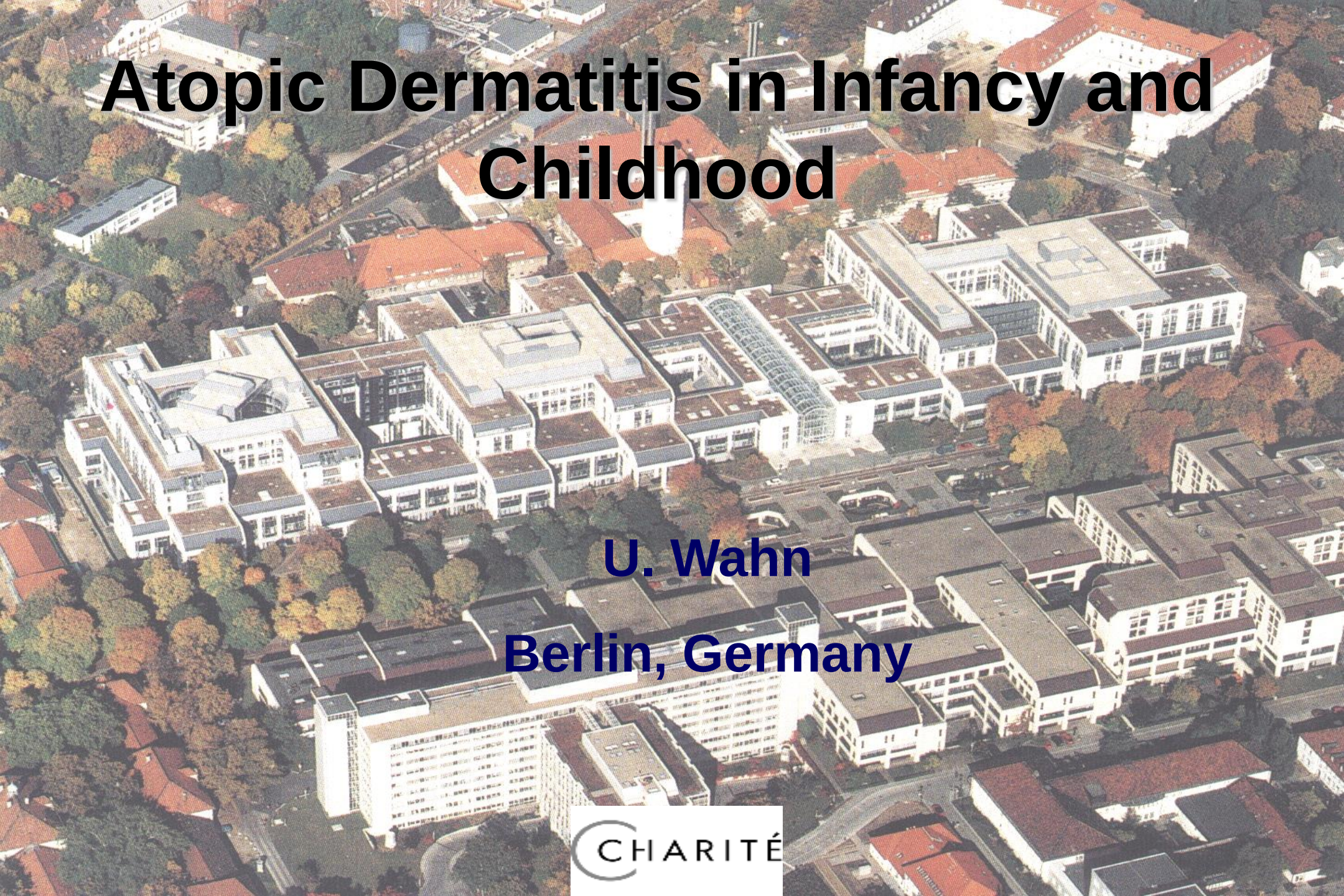
Atopic Dermatitis in Infancy and Childhood

