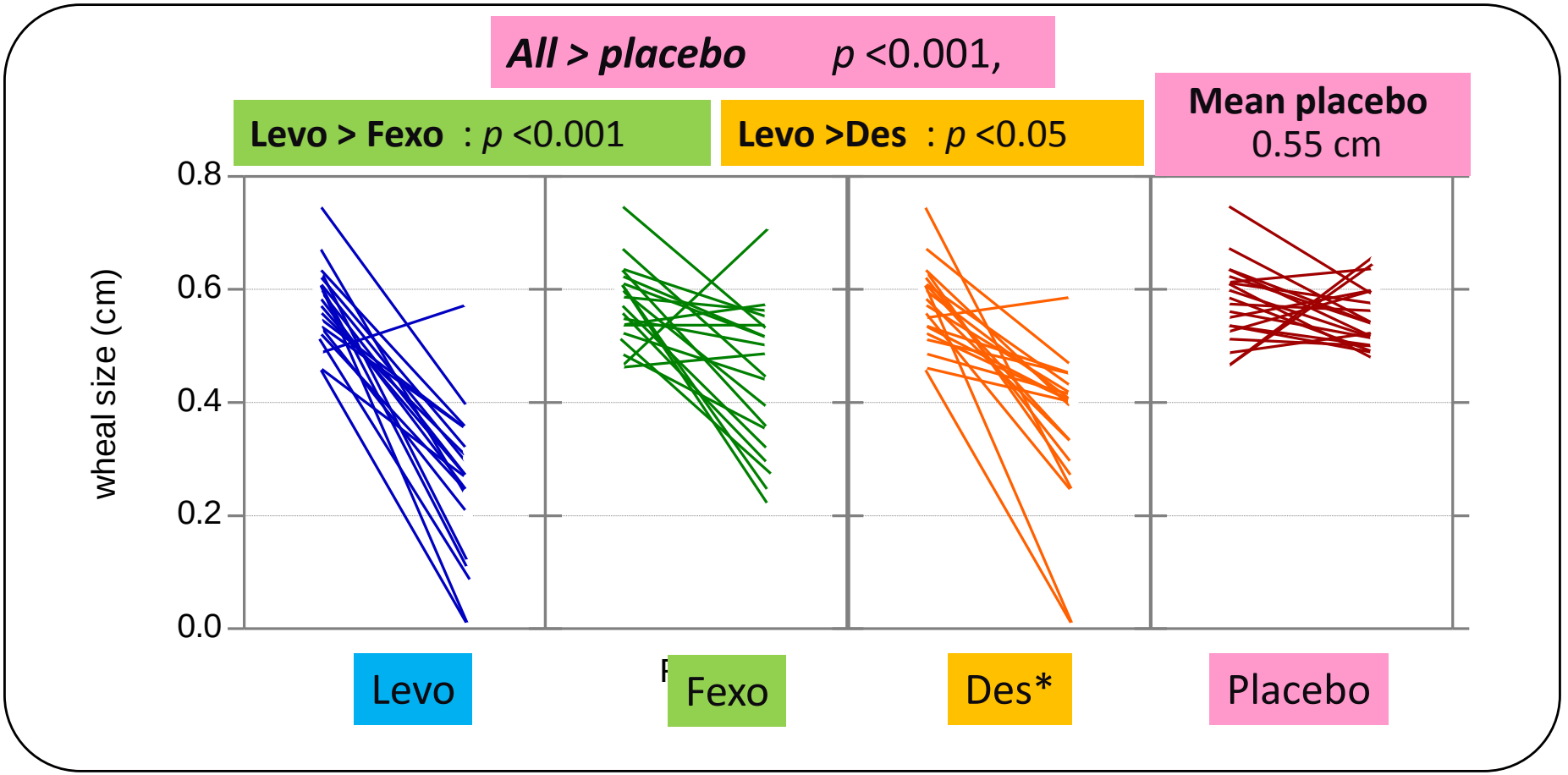
Desloratadine, Fexofenadine, and Levcetirizine

Pavarat Saengaram, MD

With no any pharmaceutical industry support

Histamine-induced Wheal Reduction

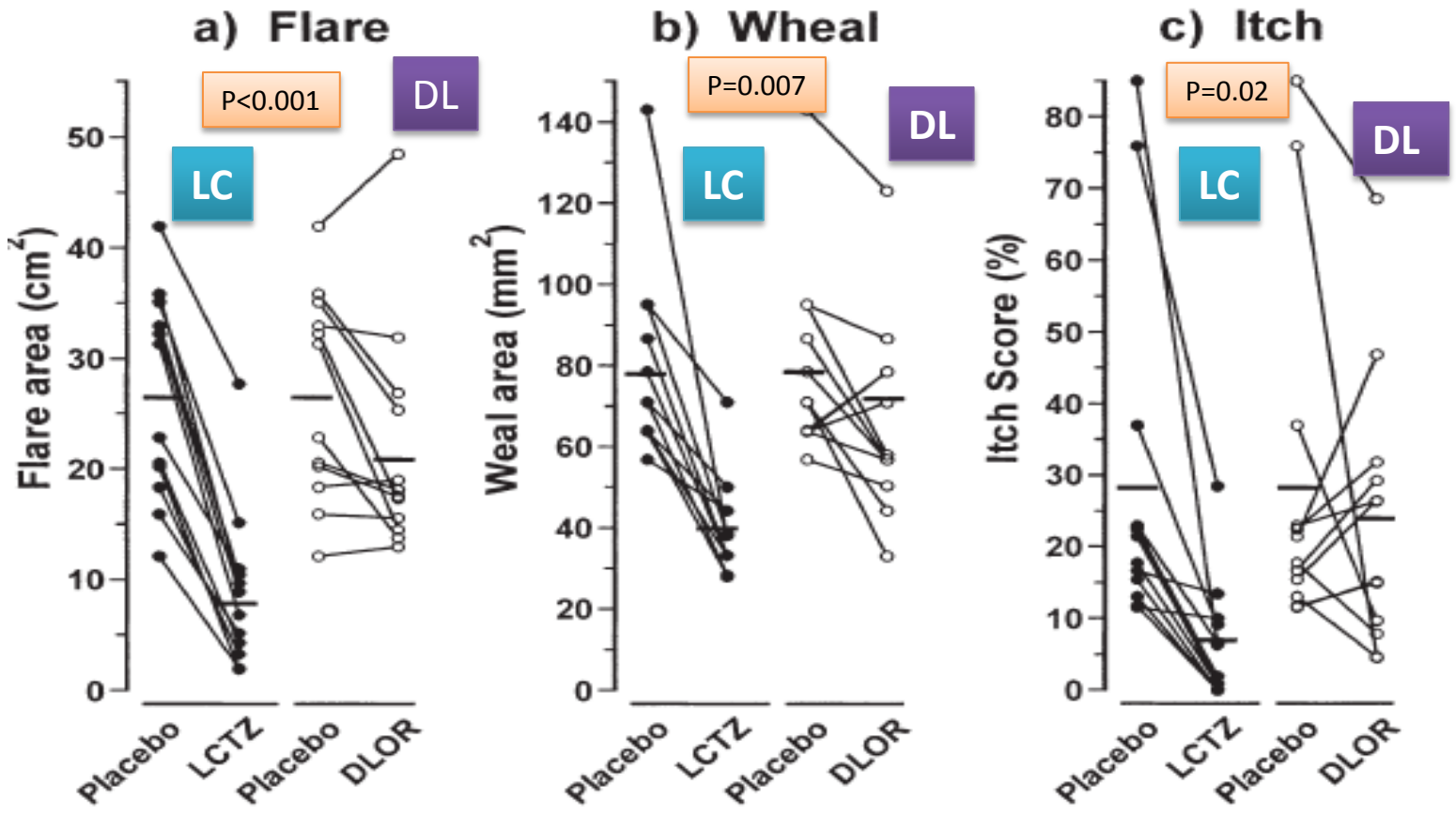
On antihistamines for 7 days, mean last dose taken =17 h



