

**L'alimentazione del bambino...
sano, allergico, con malattia cronica**
Una esigenza della famiglia a cui il pediatra risponde
con evidenze e... buon senso

VI Giornate Pediatriche "A. Laurinsich"
SIPPSAGGIORNA



POLIAMBULATORIO
DALLA ROSA PRATI
Centro Diagnostico
Europeo - Parma

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Centro Congressi della Camera di Commercio di Parma
via Giuseppe Verdi n°2, Parma



Dieta o terapia topica

Giampaolo Ricci

Allergologia Pediatrica

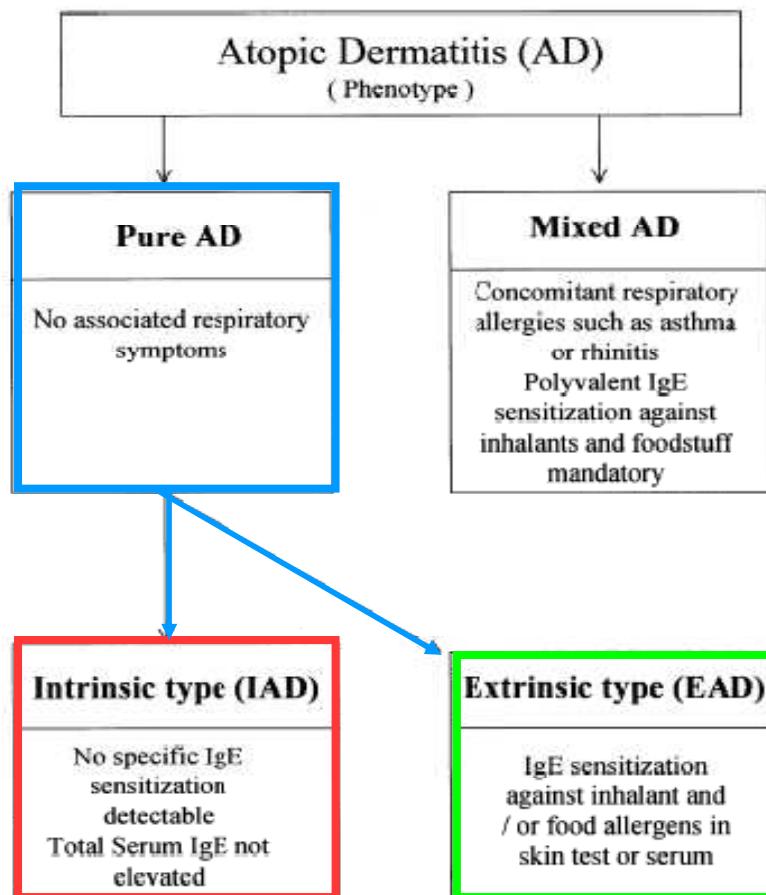
Alma Mater Studiorum -
Università di Bologna



❖ Quantificare la componente allergica nella DA



Associazione



On basis of results of accurate allergologic investigation by means of **skin tests** and **specific IgE determinations**, “pure” AD can be subdivided into subtypes:

- **extrinsic (EAD)**
- **intrinsic (IAD)**

Wüthrich B. *Akt Dermatol* 1983

Epidemiology, clinical features, and immunology of the “intrinsic” (non-IgE-mediated) type of atopic dermatitis (constitutional dermatitis)

Schmid-Grendelmeier, Wüthrich B. et al. *Allergy* 2001

Frequency of IAD in various studies (12)

Reference	No. of patients	Patients with IAD	Age (years)	Mean total serum IgE (kU/l)
Wuthrich et al. 1990	37	9 (24%)	14–60	62
Hochreutener 1991	40	15 (30%)	1–5	
Walker et al. 1993	25	5 (20%)	28 (17–56)	134±39
Somos et al. 1993	58	11 (16%)		71.4
Kagi et al. 1994	33	14 (42%)	35.5 (19–55)	77.7±88.6
Cabon et al. 1996	59	27 (45%)	5.2 (0–12)	89.3
Wedi et al. 1997	21	9 (43%)	39±17	22.2
Wuthrich et al. 1999	93	17 (18%)	37	<150
Schafer et al. 1999 *	2201	726 (25%)	5–14	76.7
Fabrizi et al. 1999	72	8 (11%)	1–25	n.g.
Akdis et al. 1999	1151	117 (10%)		<200
Oppel et al. 2000	69	7 (10%)	Adults	76.7±28.4

“Studio sulla predisposizione genetica alla dermatite atopica in età pediatrica” (Allergene2) con l’obiettivo di individuare caratteristiche genetiche peculiari dei due fenotipi di DA. (Unibo)

- **Pazienti:**

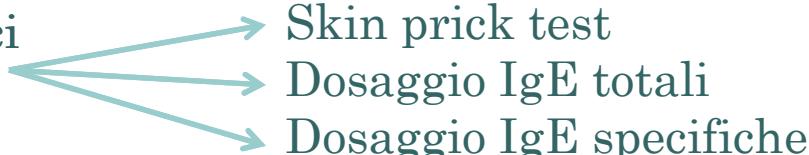
- ✓ Campione di 184 pazienti consecutivi provenienti dall’ambulatorio di Dermatologia Pediatrica e dall’ambulatorio di Allergologia Pediatrica
- ✓ Diagnosi di DA secondo i criteri di Hanifin e Rajka
- ✓ Età media 1^a visita: 2 anni e 10 mesi, range: 3 mesi - 14 anni
- ✓ Follow up medio: 8 anni, range: 3 - 13 anni

