# DEVELOPMENT OF NEW TECHNIQUES IN SPECIFIC ORAL TOLERANCE INDUCTION




## 3rd International Conference on Pediatrics

San Antonio (Tx)
18-21 May 2015

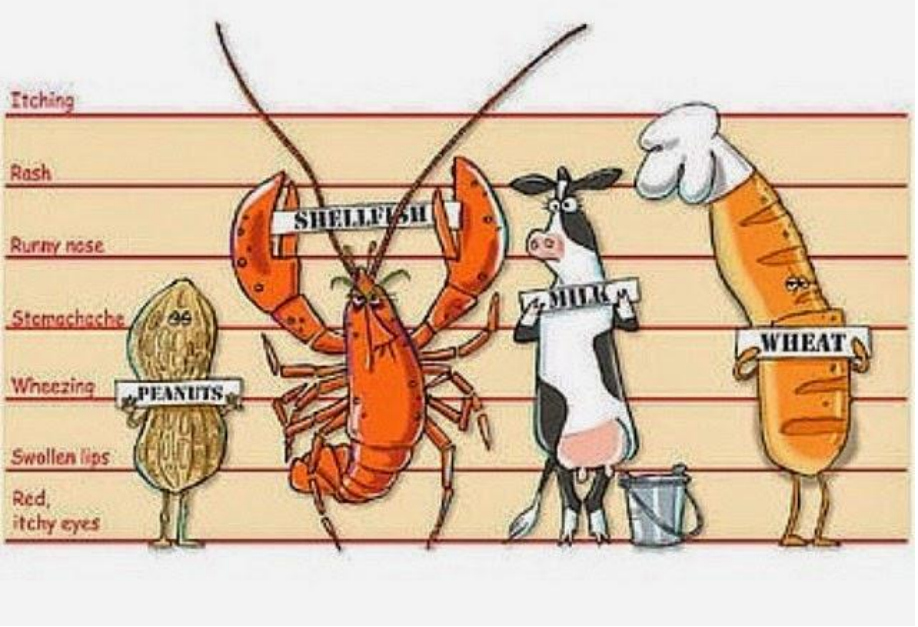

## Dr. Carlos Sánchez Salguero MD. PhD.

Director of Paediatric Allergy Department
University Hospital Puerto Real (Spain)
President of Allergy and Clinical Immunology of the South
Member of Food Allergy Commite
Professor Cadiz University


SEICAAP
Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica

AICIS
Asociación de Alergia e Inmunología Clínica Infantil del Sur

# FOOD ALLERGY




**Tolerance Induction:**
**Today is yesterday's tomorrow.**

**Is an old problem but result new:**

**•Increasing prevalence**

**•Increasing persistent food allergy which have a good forecast in infants**

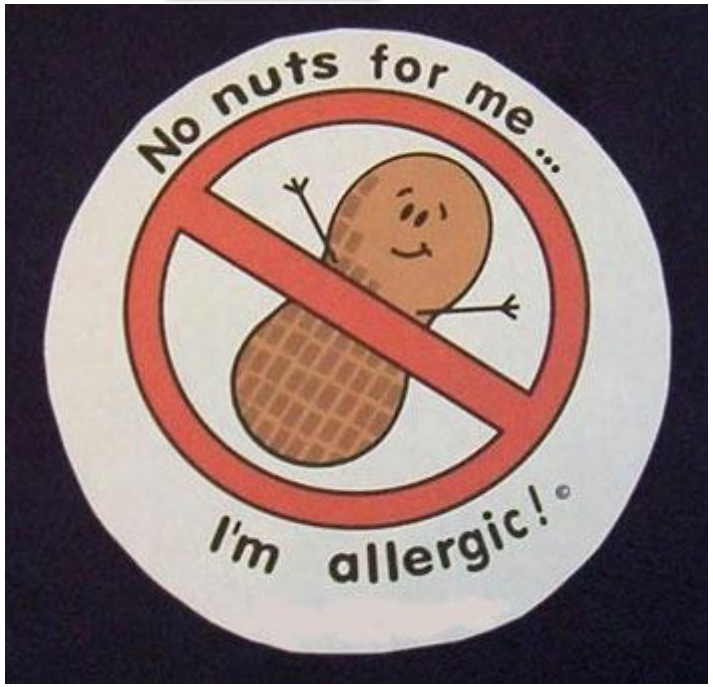
**•The involment of an increasing number of food**

**• Changes in our lives that make us increasingly take industrially processed foods and outside the domestic sphere**

**We have lost the control of our food**

# Treatmet indicated in food allergy

**Diet**




1. It is easy to prescribe
2. It is effective ¿ 100%?
3. It is safe ¿ ?
4. It is economic ¿ ?
5. It is easy to make ¿ ?

**Good notice: in some foods and in some ages the evolution at the tolerance is frecuent in a high porcentage of patients**

# Is it necesary to make anything more than the diet?

**Clinic dates about childs allergic to cow´s milk**
**240 childrens**

**Age: medium 4,6 years (1-12 y)**

**72,9% < 5**
**27,1**
**isten allergy = bad evolution**

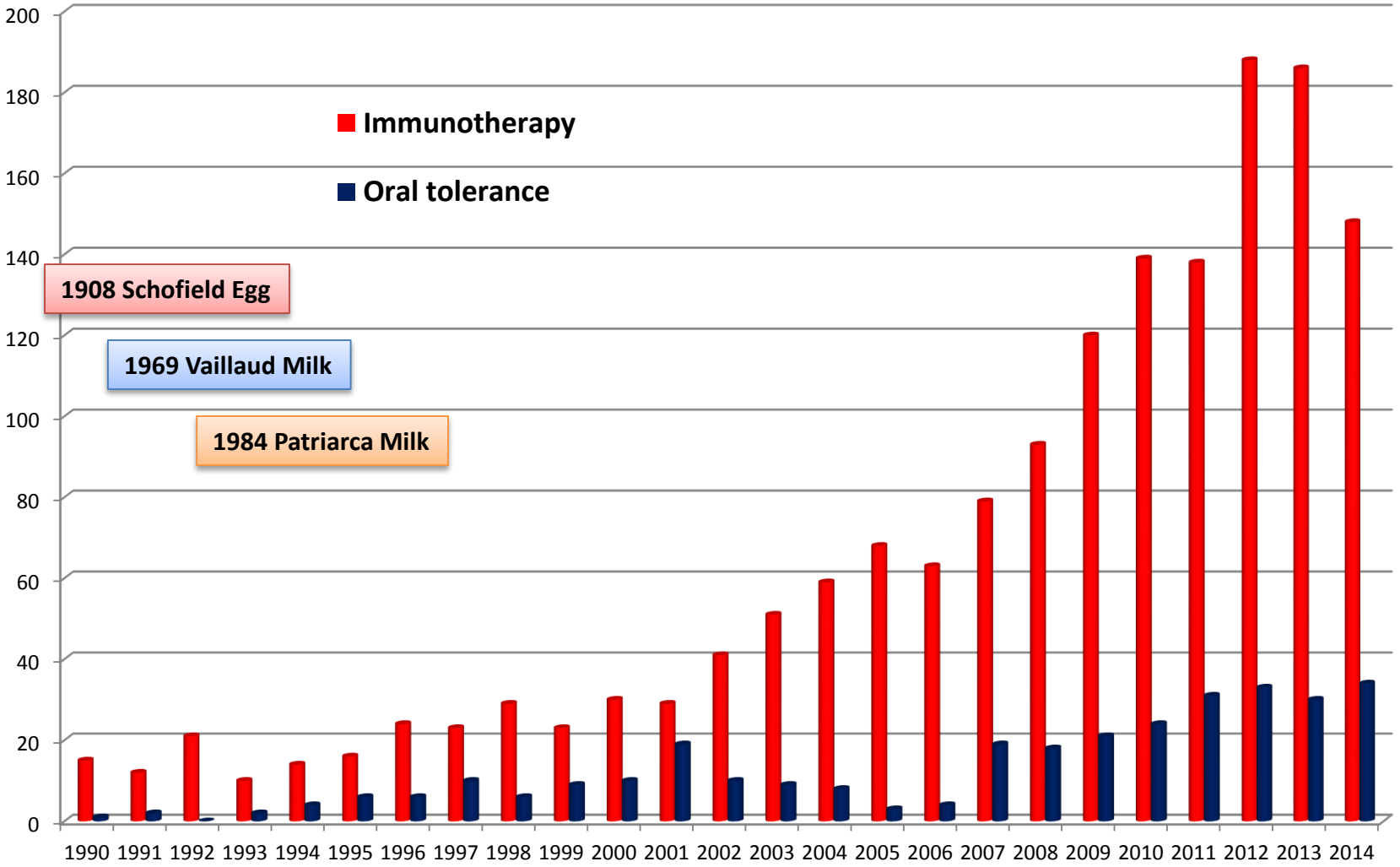
**Cow´s Milk Allergy (CMA)**
**Associated with oth**
**42,5%**
**13,3% Fish**
**ies**
**15% Nuts**
**esh fuits**
**3,3% Shellfish**

**2 3 food groups**

**At 5 years old is a child with many problems**

**Comorbilities: Asthma: 38,3% (< 5y: 30,2%; > 5 y: 62,5% )Dermatitis 11,7%**

Database: Univ. Hospital PR, 2014




**Pub Med: 1990-2014**

**Food Allergy & Immunotherapy: 1619**

**Food allergy & Oral Tolerance: 319**

# Desensitization or Tolerance induction
# Conceptual diferences

**Desensitization :** Ability to tolerate the allergens that cause adverse reaction after application of a treatment.
Requires immediate exposure
It is not known how long the interruption of exposure tolerance would be lost
Sometimes it's just an elevation of the threshold dose reactive

**Tolerance:** Permanent state of loss of adverse reaction to a substance with which previously appeared allergic reaction.
Tolerance can be spontaneous or induced

The permanent tolerance is **ALLERGY CURED**

# SPECIFIC ORAL DESENSITIZATION INDUCTION (SODI)

**Administration of the product (food allergen) which cause the allergic reaction begining with small amounts until get the normal amount or the highest dosage tolerated.**

We try to get an immunological tolerance, reeducating the complex cellular and serologic mechanism, to correct an inadequate reaction.

**Our whole life is a history of gradual tolerance towards the environment around us**

# SPECIFIC ORAL TOLERANCE INDUCTION (SOTI)

WHO?

AT WHAT AGE ?

WITH WHAT PROTOCOL?

WHERE?

FOR WHAT FOOD?