*Desloratadine was open-labeled

Pavarat Saengaram, Kiat Ruxrungtham 2006 (AAAAI 2013 poster)

Comparisons on Histamine Skin test: Levocetirizine vs Desloratadine



ID : 20 *µl of 100 µM histamine, 4 hr after taken H1 blockers*

Denham KJ. Inflamm. res. 52 (2003) 424–427

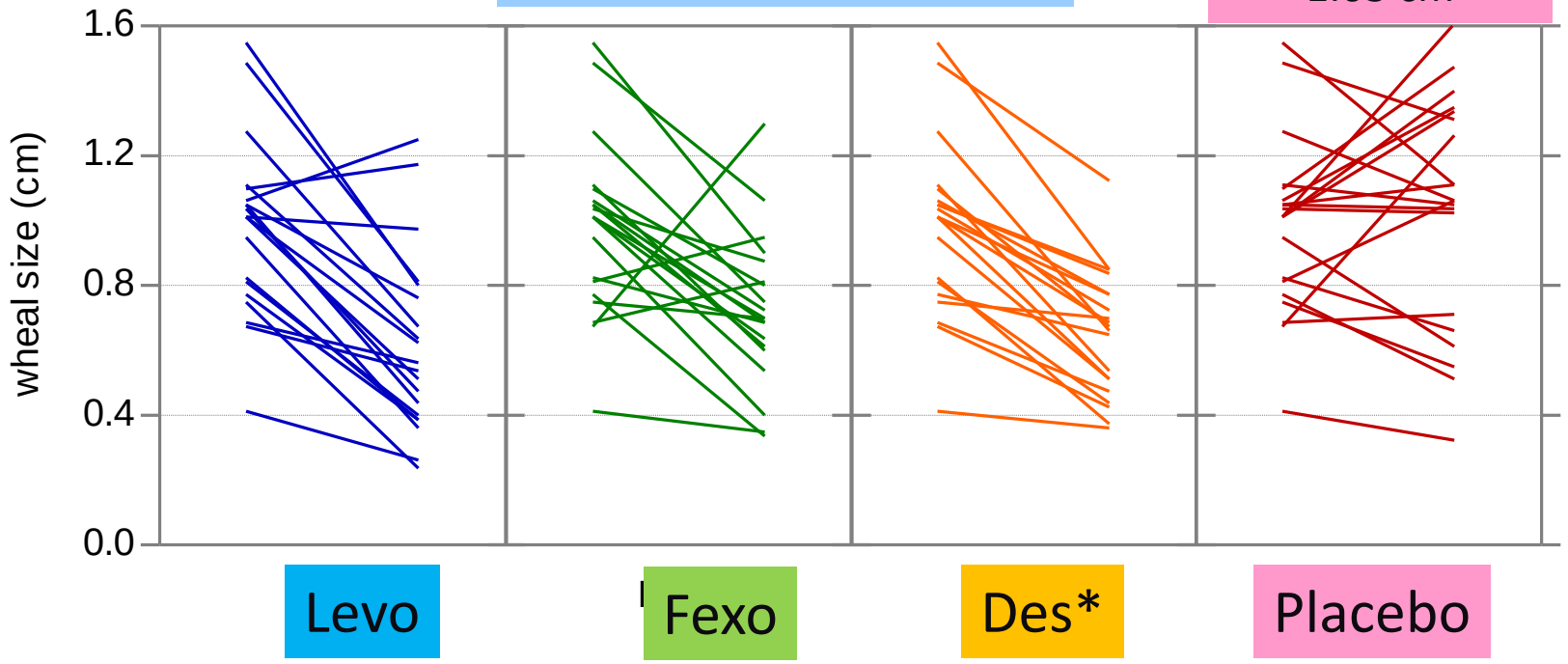
Allergen-induced Wheal Reduction

On antihistamines for 7 days, mean last dose taken =17 h

All > placebo *p* <0.001 (except Fexo *p <0.01*)

Levo ,Fexo , Des : *p =NS*

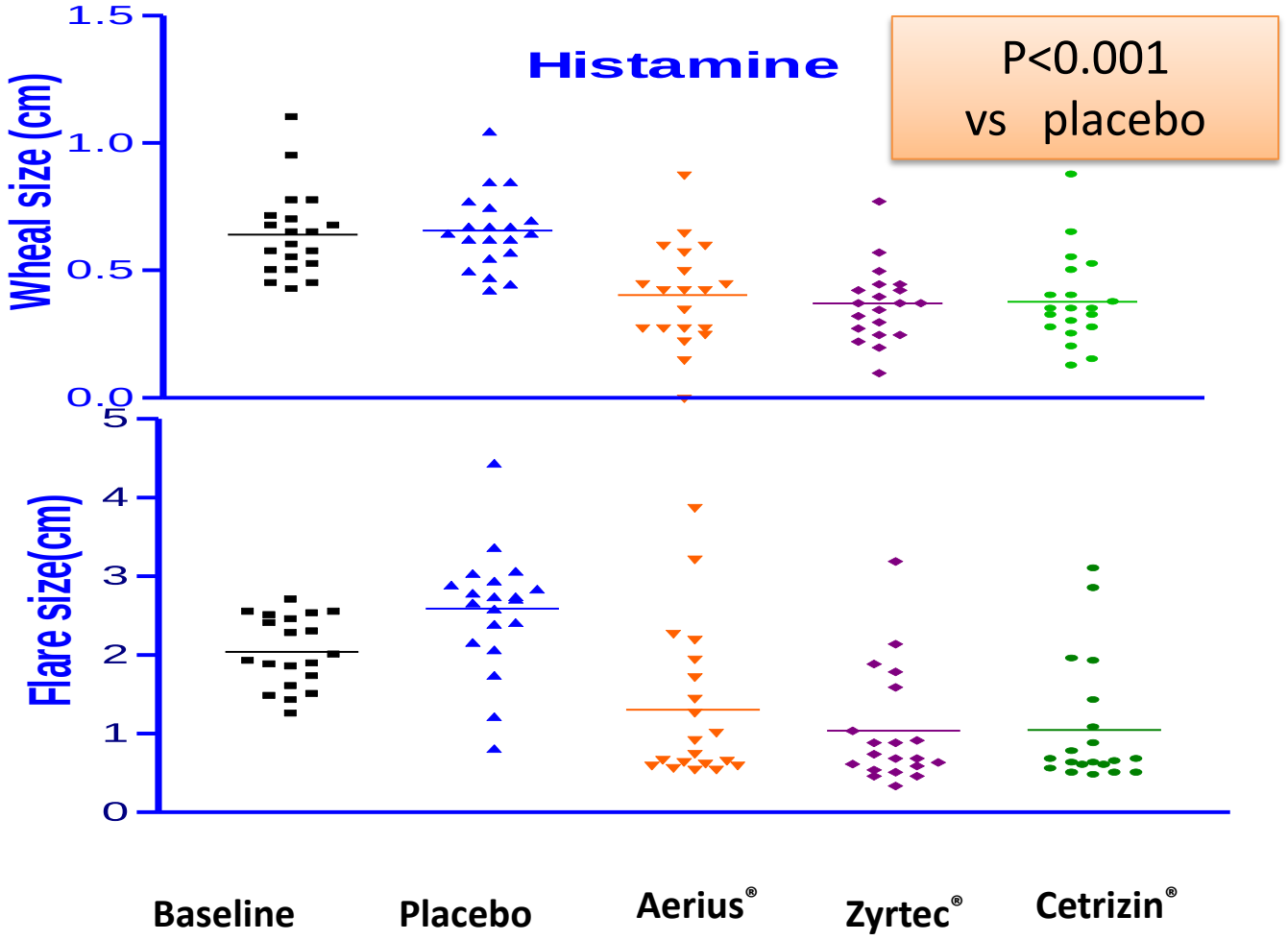
Mean placebo 1.03 cm



*Desloratadine was open-labeled

Pavarat Saengaram, Kiat Ruxrungtham (unpublished data)

