Tratamiento de las alergias alimeNtarias

DE DONDE VENIMOS?

DONDE ESTAMOS?

HACIA DONDE VAMOS?

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20 de junio 2013

ALERGIA= ENFERMEDAD GENETICA

La sintomatologia establece el diagnostico y guía las conductas terapeuticas a seguir

DE DONDE VENIMOS?

Y ante situaciones inesperadas….

* Antihistamínicos y corticoides para reacciones locales (cutáneas)

* Adrenalina ante reacciones anafilácticas, seguida de antihistamínicos y cortis para evitar la reacción bifásica

Dieta de exclusión

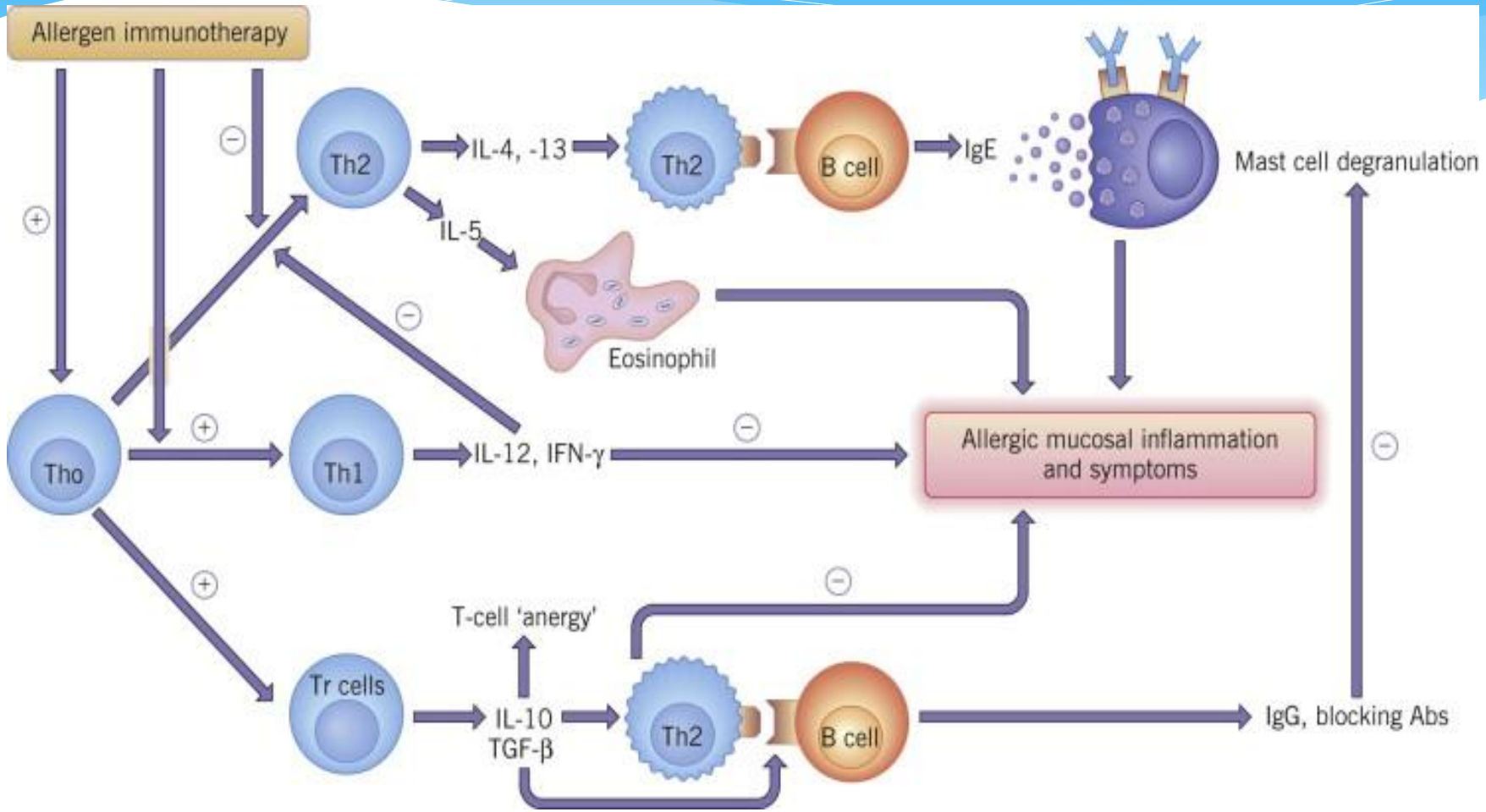
* Va asociada con restricciones en la dieta que pueden provocar déficits nutricionales

* Pueden ocurrir ingestas accidentales cuyas consecuencias pueden ocasionar reacciones impredecibles y hasta fatales

DONDE ESTAMOS?

