



2012 대한임상건강증진학회 춘계 통합학술대회 / 연수강좌

# 일차진료에서 만나는 비염의 치료

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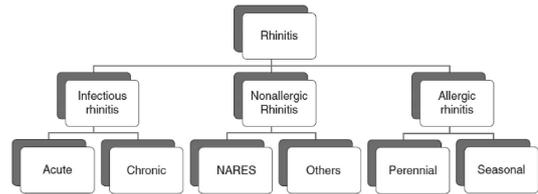
## Nose is ...

- ❖ Sensory organ
  - Smell (Olfactory / Trigeminal)
  - Airflow sensation
- ❖ Immunologic organ
  - Innate immunity
    - Epithelial barrier
    - Mucus
      - Antimicrobial peptides
      - Mucociliary clearance
  - Adaptive immunity
- ❖ Humidifier / Warmer / Filter
- ❖ 비강공명기능

## Classification of "Rhinitis"

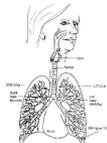
"비염"이란?

비강내 비점막의 염증성 병변으로 인한 비루, 재채기, 소양증 및 비폐색 중 한 가지 이상의 증상을 동반하는 비점막의 염증성 질환



## Acute rhinitis

- ❖ Known as
  - "nasopharyngitis, rhinopharyngitis, acute coryza, common cold"
- ❖ Upper respiratory tract infection, divided by area affected
- ❖ Virus : rhinoviruses, adenoviruses, influenza viruses, etc
- ❖ 증상
  - Immune response > Tissue destruction
  - 전구시기 ; Fever, chill, muscle aches, cough, headaches
  - 비염성 시기 ; 전신증상의 악화, 수양성 비루, 비폐색, 후각상실증 (hyperemic stage)
  - 점액기 ; 점액성 비루
  - 흡수기 (resolution stage) ; 5-10일 후 정상화
  - 이차 감염기 (secondary infection stage) ; 부비동염, 인두염, 편도선염, 기관지염 이행



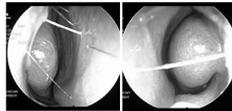
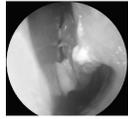
## Acute rhinitis



- ❖ 내시경 소견
  - Hyperemic
  - Swollen
  - Serous secretion
- ❖ 치료
  - 증상에 대한 치료
  - 진통 해열제, 휴식, 수분섭취, 습도 및 온도조절, 충분한 영양공급
  - 항히스타민제, 국소용 점막수축제
  - 국소용 스테로이드분무

## Chronic rhinitis

- ❖ 감염성 (serous, mucoid, purulent discharge)
- ❖ 비감염성
  - Chr hypertrophic rhinitis
  - Septal deviation
- ❖ 치료
  - 내과적 치료
    - Nasal steroid spray
    - Oral decongestant
  - 외과적 치료
    - Partial turbinectomy
    - Turbinoplasty
    - Cold knife
    - Electrocautery
    - Laser
    - Coblation
    - Combined septoplasty



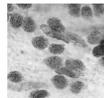
## Non Allergic rhinitis

- Difficult !
- Symptoms
  - Similar to AR, nonspecific
  - Rhinorrhea, nasal congestion, sneezing
  - Having No history of allergies
  - Negative results of allergic test (MAST, skin test)

## Non Allergic rhinitis

- ❖ Non Allergic Rhinitis with Eosinophilia Syndrome (NARES)
  - First described by *Jacobs et al.(1981)*
  - Perennial symptoms
    - Watery rhinorrhea, pruritus, epiphora, sneezing
  - Negative to common allergens (skin test or MAST)
  - Cytology of nasal secretion ; Eosinophilia
  - Localized IgE-mediated reactions
  - Nasal neural dysfunction

Eosinophilic mucin



Eosinophilic mucin  
Sticky, thick  
Yellow-green



## Non Allergic rhinitis

- ❖ Hormone-related
  - Hypothyroidism, Acromegaly, Puberty,
  - Pregnancy, Postmenopausal status
- ❖ Irritants
  - Temperature, Humidity, Gustatory exposure
- ❖ Chemical exposure
  - Animal proteins, wheat, perfumes, floral fragrances, cosmetics
  - Air pollution
  - Tobacco smoke
  - Formaldehyde
- ❖ Atrophic
  - Cocaine abuse, surgery, aging, external beam radiation treatment
- ❖ Emotional
- ❖ Exercise-induced
- ❖ Idiopathic

## Non Allergic rhinitis

### ❖ Medications contributing to Rhinitis

- Intranasal decongestants
- Antihypertensives
  - B-blockers, Hydralazine, Reserpone, ACE inhibitors
- Phosphodiesterase type 5 inhibitors
  - Sildenafil, Tadalafil, Vardenafil
- Hormones
  - Oral contraceptives
  - Hormone replacement therapy
- Anti-depressants
  - Selective serotonin reuptake inhibitors
- Psychotropic agents
  - Chlorpromazine, Amitriptyline, Alprazolam