Comparison of Generic cetirizine, Zyrtec, and Aerius on histamine skin test



A. Sukkul and K. Ruxrungtham (AAAAI 2007 poster)

No difference between the 3 antihistmaines

Antihistamines Comparison in AR

Author Year	Type of AR	Sample size	Results	p value
Day 2004	SAR	574	TSSC in 24 h: **CET>FEX** Stuffy noses : CET=FEX	p<0.001
Day 2004	SAR	373	**LEV>DL**	p=0.007
Day 2005	SAR	595	TSSC+ stuffy noses **CET > FEX**	p<0.01
Howarth 1999	SAR	821	FEX ,CET> placebo	p<0.01
van Cauwenberge 2000	SAR	688	FEX, LOR>placebo	p≤0.05
Berger 2006	SAR	722	DL , FEX> Placebo	p=0.013

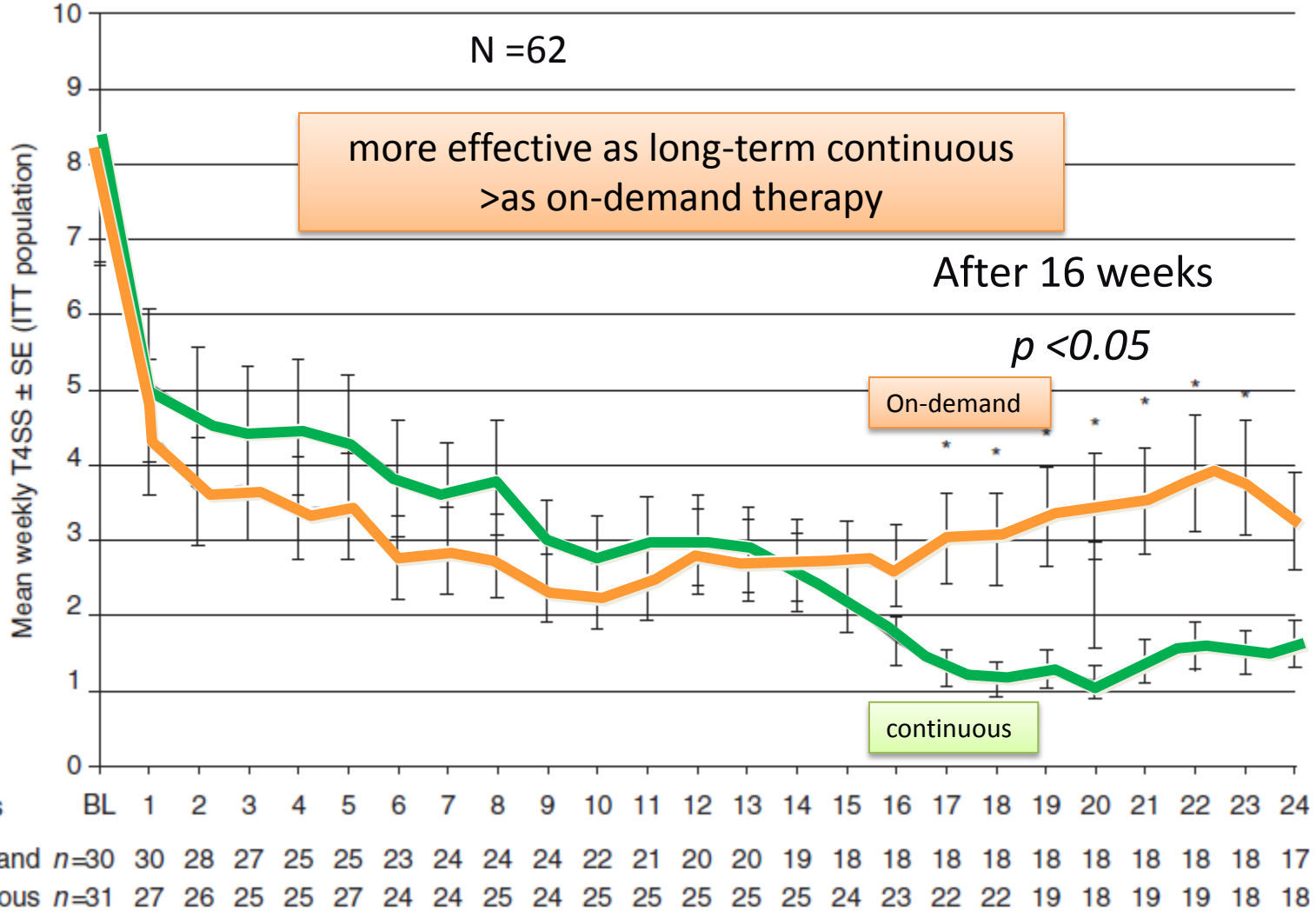
Modified from Bachert C. *Clin Ther. 2009;31:* 921–944

Antihistamine treatment in Persistent Allergic Rhinitis

Continuous versus on-demand ?