* DIETA DE EXCLUSION
* **INDUCCION DE TOLERANCIA ORAL AISLADA O ASOCIADA CON ANTI IGE**
* INMUNOTERAPIA SUBLINGUAL
* MEDICINA TRADICIONAL CHINA

INDUCCION DE TOLERANCIA ORAL



Que se ha avanzado hasta hoy??

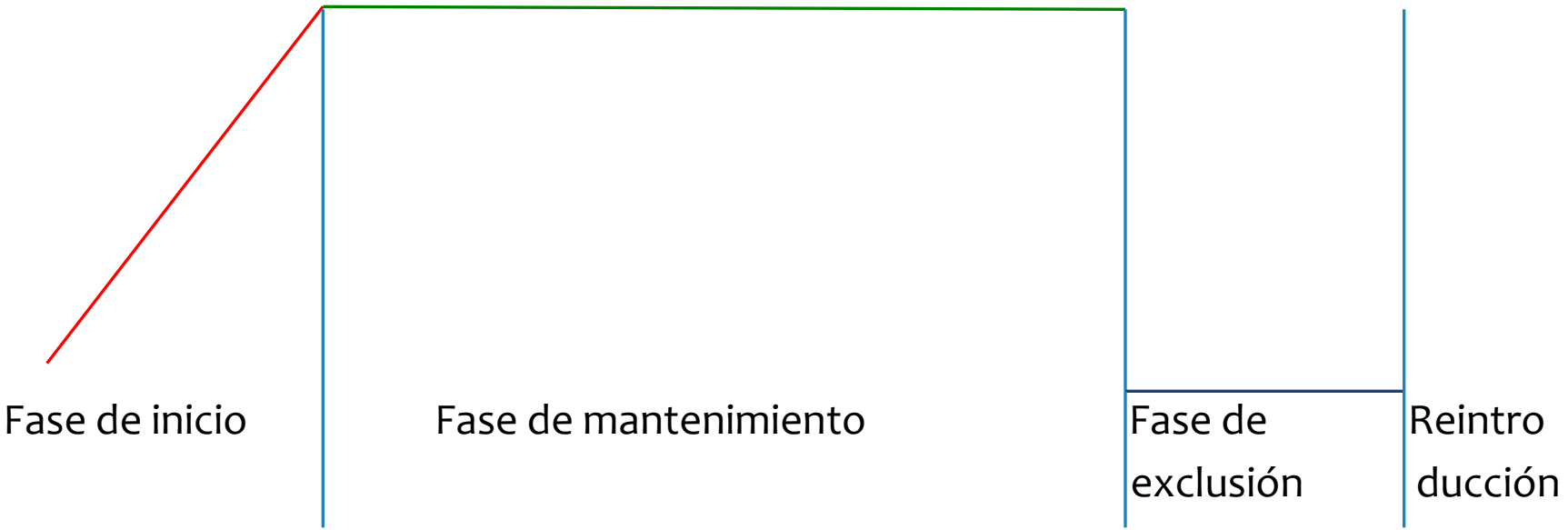
* Se han conseguido resultados con alimentos cuya prevalencia en alergia alimentaria es alta ➔ leche, huevo y cacahuetes; como lo demuestran múltiples estudios publicados en los últimos años

En que consiste?

