

**Immunotherapy: prevention!**



Hugo Van Bever  
Department of Pediatrics  
NUHS  
Singapore

WISC, December 2012, Hyderabad, India

Two Statements

- We are starting immunotherapy (SLIT – SCIT) too late in children
- We are starting immunotherapy (SLIT – SCIT) only when symptomatic treatment is unable to control symptoms.

→ **WRONG APPROACH?**

**Start of immunotherapy**

*Situation at its start: > 5- 7 years-old*

|                    |                                 |
|--------------------|---------------------------------|
| • <b>RHINITIS:</b> | rhino-sinusitis / restructuring |
| • <b>ASTHMA:</b>   | remodeling                      |
| • <b>ECZEMA:</b>   | bacterial colonization          |

*... SIT is started when complications have settled!*

*Allergists prefer symptomatic treatment over causal treatment...*

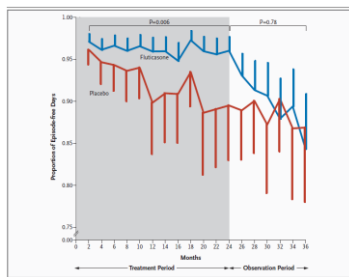
**SYMPTOMATIC TREATMENT**

1. established (habit)
2. more studies – more companies involved
3. safe – effective
4. cheaper

Long-Term Inhaled Corticosteroids in Preschool Children at High Risk for Asthma

Theresa W. Guilbert, M.D., Wayne J. Morgan, M.D., Robert S. Zeiger, M.D., Ph.D., David T. Meager, Ph.D., Susan J. Boehmer, M.A., Stanley J. Szefler, M.D., Ph.D., Leonard B. Bacharier, M.D., Robert F. Lemanske, Jr., M.D., Robert C. Strunk, M.D., David B. Allen, M.D., Gordon R. Bloomberg, M.D., Gregory Fields, M.D., Marzena Krawiec, M.D., Gary Larsen, M.D., Andrew H. Liu, M.D., Vernon M. Chinchilli, Ph.D., Christine A. Sorokens, Pharm.D., Lynn M. Tarzagg, M.D., and Fernando G. Martinez, M.D.

NEJM, 2006



**SLIT or SCIT?**



## SLIT!

- **SAFE**
- **CHILD FRIENDLY**
- **CONVENIENT**
- **Con: EXPENSIVE...**

### STATEMENTS:

**Allergy is a non-curable feature  
of the human body**

**The human race is getting more  
and more allergic**  
*(cfr 2<sup>nd</sup> wave of food allergy)*

### **By 2020...**

- \* > 50% of all children will be allergic.
- \* New approaches are urgently needed.

### Treatment of asthma



### New treatment for allergy

1. For prevention
2. For control
- 3 For cure

### Allergy treatment - problems

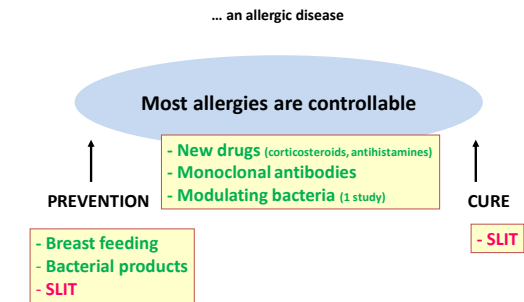
1. Compliance: **PROBLEMS**
2. Prevention: **IMPOSSIBLE**
3. Cure: **IMPOSSIBLE**

### Growing out of an allergy

|                |          |
|----------------|----------|
| - Eczema       | > 80%    |
| - Asthma       | ± 50%    |
| - Rhinitis     | only 20% |
| - Food allergy | variable |

SUMMARY OF WHAT IS NEW...

### New treatment for allergy



### SLIT – current weaknesses

1. Company-sponsored research.
2. No standardization in extracts.
3. Expensive.

### SLIT is more effective in AR > AA > AD

|   | AD                   | AA          | AR              |
|---|----------------------|-------------|-----------------|
| Age of onset  | First years of life  | 3 – 5 years | 5 – 7 years     |
| Pathophysiology at the time of SLIT (7-yrs onwards) | Chronic colonization | Remodeling  | Rhino-sinusitis |

### SLIT is more effective in AR > AA > AD

|   | AD                          | AA                       | AR                       |
|---|-----------------------------|--------------------------|--------------------------|
| Age of onset  | First years of life         | 3 – 5 years              | 5 – 7 years              |
| Pathophysiology at the time of SLIT (7-yrs onwards) | Chronic colonization        | Remodeling               | Rhino-sinusitis          |
| Start SLIT (in theory)                              | Neonatal period (hen's egg) | At the age of 3yrs (HDM) | At the age of 5yrs (HDM) |

### Why SLIT?

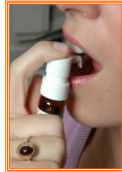
- ❖ Effective (if indicated...)
- ❖ Safe (no anaphylaxis...)
- ❖ Child friendly (at home – no pain...)