- **Valutazione clinica (I visita)
(objective SCORAD)**



- DA lieve ≤ 15
- DA moderata ≥ 16 e ≤ 39
- DA severa ≥ 40

- **Test allergometrici**



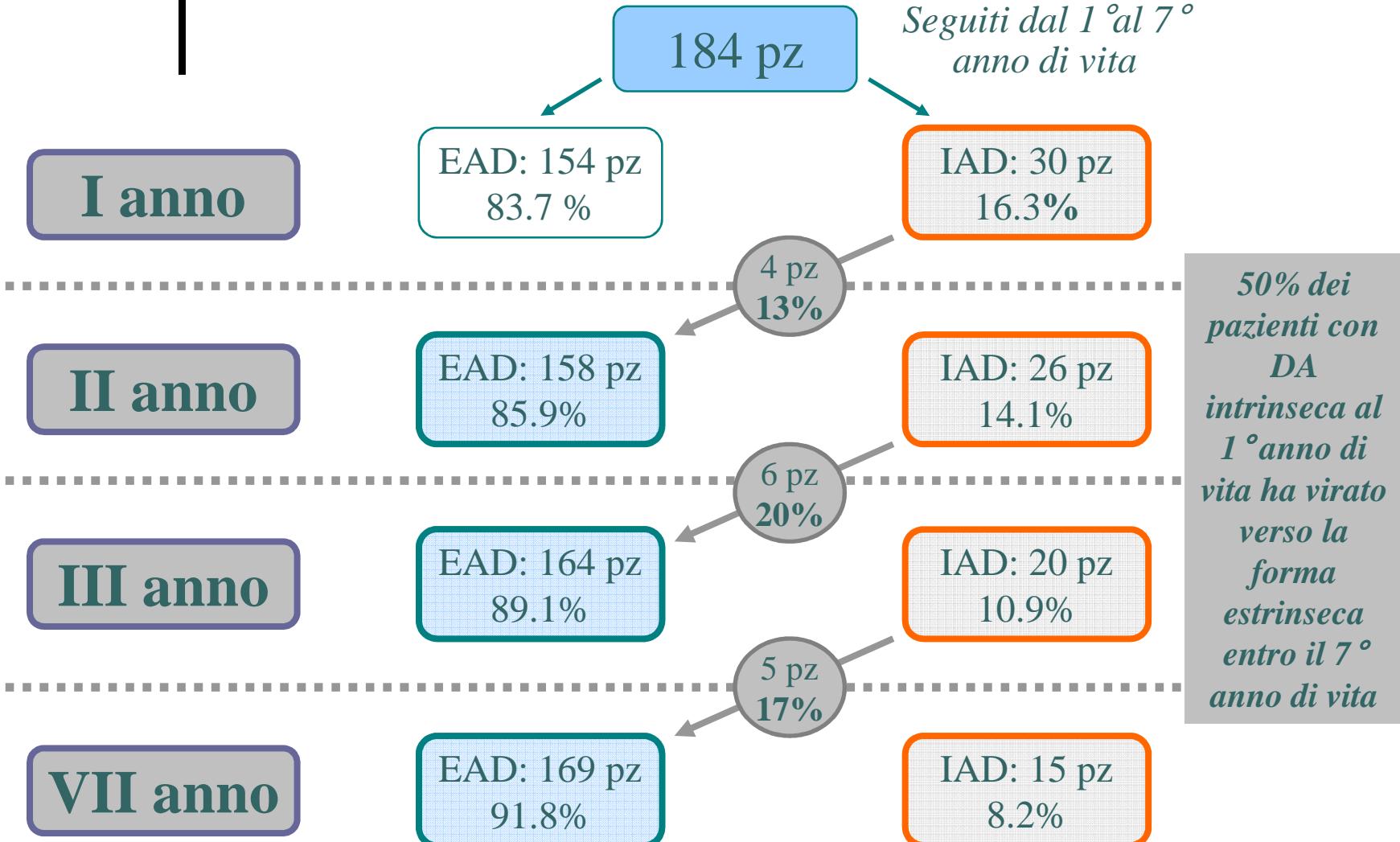
RISULTATI

QUANTIFICAZIONE DEL FENOTIPO ESTRINSECO – INTRINSECO *all'ultimo follow-up*

	DA estrinseca	DA intrinseca	Totale
Numero (%)	169 (92%)	15 (8%)	184
M/F (M %)	95/74 (M 56%)	7/8 (M 47%)	102/82 (M 55%)
Età media attuale (anni)	11	10	11
Fam. atopica grado)	(I 108 (63%))	8 (53%)	116 (63%)
Fam. DA (I+II grado)	23 (13%)	1 (6%)	24 (13%)
Allergia alimentare	125 (74%)	/	125 (68%)
Asma	62 (37%)	/	62 (34%)
Rinocongiuntivite	112 (67%)	/	112 (61%)



PASSAGGIO DA UN FENOTIPO ALL'ALTRO: INTRINSECO → ESTRINSECO



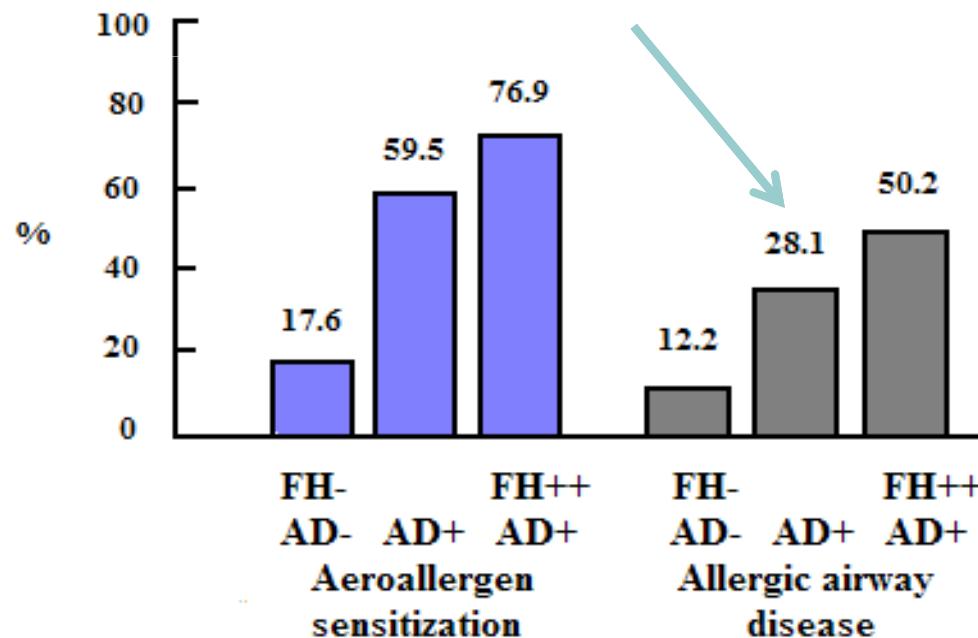


❖ Se rovesciamo la domanda:
quanta DA c'è nell'allergia?



Atopic dermatitis in early infancy predicts allergic airway disease at 5 years

- 1314 children of a German perspective birth cohort study MAS 90
- followed from birth up to 5 years of age
- Aeroallergen sensitization if IgEs >0.35 kU/L



Bergmann et al. *Clin Exp Allergy* 1998

Atopic dermatitis, extrinsic atopic dermatitis and the hygiene hypothesis: results from a cross-sectional study

ISAAC phase II

→ 11094 bambini in età scolare (6-10 anni- Monaco)



SPT inalanti effettuati su 6174 bambini:

- 33% EAD (compresi asmatici e rinitici)
- 23% EAD (esclusi asmatici e rinitici)

- Non testati allergeni alimentari
- IgE tot. e specifiche non dosate

Zutavern et al. *Clin Exp Allergy* 2005

The Prevalence of Atopic Dermatitis, Asthma, and Allergic Rhinitis and the Comorbidity of Allergic Diseases in Children- (South Korea)

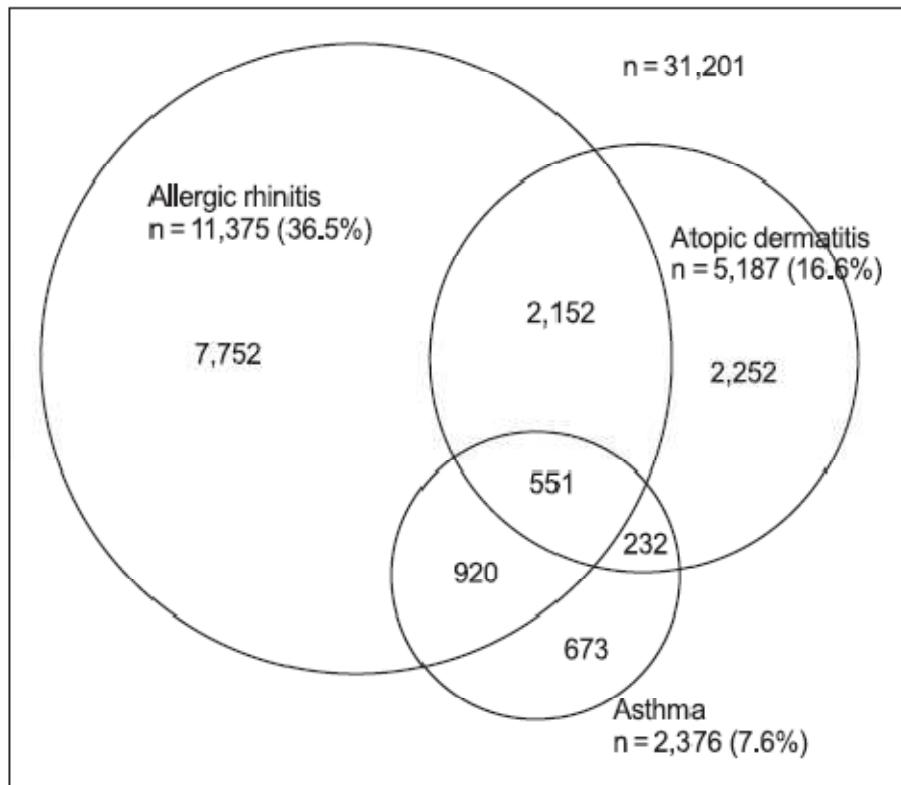


Figure 1. Venn diagrams illustrating the associations among the symptoms of atopic dermatitis, asthma, and allergic rhinitis in the past 12 months.