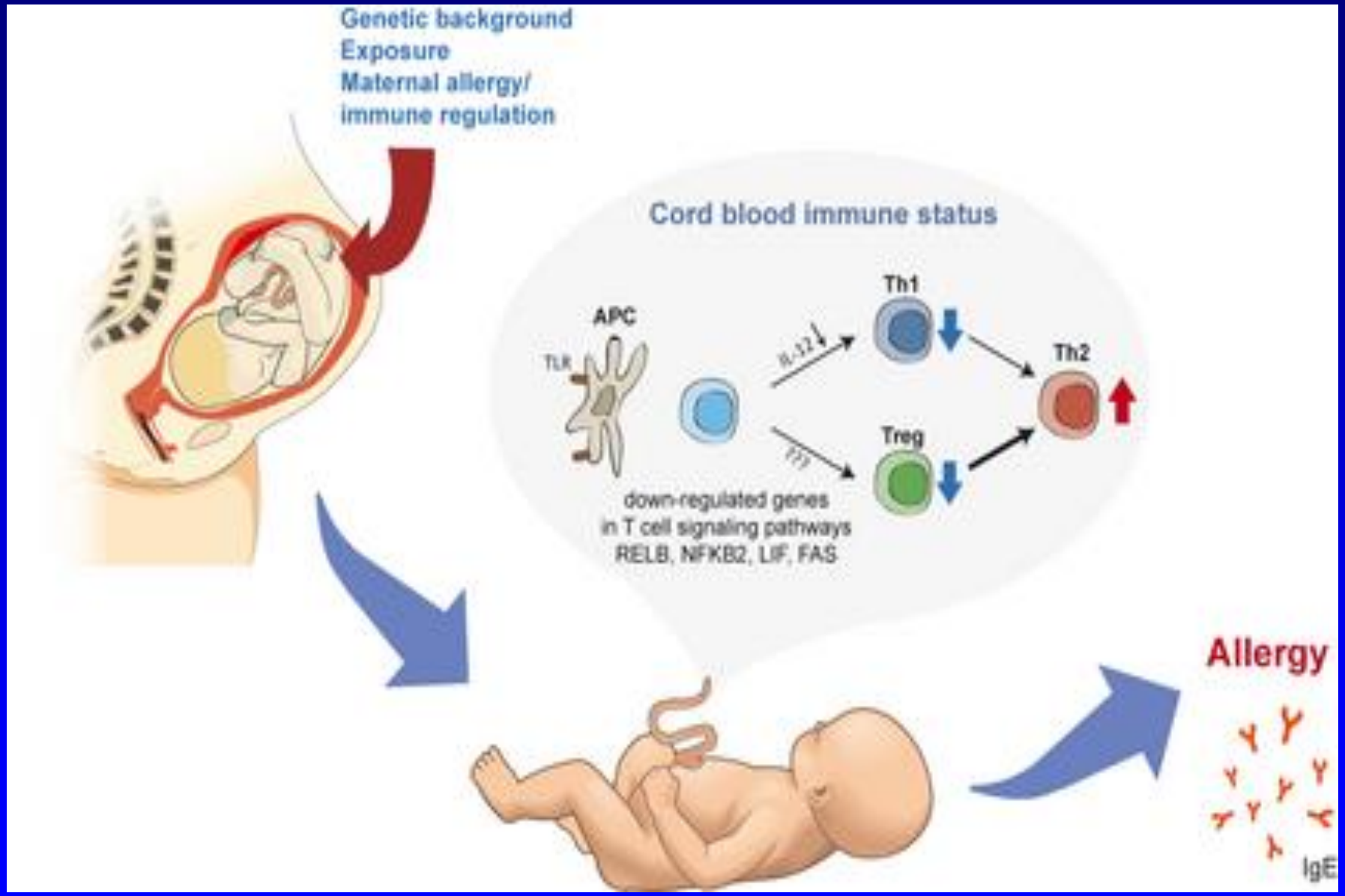


U. Wahn

Berlin, Germany

CHARITÉ

The atopic infant



MAS birth cohort: Multicenter Allergy Study

n = 1314 1/3 with high CB-IgE and/or atopy in the family

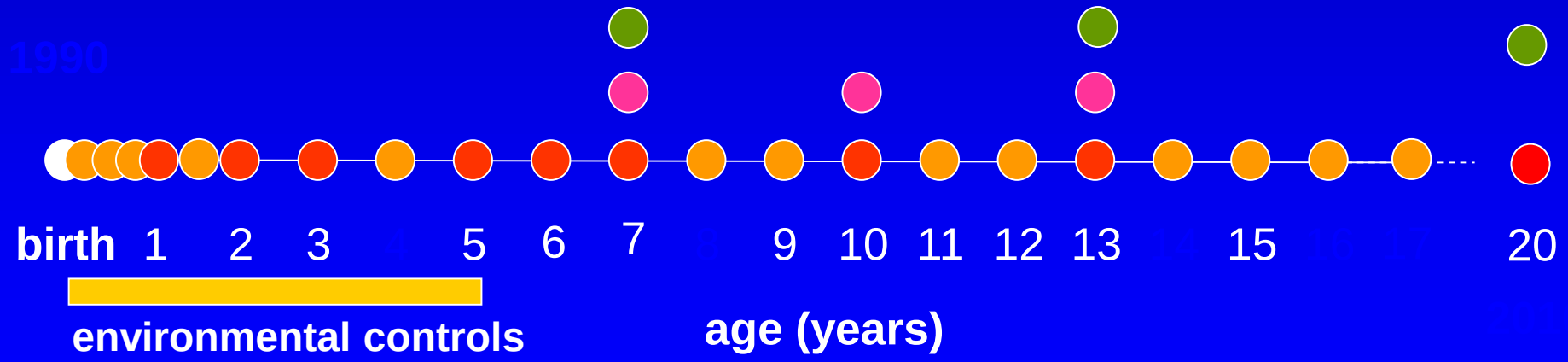
IgE-Ab vs
mites, cat, dog, grass, birch
milk, egg, soy, wheat
total IgE