* Administrar dosis progresivas del alimento involucrado en el ámbito hospitalario para luego continuar con la misma dosis en el domicilio cumpliendo una serie de condiciones:

1. Compromiso familia
2. Recaudos de administración de la dosis
3. Disposición para actuar en caso de reacciones adversas

* Hasta llegar a una dosis de mantenimiento que luego se administra por un tiempo variable (12-24 meses), se hace nuevamente dieta de exclusión (4-8 semanas) y se vuelve a reintroducir de manera vigilada


Fase de inicio
Fase de mantenimiento
Fase de exclusión
Reintro ducción

A randomized, double-blind, placebo-controlled study of milk oral immunotherapy for cow's milk allergy

Justin M. Skripak, Mda, Scott D. Nash, MDb, Hannah Rowley, RDa, Nga H. Brereton, Rda, Susan Oh, Rda, Robert G. Hamilton, PhDa, Elizabeth C. Matsui, Mda, A. Wesley Burks, MDb, Robert A. Wood

* **Objective**

  We sought to determine whether milk oral immunotherapy (OIT) is safe and efficacious in desensitizing children with cow's milk allergy

* **Results**

  Nineteen patients, 6 to 17 years of age, completed treatment: 12 in the active group and 7 in the placebo group. Baseline median milk IgE levels in the active (n = 13) versus placebo (n =) groups were 34.8 kUa/L versus 14.6 kUa/L. The median milk threshold dose in both groups was 40 mg at the baseline challenge. After OIT, the median cumulative dose inducing a reaction in the active treatment group was 5140 mg, whereas all patients in the placebo group reacted at 40 mg (P = .0003). Milk-specific IgE levels did not change significantly in either group. Milk IgG levels increased significantly in the active treatment group, with a predominant milk IgG4 level increase.

* **Conclusions**

  Milk OIT appears to be efficacious in the treatment of cow's milk allergy. The side-effect profile appears acceptable but requires further study.

JACI 2008

Egg oral immunotherapy in nonanaphylactic children with egg allergy

Ariana D. Buchanan, Todd D. Green, Stacie M. Jones, Amy M. Scurlock, Lynn Christie, Karen A. Althage, Pamela H. Steele, Laurent Pons, Rick M. Helm, Laurie A. Lee, A. Wesley Burks

* **Objective**

The purpose was to study the safety and immunologic effects of egg oral immunotherapy (OIT). The short-term goal was to desensitize subjects to protect against accidental ingestion reactions

* **Results**

Seven subjects completed the protocol. Egg-specific IgG concentrations increased significantly, whereas egg-specific IgE concentrations did not significantly change. During double-blind, placebo-controlled food challenges at study conclusion, all tolerated significantly more egg protein than at study onset and than that found in the typical accidental exposure. Two subjects demonstrated oral tolerance

* **Conclusion**

This study provides proof of concept that OIT can be safely used for patients with egg allergy without a history of anaphylaxis to egg.

Whether OIT will induce clinical oral tolerance cannot be concluded from this initial cohort.

JACI 2007

Efficacy and safety of oral desensitization in children with cows milk allergy according to their serum specfic IgE level

Carmen García-Ara; María Pedrosa; María Teresa Belver;
María Flor Martín-Muñoz; Santiago Quirce; and Teresa Boyano-Martínez,
Hospital La Paz, Madrid

* **Objective:**To analyze the efficacy and safety of the oral desensitization according to specific IgE (sIgE) level and adverse events during the maintenance phase.
* **Methods:** Thirty-six patients allergic to cow's milk (mean age, 7 years) were included in an oral desensiti-zation protocol. **Patients were grouped according to sIgE levels into groups** . Nineteen children were included as a control group. Serum sIgE levels to cow's milk and its proteins were determined at inclusion and 6 and 12 months after finishing the desensi-tization protocol
* **Results:** Thirty-three of 36 patients were successfully desensitized (200 mL): 100% of group 1 and 88% of groups 2 and 3. Desensitization was achieved in a median of 3 months (range, 1-12 months); 90% of the patients ingroup1,50% of the patients ingroup 2, and 30% of the patients in group achieved tolerance in less than 3 months (P 0.04). In the control group only 1 child tolerated milk in oral food challenge after 1 year. During the induction phase, there were 53 adverse events in 27 patients (75%). Patients of groups 2 and 3 had more severe adverse events compared with group 1. During the maintenance phase, 20 of 33 patients (60%)had an adverse event.
* **Conclusion:** Oral desensitization is efficacious. Tolerance is achieved earlier when sIgE is lower. Severe adverse events are frequent, especially in patients with higher sIgE levels

Ann Allergy, Asthma and Immunol 2013

Oral desensitization as a useful treatment in 2-year-old children with cow's milk allergy.

Martorell A, De la Hoz B, Ibáñez MD, Bone J, Terrados MS, Michavila A, Plaza AM, Alonso E, Garde J, Nevot S, Echeverria L, Santana C, Cerdá JC, Escudero C, Guallar I, Piquer M, Zapatero L, Ferré L, Bracamonte T, Muriel A, Martínez MI, Félix R.