STUDY DESIGN

- 31,201 children studied
- age: 0-13 yrs
- ISAAC questionnaire

In AR = 23.7% AD
In Asthma= 33% AD

In AD = 21.3% Asthma e/o AR
AD = 37.5% Asthma+AR



○ Associazione, esacerbazione
o rapporto causale con
alimenti/inalanti ?





Review: Dietary exclusions for established atopic eczema 2008

Egg and cows milk exclusion diets

Six RCTs, three of which were cross-over studies (Atherton 1978; Cant 1986; Neild 1986) and three were parallel studies (Isolauri 1995; Lever 1998; Niggemann 2001)

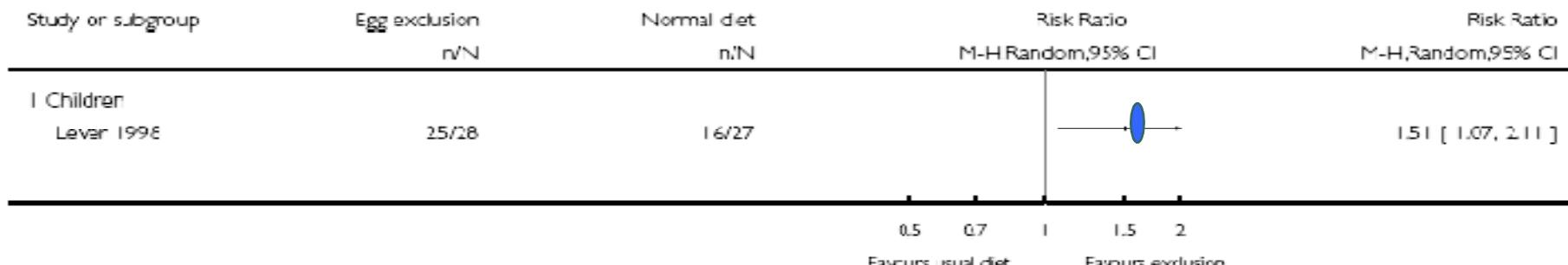
- Egg and cow's milk exclusion diet (with soya substitute) vs egg and cows' milk (Atherton 1978)
- Egg and cow's milk exclusion diet (with soya substitute) vs egg and cows' milk in breastfeeding mothers (Cant 1986)
- Whey hydrolysate vs amino acid derived formula (Isolauri 1995)
- Egg and cow's milk exclusion diet (with soya substitute) vs normal diet (Neild 1986)
- General advice on care of atopic eczema and specific advise about egg exclusion diet vs general advise from dietician only (Lever 1998)
- Amino-acid-based (AA)formula vs extensively hydrolysed whey formula (Niggemann 2001)



Review: Dietary exclusions for established atopic eczema

Egg exclusion vs normal diet

OUTCOME 1-2: Number of pts whose body surface are improved -Change in body surface area at 6 weeks



OUTCOME 3: Change in severity score – end of treatment



Bath-Hextall FJ *et al.* 2008



Food allergen-free diet in severe atopic dermatitis related to food allergy. Marie-Helene G, Anyfantakis V, Guillet G. *Indian J Dermatol Venereol Leprol* 2011;77:332-3

Food allergy was suspected on the basis of a detailed history by skin prick tests (SPT), with specific standard extracts or fresh food allergens.

Patients with positive SPT were further evaluated for specific serum IgE

Food allergy was confirmed by elimination and later by double-blind placebo-controlled food challenges, prior to initiation of the appropriate dietary intervention.

Food allergy was related to egg in 67%, peanut in 54%, milk in 30%, sea shells in 26.9%, wheat flour in 16.8%, fish in 11.2%, soy in 8.9%, mustard in 4.5%.



Table 1: Effect of specific food allergen-free diet on the clinical score, topical corticosteroid consumption, and total IgE level in a prospective five-year follow-up of 97 children with food allergy triggered flares of AD

	Inclusion Day	3 months	1 year	3 years	5 years
Clinical Score	53.6	-78% (11.94)	-70% (16.1)	-75.6% (13)	-76% (12)
Topic Steroids	30g	- 84% (5g)	- 73% (8g)	-75% (7g)	-90% (3g)
IgE level (kU/l)	1272	1022	943	720	340

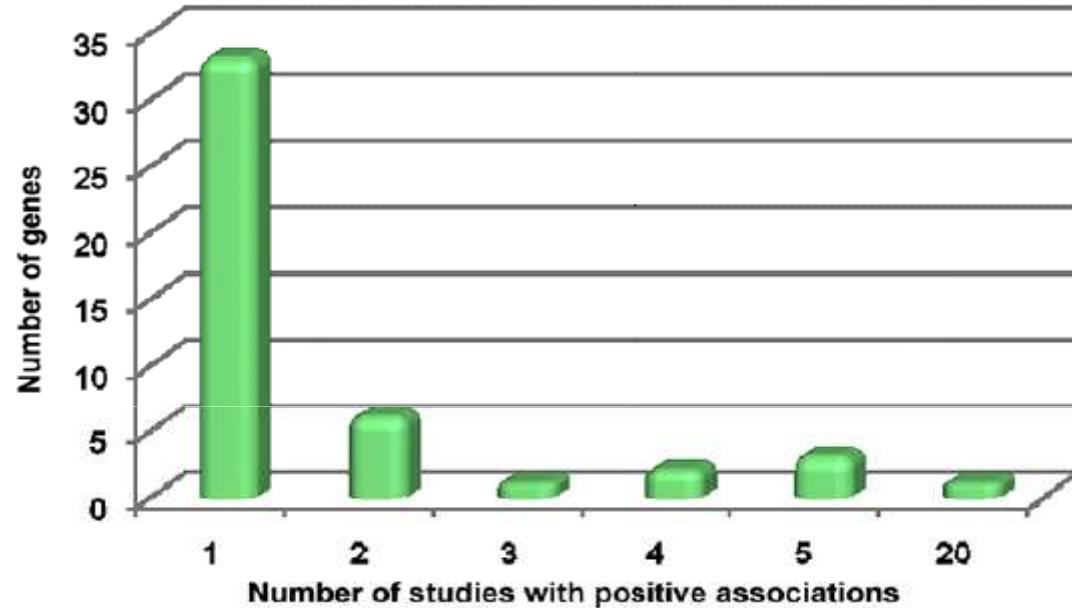
Guidelines for treatment of atopic eczema (atopic dermatitis) 2012 Sep;26(9):1176-1193

Recomendations:

Patients with moderate to severe AE should observe a diet eliminating those foods that elicited clinical early or late reactions upon controlled oral provocation tests (2bB)



Geni associati alla DA in almeno uno studio



ADAM33	IL12B*
BDNF*	IL12RB1
BFL1	IL5
CARD12	IRF2
CARD15*	NAT2*
COL29A1	PHF11
CSF2*	SCCE
CSTA	SMPD2
CTLA4	SOCS3
CYSLTR1	ST2
EOTAXIN*	TAP2
FCER1B	TGFB1
GATA3	TIM4
GSTM1	TLR2
HNMT	TLR9
IL10*	TOLLIP
	VEGF