## Atrophic rhinitis



- ❖ Klebsiella ozaenae, Bacillus mucosus, etc
  - No direct evidence
  - Possibly secondary bacterial infection
- ❖ More often as a result of
  - Aggressive surgery for nasal obstruction
  - Trauma
  - Granulomatous disease
  - Chronic cocaine abuse
  - Radiation therapy
- ❖ Associated with increasing age

- ❖ Mucosal changes
  - Ciliated respiratory epithelium
    - Nonfunctioning nonciliated squamous metaplasia
  - Loss of mucociliary clearance
- ❖ Treatment
  - Limited and unsatisfactory
  - Antibiotics
  - Nasal irrigation / humidification
  - Surgeries to alter nasal airflow



### Useful Questions for Diagnosis of Nonallergic Rhinitis

What are your nasal and sinus symptoms?  
Are your symptoms intermittent or persistent?  
Which of the following do they include?

- Nasal discharge
- Congestion/blockage
- Postnasal drainage
- Episodes of sneezing
- Nasal itching
- Itchy eyes

Epiphora

Do you have environmental allergies (e.g., hay fever)?  
Have you undergone allergy testing?

Have you been treated for allergies?

Are there certain situations or environments in which your symptoms are worse or in which they are better? For example, home, work, indoors, or outdoors?

Are there certain times of the day or year during which your symptoms are worse or better?

What type of work do you do?

Are you exposed to chemicals in your occupation?

Have you noticed an increase in nasal or sinus symptoms around certain chemicals/aromas/foods?

Did your symptoms begin when you started taking certain medications?

What medications have you tried for your symptoms?  
Of the medications you have tried, have any resulted in the improvement of your symptoms?

When using nasal sprays, have you used them regularly?  
Do you have a history of chronic sinusitis? Nasal and/or sinus polyps?

Are you sensitive or allergic to aspirin?

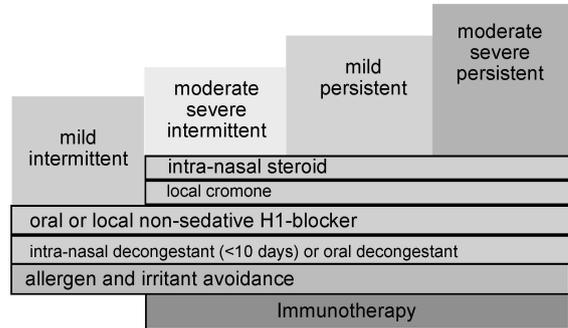
Have you undergone sinus surgery?

Do you have asthma?

Do you have a history of head or nasal trauma?



### Treatment of allergic rhinitis (ARIA)



### Allergen-Specific Immunotherapy (ASIT)

- ❖ To overcome deviated immune response
- ❖ Induction of peripheral tolerance to responsible allergen
- ❖ Repeated administration of sensitizing allergens

- Subcutaneous injection
- Mucosal route



### 면역치료의 대상

- ❖ 알레르겐 특이 IgE 항체가 존재 (Skin prick test, MAST)
- ❖ 알레르겐에 노출시 증상 발현
- ❖ 의심 알레르겐에 실제 폭로
- ❖ 약물치료에도 증상 호전이 적음
- ❖ 지속적인 약물의 사용이 불가능
- ❖ 환자가 적극적인 알레르기 원인 치료 원함

### 면역치료의 금기증

- ❖ 심한 전신 면역계 질환
- ❖ 약성 중량이 동반
- ❖ 중증 고혈압 환자
- ❖ 관상동맥 질환자
- ❖ 베타차단제 복용 환자
- ❖ 순응도가 떨어지는 환자
- ❖ FEV<sub>1</sub> 70 % 미만의 중증 천식환자