Levocetirizine in PER: Continuous vs On-demand

T4SS: sneezing, rhinorrhoea, nasal pruritus and ocular pruritus

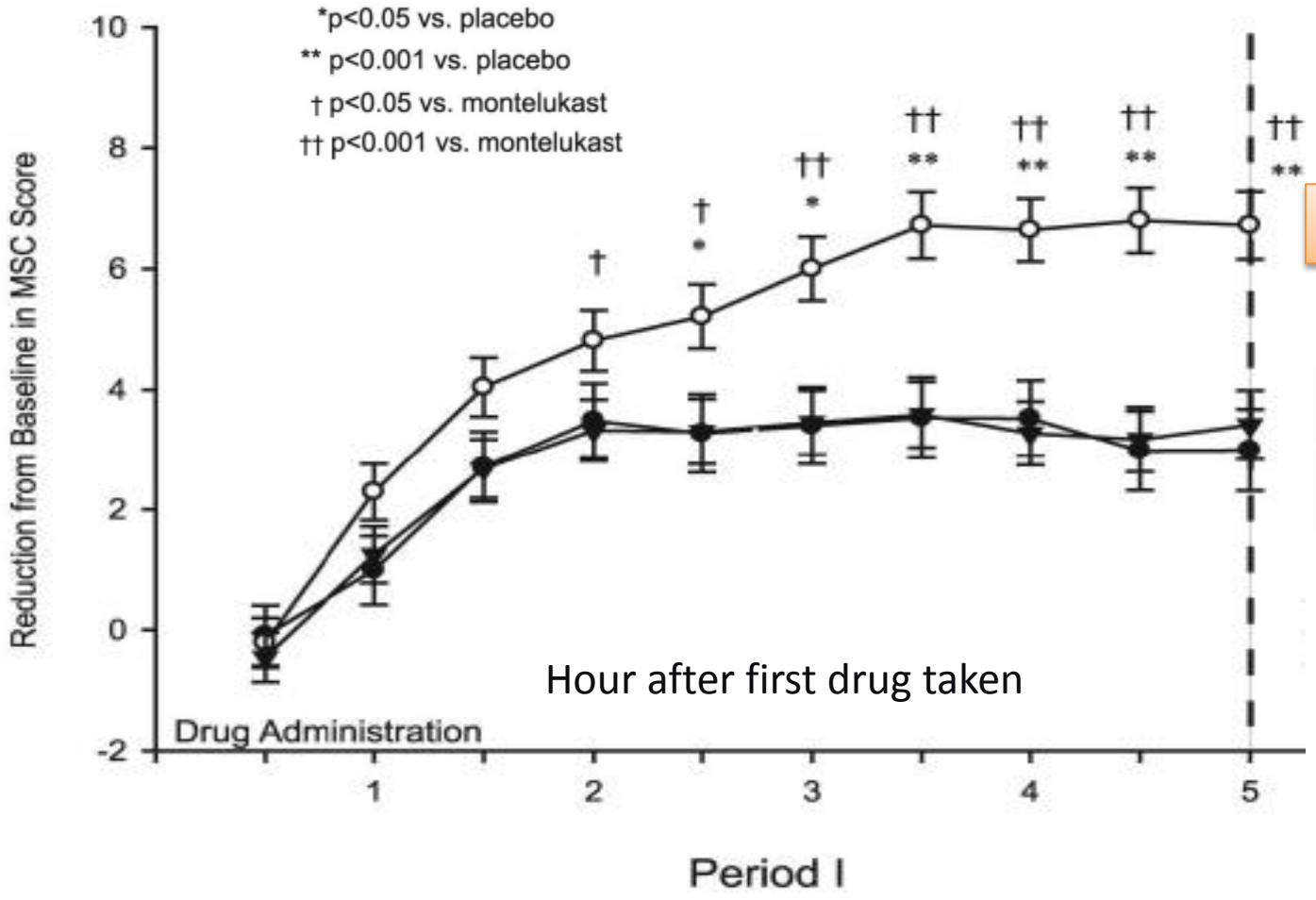


Canonica et al. Current Med Research and Opinion 2008; 24: 2829–2839

Antihistamines *versus* Montelukast

Levocetirizine vs Montelukast in Ragweed AR DBPC trial (N=403)

Reduction of Major Symptom Complex from Baseline



Patel et al. Ann Allergy Asthma Immunol. 2008;101:287–294.

Leukotriene receptor antagonists

A weak monotherapy for AR

"The effects of **leukotriene antagonists** are ***modest and less predictable*** than for intranasal steroids or antihistamines."

A meta-analysis of 11 studies demonstrated that when compared to placebo the overall mean daily rhinitis symptom scores reduction is

- **5% by Antileukotrienes**
- 7% by Antihistamines
- 17% by Intranasal corticosteroids

Plaut M, Valentine M: Clinical practice:Allergic rhinitis**.** ***N Engl J Med 2005,*** 353(18):1934-44.

Wilson A, O'Byrne P, Parameswaran K: Leukotriene receptor antagonists for allergic rhinitis: A systematic review and meta-analysis**.** ***Am J Med*** 2004, 116(5):338-44.

Middleton's Allergy 7th Ed. 2008

Oral Antihistamines: Somnolence/Drowsiness

H1 locker	Active	Placebo	Data Source
Desloratadine 5 mg qd	**2.1%**	1.8%	www.PDR.net
Fexofenadine 60 mg bid	**1.3%**	0.9%	www.PDR.net
Levocetirizine 5 mg qd	**6.8%**	1.8%	Bachert et al JACI 2004;114:838
Cetirizine 10 mg qd	**13.7%**	6.3%	www.PDR.net
Loratadine 10 mg qd	**8%**	6%	www.PDR.net
Rupatadine 10 mg qd	**9.5%**	3.4%	Mullol Allergy 2008: 63 : s5–28

All except fexofenadine cross blood brain barrier, therefore are dose-dependent associated with somnolence/drowsiness[1]

Adapted from GLORIA module; [1]Greiner and Meltzer JACI 2006; 118: 985-96)

First generation antihistamines and its *Side Effects:*

- Impaired alertness or performance
- Anxiety, confusion
- **Sedation,** perturbs the normal sleep cycle
- **Disequilibrium**
- Postural hypotension
- **Constipation**
- **Urinary retention**
- **Worsening of glaucoma**

Decongestants and its SEs

The most common side effects of oral form

- CNS stimulation : Nervousness, **Insomnia**
- Dizziness
- Cardiac stimulation : palpitations
- Hypertension
- Urinary retention
- Increase intraoccular pressure in narrow angle glaucoma

Topical form: Rhinitis medicamentosa

NASAL STEROIDS

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use NASACORT AQ safely and effectively. See full prescribing information for NASACORT AQ.

Nasacort® AQ (triamcinolone acetonide)
Nasal Spray
For intranasa
Initial U.S. Ap

- Indications
- Dosage and

- NASACORT
symptoms
of age and

- *Adults and*
(two sprays
- *Children 6 t*
once daily).
- *Children 2 t*
each nostril
- *Priming/Use*
5 sprays int
2 weeks, rel

BECONASE
(beclomethasone
monohydrate)
Nasal Spray, 42

For Intranasal Us

DESCRIPTION

Beclomethasone d
Spray, is an anti-infla
16β-methylpregna-1,
chemical structure:

300475

RHINO
(budesonide
Nasal Spr

For Intranasal Use Only.
Rx only

DESCRIPTION
Budesonide, the active
anti-inflammatory synthe
It is designated chemicall
1,4-diene-3,20-dione cyc
Budesonide is provided a
The empirical formula of
Its structural formula is:

AVAMYS®

28
HO
19
1
1
9
2
10
F
3
O
5
4
6
F

PRODUCT INFORMATION

NASONEX®
(mometasone furoate monohydrate)
Nasal Spray, 50 mcg*
FOR INTRANASAL USE ONLY