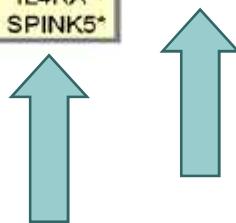
CD14*
DEFB1
GSTM1
IL18*
NOD1
TIM1

RANTES*
IL13*

CMA1
IL13*

IL4*
IL4RA*
SPINK5*

FLG*

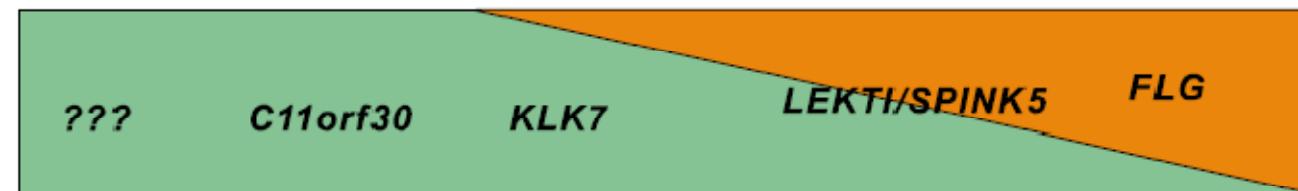


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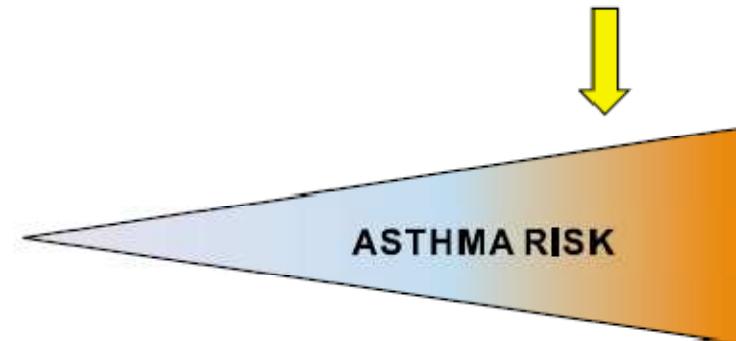
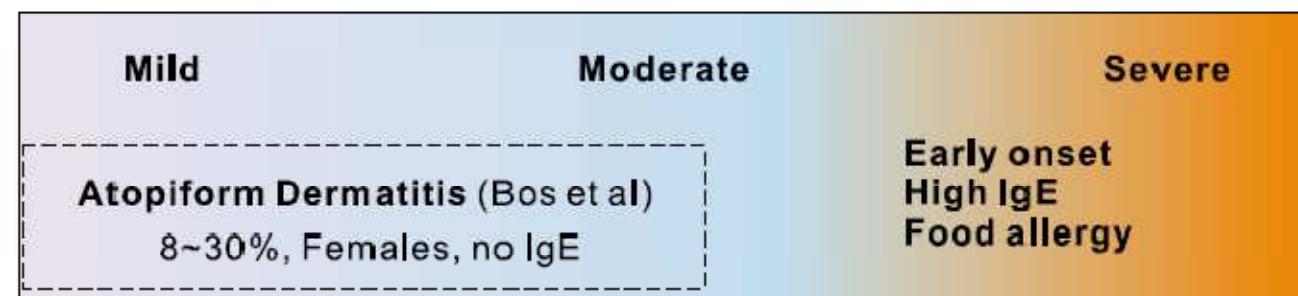
Barnes. JACI 2010