## SLIT in children

1. Effective
2. Safe

### 3. Additional effects

- carry-over effect (4 - 5 years)
- prevention of new sensitizations
- prevention of asthma in rhinitis pts



Prevention of new sensitizations in asthmatic children monosensitized to house dust mite by specific immunotherapy.

Pajno et al. Clin Exp Allergy 2001, 31, 1392-7.

Table 3. Drop-outs and new sensitizations

| Patients                         | SIT Group | Control Group |
|----------------------------------|-----------|---------------|
| Number of patients enrolled      | 75        | 63            |
| Drop-outs                        | 6         | 9             |
| Patients followed-up for 6 years | 69        | 54            |
| New sensitizations               |           |               |
| None                             | 52        | 18            |
| Parietaria                       | 11        | 16            |
| Grass                            | 5         | 12            |
| Olive tree                       | 5         | 8             |
| Cat                              | 3         | 7             |
| Dog                              | 0         | 2             |
| Alternaria spp.                  | 1         | 5             |
| Mugwort                          | 1         | 2             |

Long-lasting effect of sublingual immunotherapy in children with asthma due to house dust mite.

Di Rienzo et al. Clin Exp Allergy 2003, 33, 206-10.

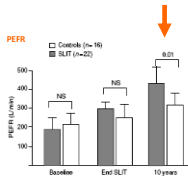


Fig. 2. Mean PEFR (L/min) ± SEM in the two groups of patients at the three time points. Intra-group P-values are indicated above the bars.

### CONCLUSIONS: (SLIT versus control)

- improvement of asthma
- less asthma medication
- clinical effects persist for 5 years after discontinuation

## Long-lasting effects of sublingual immunotherapy according to its duration: A 15-year prospective study

Maurizio Marogna, MD,\* Igino Spadolini, MD,<sup>†</sup> Alessandro Massolo, BS,<sup>†</sup> Giorgio Walter Canonica, MD,<sup>‡</sup> and Giovanni Passalacqua, MD<sup>§</sup> - *Norcia, Florence, and Genoa, Italy, and Calgary, Alberta, Canada*

- In the patients receiving SLIT for 3 years the clinical benefits persisted for 7 year.

- In those receiving SLIT for 4 – 5 years the clinical benefits persisted for 8 years

**CONCLUSION:** 4 years of SLIT is the optimal duration

JACI, 2010, 126, 969 - 75

## SLIT in allergy

PREVENTION



CURE



Allergies are controllable in most children

## SLIT - Unmet Needs (1)

(WAO Position Paper, November 2012)

### DOSING:

- Optimal dose in children
- Bio-availability of drops and tablets
- Drops vs. tablets
- Efficacy of multiple allergens
- Optimal duration
- SLIT in preschoolers (infants)

## SLIT - Unmet Needs (2)

(WAO Position Paper, November 2012)

### INDICATIONS:

- Early administration of SLIT
- Efficacy in children unresponsive to pharmacotherapy.
- Long-term efficacy
- Preventive effects

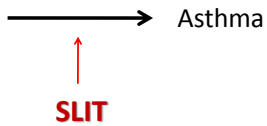
## SLIT - Unmet Needs (3)

(WAO Position Paper, November 2012)

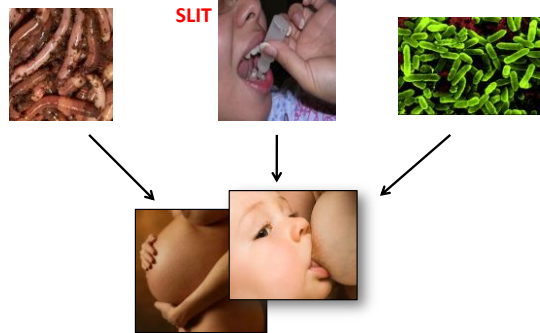
### OTHER ALLERGENS:

- Latex allergy
- Food allergy (milk, peanut, hazelnut)

Young children – Infants...



Interventions during pregnancy - lactation?



## *Conclusion...*

1. SLIT: promising! (safe – effective)
2. SLIT: not necessary to control most allergic diseases.
- 3. SLIT: PREVENT & CURE**
4. More studies are needed in young children.