*calculated on the anhydrous basis

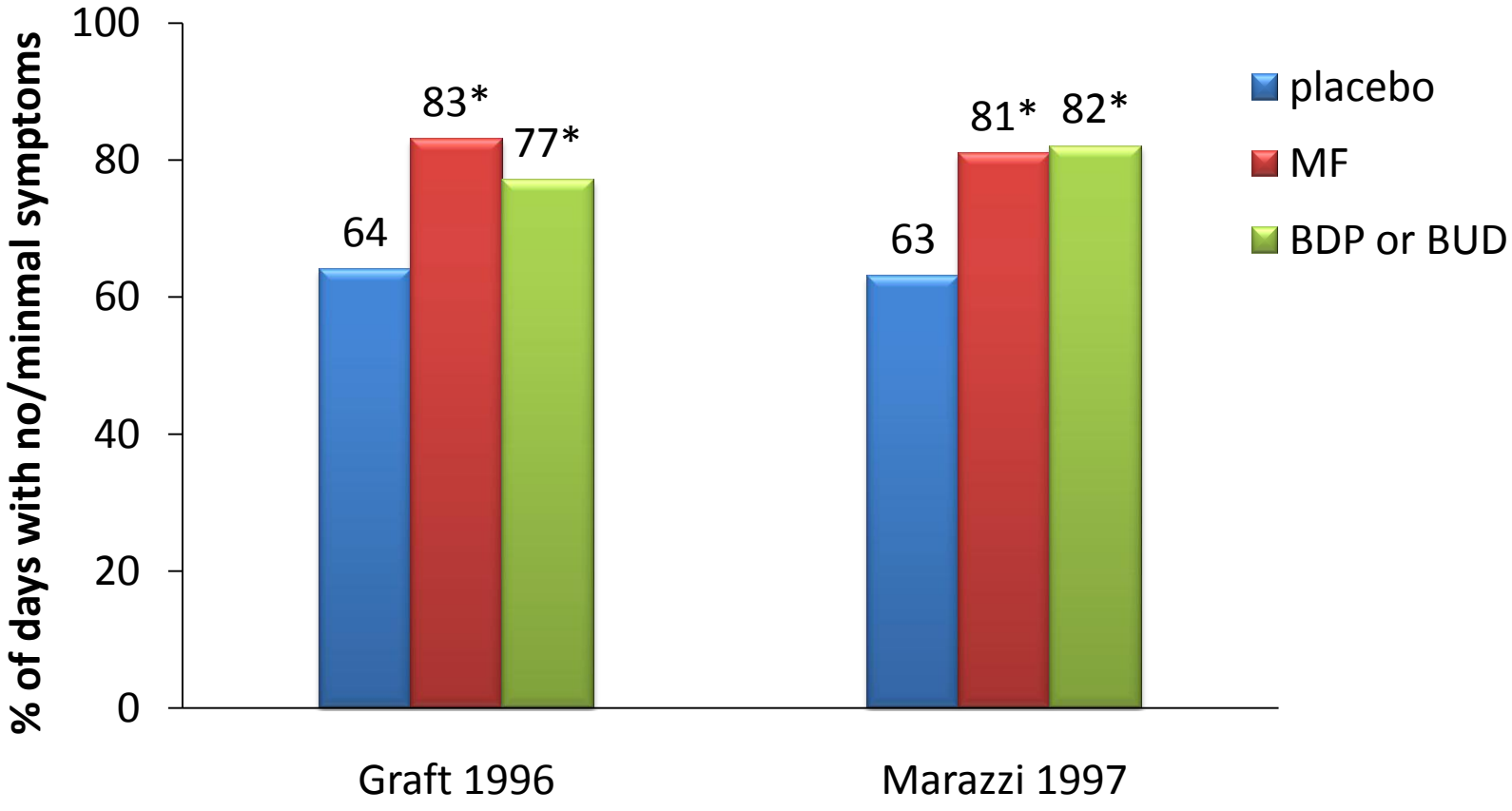
DESCRIPTION Mometasone furoate monohydrate, the active component of NASONEX Nasal Spray, 50 mcg, is an anti-inflammatory corticosteroid having the chemical name, 9,21-Dichloro-11β,17-dihydroxy-16α-methylpregna-1,4-diene-3,20-dione 17-(2 furoate) monohydrate, and the following chemical structure:

CH_2Cl
$C{=}O$
CH_3
O
C
HO
CH_3
CH_3
$\cdot H_2O$
Cl
O

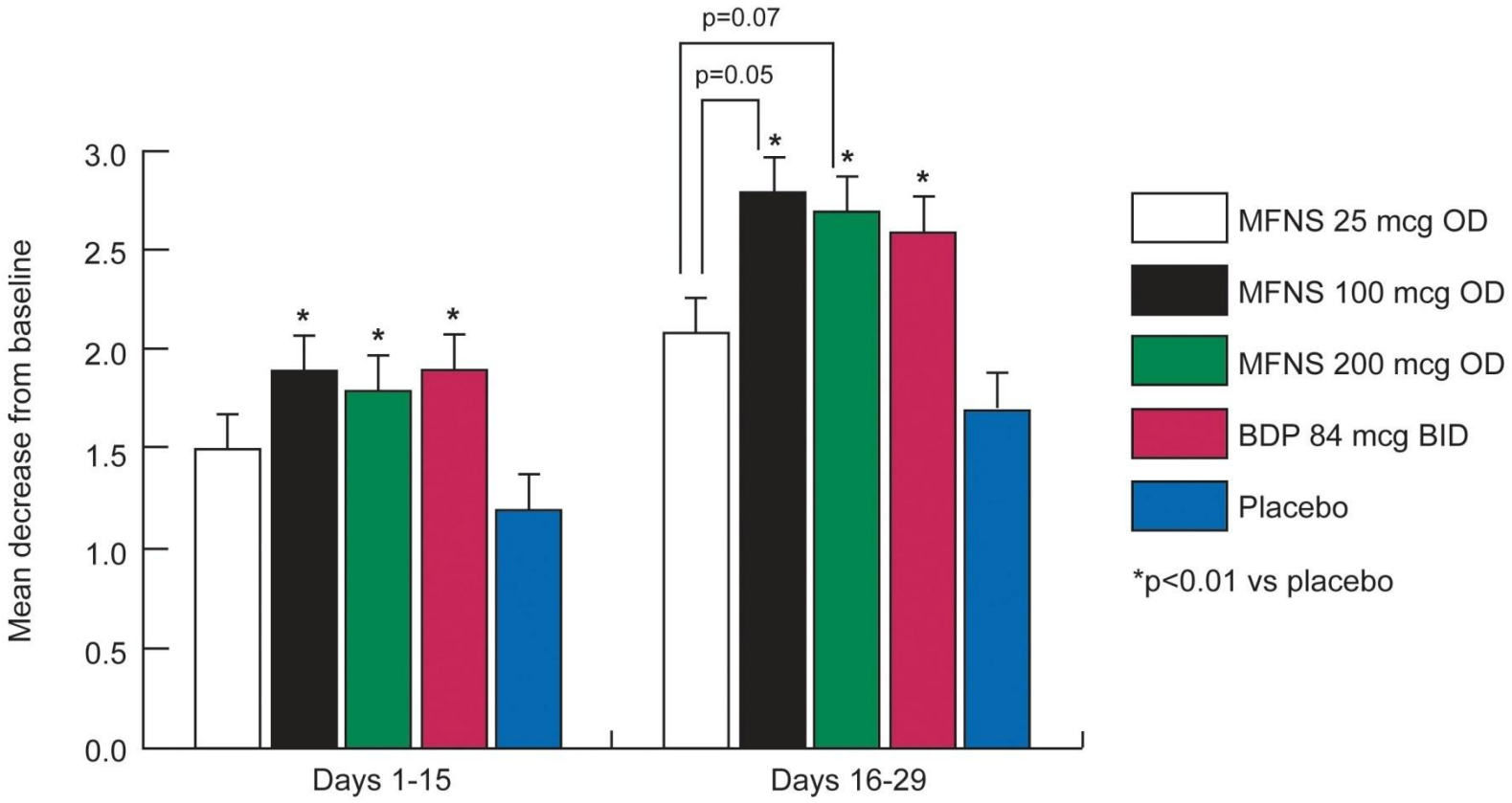
Nasal Steroids: Are they different ?

Pre-seasonal INCS Prophylaxis in SAR

(4-4 wks pre/during season)



Efficacy of INCS in children with allergic rhinitis and seasonal symptoms



Meltzer E. et al. J Allergy Clin Immunol. 1999;104:107. (source –GLORIA)

A comparative review: INCS

- BANS (Bud Aq), FPNS, MFNS, and TANS have similar efficacy and safety profiles.
- Differences in sensory attributes,
- cost may contribute to better patient acceptance of one INS versus another.”

Herman H. Am J Rhinol. 2007; 21:70-9.