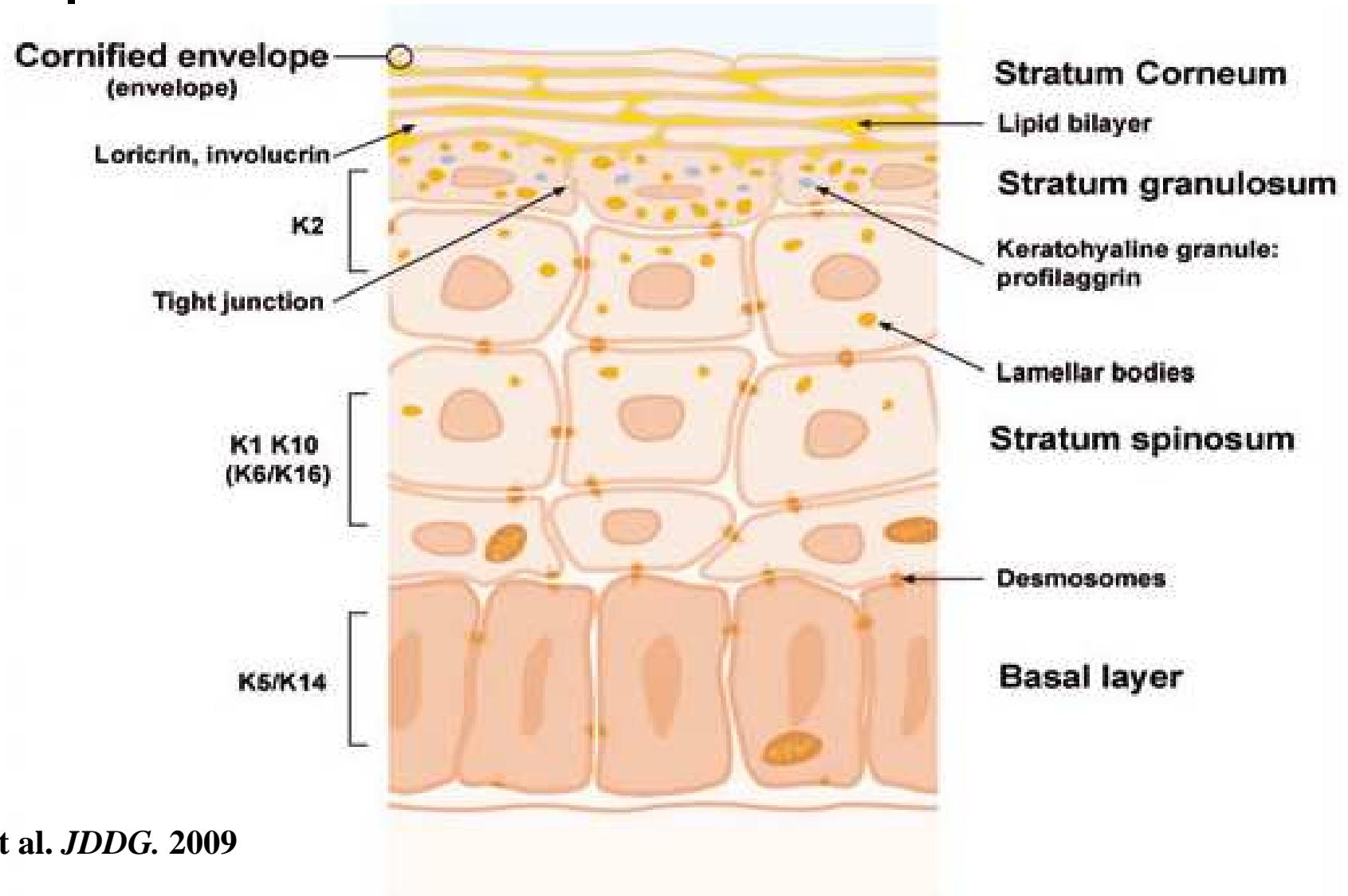
GENOTIPO



FENOTIPO



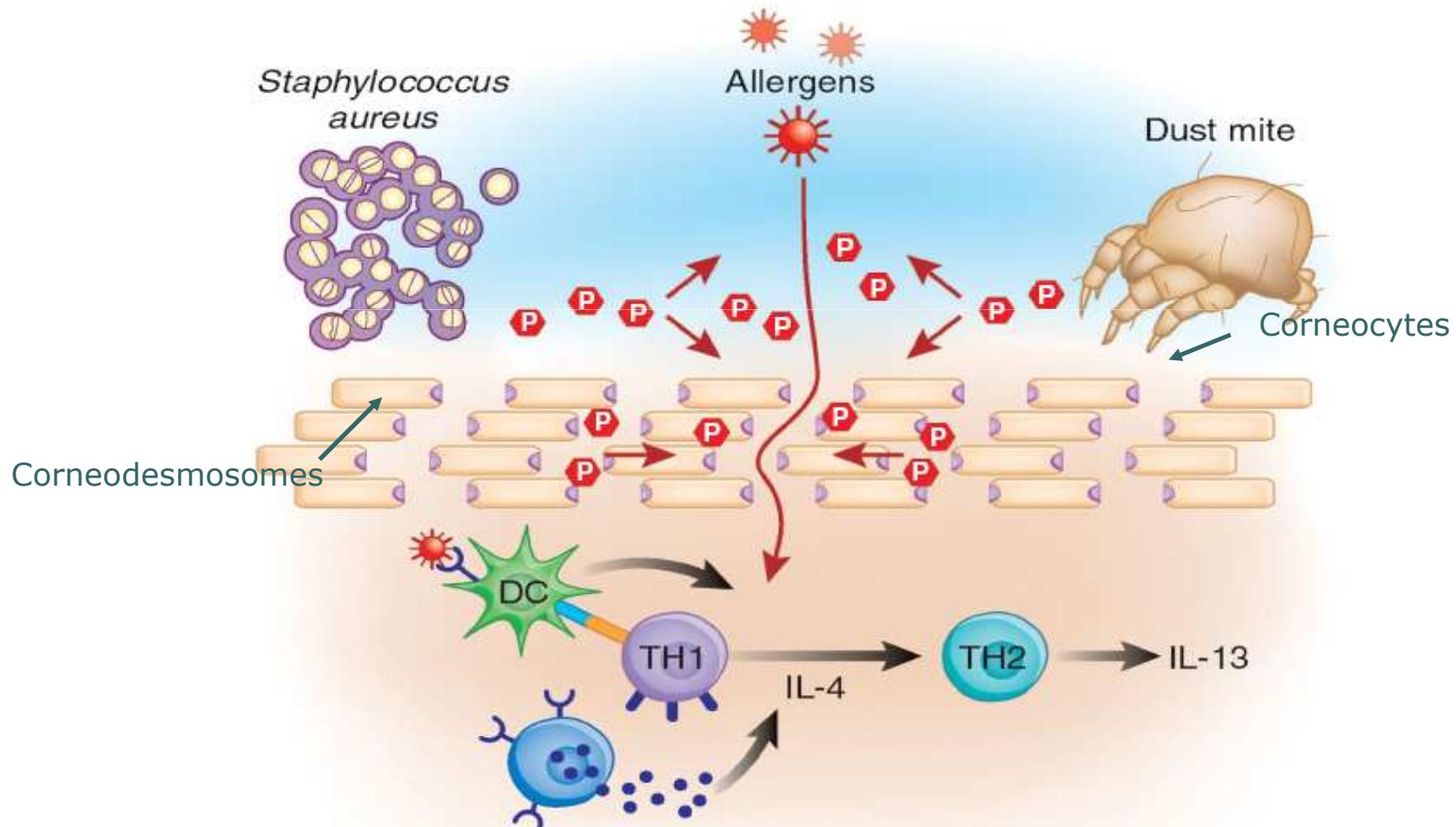
Il processo di differenziazione epidermica



Epidermal Barrier Dysfunction in Atopic Dermatitis



P = proteases exogenous



Cork et al. *J Invest Dermatol.* 2009



Trattare la cute anche in fase di remissione

EMOLLIENZA PASSIVA		EMOLLIENZA ATTIVA
DIRETTA	INDIRETTA	
Apporto di acqua Effetto igroscopico Emulsioni O/W	Apporto di lipidi Effetto occlusivo Emulsioni W/O	Miglioramento delle proprietà di barriera dello strato corneo
		Effetto nutritivo



L' EMOLIENTE VA APPLICATO:

- più volte al giorno con regolarità
- su tutta la superficie corporea
- entro 3 minuti dopo il bagno
- evitare le parti molto infiammate o sovra infettate



CONTROLLO DELL'INFIAMMAZIONE

Terapia topica



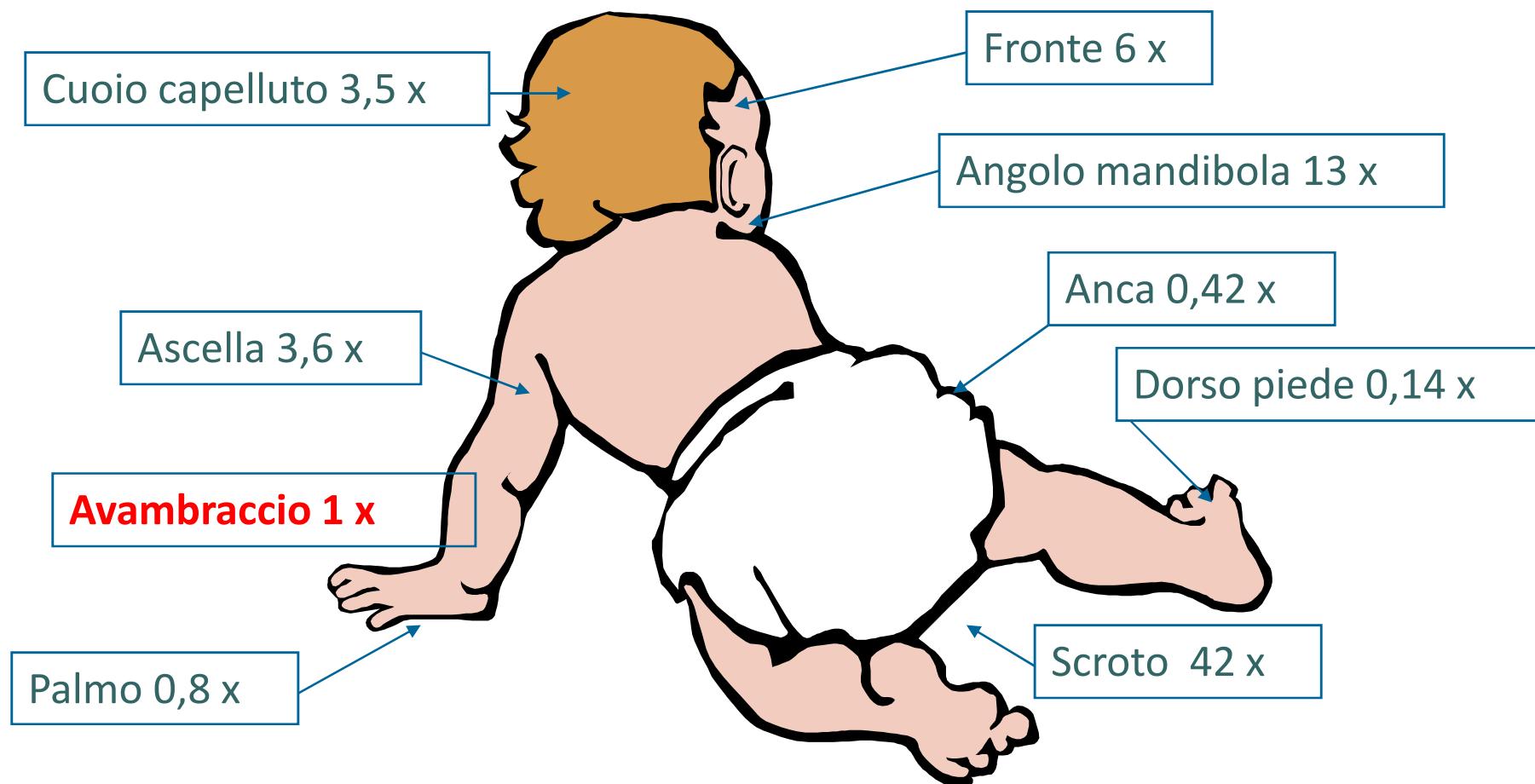
Corticosteroidi
Tacrolimus
Pimecrolimus

Terapia sistemica



(Antistaminici)
Corticosteroidi
Ciclosporina A
Azatioprina, Etc

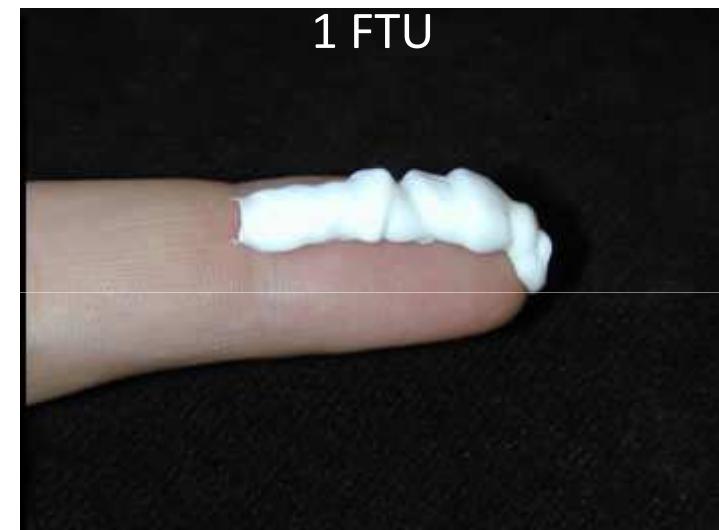
COEFFICIENTE DI ASSORBIMENTO NELLE DIVERSE SEDI CORPOREE





FINGER-TIP UNIT O “FALANGETTA”