telephone interview

id. + direct exam + blood drawing

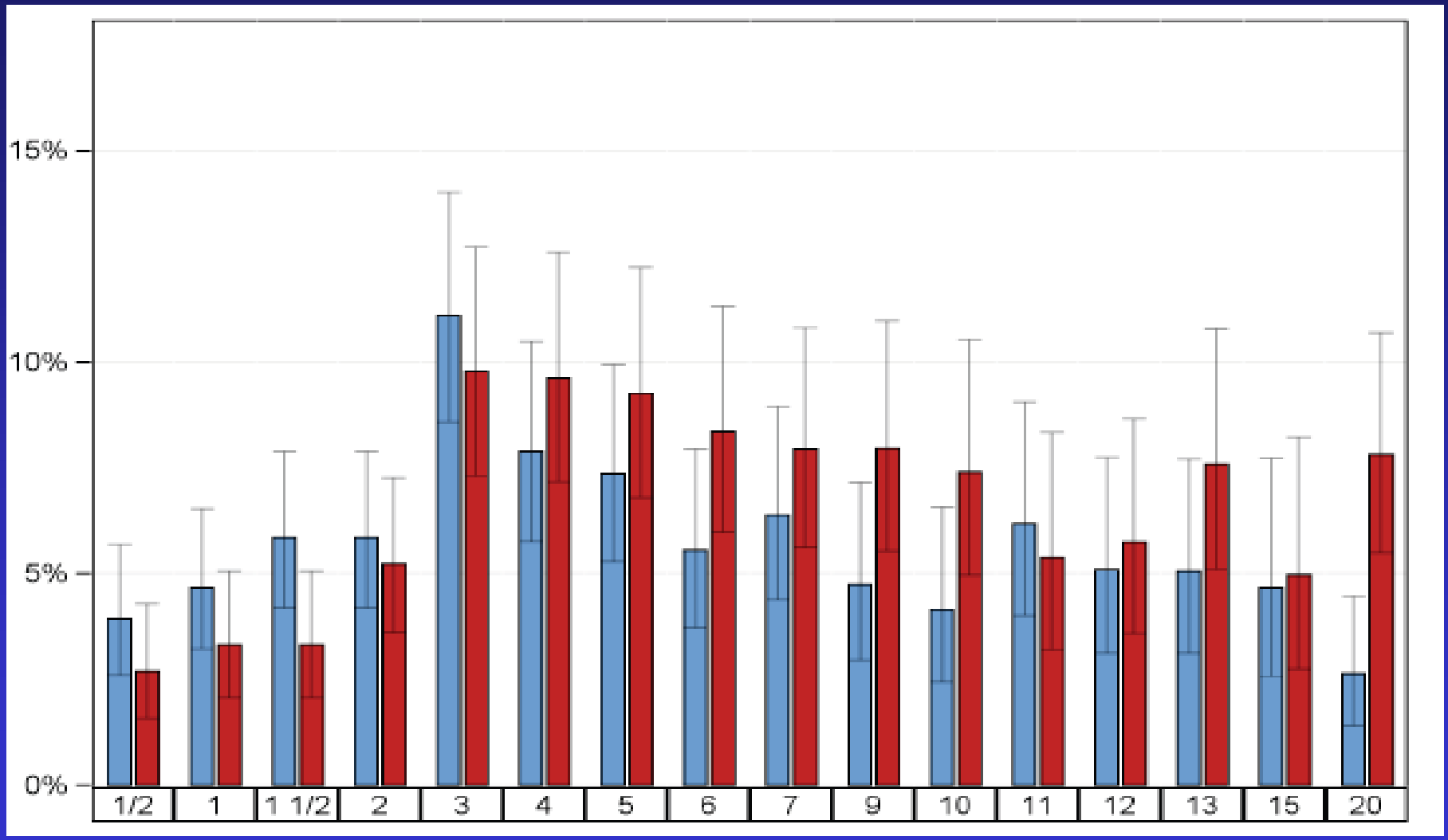
lung function test

bronchial provocation test
(histamine/cold air)