WHO SHOULD BE PERFORMED?

WHERE TO GET?

HOW MANY FOOD?

ALWAYS POSSIBLE?

# METHODOLOGY OF ORAL TOLERANCE INDUCTION

There are many guidelines or protocols:

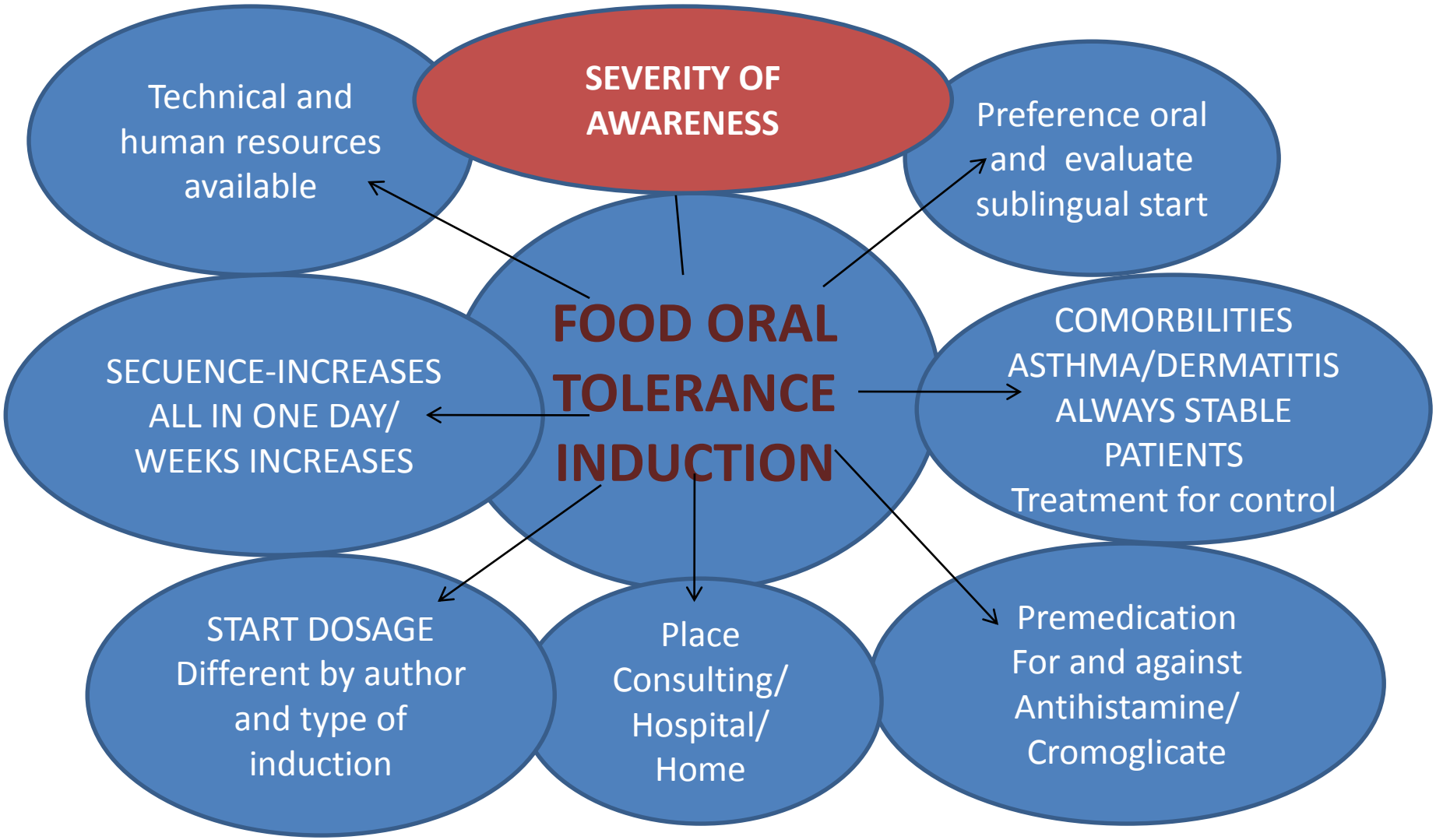
1.- It depends on the means you count

2.- It depends of the type of center

3.- It depends of the type of patient: age
level of sensitization
disponibility
comorbilities

4.- It depends of the type of geographical area and the comunications

5.- It depends of the circumstances of the center, of the family and of the patient


SEVERITY OF AWARENESS
Technical and human resources available
Preference oral and evaluate sublingual start
FOOD ORAL TOLERANCE INDUCTION
SECUENCE-INCREASES ALL IN ONE DAY/ WEEKS INCREASES
COMORBILITIES ASTHMA/DERMATITIS ALWAYS STABLE PATIENTS Treatment for control
START DOSAGE Different by author and type of induction
Place Consulting/ Hospital/ Home
Premedication For and against Antihistamine/ Cromoglicate

**VIA**

Oral with ingestion, sublingual without ingestion
Subcutaneous

**TIME**

Slow, very much slow
Short, cluster
Semicluster: first quick and after each week

**IS A BESPOKE SUIT**

**PLACE**

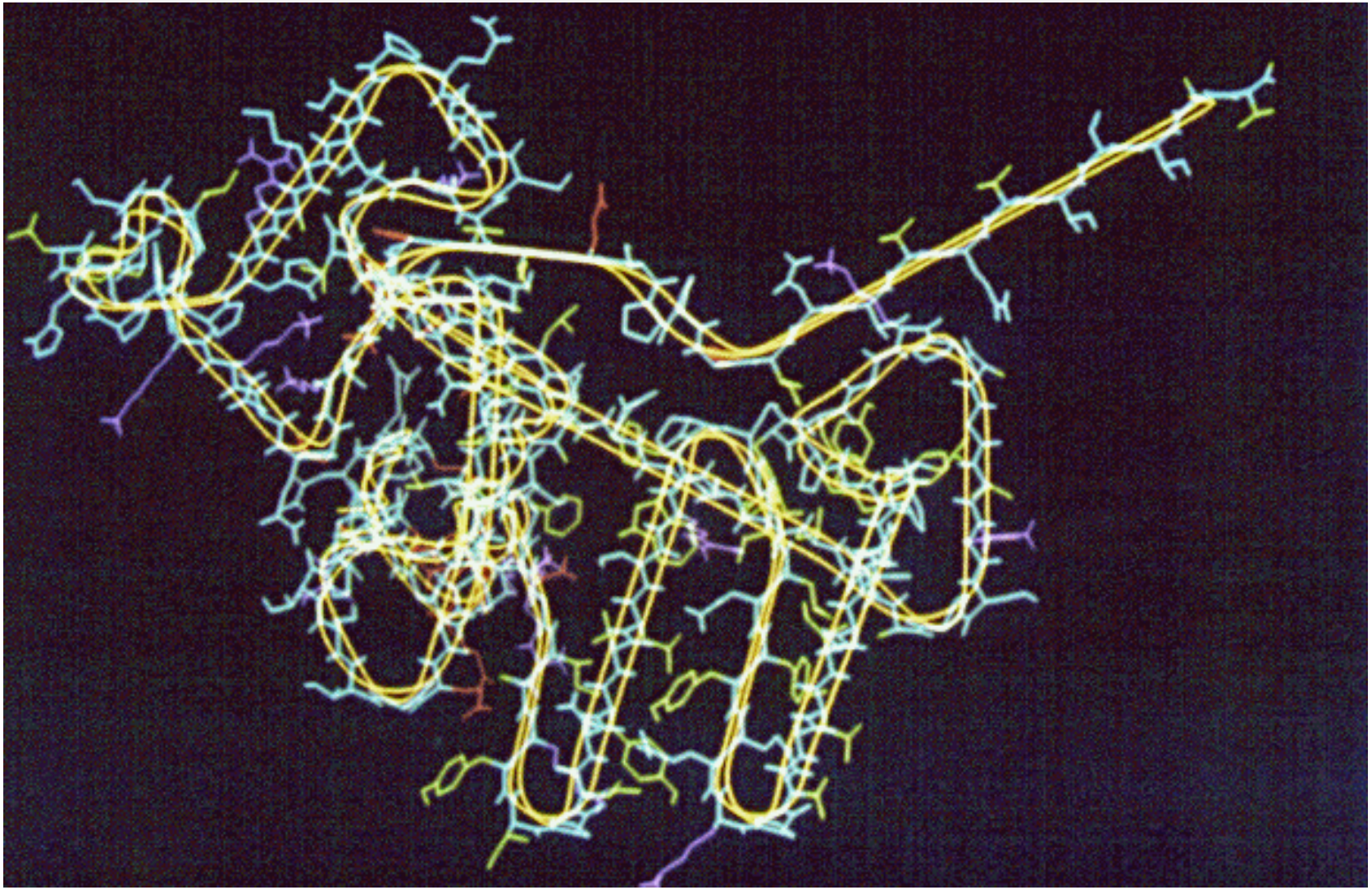
Admitted to hospital
With partial admitted
With increases in the hospital
With increases at home
Increases by week, daily….