- 1 FTU una mano o
regione genitale
- 2 FTU viso o un
piede
- 3 FTU un arto
superiore
- 6 FTU un arto
inferiore
- 14 FTU tronco



Utilizzo Max : 15-20 gr di crema alla settimana (1 tubo circa) = 40 FTU



DOSAGGIO MASSIMO MENSILE CONSIGLIATO

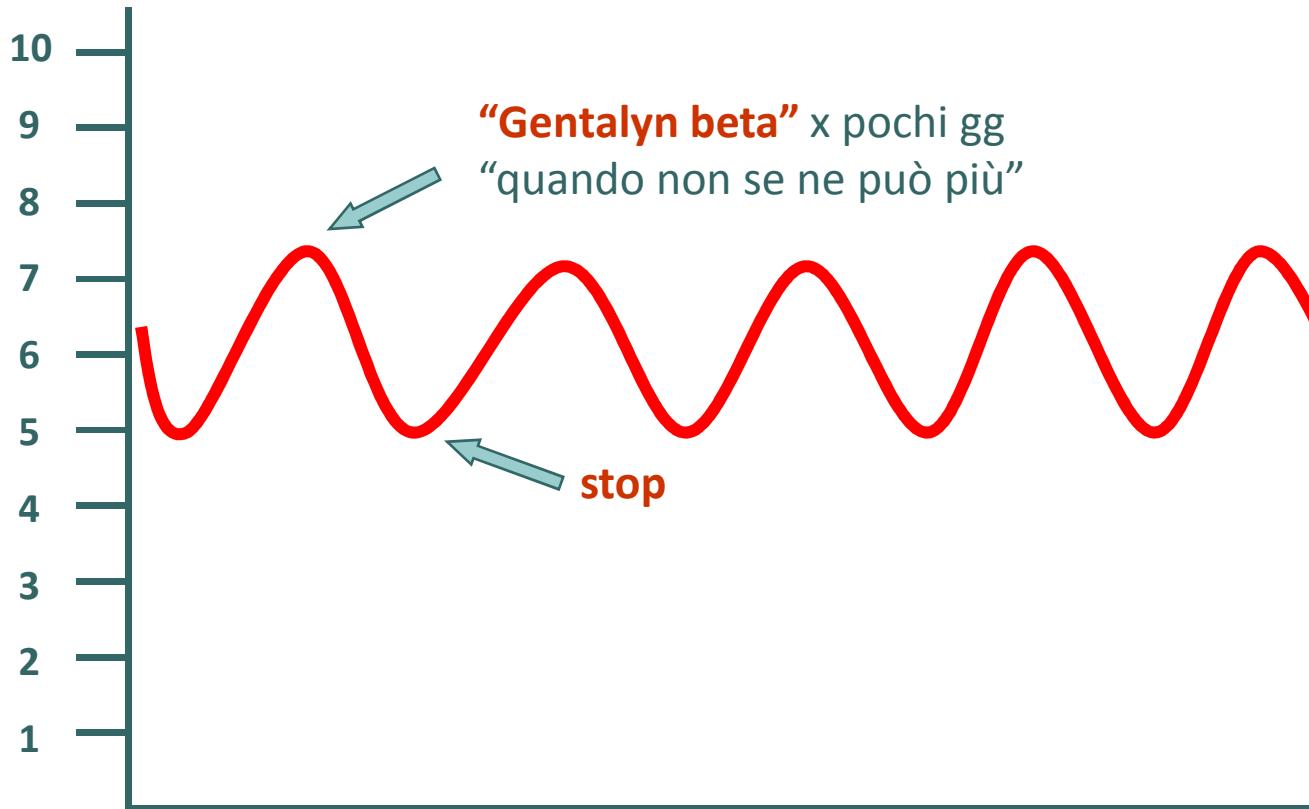
- 15 gr nel neonato e nel 1° anno di vita
 - $\frac{1}{2}$ tubo di crema
- 30 gr nel bambino
 - 1 tubo di crema
- 60-90 gr nell'adolescente e nell'adulto
 - 2-3 tubi di crema

LO SCHEMA PERDENTE

(reactive management)



gradi della DA



Courtesy G. Longo

LO SCHEMA VINCENTE

(proactive management)



gradi della DA

10
9
8
7
6
5
4
3
2
1

steroide topico
antibiotico antistafilo per 10 gg
cortisone per os per 4-14 gg

“applicazione continua di emollienti”

steroide topico alla sera
per 2 gg consecutivi settimana



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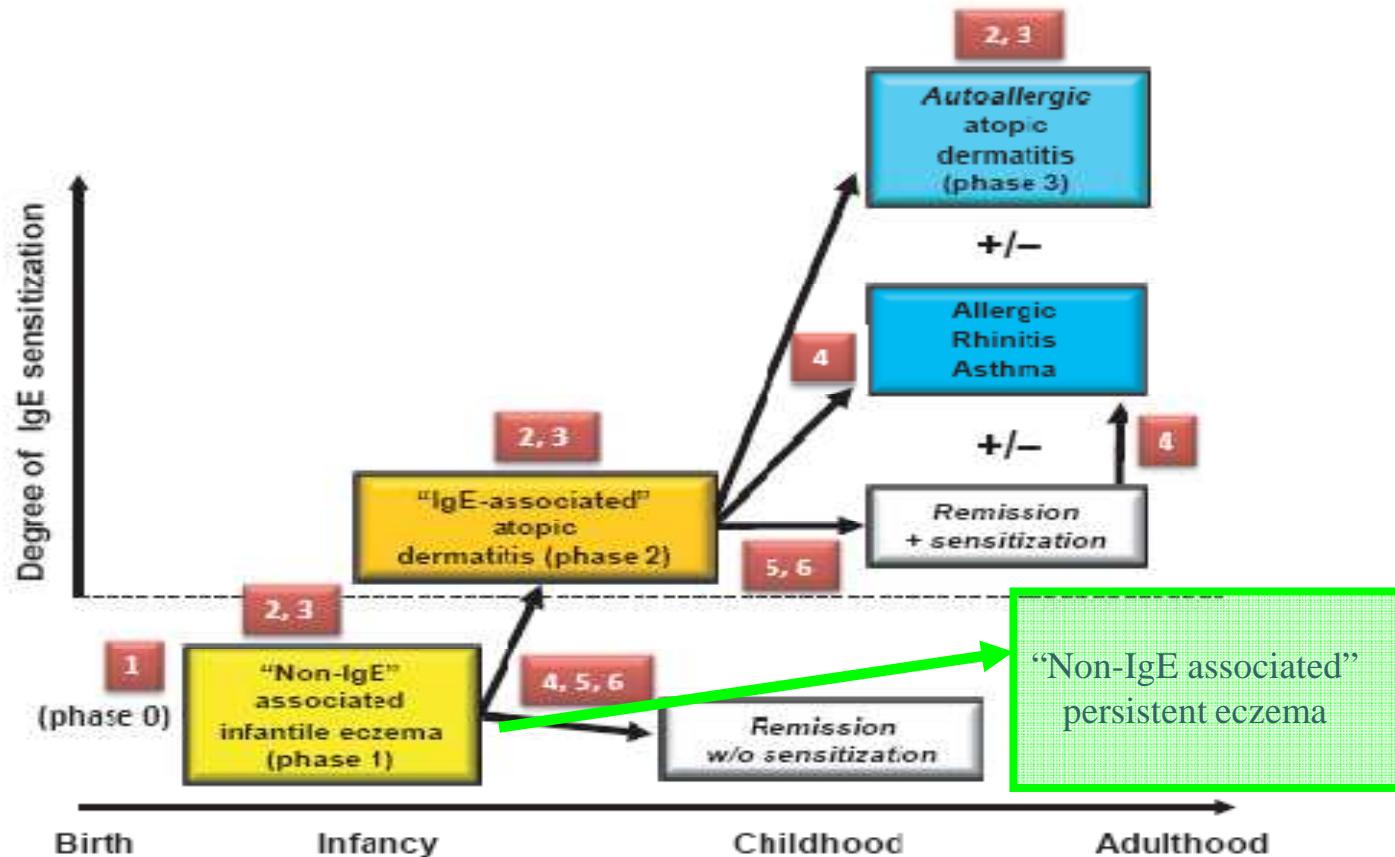
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Riepilogo finale