Prevalence of atopic eczema during the last 12 months according to age and sex

Grabenhenrich et al; in preparation

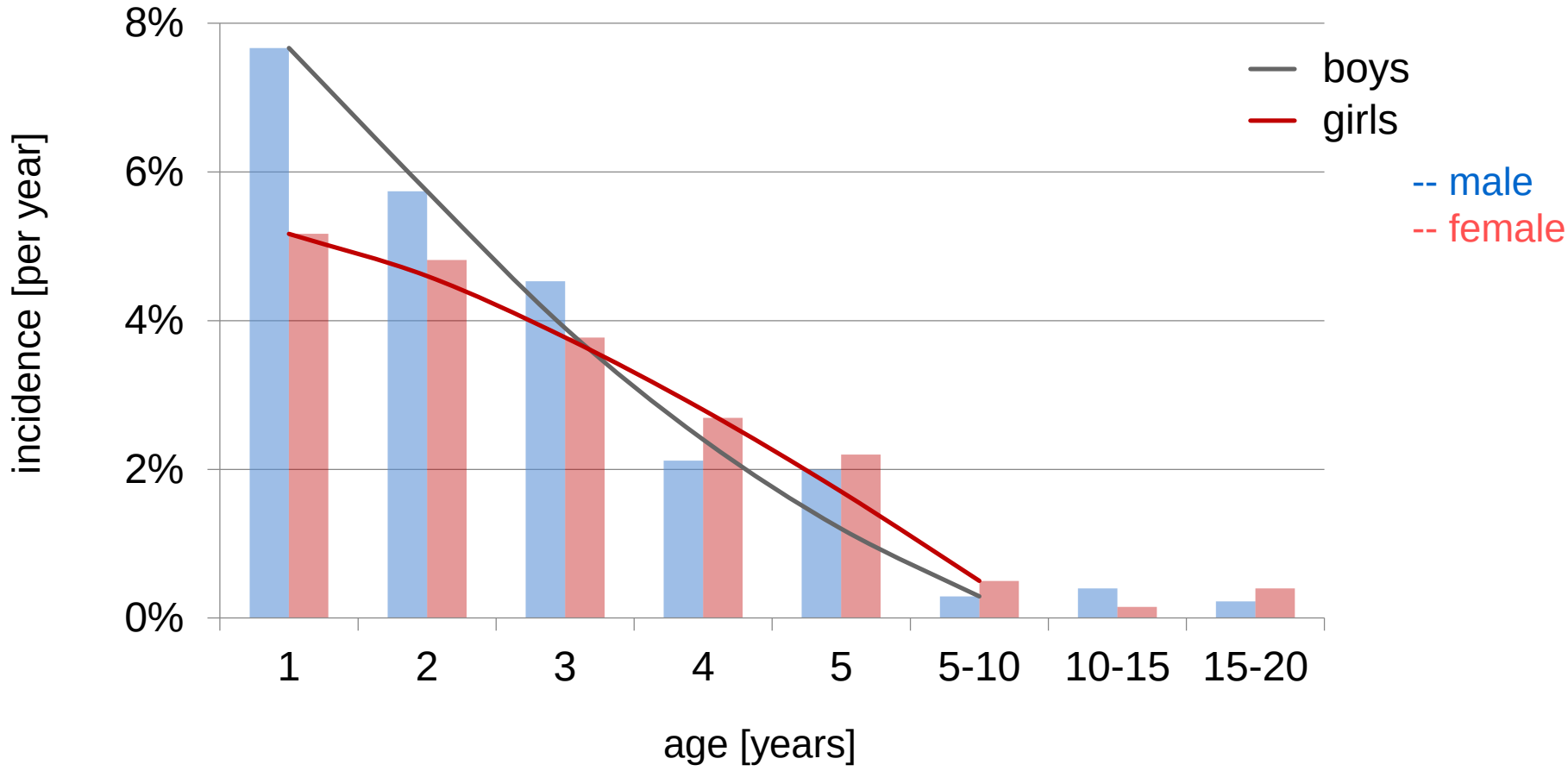


Early life predictors of eczema

				Hazard Ratio	CI (Wald)
Atopy in family	1 or 2	**vs.**	0 atopic parents	**1,35***	**[1.05;1.73]**
Early sensitization	< 0.35 kU/l sensitized	**vs.**	Not sensitized	**2,67****	**[2.02;3.53]**
Sex	male	**vs.**	female	1.03	[0.81;1.31]
Education	low	**vs.**	medium/high	**0.68**	**[0.48;0.96]**
Living environment	village	**vs.**	city	0,77*	[0.55;1.08]
Age of mother	<25	**vs.**	>= 25 years	0,83*	[0.56;1.24]
Cord blood cotinin	>=5	**vs.**	<5 ng/ml	0,96*	[0.65;1.40]