**MEDICATION**

Without medication
With premedication: antihistamine, Salbutamol, etc

**We make a protocol for “easy” patients versus “anafilactics” and adapted at the circumstances**

# SPECIFIC ORAL TOLERANCE INDUCTION COW´S MILK



Patriarca G, Schiavino D, Nucera E, Schingo G, Milani A, Gasbarrini GB. Food Allergy in children: Results of a standarized protocol for oral desensitization. HepatoGastroenterology 1998; 45: 52-58

**MILK**

Table 1. Protocol for oral desensitization with cow's milk (modified from Patriarca *et al.*[26])

| Days | Daily dose | Days | Daily dose |
|---|---|---|---|
| Starting dilution: 10 drops of milk in 100 mL of water | | Pure milk | |
| 1–3 | 1 drop | 65–68 | 40 drops × 4 |
| 4–6 | 4 drops | 69–72 | 50 drops × 4 |
| 7–9 | 6 drops | 73–76 | 60 drops × 4 |
| 10–12 | 10 drops | 77–80 | 4.5 mL × 3 |
| 13–15 | 12 drops | 81–84 | 6 mL × 3 |
| 16–18 | 18 drops | 85–88 | 6 mL × 4 |
| Pure milk | | 89–92 | 7 mL × 4 |
| 19–21 | 1 drop | 93–96 | 12 mL × 4 |
| 22–24 | 2 drops | 97–100 | 15 mL × 4 |
| 25–27 | 3 drops | 101–104 | 15 mL × 5 |
| 28–30 | 4 drops | 105–108 | 20 mL × 3 |
| 31–33 | 6 drops | 109–112 | 30 mL × 3 |
| 34–36 | 8 drops | 113–116 | 40 mL × 3 |
| 37–40 | 10 drops | 117–120 | 50 mL × 2 |
| 41–44 | 16 drops | 121–124 | 65 mL × 2 |
| 45–48 | 24 drops | 125–128 | 80 mL × 2 |
| 49–52 | 32 drops | 129–132 | 100 mL |
| 53–56 | 40 drops | 133–136 | 120 mL |
| 57–60 | 40 drops × 2 | Maintenance dose: 120 mL of milk (about 1 glass) at least 2–3 times a week | |
| 61–64 | 40 drops × 3 | | |

Total daily dosage 120 cc
Time: 19,4 weeks
Success: 79,2%

# Experience in Specific Oral Tolerance Induction

Food allergy immunotherapy trials

| Study, y of publication | Targeted food | Modality | Blinded | Total subjects, n (age [y]) | Duration | Success rate[a] [n (%)] | Withdrawals [n (%)] | Tolerance [n (%)] |
|---|---|---|---|---|---|---|---|---|
| Patriarca et al.,[18] 2003 | Milk, egg, other | OIT | No | 59 (3–55) | 2–3 mo | 45/54 (83.3) | 9 (16.7) | NA |
| Meglio et al.,[19] 2004 | Milk | OIT | No | 21 (6–10) | 6 mo | 15 (72) | 3 (14) | NA |
| Staden et al.,[20] 2007 | Milk, egg | OIT | No | 25 (0.6–12.9) | 11–59 mo | 12 (48) | 9 (36) | 9 (36)<br>– off 2 mo |
| Buchanan et al.,[21] 2007 | Egg | OIT | No | 7 (1–7) | 24 mo | 7 (100) | 0 | 2 (29<br>– off 3–4 mo |
| Longo et al.,[22] 2008 | Milk | OIT | No | 30 (5–17) | 1 y | 11 (36) | 3 (10) | NA |
| Skripak et al.,[23] 2008 | Milk | OIT | Yes | 13 (6–17) | 5–6 mo | 12 (92) | 1 (8) | NA |
| Clark et al.,[24] 2009 | Peanut | OIT | No | 4 (9–13) | 6–7 mo | 4 (100) | 0 | NA |
| Jones et al.,[25] 2009 | Peanut | OIT | No | 39 (1.1–9.4) | 36 mo | 29 (74) | 10 (26) | NA |
| Blumchen et al.,[26] 2010 | Peanut | OIT | No | 23 (3–14) | 9 mo | 14 (61) | 9 (39) | NA |
| Pajno et al.,[27] 2010 | Milk | OIT | Yes | 15 (4–13) | 4–5 mo | 10 (67) | 5 (3.3) | NA |
| Martorell et al.,[28] 2011 | Milk | OIT | No | 30 (2–3) | 12 mo | 27 (90) | 2 (0.07) | NA |
| Garcia Rodriguez et al.,[29] 2011 | Egg | OIT | No | 23 (5–17) | 3 mo | 20 (86.9) | 1 (0.04) | NA |
| Anagnostau et al.,[30] 2011 | Peanut | OIT | No | 22 (4–18) | 2–9 mo | 19 (86.4) | 1 (0.05). | NA |
| Burks et al.,[31] 2012 | Egg | OIT | Yes | 40 (5–11) | 22 mo | 30 (75) | 6 (15) | 11 (28)<br>– off 4–6 wk |
| Enrique et al.,[32] 2005 | Hazelnut | SLIT | Yes | 12 (19–53) | 5 mo | 11 (92) | 1 (8) | NA |
| De Boissieu and Dupont,[33] 2006 | Milk | SLIT | No | 8 (6–17) | 6 mo | 7 (87) | 1 (13) | NA |
| Fernandez-Rivas et al.,[34] 2009 | Peach | SLIT | Yes | 37 (18–65) | 6 mo | 33 (89) | 4 (11) | NA |
| Kim et al.,[35] 2011 | Peanut | SLIT | Yes | 11 (1.6–10.5) | 12 mo | 11 (100) | | NA |
| Keet et al.,[36] 2012 | Milk | OIT/SLIT | No | 30 (6–17) | 60 wk | 28 (93) | 2 (7) | 9 (30)<br>– off 6 wk |

[a]Success rate is defined as number of subjects who successfully finished treatment and were able to include the targeted food into the diet or finished treatment and underwent post-treatment food challenge.

**NA** = not applicable; **OIT** = oral immunotherapy; **SLIT** = sublingual immunotherapy.

# My experience



**1st DAY**
**Intervals: 1 hour**

| DOSAGE | HOUR | REACTION |
|---|---|---|
| 1 ml dilution 1/100 | | |
| 2 ml 1/100 | | |
| 4 ml 1/100 | | |
| 8 ml 1/100 | | |
| 1,6 ml 1/10 | | |

**2nd DAY**
**Intervals: 1 hour**

| DOSAGE | HOUR | REACTION |
|---|---|---|
| 1,6 ml 1/10 | | |
| 3,2 ml 1/10 | | |
| 6 ml 1/10 | | |
| 12 ml 1/10 | | |
| 2,5 ml pure milk | | |

# Milk without dilution. Incresing by weeks

| | DOSAGE | DAY | REACTION IN HOSPITAL | REACTION AT HOME |
|---|---|---|---|---|
| 1 | 5 ml | | | |
| 2 | 10 ml | | | |
| 3 | 20 ml | | | |
| 4 | 40 ml | | | |
| 5 | 60 ml | | | |
| 6 | 80 ml | | | |
| 7 | 100 ml | | | |
| 8 | 140 ml | | | |
| 9 | 180 ml | | | |
| 10 | 250 ml | | | |

SOTI with milk in our hospital

40 childs (2010-2014)

- Age: 6-14 y
- Medium IgE casein: 45 UI/ml (4->100)
- Weeks for SOTI: medium 10,5 w. (intervals 9- 15)
- **CAREFOUL WITH PATIENTS WITH HIGH RISK OF ANAPHYLAXIS**

Number of patients with total tolerance to milk: 35

Quantity: 240 ml but with individual increases if the patient want to drink o eat foods with milk.

5 patient only got 100 ml of tolerance and actually maintance this dosage

**Adverse reactions:**

- **abdominal pain (5)**
- **eosinophilic esophagitis (1)**
- **ANAPHYLAXIS (10): treatments with Adrenaline via IM**