Dieta, quando opportuna, e terapia topica

Conclusioni



Modificato da: Bieber et al. *Allergy* 2012



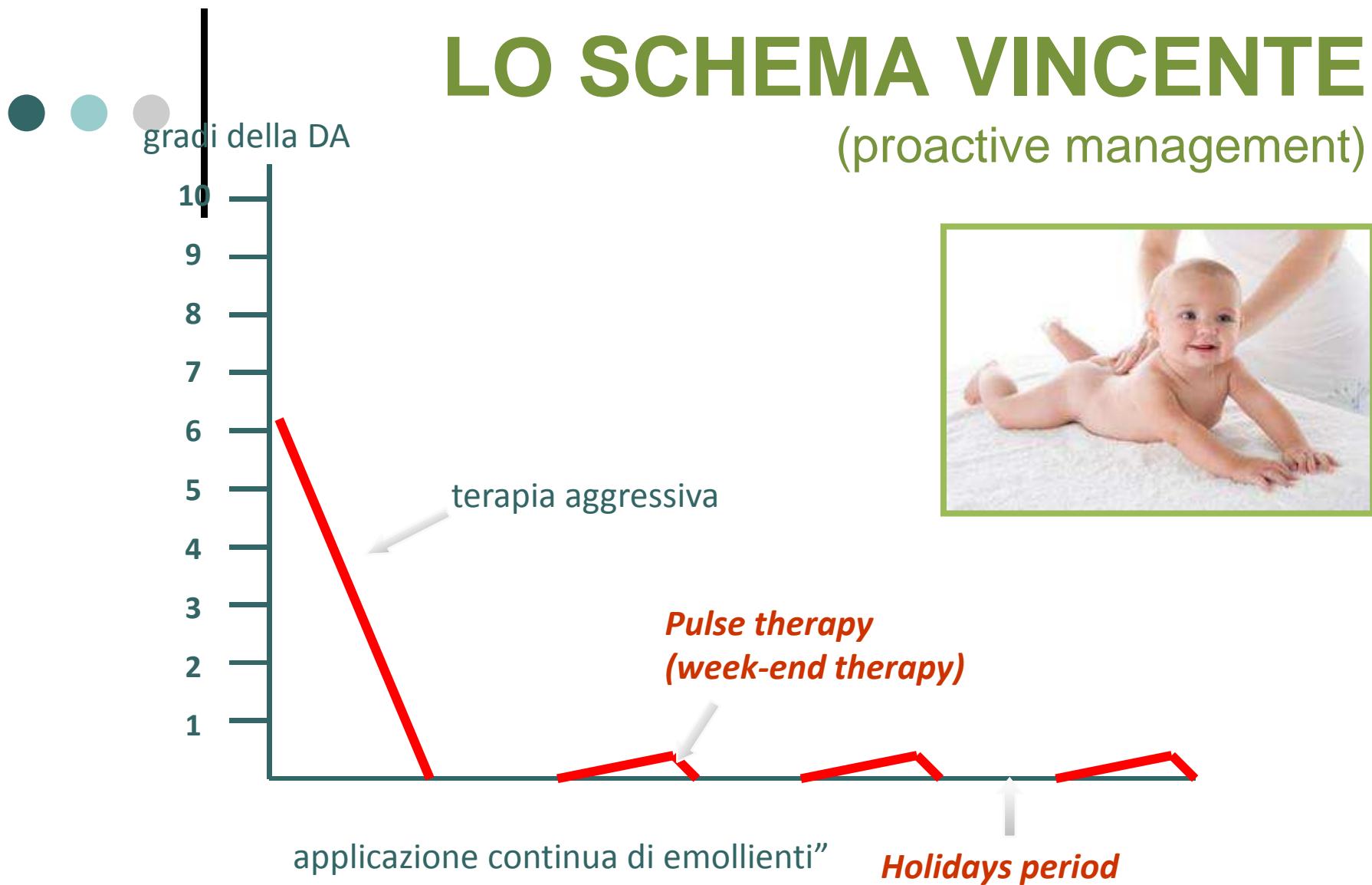
TERAPIA SISTEMICA

*La terapia sistemica solo ai casi
più severi e resistenti.*



LO SCHEMA VINCENTE

(proactive management)





Riepilogo finale

- Possibili esacerbazioni correlate alla allergia
- Test allergici vanno eseguiti
- La dieta può essere opportuna nei soggetti con forme moderato-severe dove ci sia una evidenza di legame mediante challenge
- Difetto di barriera
- Idratare, idratare, idratare
- Non aver paura del cortisone topico

The dietary paradox in food allergies: yesterday's mistakes, today's evidence and lessons for tomorrow

E, Berti, Radillo, O, Matarazzo, L, Vent

Ventura A, Longo G Curr Pharm Des. 2012 Jun 21.

- During the last decades the prevalence of food allergies has significantly increased among children and antigen avoidance still remains the standard care for the management of this condition.

Most reactions are IgE-mediated with a high risk of anaphylaxis requiring emergency medical intervention in case of inadvertent ingestion.

- Recent studies showed that continuous administration of the offending food, rather than an elimination diet, could promote the development and maintenance of oral tolerance.
- Indeed, intestinal transit of food proteins and their interaction with gut-associated lymphoid tissue (GALT) is the essential prerequisite for oral tolerance.
- On the contrary, low-dose cutaneous exposure to environmental foods in children with atopic dermatitis and altered skin barrier facilitates allergic sensitization.
- The timing and the amount of cutaneous and oral exposure determine whether a child will have allergy or tolerance.
- Furthermore, previous preventive strategies such as the elimination diet during pregnancy and breastfeeding, prolonged exclusive breastfeeding and delayed weaning to solid foods did not succeed in preventing the development of food allergy.
- On the other hand, there could be an early narrow window of immunological opportunity to expose children to allergenic foods and induce natural tolerance.
- Finally, the gradual exposure to the offending food through special protocols of specific oral tolerance induction (SOTI) may be a promising approach to a proactive treatment of food allergy.

22726112

[PubMed - as supplied by publisher]

The natural history of food sensitization in children with atopic dermatitis and the prognostic role of specific serum IgE

Fig.4A.