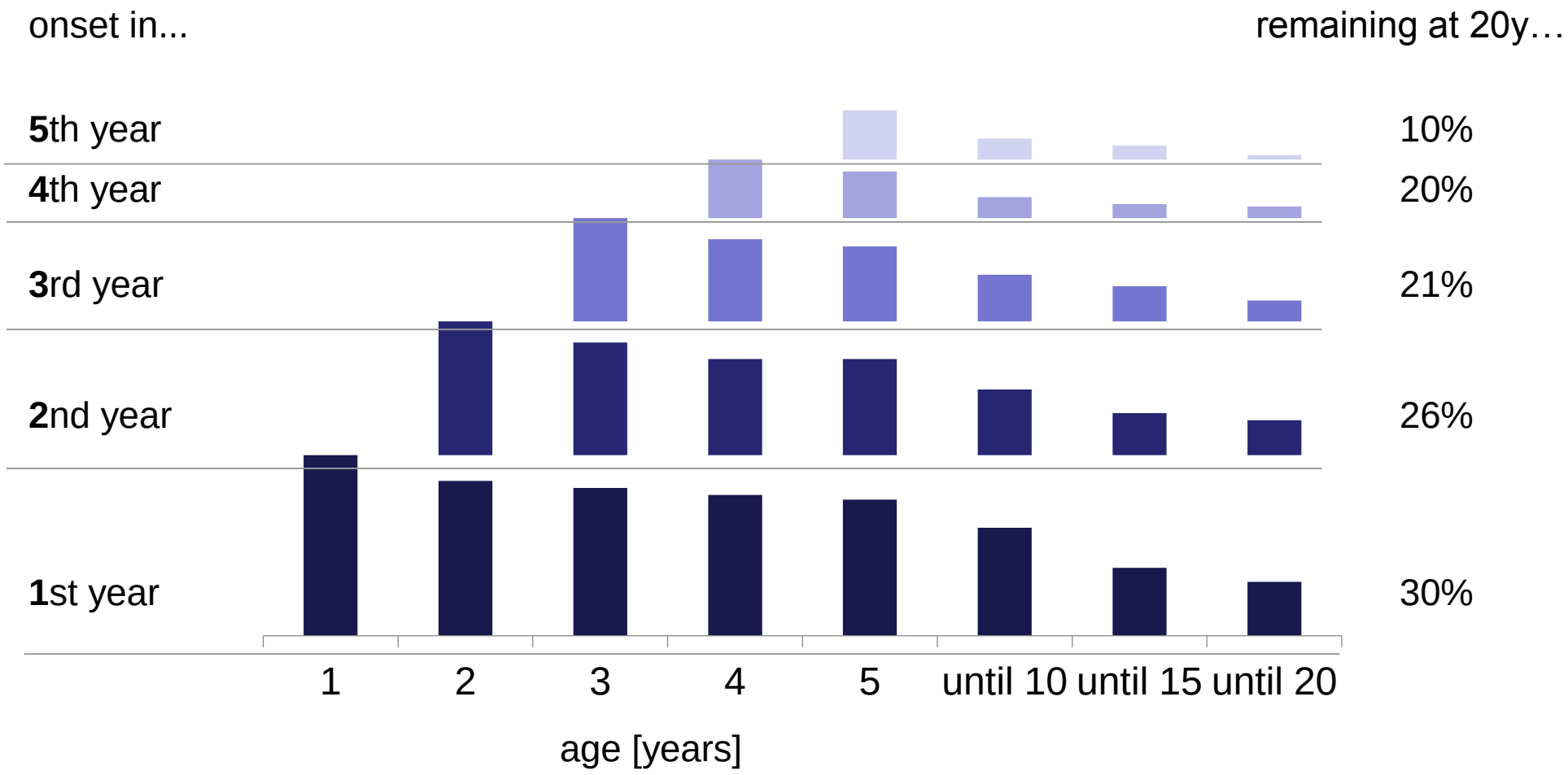
* adjusted for educational status of parents, ** for all other factors, proportional Hazards (PH) model, CI: 95% confidence interval