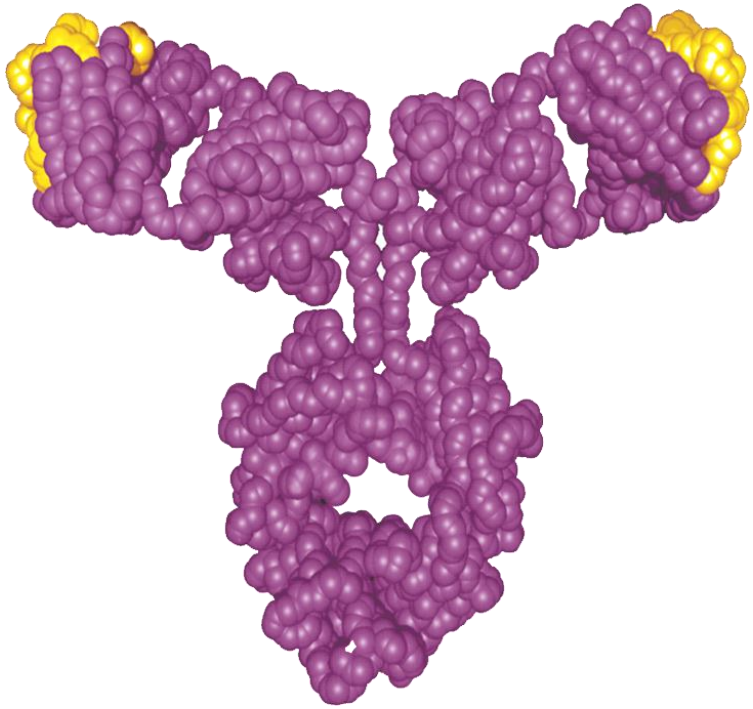
# Omalizumab: high risk of anaphylaxis

Human and monoclonal antibody

It binds to circulating IgE despite
Their specificity

It builds small comlex biologically inert
of Omalizumab:IgE

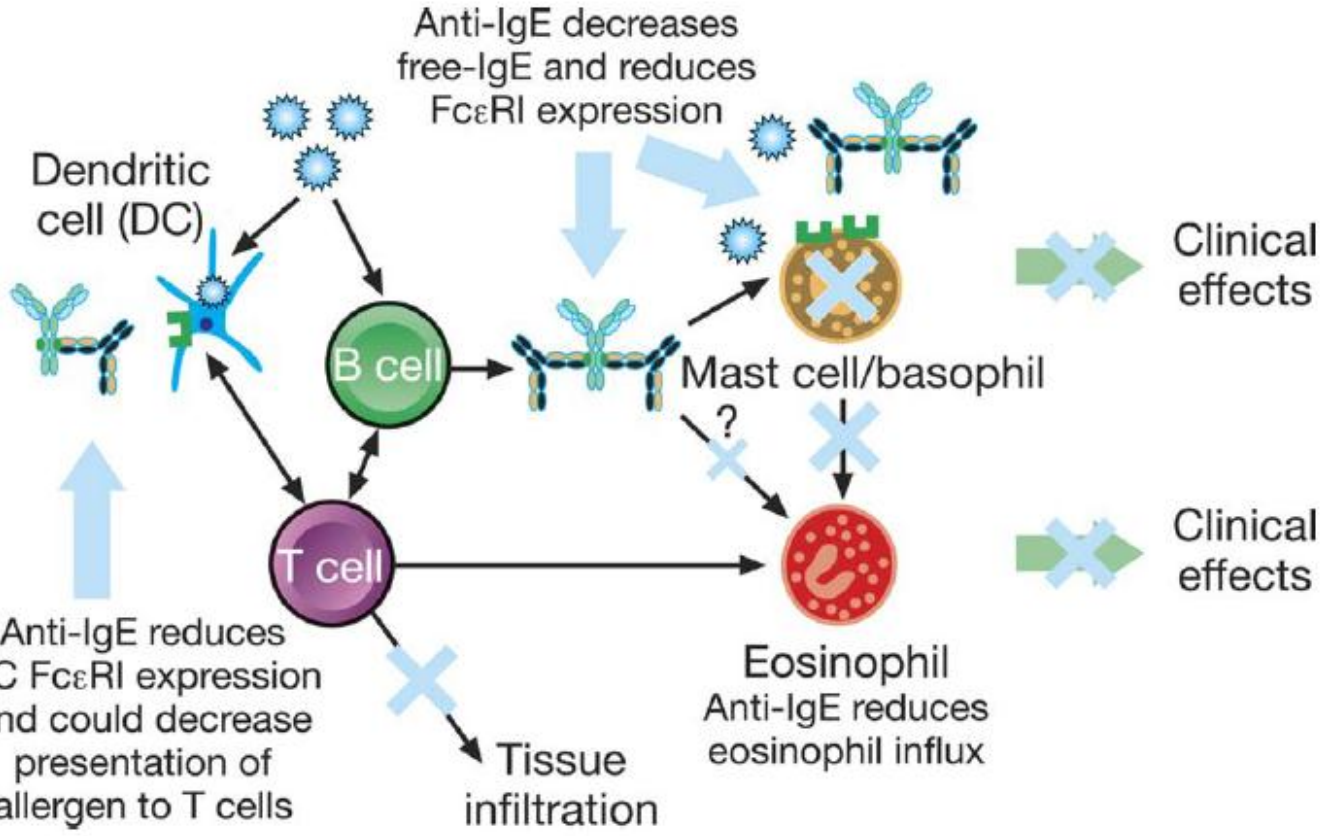
Don´t activethe complement way



**Decreases the IgE levels, depending of the doses**

**Inhibits the delivery of hisyamine and others precharged mediators**

**It cause the down regulation of the high affinity receptors**



Leung DY, Effect of Anti-IgE Therapy in Patients with Peanut Allergy N Engl J Med 2003;348:986-93

- **Results**:



**Placebo**: 735 mg
913 mg in the group given **150 mg of TNX-901**.
1650 mg in the group given **300 mg of TNX-901**
2627 mg in the group given **450 mg of TNX-901**

P<0.001 for the comparison of the 450-mg dose with placebo, and P<0.001 for trend with increasing dose

**TNX-901 was well tolerated**

Efficacy of Omalizumab for the Treatment of Food Allergy
*Journal of Allergy and Clinical Immunology*, 2008 Volume 121, Issue 2, Pages S252-S252
C. Watson, A. Rafi, L. Do, L. Sheinkopf, R. Katz

- **Objetive**: evaluate the efficacy of Omalizumab in food allergy
- **Method**: retrospective analysys to test the effectiveness of Omalizumab in 22 patients with persistent asthma and IgE mediated food allergy. Were analyzed: Juniper quality life measurements and Investigator Global Assessment scores.
- **Results:** 13 women y 9 men, age: 28 años (14-66 ).

  All the patiernts with Prick test positive to foods. And all of them get a significative improvement of the clinical symptoms when they were reexposure with the food
- **Conclusiones:** Omalizumab could be effective as treatment in patients with food allergy IgE mediated

# Abstract nº 87: AAAAI New Orleans . JACI Feb 2010 .

- **Omalizumab in peanut-allergic patients reduces free anti-IgE peanut and Skin Prick test to peanut**

- Not all the patients respond similar to Omalizumab.

- **Hypotesis**: the decrease og free IgE and Prick test after the treatment with 12 weeks of Omalizumab can be predicted to happen to make the oral provocation.

- **Method**: 5 patients of 5-25 years. Prick test:> 8mm,Cap:>15 KU/ml. IgE free and Prick test when free IgE less of 15 KU/ml.

- **Results:** Decrease of free IgE from 119,4 KU/ml. to 6 KU/ml. 1 patient negative the Prick tests after 4 weeks of treatment with Omalizumab, oral provocation negative

# Treatment with Omalizumab in childs with anafylactics reactions to cow´s milk proteins

**Objetive:**

- To evaluate the tolerance to cow´s milk allergy, after 16 weeks of treatment,1 year and 2 years with Omalizumab

**Material and methods:**

- Is an observational study
- Childs with more than 5 years, anaphylactics with cow´s milk protein, prick test positive, specific IgE positive.

# Material and Methods

- At 16 weeks,1 year and 2 years of treatment with Omalizumab, each 2-4 weeks, depending the dosage

- We did:
  - 1. Oral provocation,
  - 2. Prick test,
  - 3. Specific IgE to cow´s milk

- Oral provocation: lips contact with 1 drop of milk, each 30 minutes: 1 ml, 2´5ml, 5ml , 10ml, 20 ml, 50ml y 100 ml .

- Place: Pediatric Hospital Day

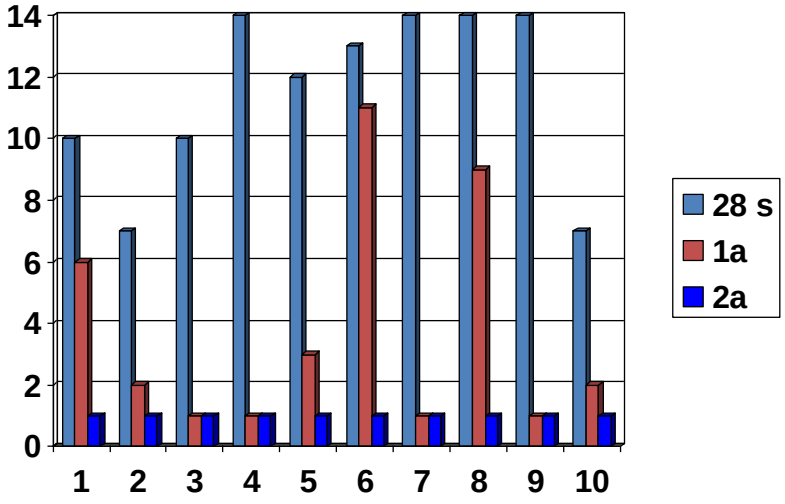
# Results

| **Características de los pacientes** | | | | |
|---|---|---|---|---|
| Number | 10 childs | 4 boys | 6 girls | |
| Asthma | 10 childs | 100% | | |
| Anaphylaxis | 10 childs | 100% | | |
| Age (years) | medium | 8,7 years | Range | 5 y – 15y |
| IgE | medium | 1321 Ul/ml | Range | 150-2500 |
| Weight | medium | 37Kg | Range | 20-57Kg |
| IgE level | medium | 75 KU/ml | Range | 7-100 KU/ml |
| Prick test | medium | 7 x 5mm | Range | 4x5 - 14x14 |
| Omalizumab dosage | | | Range | 75mg/4s<br>300mg/2s |

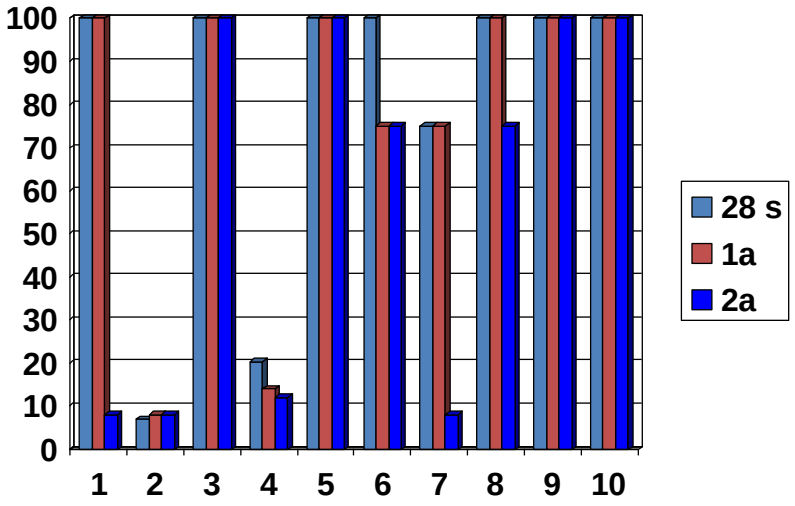
# Results oral provocation with 1 year / 2 years

- Neither child presented reaction with 1 year and with 2 years of treatment

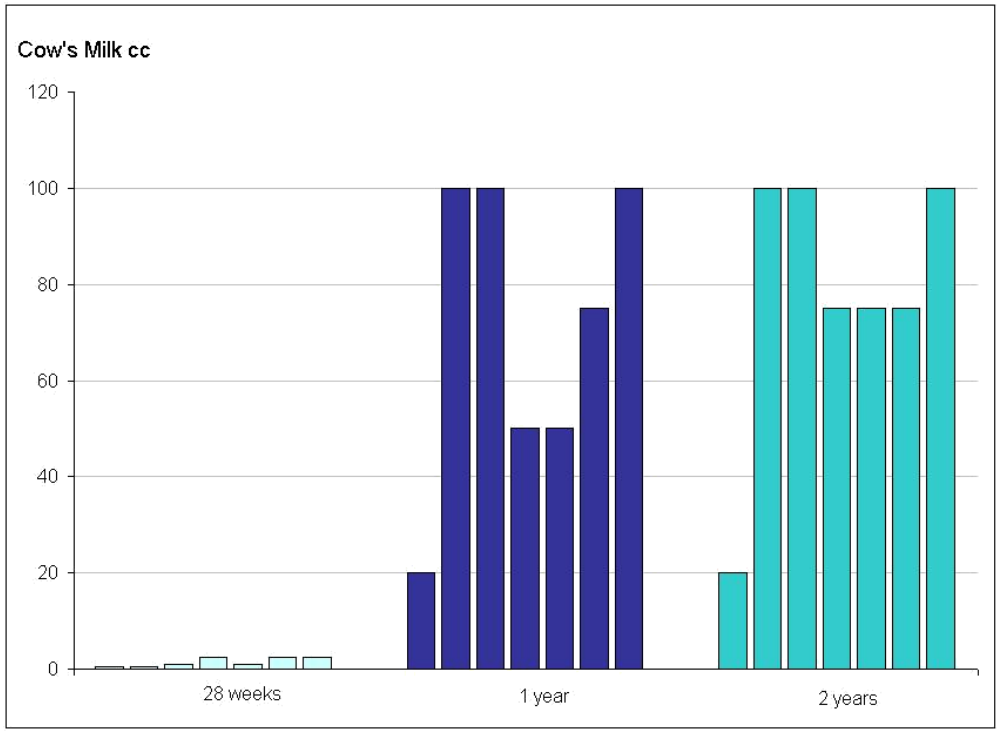
- Oral provocation: 1 ml, 2´5ml, 5ml , 10ml, 20 ml, 50ml y 100 ml .