Patient's friendly and preference particularly for children/adolescents

Easy to use device

Nozzle is short and ergonomically designed

- Comfortable for patients

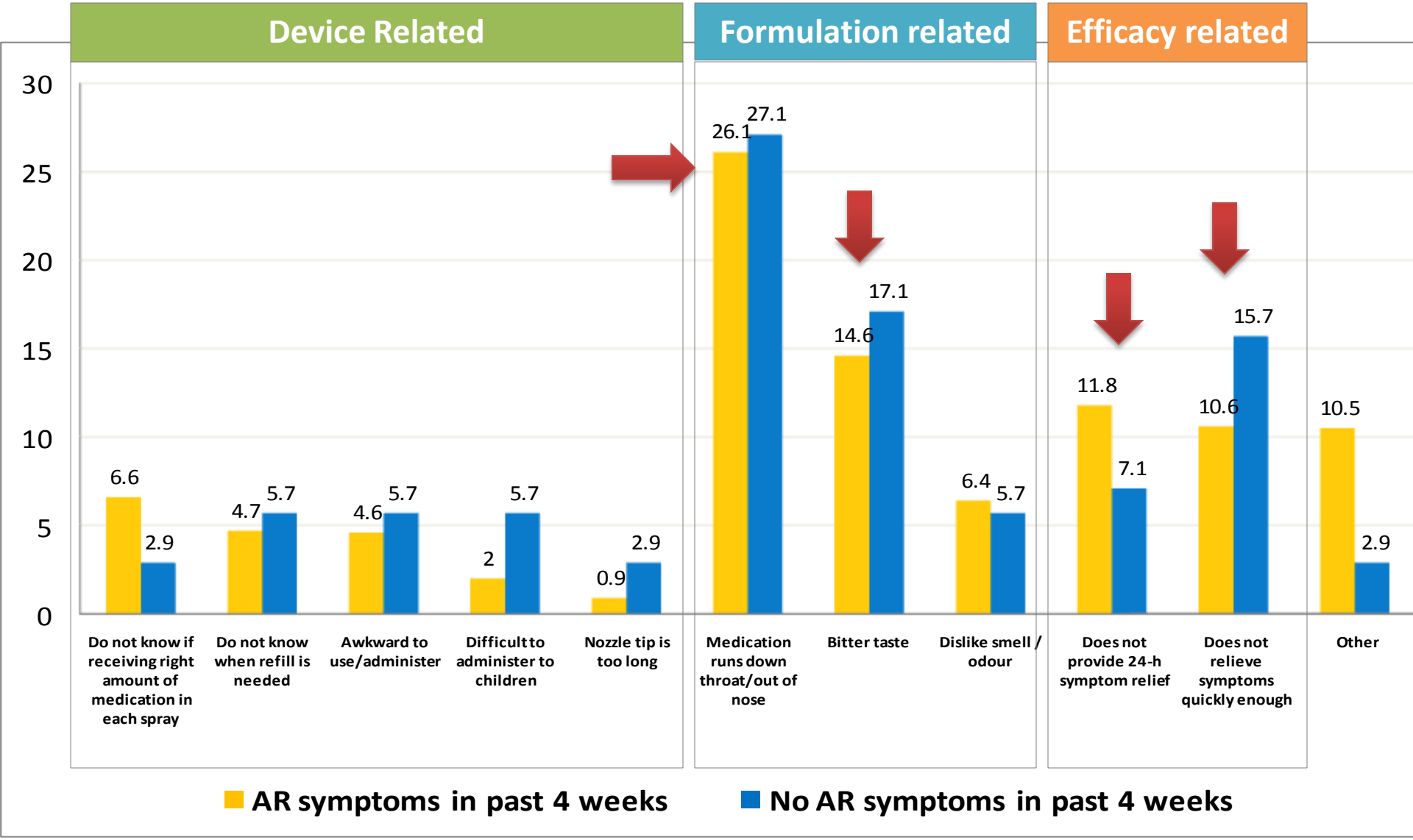
Easy to grip with side actuation

Viewing window

- See how much is left

Berger W.E. Godfery J.W. Slter A.L. et alEpert Opin. Drug Deliv. 2007; 4(6): 1-13

The most likely reasons for stopping ICS use



Berger WE et al. *Expert Opin Drug Deliv* 2007;4:689–701.

Glucocorticoid doses per single spray and estimated volume

Compound	Dose per spray (µg)	Volumew per spray (µL)	Sprays per nostril	Volume per application (µL)
Triamcinolone acetonide	55	60 ±0.4	1 qd	**60**
Budesonide	50	69 ±0.9	1 bid	**69**
Fluticasone propionate	50	147 ±1.7	1 qd	**147**
Mometasone furoate	50	102 ±1.9	1 qd	**102**
Fluticasone furoate	27.5	56 ±1.2	1 qd	**56**

- Any excess volume of an intranasally administered dose will be rapidly runoff or drip down the throat with subsequent swallowing. This translates into **loss of active drug** that is not available **to the target tissue**.
- It has been suggested that the volume applied into the nasal cavity **should not exceed 100 µL to 150 µL per nostril.**

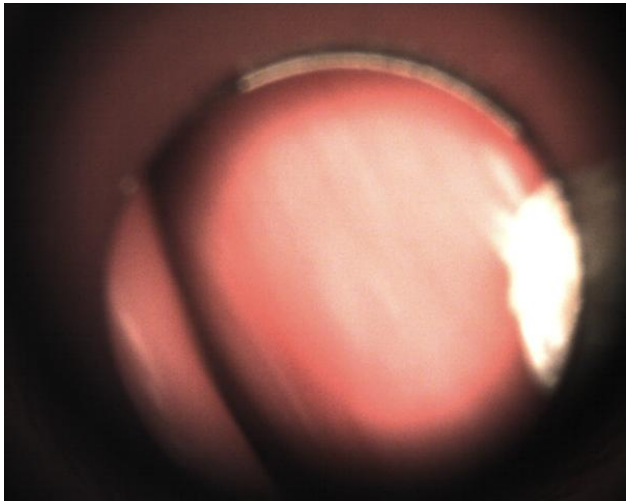
Baumann D. Bachert C. H¨ogger P. et al. Dissolution in nasal fluid, retention and anti-inflammatory activity of fluticasone furoate in human nasal tissue ex vivo. Clinical & Experimental Allergy 2009; 39: 1540–1550

Generic name	Futicasone furoate (FF)	Beclo-methasone dipropionate	Fluticasone propionate (FP)	Budesonide (BUD)	Mometasone furoate (MF)	Triam-cinolone Acetonide
Company	GSK	GSK	GSK	AstraZeneca	MSD	Sanofi Aventis
Indications	1) Nasal symptom (SAR & PAR) 2) Ocular symptom (SAR)*	1) Prophylaxis and treatment of PAR & SAR 2) Vasomotor rhinitis.	Allergic Rhinitis (SAR & PAR)	1) Allergic Rhinitis (SAR& PAR) 2) Nasal polyp 3) Prevention of nasal polyp after polypectomy	1) Allergic Rhinitis (SAR + PAR) 2) Adjunctive Acute Rhinosinusitis 3) Nasal Polyp	Nasal symptom (SAR & PAR)
Prescribe age (TH)	**≥ 2 years**	**≥ 6 years**	**≥ 4 years**	**≥ 6 years**	**≥ 3 years**	**≥ 2 years**
Onset	**8 hrs**	**3 days -3 weeks**	**12 hrs**	**4-48 hrs**	**12-72 hrs**	**24 hrs**
บัญชียาหลัก NED	**No**	**บัญชี ข**	**บัญชี ง**	**บัญชี ข**	**No**	**บัญชี ง**