Eczema: new onset in last 12 months



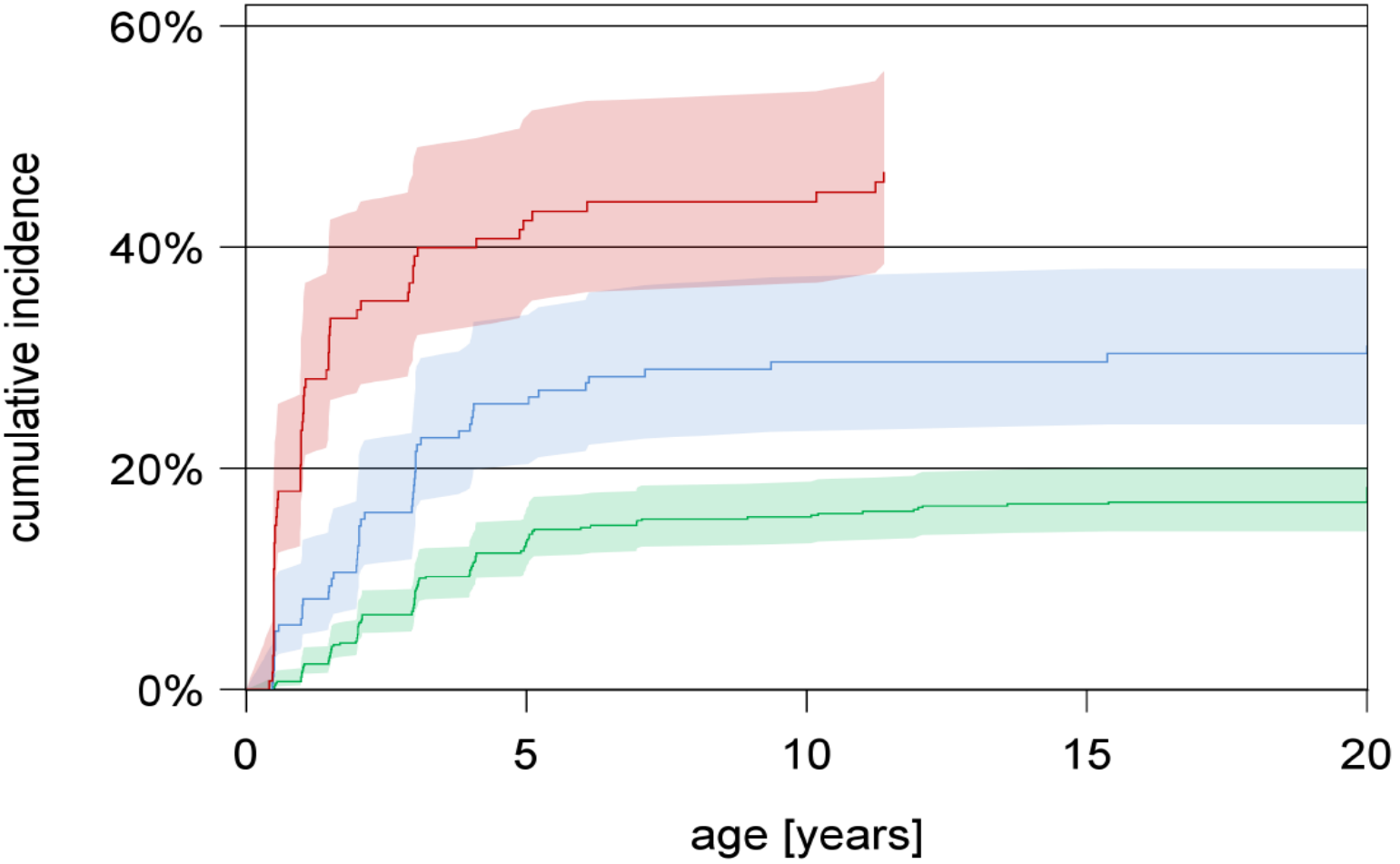
MAS – birth cohort (Germany)

Eczema: prognosis by age at onset



at birth n=1314

Eczema and atopic status



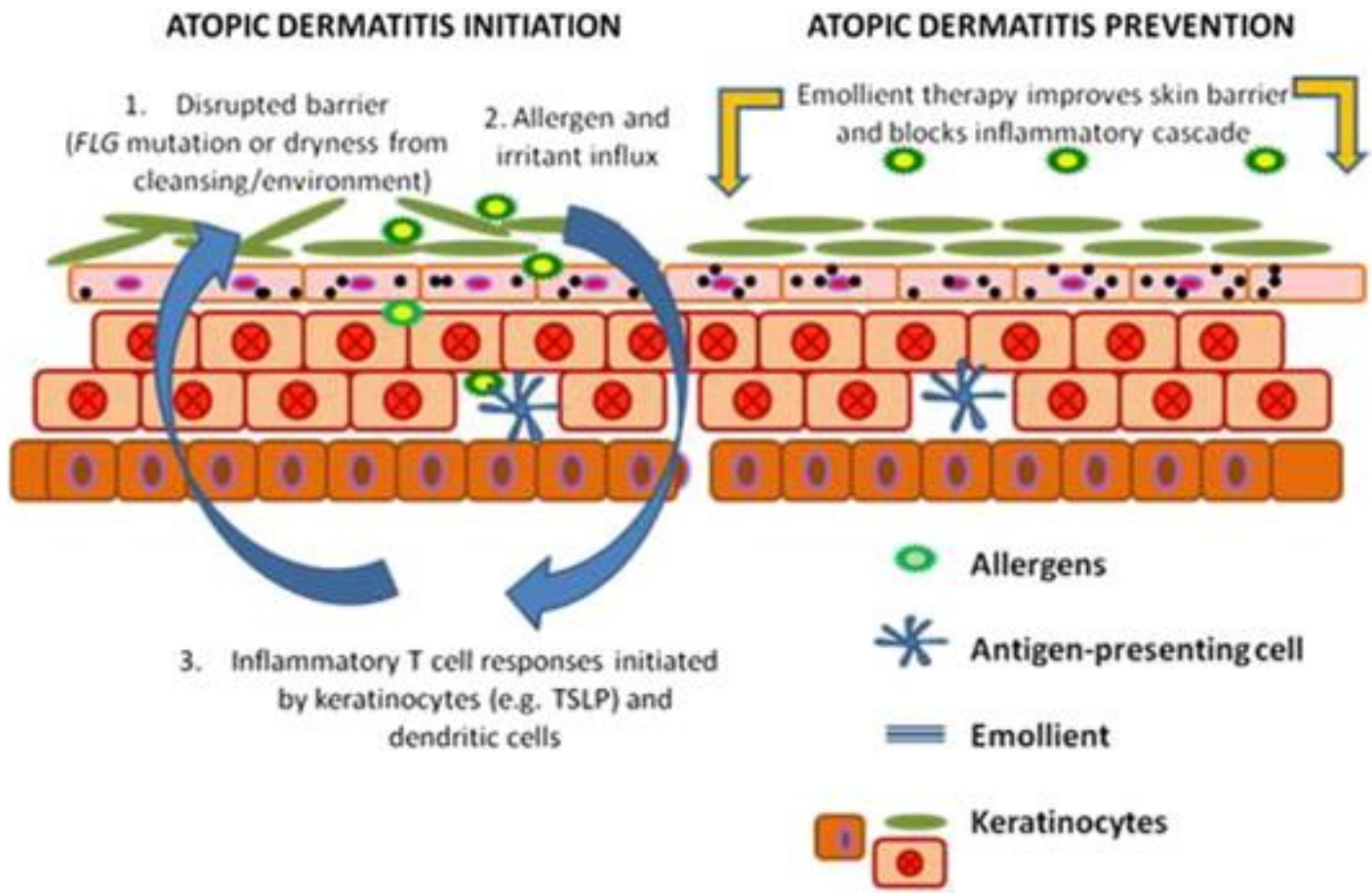
multi-sensitized
(first 3y)