## Prick Test




## CAP to casein




## Quantity of milk tolerated

# No adverse effects during treatment with Omalizumab

- Headache: 0 casos
- Urticaria: 0 casos
- Local reactions: 0 casos

## Conclusions:

Omalizumab is sure and efficacy in childs with anaphylaxis to cow´s milk protein allergy

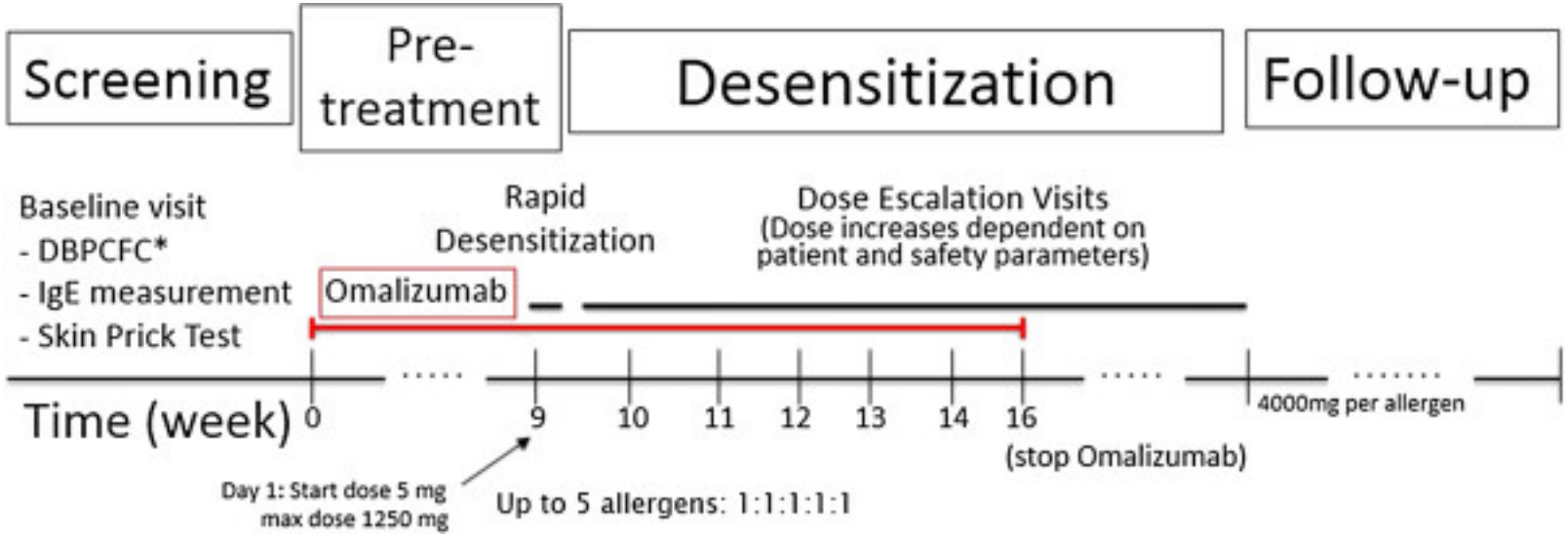
Bégin P. Phase 1 results of safety and tolerability in a rush oral immunotherapy protocol to multiple foods using Omalizumab.
Allergy Asthma Clin Immunol. 2014; 10(1): 7.

**Objetive**

- To evaluate the security and tolerability of Omalizumab to do the desensitization to many foods with a sura and fast method.
- Protocol Phase I  unicentric

**Methods**

- Multiallergic patients to food, OIT 5 o more allergens in the same time + omalizumab (rush OIT). The reactions in their home were recorded daylyLas reacciones  en el domicilio se registraban diariamente



# Protocol dosage OIT

**Table 1**

Rush mOIT initial escalation day schedule

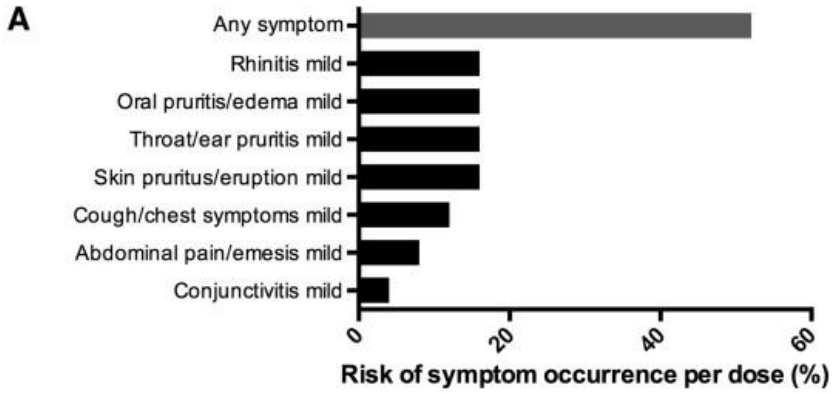
| Dose in mg of protein | Dosing interval in minutes |
|---|---|
| 5 | 30 |
| 50 | 30 |
| 150 | 30 |
| 300 | 30 |
| 625 | 30 |
| 1250 | 120 |

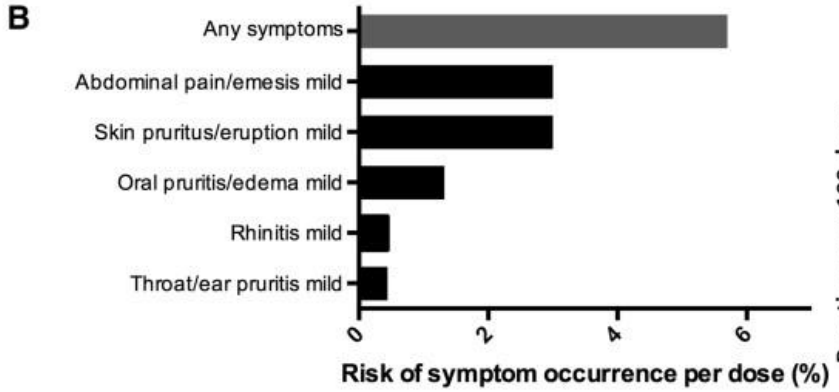
**Table 2**

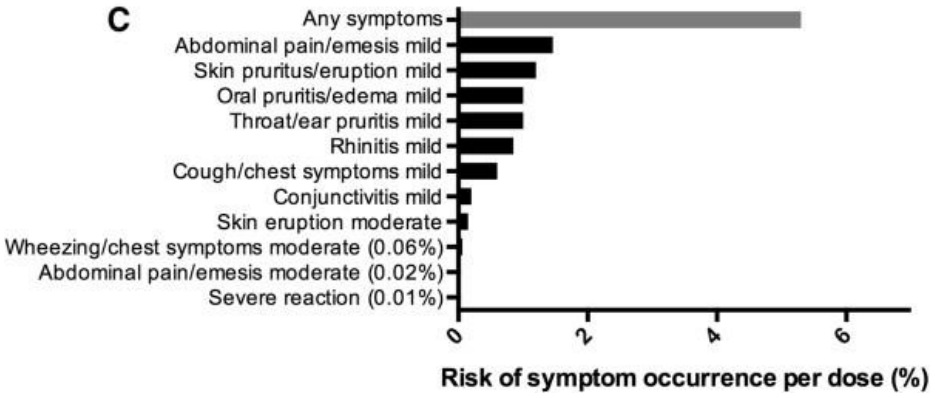
Rush mOIT dose escalation schedule

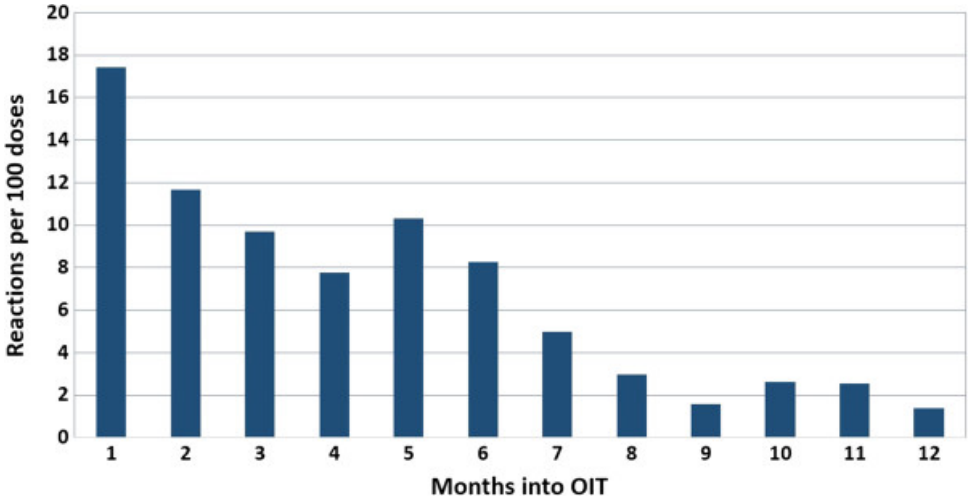
| Dose of protein (mg) | Interval in weeks | % of increase from previous |
|---|---|---|
| 2350 mg | 2 | 88% |
| 4000 mg | 2 | 70% |
| 5800 mg | 2 | 45% |
| 7600 mg | 2 | 50% |
| 9400 mg | 2 | 30% |
| 11200 mg | 2 | 20% |
| 14000 mg | 2 | 25% |