### SLIT 투여방법

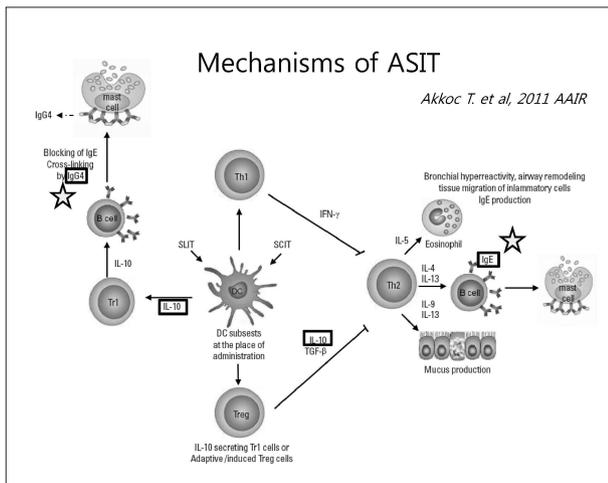
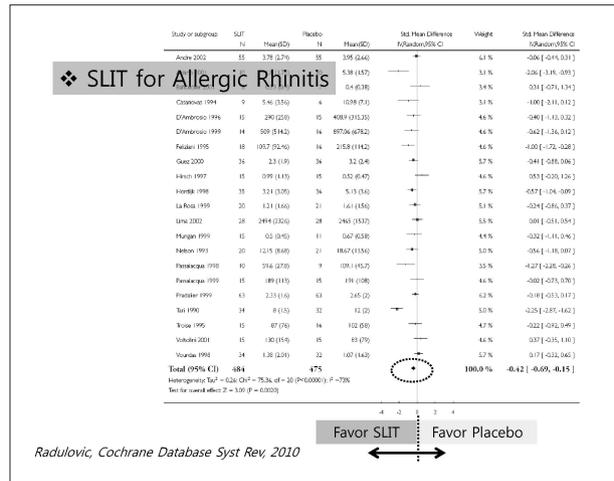
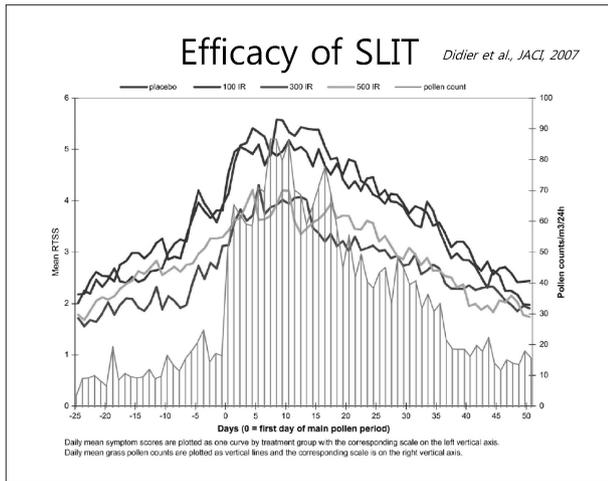


- ❖ Sublingual Swallow or Spit ?
  - Keep under tongue for 1 ~ 2 minutes and then swallowed (Passalacqua G. et al., Allergy, 2001)
  - At least 2 minutes
- ❖ Allergen dosing
  - Low vs. High concentration ?
    - Low < High (Marcucci F. et al., Allergy 2005)
    - (Durham SR et al., JACI, 2006)
  - How frequently ?
    - Daily Low con. > Alternative High con. (Bordignon V. et al., J Investig Allergol Clin Immunol, 2003)

### Optimum dosing for SLIT ?

- ❖ Optimum dose for SCIT
  - Inducing clinically relevant effect without unacceptable S/E
  - 5 ~ 20 µg of major allergen per dose
- ❖ Recommended dose for SLIT is less clear
  - No universally accepted SLIT dosing schedule
  - Different antigen production
  - Different standardization techniques world wide
- ❖ Published SLIT doses are much higher than SCIT doses
  - Individual SLIT dose ; ~ 21 times ↑
  - Median monthly SLIT dose ; ~ 49 times ↑
- ❖ Moderate-to-high SLIT doses
  - More frequently improved
  - Grass pollen antigen ; 15 ~ 25 µg daily





### 면역치료의 효능 평가

- ❖ IgE  
Variable (increase / decrease / no change)
- ❖ IgG4  
Increased 2 ~ 30-fold by 12 mo → reached plateau  
Not correlated with Clinical Symptoms
- ❖ IgA, ICAM, ECP, IFN- $\gamma$ , IL-2, -10, -12, -13, etc
- ❖ Skin prick test, Provocation test
- ❖ 환자의 증상점수, 약물사용 점수 및 삶의 질 변화로 평가

### Compliance of SLIT

- ❖ Drop out rate
  - 국내 (31%), 국외 (7~30%)
  - First 3 month ↑
- ❖ The reasons of drop out
  - 스케줄에 맞추어 약의 투여가 어렵다
  - 효과가 없는것 같다
  - 정기적으로 병원을 방문하기가 어렵다
  - 부작용이 있었다

### Adverse effects by SLIT

Adverse effects	Up-dosing phase	≥6 months
Aggravation of symptoms	31 (33.7%)	7 (7.6%)
Itching sense of the oral cavity or insert the lip	9 (9.8%)	1 (1.1%)
Itching sense or discomfort of the eye	23 (25.0%)	3 (3.3%)
Skin itching or rash	15 (16.3%)	3 (3.3%)
Gastrointestinal trouble	14 (15.2%)	1 (1.1%)
Breathing discomfort	2 (2.2%)	5 (5.4%)
Wheezing	2 (2.2%)	0