mono-sensitized
(first 3y)

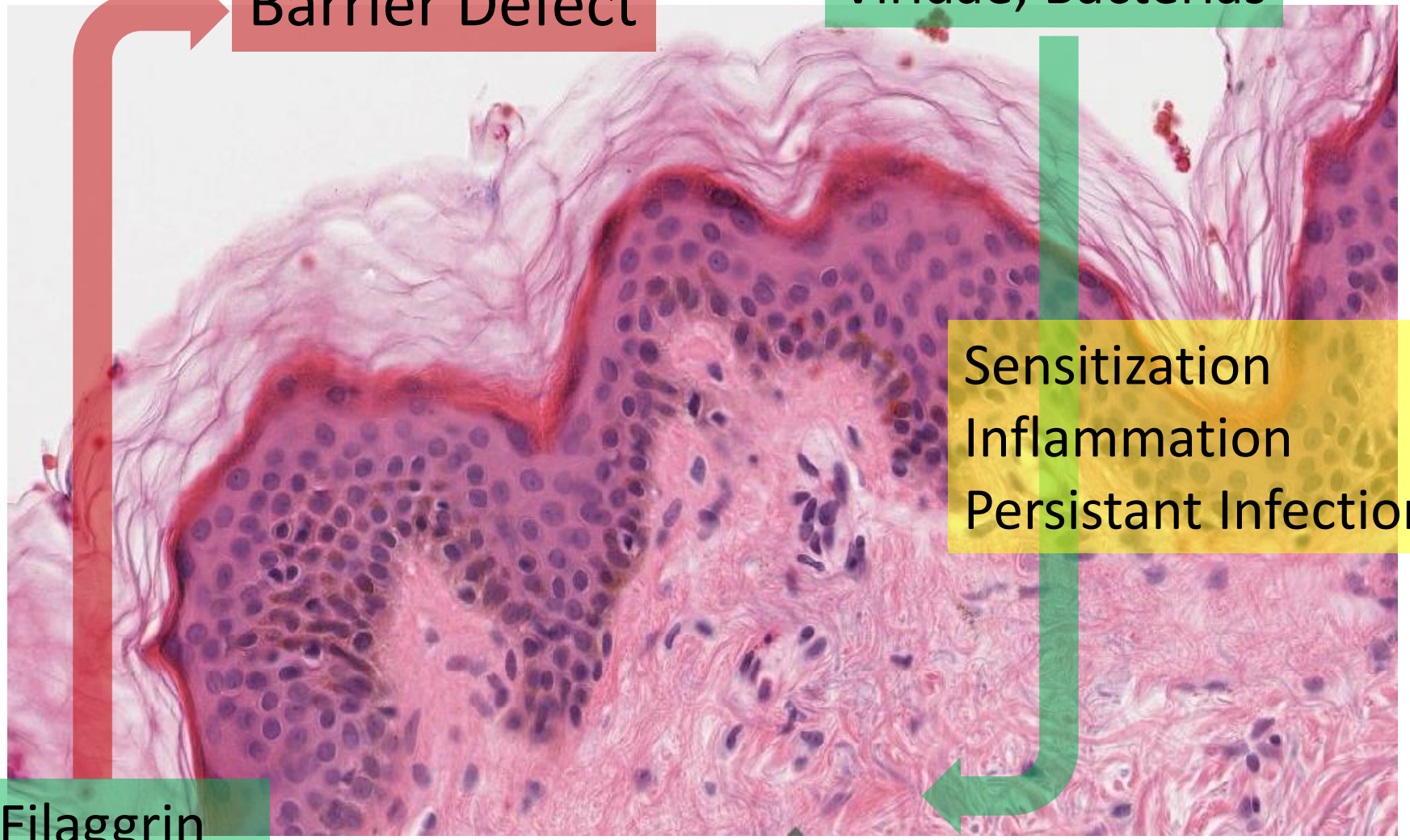
not sensitized
(first 3y)