Omalizumab was stopped at 16 weeks, 8 weeks before and 8 weeks OIT+ Omalizumab

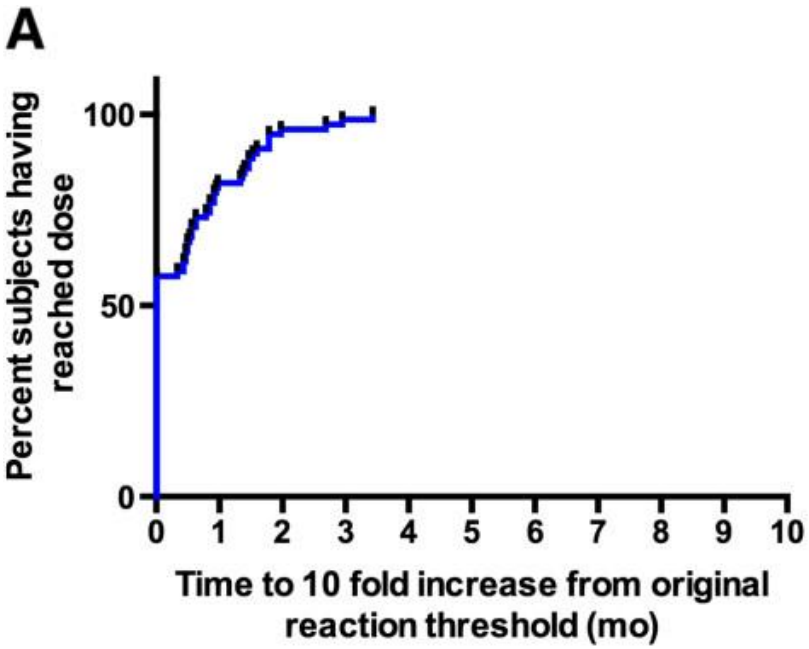


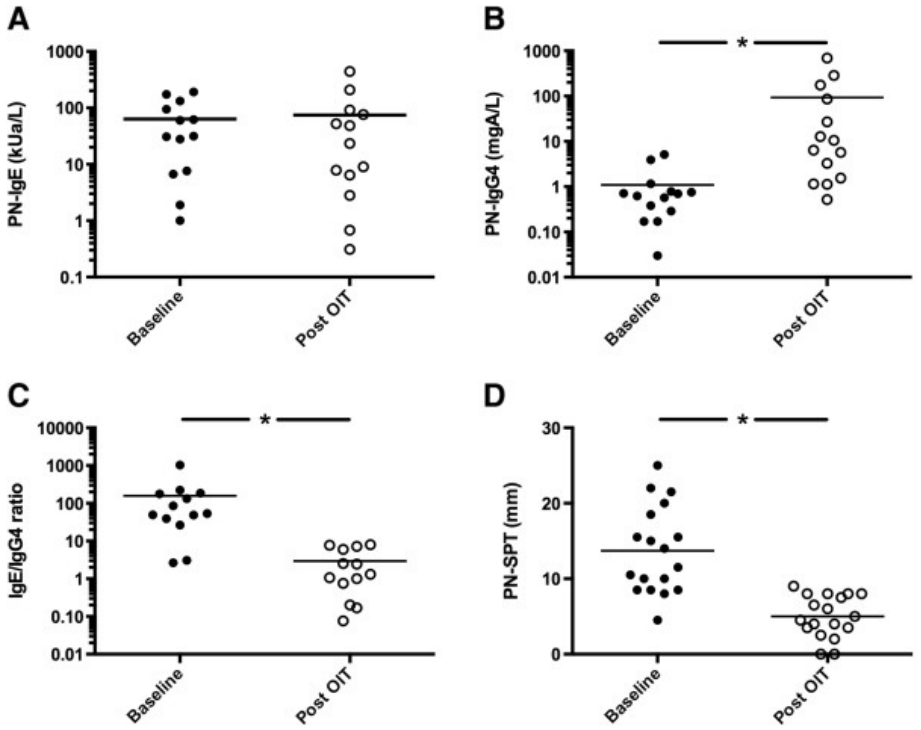



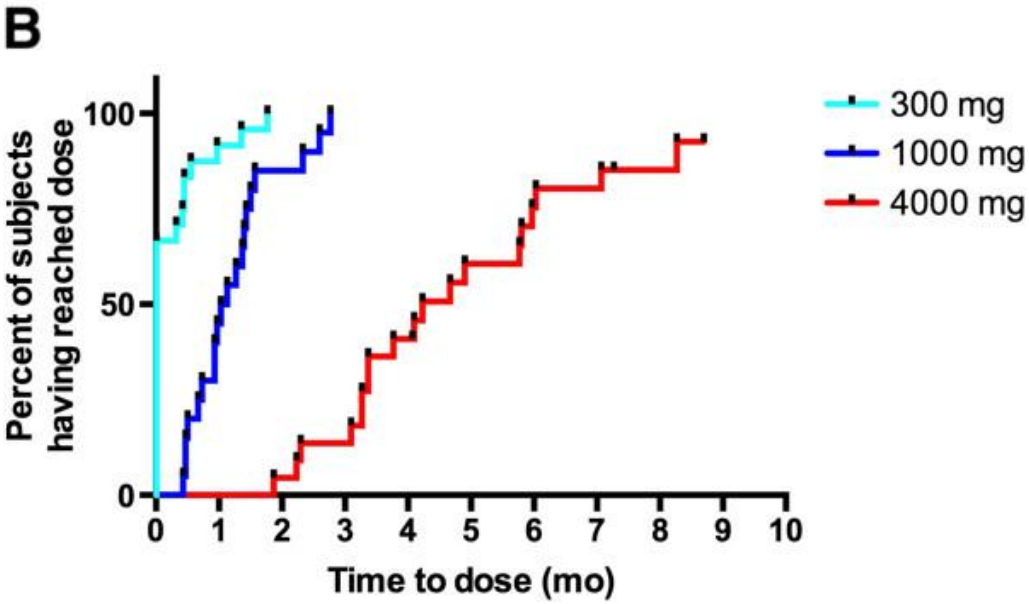




**Reactions/months 1st year**



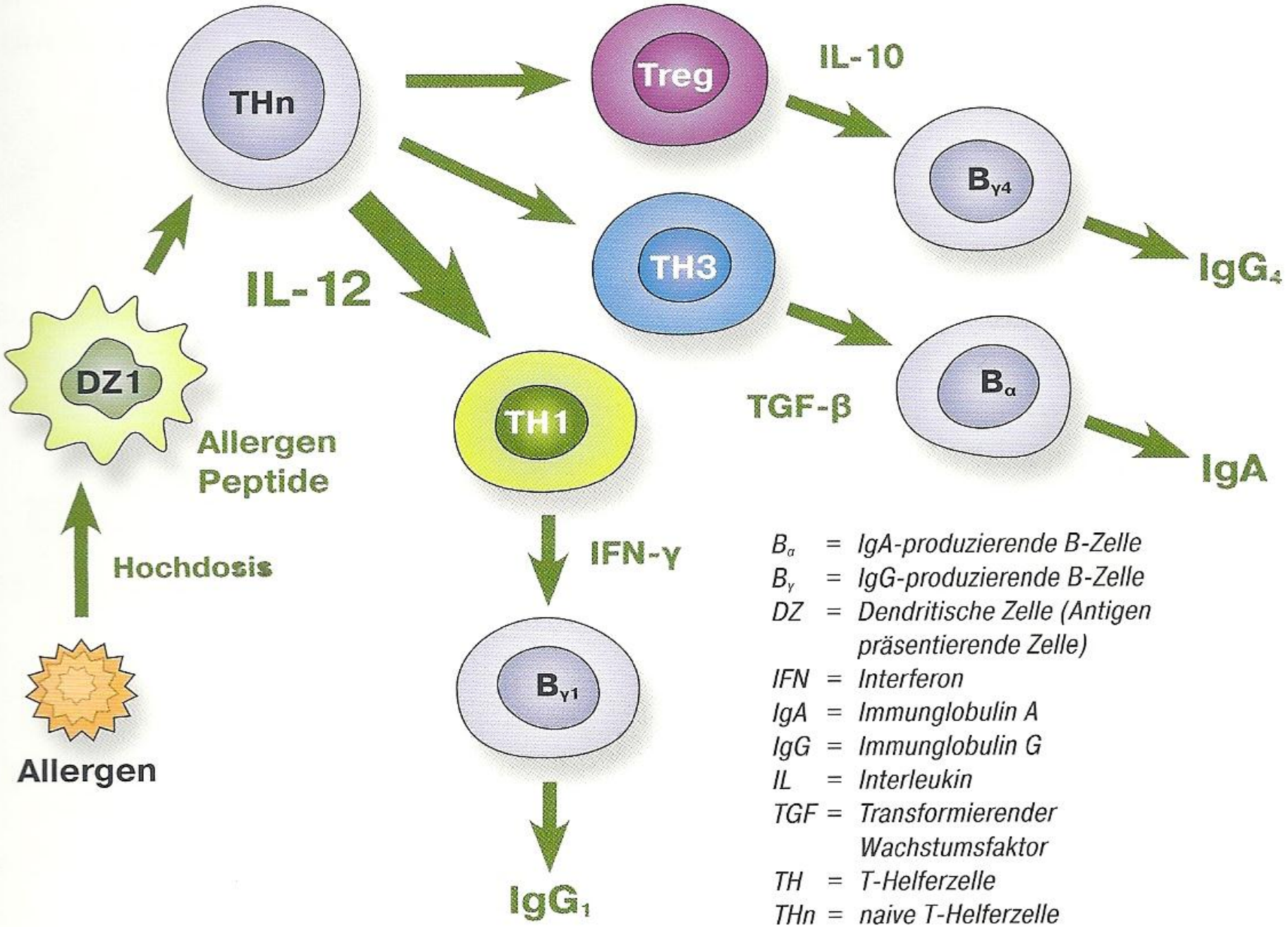



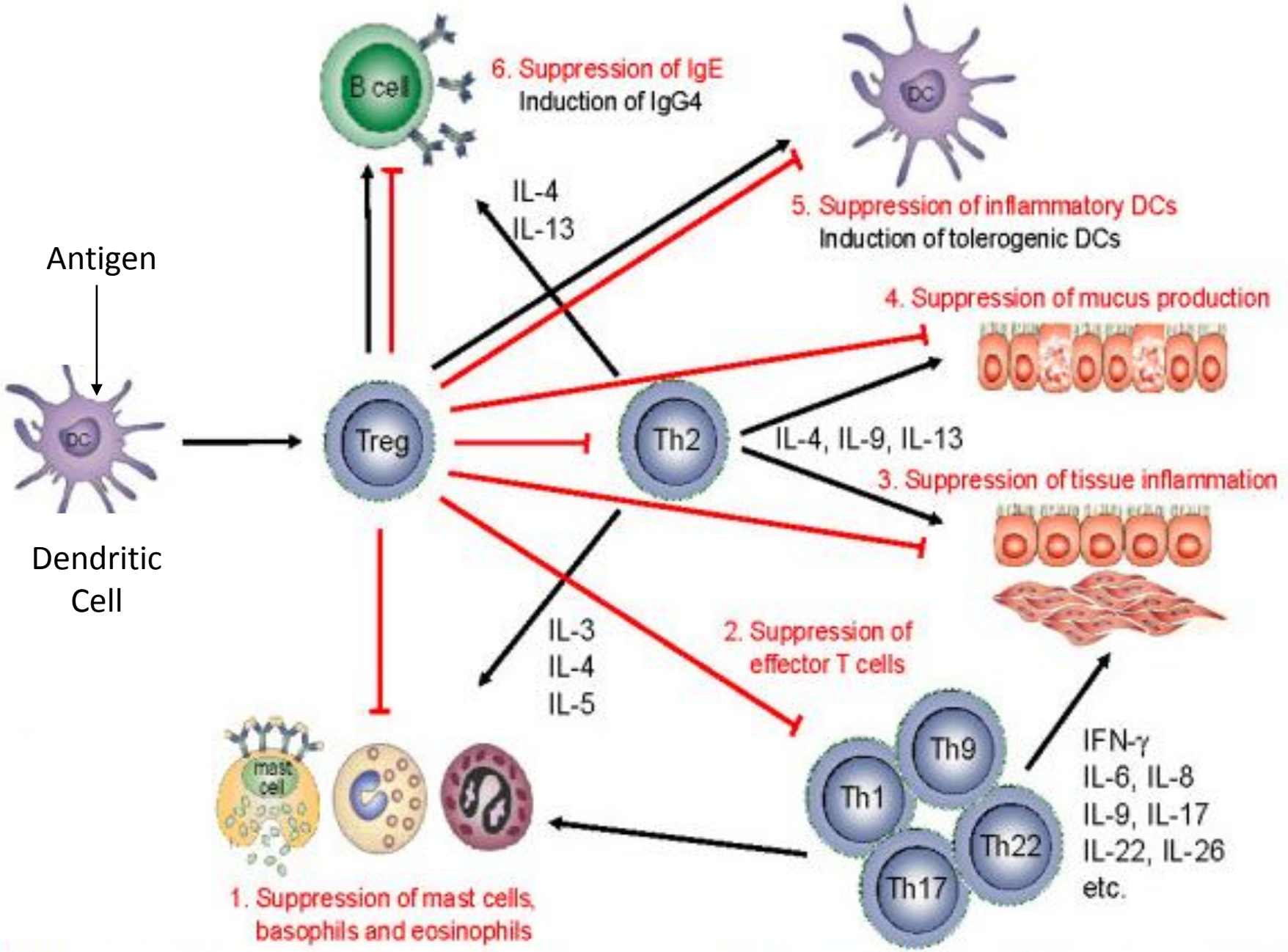

## Results

**Conclusions:**

- OIT+Omalizumab many foods
- Sure
- Eficacy
- Specialist and training personal
- Place: quiet and with equipment



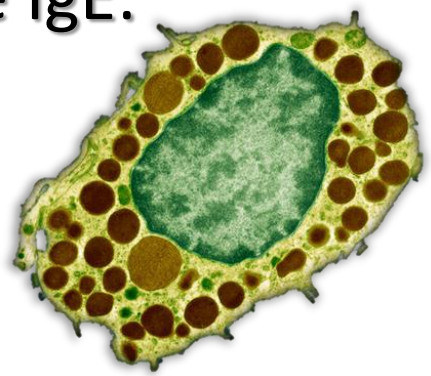

$B_\alpha$ = *IgA-produzierende B-Zelle*
$B_\gamma$ = *IgG-produzierende B-Zelle*
*DZ* = *Dendritische Zelle (Antigen präsentierende Zelle)*
*IFN* = *Interferon*
*IgA* = *Immunglobulin A*
*IgG* = *Immunglobulin G*
*IL* = *Interleukin*
*TGF* = *Transformierender Wachstumsfaktor*
*TH* = *T-Helferzelle*
*THn* = *naive T-Helferzelle*
*Treg* = *T-Regulatorzelle*