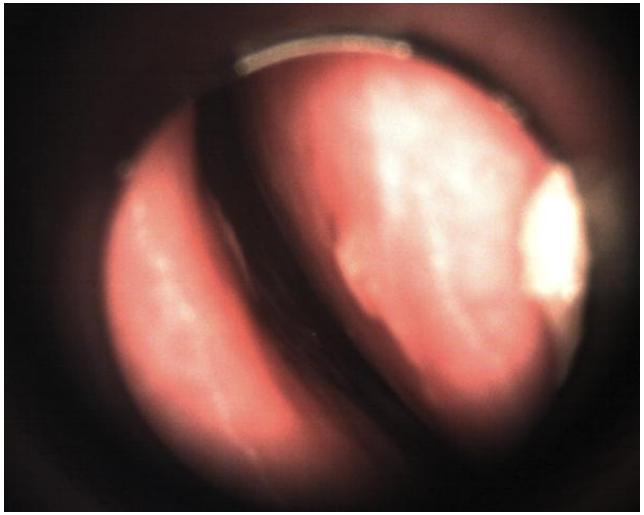
Product informatio n *Approved indication in adult Katial RK. Allergy Asthma Proc 2009:30:595-604.

Why some of the **very well complied** patients in using INCS **still failed** to improve their AR symptoms ?

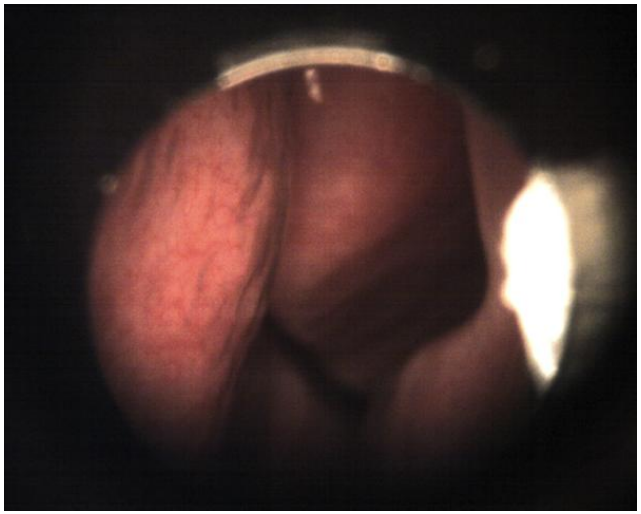
Pretreated finding



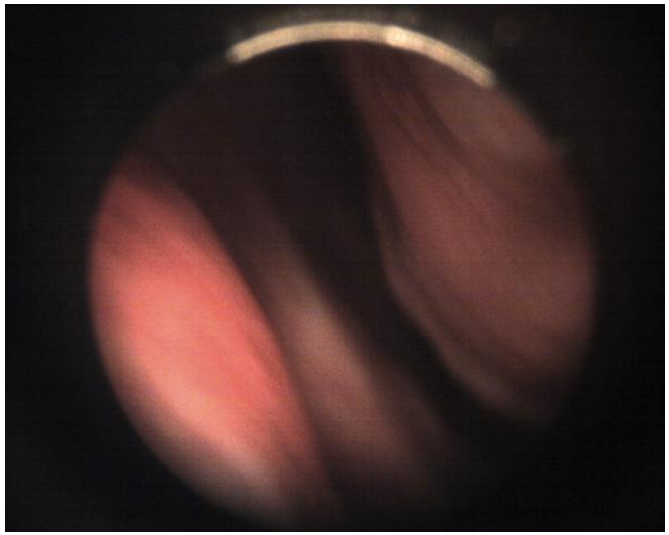
% NaCl spray



First decongestant spray



Second decongestant spray



Accessibility of the nasal corticosteroid into most parts of nasal mucosa is critical and is **depend mainly on the patency** of the nostrils

Oxymetazoline adds to the effectiveness of fluticasone furoate in the treatment of perennial allergic rhinitis

Fuad M. Baroody, MD, David Brown, MD, Laura Gavanescu, MD, Marcy DeTineo, BSN, and Robert M. Naclerio, MD *Chicago, Ill*

Rational: Only 60% of AR respond to INCS, thus adjunct treatment option is needed

Design: DBPC 4 arms trial

The 4 groups received the following treatments:

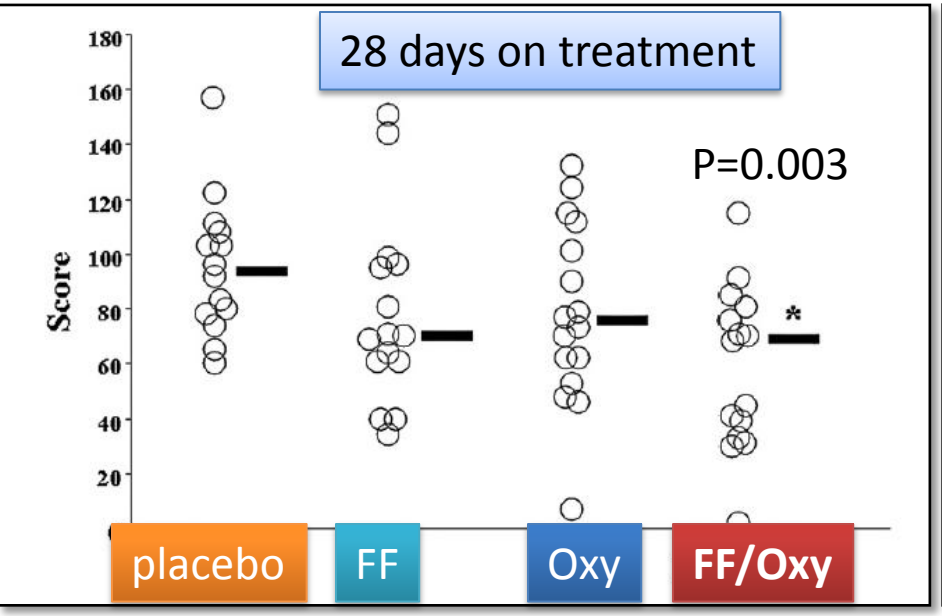
1. Placebo
2. OXY (0.05%, 2 puffs in each nostril every evening)
3. FF nasal spray (110 mg per day)
4. FF nasal spray plus OXY (FF/OXY)