* Evaluate the safety and efficacy of oral desensitization in 2-year-old children with cow's milk allergy, as a treatment alternative to elimination diet.
* **METHODS:** 60 children aged 24-36 months with IgE-mediated allergy to CMPs were included and were randomized into two groups. Thirty children (group A: treatment group) began oral desensitization immediately, whereas the remaining 30 (group B: control group) were kept on a milk-free diet and followed-up for 1 year.
* **RESULTS:** After 1-year follow-up period, 90% of the children in group A had become completely tolerant vs. 23% of the children in group B. In group A, cow's milk skin reactivity and serum-specific IgE to milk and casein decreased significantly from the initial assessment, whereas group B showed no significant change after 1 year of follow-up. Twenty-four patients (80%) developed some reaction during the treatment period: 14 children developed moderate reaction (47%) and 10 mild reaction (33%). The most common manifestations were urticaria-angioedema, followed by cough.
* **CONCLUSIONS AND CLINICAL RELEVANCE:** In this study, oral desensitization was found to be effective in a significant percentage of 2-year-old children with cow's milk allergy. The side-effect profile appears acceptable but requires further study

Clin Exp Allergy. 2011

Rapid oral desensitization in combination with omalizumab therapy in patients with cow's milk allergy

Kari C. Nadeau, Lynda C. Schneider, Lisa Hoyte, Irene Borras, Dale T. Umetsu

* We conducted a pilot phase I study in 11 children (age, 7-17 years) with cow's milk allergy by using omalizumab in combination with relatively rapid oral milk desensitization. We hypothesized that oral desensitization might occur rapidly and with few side effects when performed with omalizumab. Our primary objectives were to examine the safety of this approach and to determine whether subjects could be dosed up to 2000 mg milk within 7 to 11 weeks of initiating the desensitization
* In summary, we demonstrated that omalizumab treatment combined with oral milk desensitization in children with clinical reactions to cow's milk permitted rapid milk dose escalation in the majority of subjects. This study is the first to use omalizumab in combination with oral desensitization and demonstrates a potential value of this approach for the treatment of food allergy, although it must be first confirmed by future phase II and III trials. Nine of the 11 patients achieved the primary objective, tolerating desensitization to a dose of 2000 mg/d within a period of 7 to 11 weeks. Moreover, 9 of the 10 patients who completed the study passed a DBPCFC and an open challenge of milk without symptoms. Importantly, the 9 patients, after passing the DBPCFC, began tolerating almost normal amounts of milk in their diet (≥240 mL, equivalent to >8000 mg/d). The tenth patient is tolerating 4000 mg/d.

JACI 2011

En definitiva

* Si bien los datos iniciales con respecto a la ITO son esperanzadores la falta de protocolos estandarizados, la aparición de reacciones adversas con relativa frecuencia hacen que aún no sea considerada una técnica de uso clínico rutinario
* De todas formas los resultados han de ser analizados no solamente desde el punto de vista de la tolerancia completa o la desensibilización total dado que lograr un aumento de umbral de la cantidad de alimento tolerado es un éxito per se que puede mejorar significativamente la calidad de vida de muchos pacientes

Inmunoterapia Sublingual

* Es otra forma de administrar pequeñas cantidades de alérgeno para generar tolerancia inmunológica

* Se ha utilizado en pacientes alérgicos a kiwi, melocotón, avellana y cacahuete aunque podría ser útil su extensión a otras alergias alimentarias

Sublingual immunotherapy for hazelnut food allergy: A randomized, double-blind, placebo-controlled study with a standardized hazelnut extract

Ernesto Enrique, Fernando Pineda, Tamim Malek, Joan Bartra, María Basagaña, Raquel Tella, José Vicente Castelló, Rosario Alonso, José Antonio de Mateo, Teresa Cerdá-Trias, María del Mar San Miguel-Moncín, Susana Monzón, María García, Ricardo Palacios, Anna Cisteró-Bahíma

* **Objective**

Evaluate the efficacy and tolerance of sublingual immunotherapy with a standardized hazelnut extract in patients allergic to hazelnut

* **Results**

Twenty-three patients were enrolled and divided into 2 treatment groups. Twenty-two patients reached the planned maximum dose at 4 days. Systemic reactions were observed in only 0.2% of the total doses administered. Mean hazelnut quantity provoking objective symptoms increased from 2.29 g to 11.56 g (P = .02; active group) versus 3.49 g to 4.14 g (placebo; NS). Moreover, almost 50% of patients who underwent active treatment reached the highest dose (20 g), but only 9% in the placebo. Laboratory data showed an increase in IgG_4 and IL-10 levels after immunotherapy in only the active group.