Chang H et al, 2009, CEO

House dust mite extract

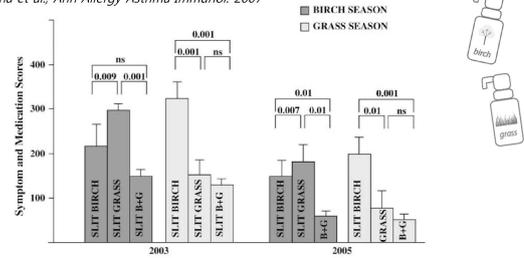


## Safety of SLIT

- Excellent safety profile in > 20 years of clinical trials
- No life-threatening events
- Safety profile in children less than 5 years old
  - Local itching, oral discomfort, abdominal pain, diarrhea
  - Reduced by temporary dose decrease
- Worsening of allergic symptoms is uncommon
- Mild to moderate systemic adverse events should be considered !

## Single Antigen vs. Multiantigen Tx

Marogna et al, Ann Allergy Asthma Immunol, 2007



- ❖ Simultaneous delivery of multiple unrelated allergens can be clinically effective
- ❖ But, more studies are required *Nelson H, JACI, 2009*

## SLIT in polyallergen sensitized pts with AR

Lee JE et al, Ann Allergy Asthma Immunol, 2011

❖ Total nasal symptom score

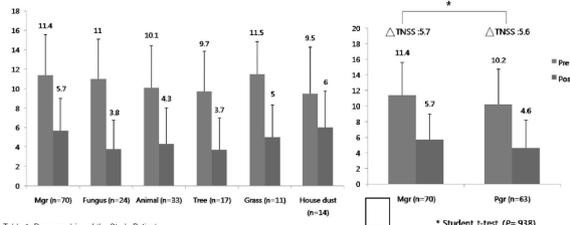


Table 1. Demographics of the Study Patients

Demographics	Monovalent sensitized group	Polyallergen sensitized group
No. of patients	70	64
Male/female	52/18	42/22
Age, mean (SD), y	14.2 (9.0)	15.3 (10.4)
Duration of symptoms, mean (SD), y	6.6 (5.3)	6.9 (6.3)
No. (%) with asthma history	11 (15.7)	18 (28.6)

SLIT for *Dp / Df*

## SLIT in pregnancy

Shaikh WA, 2012, Allergy

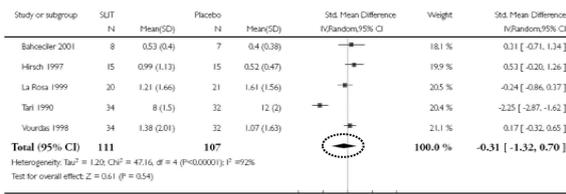
	Avoidance = SLIT (total = 185)		Avoidance = budesonide (total = 96) (group A)		Avoidance = rescue ephedrinol (group B)		General population
	No.	%	No.	%	No.	%	
Abortion	8	4.32*	15	16*	10	25**	10-20% of all pregnancies*
Perinatal deaths (stillbirth and neonatal deaths)	1	0.54	2	2.08	1	2.22	44/1000 births (4.4%)
Prematurity (<2500 g weight)	5	2.70	4	4.17	6	13.33	31% of all live births
Toxaemia	3	1.62	3	3.13	4	8.88	5-15%
Congenital malformation	0	0	0	0	0	0	2.5-4%

- ❖ SCIT 및 SLIT 모두 안전
- ❖ 유지용량으로 시행중인 경우 지속 가능
- ❖ 일반적으로 면역치료가 권고되지는 않음



## Controversies in Pediatrics

- ❖ SLIT for Allergic Rhinitis
  - Allergic Rhinitis symptom score



Radulovic, Cochrane Database Syst Rev, 2010

## Differential diagnosis of Rhinitis

- ❖ Polyps
- ❖ Chronic sinusitis
- ❖ Mechanical factors
  - Septal deviation
  - Turbinate hypertrophy
  - Adenoidal hypertrophy
  - Foreign bodies
  - Choanal atresia
- ❖ Tumors
  - Benign
  - Malignant
- ❖ Granulomas
  - Wegener granulomatosis
  - Sarcoidosis
- ❖ CSF fistula



### Rhinitis vs. Sinusitis

	Rhinitis	Sinusitis
비내 충혈, 음혈	++++	++++
재채기	+++	+
가려움증	+++	-
콧물		
맑은 콧물	++++	+
찜득한 콧물	+	++++
후비루	+ or ++	++++
두통	+	+++
안면 압박감	+	+++ or ++++
후각 장애	+ or ++	+++ or ++++
기침	+	+++
목 이물감	+	+++
발열	- or +	++