Fujita H, Soyka MB, Akdis M, Akdis CA. Mechanisms of allergen-specific immunotherapy. Clin Transl Allergy. 2012; 2: 2.

# Changes in the immunology

- $iT_{reg}$ and $nT_{reg}$ inhibiting respone Th2
- $IgA_1$ and $IgA_2$ induce production of IL-10 by Mo/Mϕ
- IL-10 favors great production towards $IgG_4$
- $IgG_4$, $IgA_1$ e $IgA_2$ compete for the Ag with the IgE:
  - ✓ Less sensibilization
  - ✓ Less presentation provide of Ag
  - ✓ Less activation of mast cells and basophils



## Investigation group nº 1

Cluster protocol

6 patients

**1st day:** diluted milk 1/100: 1 ml-2ml-4ml-6ml-8ml-16 ml.
Intervals: 1 hour between them

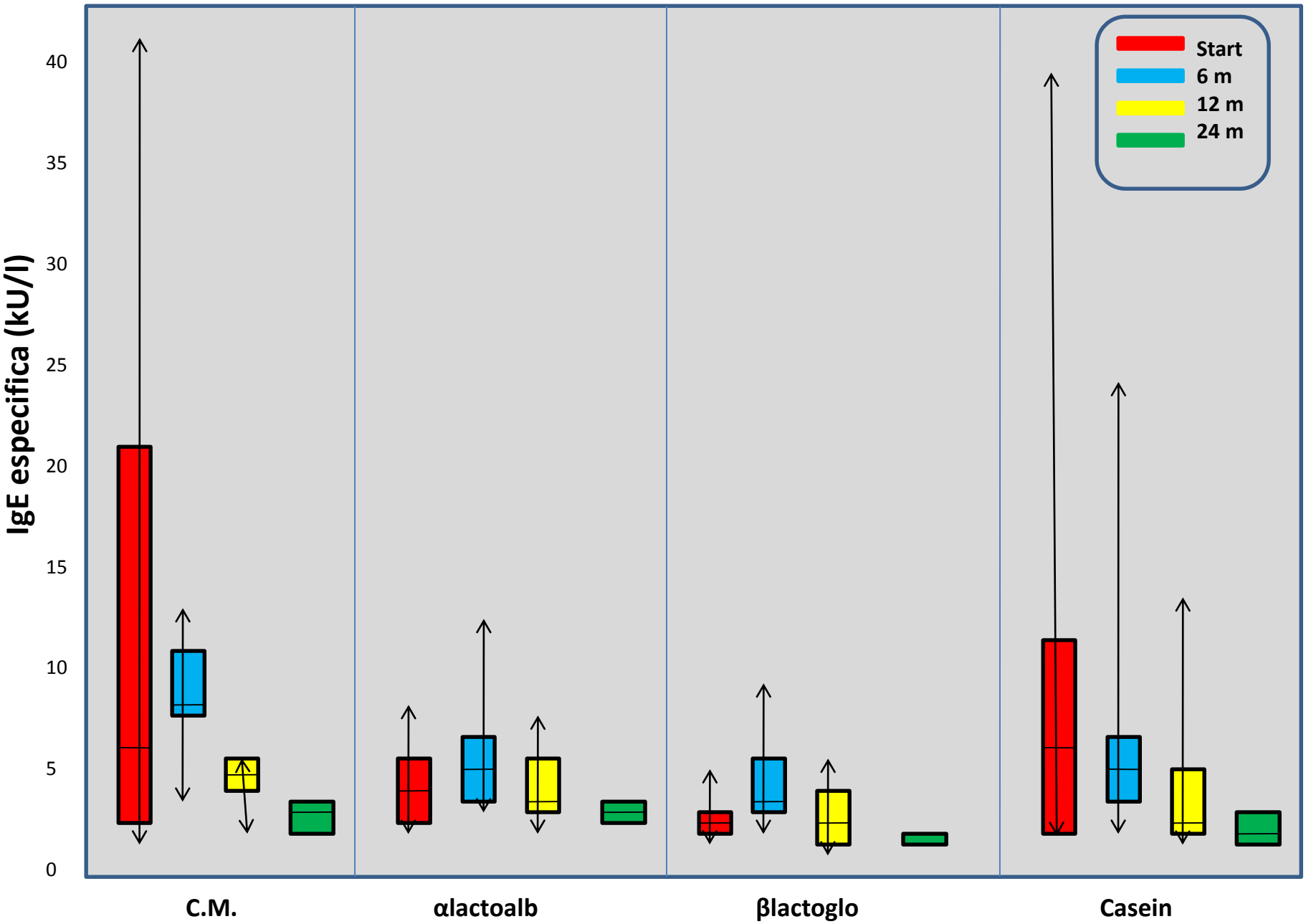
**2nd day:** diluted milk 1/100: 16 ml-32 ml and after dilution 1/10: 6-12-24 ml. Intervals: 1 h

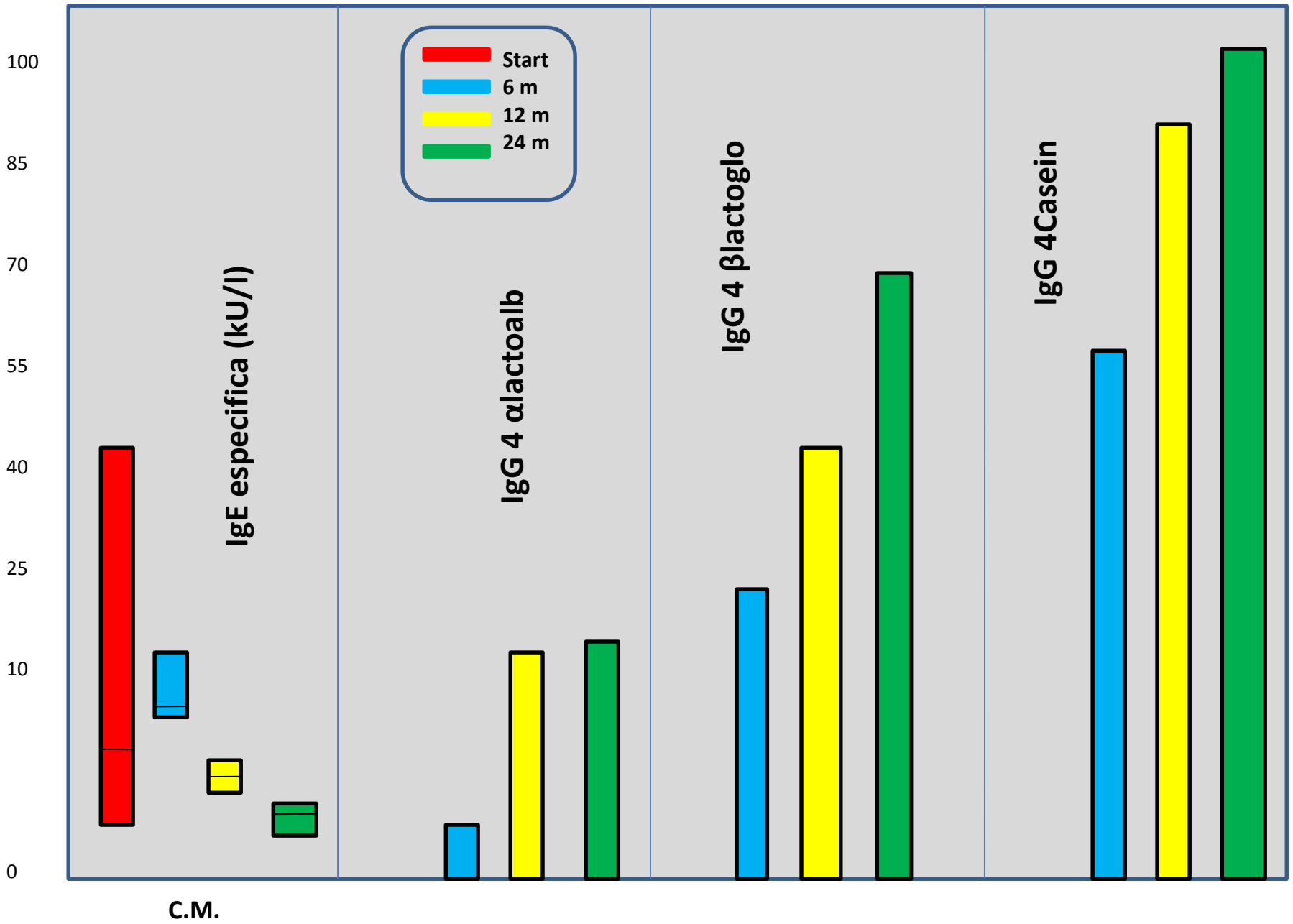
**3rd day:** diluted milk 1/10: 24-48 ml and after pure milk: 8-16-32 ml. Intervals: 1 h