* **Conclusion**

Our data confirm significant increases in tolerance to hazelnut after sublingual immunotherapy as assessed by double-blind, placebo-controlled food challenge, and good tolerance to this treatment.

JACI 2005

Sublingual immunotherapy for peanut allergy: A randomized, double-blind, placebo-controlled multicenter trial

David M. Fleischer, A. Wesley Burks, Brian P. Vickery, Amy M. Scurlock, Robert A. Wood, Stacie M. Jones, Scott H. Sicherer, Andrew H. Liu, Donald Stablein, Alice K. Henning, Lloyd Mayer, Robert Lindblad, Marshall Plaut,Hugh A. Sampson

* **Objective**

  We sought to investigate the safety, efficacy, and immunologic effects of peanut sublingual immunotherapy

* **Results**

  After 44 weeks of SLIT, 14 (70%) of 20 subjects receiving peanut SLIT were responders compared with 3 (15%) of 20 subjects receiving placebo ($P < .001$). In peanut SLIT responders, median SCD increased from 3.5 to 496 mg. After 68 weeks of SLIT, median SCD significantly increased to 996 mg . The median SCD at the Week 44 Crossover OFC was significantly higher than baseline (603 vs 71 mg, $P = .02$). Seven (44%) of 16 crossover subjects were responders; median SCD increased from 21 to 496 mg among responders. Of 10,855 peanut doses through the Week 44 OFCs, 63.1% were symptom free; excluding oral-pharyngeal symptoms, 95.2% were symptom free.

* **Conclusions**

  Peanut SLIT safely induced a modest level of desensitization in a majority of subjects compared with placebo. Longer duration of therapy showed statistically significant increases in the SCD

JACI 2013

The safety and efficacy of sublingual and oral immunotherapy for milk allergy

Corinne A. Keet, Pamela A. Frischmeyer-Guerrerio, Ananth Thyagarajan, John T. Schroeder, Robert G. Hamilton, Stephen Boden, Pamela Steele, Sarah Driggers, A. Wesley Burks, Robert A. Wood

* **Objective**

  We sought to explore the safety and efficacy of OIT and SLIT for the treatment of cow's milk (CM) allergy.

* **Results**

* Thirty subjects aged 6 to 17 years were enrolled. After therapy, 1 of 10 subjects in the SLIT group, 6 of 10 subjects in the SLIT/OITB group, and 8 of 10 subjects in the OITA group passed the 8-g challenge ($P = .002$, SLIT vs OIT). After avoidance, 6 of 15 subjects (3 of 6 subjects in the OITB group and 3 of 8 subjects in the OITA group) regained reactivity, 2 after only 1 week. Although the overall reaction rate was similar, systemic reactions were more common during OIT than during SLIT. By the end of therapy, titrated CM skin prick test results and CD63 and CD203c expression decreased and CM-specific IgG_4 levels increased in all groups, whereas CM-specific IgE and spontaneous histamine release values decreased in only the OIT group.

* **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

JACI 2012

Medicina tradicional China

* En los últimos años la Medicina Tradicional China ha generado interés en los países occidentales
* Una fórmula en particular constituida por 9 hierbas, la FAHF , demostró bloquear completamente la anafilaxia en ratones sensibilizados al cacahuete después de la exposición a este alimento
* Ha demostrado ser segura y bien tolerada en un la fase 1 de un estudio con pacientes randomizado, doble ciego controlado con placebo

Hacia donde vamos???

* La utilización de dietas de exclusión es una alternativa que seguramente irá perdiendo validez
* El desafío es y será conseguir desensibilizar al paciente y la elaboración de alergenos más puros, que permitan ajustar la dosis es la opción más valorable
* En pacientes puntuales, que por sus características no toleren dosis mínimas de alergenos, el empleo transitorio de anticuerpos monoclonales como coadyuvantes es y será una alternativa cada vez más aceptada

Y esto recién empieza

GRACIAS