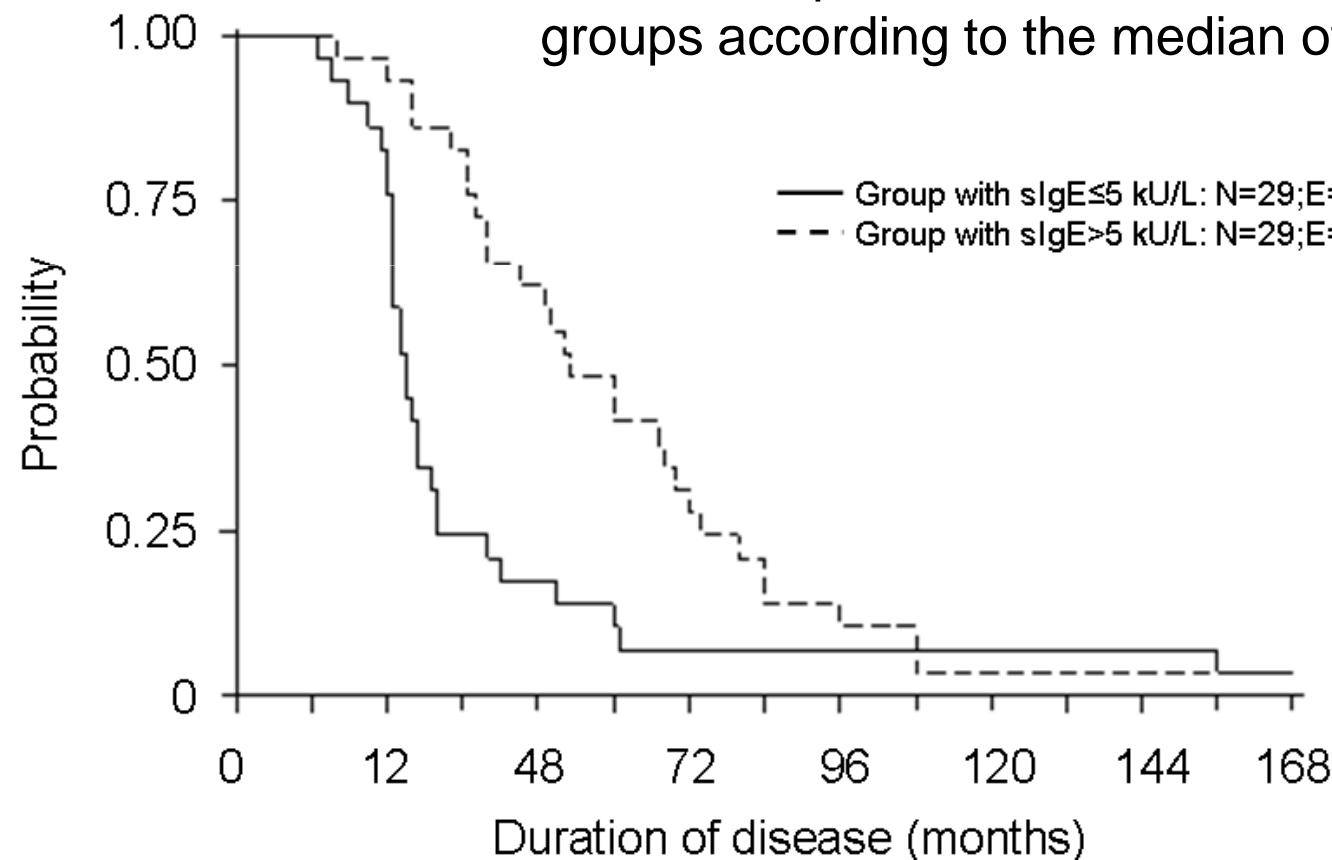


Fig.4A. Curve for duration of the disease stratified according to the **hen's egg white IgE** levels. The patients were divided into two groups according to the median of sIgE (5 U/L).

N= number of patients, E= events; Log-rank p = 0.0023

 [Cochrane Database Syst Rev.](#) 2012 Feb 15;2:CD005205.

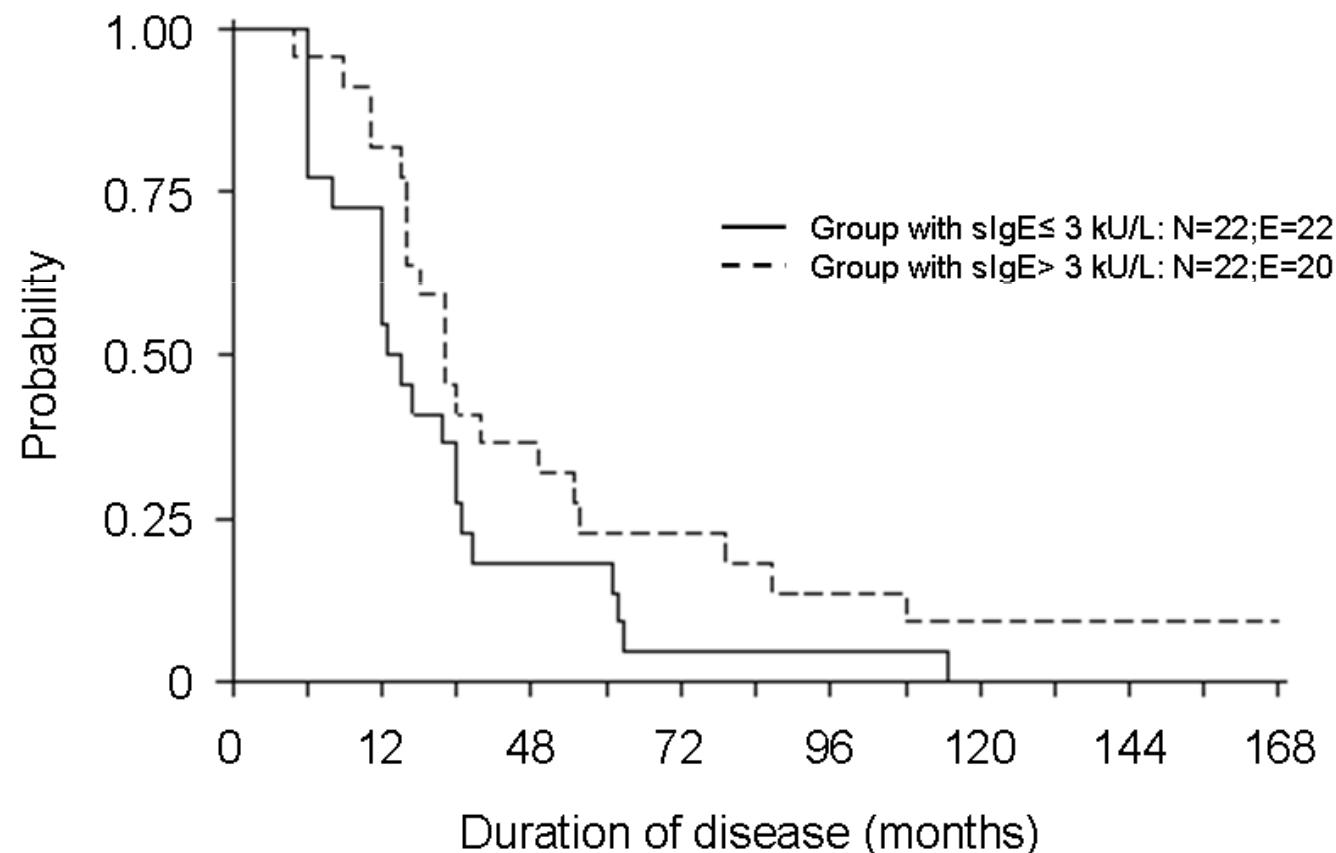
Dietary supplements for established atopic eczema.

[Bath-Hextall FJ](#), [Jenkinson C](#), [Humphreys R](#), [Williams HC](#).

- fish oil versus olive oil or corn oil placebo.
- oral zinc sulphate compared to placebo,
- selenium versus selenium plus vitamin E versus placebo,
- vitamin D versus placebo, vitamin D versus vitamin E versus vitamins D plus vitamin E together versus placebo,
- pyridoxine versus placebo,
- sea buckthorn seed oil versus sea buckthorn pulp oil versus placebo, hempseed oil versus placebo,
- sunflower oil (linoleic acid) versus fish oil versus placebo, a
- DHA versus control (saturated fatty acids of the same energy value).
- Two small studies on fish oil suggest a possible modest benefit, but many outcomes were explored. A convincingly positive result from a much larger study with a publicly-registered protocol is needed before clinical practice can be influenced.
- **AUTHORS' CONCLUSIONS:**
- There is no convincing evidence of the benefit of dietary supplements in eczema, and they cannot be recommended for the public or for clinical practice at present. Whilst some may argue that at least supplements do not do any harm, high doses of vitamin D may give rise to serious medical problems, and the cost of long-term supplements may also mount up.

Fig.4B.

Fig.4B. Curve for duration of the disease stratified according to the **cow's milk IgE** levels. The patients were divided into two groups according to the median of sIgE (3kU/L).



N= number of patients, E= events; Log-rank p = 0.095