**4th day:** 32-64-100 ml pure milk. Intervals: 2 h

**5th day:** 100-200 ml pure milk. Intervals: 2 h

| *CM (ml)* | *CM protein (mg)* |
|---|---|
| 1/100 | |
| 1 ml | 0.333 mg |
| 2 ml | 0.666 mg |
| 4 ml | 1.332 mg |
| 6 ml | 1.998 mg |
| 8 ml | 2.664 mg |
| 16 ml | 5.328 mg |
| 32 ml | 10.656 mg |
| 1/10 | |
| 6 ml | 19.8 mg |
| 12 ml | 39.6 mg |
| 24 ml | 79.2 mg |
| 48 ml | 158.4 mg |
| 1/1 | |
| 8 ml | 266.4 mg |
| 16 ml | 532.8 mg |
| 32 ml | 1065.6 mg |
| 64 ml | 2131.2 mg |
| 100 ml | 3330 mg |
| 200 ml | 6660 mg |


IgE especifica (kU/l)
0
5
10
15
20
25
30
35
40
Start
6 m
12 m
24 m
C.M.
αlactoalb
βlactoglo
Casein


100
85
70
55
40
25
10
0
Start
6 m
12 m
24 m
IgE especifica (kU/l)
IgG 4 αlactoalb
IgG 4 βlactoglo
IgG 4Casein
C.M.

# SPECIFIC ORAL TOLERANCE IN EGG ALLERGY

The general experience is less



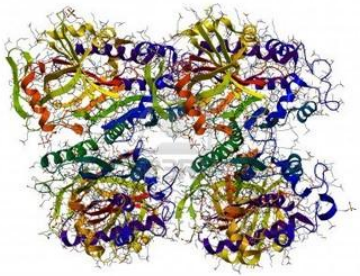
•Some studies excluded anaphilactic patients (Buchanan)

• Patriarca: beaten egg

•Staden: lyophilized egg

•Itoh: severe allergy and cluster protocol

•My hospital: we used commercial egg with capsules containing ovomucoide protein increasing the concentration at each feeding



**ovomucoid**

# OVO-DES NM

**Ingredients: Dried egg white**

Dosage 1º: 7 capsules with **4 mg**

Dosage 2º: 7 capsules with **20 mg**

Dosage 3º: 7 capsules with **50 mg**

Dosage 4º: 7 capsules with **100 mg**

Dosage 5º: 7 capsules with **225 mg**

Dosage 6º: 7 capsules with **450 mg**

Dosage 7º: 7 packet with **900 mg**

Dosage 8º: 7 packet with **1800 mg**

Dosage 9º: 1 packet with **3600 mg**

3 days after the final packet the patient is subject a double-blind placebo control trial with a omelette and after with a mixture of milk and raw clear.

During the next year the patient must eat, at least, one egg each 2-3 days (3 eggs/week)



SOTI with egg in our hospital

10 childs (2013-2014)

- Age: 6-10 y
- Medium IgE ovomucid: 35 UI/ml (4->100)
- Weeks for SOTI: medium 10 w. (9- 12)

Number of patients with total tolerance to egg: 9

1 patient only got 225 mg of tolerance and desertion by anaphylaxis

**Adverse reactions:**

- **abdominal pain (2)**
- **ANAPHYLAXIS (1): treatment with Adrenaline via IM**

# SPECIFIC ORAL TOLERANCE INDUCTION WITH OTHER FOODS

Patriarca: inductions with many foods: fish, apple, cereals, peanut, kiwi, lettuce…

Ernesto Enríquez: sublingual with hazelnut 

Ana Tabar: peach



(actually is possible administrate sublingual immunotherapy with Pru p3)

## My experience: wheat (2 patient)



- 8 years tolerated in 24 weeks one year ago.
  - IgE wheat: 935 kU/ml. 6 months after end SOTI: 87,5 kU/ml
- 12 years, actually in SOTI with cereals

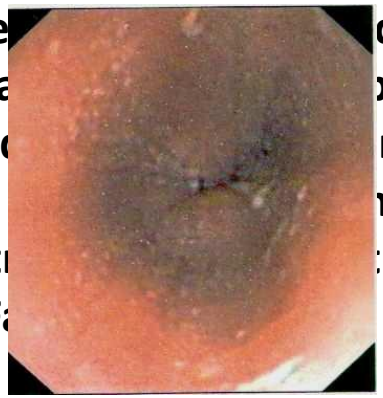
# EFFICACY AND SAFETY LONG TERM

**It is necessary to continue a medium-term control of these patients, a month, 6 months, 12 months, 2 and 3 years.**

**Patriarca: follow up 18 months. No clinical dates. Decreased prick test and milk serum IgE**

**Martorell: follow up 4 years**

**Meglio: follow up 4 years. No important incidence. No urgencies assistance. Continue tolerance.**

**My**  **up 2 ye**  **deser** 

**One ninal pa ounda**

**End med an nside sophagitis**

**eos biopsy. nded**

**Pen ic contr . Back**

**Eos -16%. Fa**

# FUTURE TREATMENTS OF FOOD ALLERGY

**Table 3.** Future treatment of food allergy

| Treatment | Allergen | Efficacy | Study (published year) |
|---|---|---|---|
| SLIT | Hazelnut | 45% of the subjects reached 20 g after 8–12 weeks of study | Enrique et al. [32] (2005) |
| | Peanut | 70% of 20 subjects were able to increase the threshold doses after 44 weeks of therapy | Fleischer et al. [33] (2013) |
| SLIT + OIT | Milk | 70% of 20 subjects were able to pass the 8-gram oral challenge after 80 weeks of therapy | Keet et al. [11] (2012) |
| OIT + omalizumab | Milk | 9 of 11 subjects reached 2,000 mg, passed the oral challenge on week 24 of the study | Nadeau et al. [36] (2012) |
| EPIT | Milk | 90% of 10 subjects tended to increase the threshold doses at follow-up oral challenge (day 90) | Dupont et al. [37] (2010) |

Int Arch Allergy Immunol 2014;164:1–9
DOI: 10.1159/000361025

SLIT: SubLingual ImmunoTherapy
OIT: Oral ImmunoTherapy
EPIT: EPicutaneous ImmunoTherapy

# The safety and efficacy of sublingual and oral immunotherapy for milk allergy.
# Keet J Allergy Clin Immunol 2011

**Methods:** We randomized children with CM allergy to SLIT alone or SLIT followed by OIT. After screening double-blind, placebo-controlled food challenges and initial SLIT escalation, subjects either continued SLIT escalation to 7 mg daily or began OIT to either 1000 mg (the OITB group) or 2000 mg (the OITA group) of milk protein. They were challenged with 8 g of milk protein after 12 and 60 weeks of maintenance. If they passed the 60-week challenge, therapy was withdrawn, with challenges repeated 1 and 6 weeks later




T1. Baseline visit:
DBPCFC, SPT, cm-IgE/IgG4, basophils
T2. Randomization:
Basophils, cm-IgE/IgG4
T3. End of dose escalation:
SPT, cm-IgE/IgG4, basophils
T4. Food challenge on therapy:
DBPCFC, SPT, cm-IgE/IgG4, basophils
T5. Food Challenge on therapy
SPT, cm-IgE,/IgG4, basophils
T6. Food Challenge OFF therapy
T7. Food Challenge OFF therapy
SPT, cm-IgE,/IgG4, basophils

FIG 1. Study timeline with key features highlighted. Subjects were randomized at T2 to either SLIT (goal dose, 7 mg), OITB (goal dose, 1000 mg), or OITA (goal dose, 2000 mg). CM-specific IgE, CM-specific $IgG_4$, and CM-titrated skin prick test *(SPT)* results were obtained in all subjects at T1, T3 to T5, and T7. Basophil studies were done at T1, T2 to T5, and T7.

**Conclusion:** OIT was more efficacious for desensitization to CM than SLIT alone but was accompanied by more systemic side effects.

Clinical desensitization was lost in some cases within 1 week off therapy.

# FUTURE PROJECTS IN 2015

SOTI to hake

Multicenter study



# What are the 14 most common allergens in Europe?

Soybean 

sesame seeds 

Fish 

Mustard 

Shellfish 

Seafood 

Milk 

Eggs 

Nuts 

sulfur dioxide
cereals containing gluten 

Peanuts 

celery 

lupins 

# INDUCTION OF TOLERANCE IN FOOD ALLERGY IS A REASONABLY SAFE AND EFFICIENT METHOD

**The benefits of SOTI method overcome difficulties**

**We need to increase our expertise in various protocols, guidelines, roads, use of allergen**

**Above all know about what we are acting**

**WE NEED TO KNOW MUCH**




**Thanks for your attention**