Duration of treatment: 4 weeks

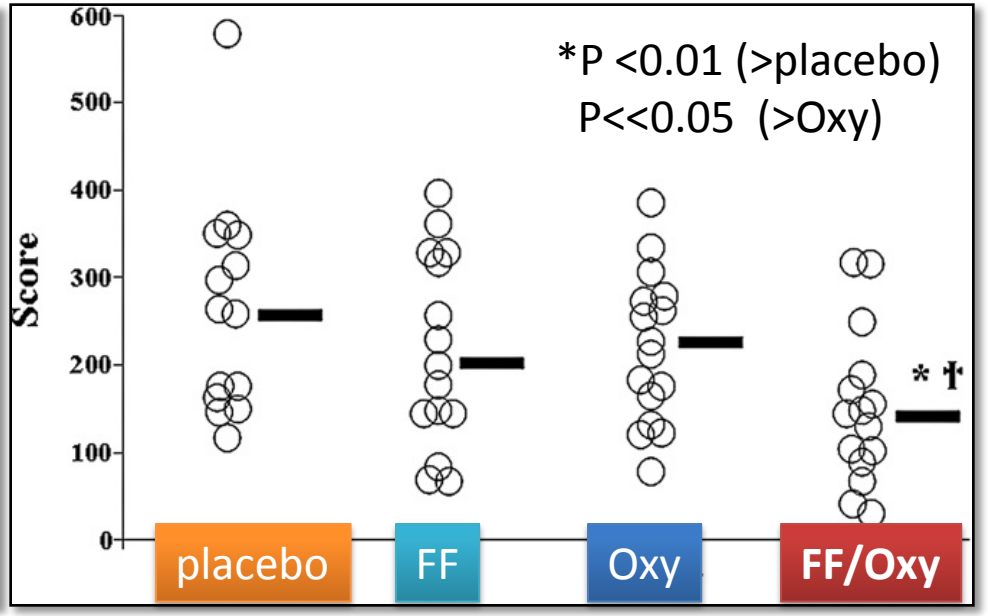
Plus 2 weeks post-treatment FU

Baroody M F., et al. J Allergy Clini Immunol 2011. Vol 127, No 4. 927-934

FF nasal spray plus Oxymetazoline



Cumulative nasal congestion score for all 28 days of active therapy.
***P =.003 versus placebo.**

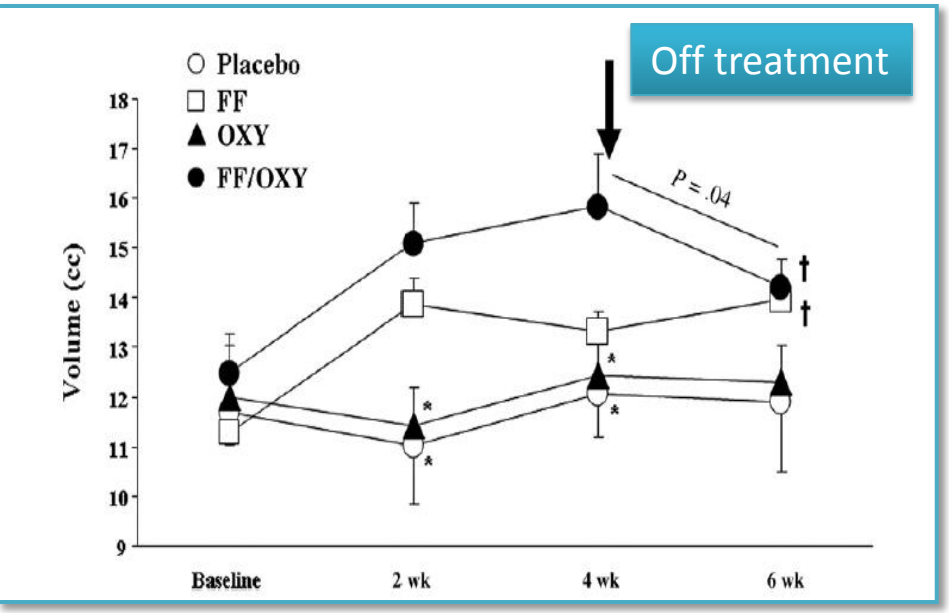


Cumulative total nasal symptom score for all 28 days of active therapy.
***P= .007 versus placebo. †P = .04 versus OXY.**

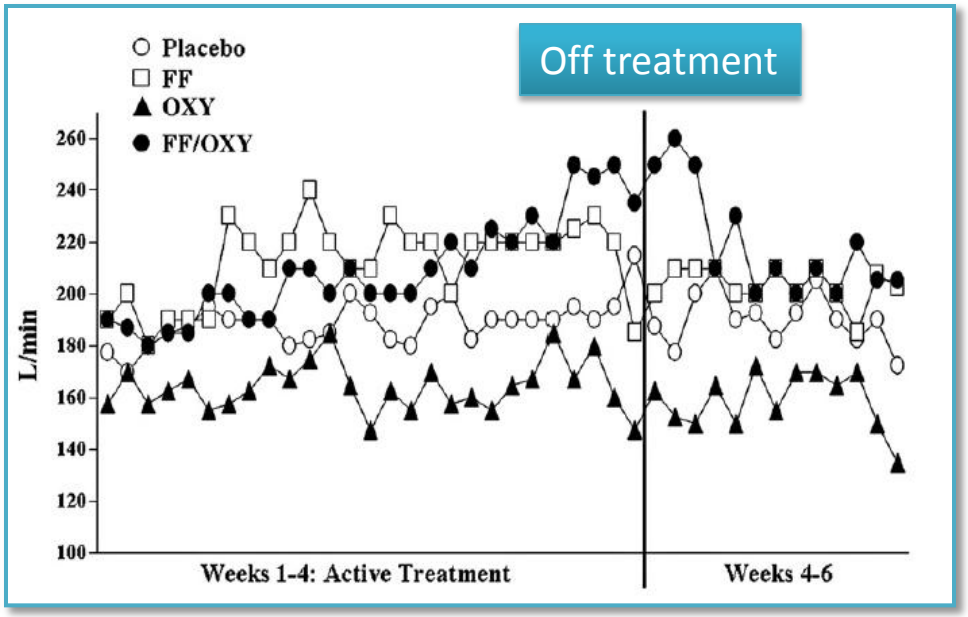
- **The nasal congestion and total nasal symptom score over the 4 weeks of treatment was lower with the combination compared with treatment with placebo and oxymetazoline alone.**

Baroody M F., et al. J Allergy Clini Immunol 2011. Vol 127, No 4. 927-934

FF nasal spray plus Oxymetazoline



Nasal volume as measured by acoustic rhinometry in mL.



NPIF (sum of AM and PM scores) in liters per minute

- **The combination of once-daily FF and oxymetazoline provides efficacy superior to that of FF without causing rhinitis medicamentosa.**

Baroody M F., et al. J Allergy Clini Immunol 2011. Vol 127, No 4. 927-934

Evidences for AIT: SCIT *vs* SLIT

TABLE III. Experimental evidence for immunotherapy

	SCIT	SLIT
Clinical efficacy: rhinitis	Ib Ia	Ia Ia
Clinical efficacy: asthma	Ia Ia	Ia Ia
Clinical efficacy: children (rhinitis)	Ib	Ia Ia
Prevention of new sensitizations	Ib	IIa
Long-term effect	Ib	IIa
Prevention of asthma	Ib*	Ib*

Ia, Evidence from meta analysis of randomized controlled trials
from at least 1 randomized controlled trial; *IIa*, evidence fr
1 controlled trial without randomization; *IIb*, evidence fro
type of quasi-experimental trial; *III*, evidence from nonex
descriptive studies (comparative, correlation, case-control);
panels of experts or clinical experience or authorities.
*One single randomized open controlled trial. Strength of e
according to Sheckelle et al.[144]

GA2 LEN network JACI 2007;119:881-91, Calderon et al Cochrane 2007

Take home messages

- Make sure that you have ***the right diagnosis*** and ***the right treatment***
- **Severe AR** suffering our patients more than what we have been appreciated
- Digital anterior nasosope is a essential tool for both Dx and for convincing our patients to be more compliance
- A right topical medicine “INCS”, ***if it couldn’t reach the affected nasal mucosa effectively***, regular use may not result to a treatment success! Thus for patients with severe nasal obstruction, initial use of INCS in combination with topical decongestant is useful.

สมาคมโรคภูมิแพ้ โรคหืด
และวิทยาภูมิคุ้มกันแห่งประเทศไทย
The Allergy, Asthma, And Immunology Association of Thailand

THANK YOU