non-adjusted Kaplan-Meier-curves

Infantile skin barrier and the role of emoillients for prevention.



Simpson, EL et al. JACI 2014, 134, 818-823.

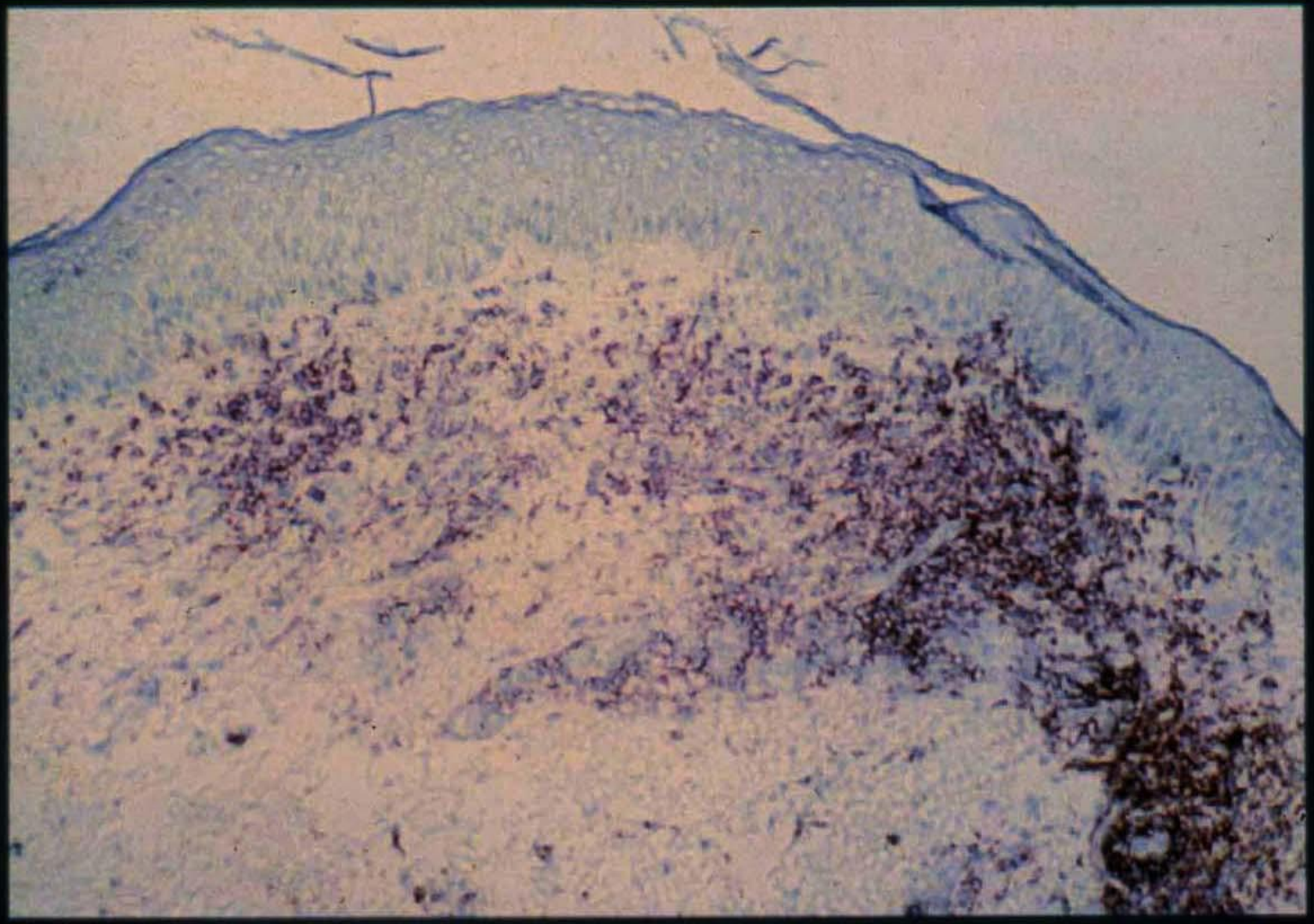

Barrier Defect
Allergens
Viridae, Bacterias
Sensitization
Inflammation
Persistant Infection
Filaggrin
Gene Defect

The skin in atopic dermatitis children

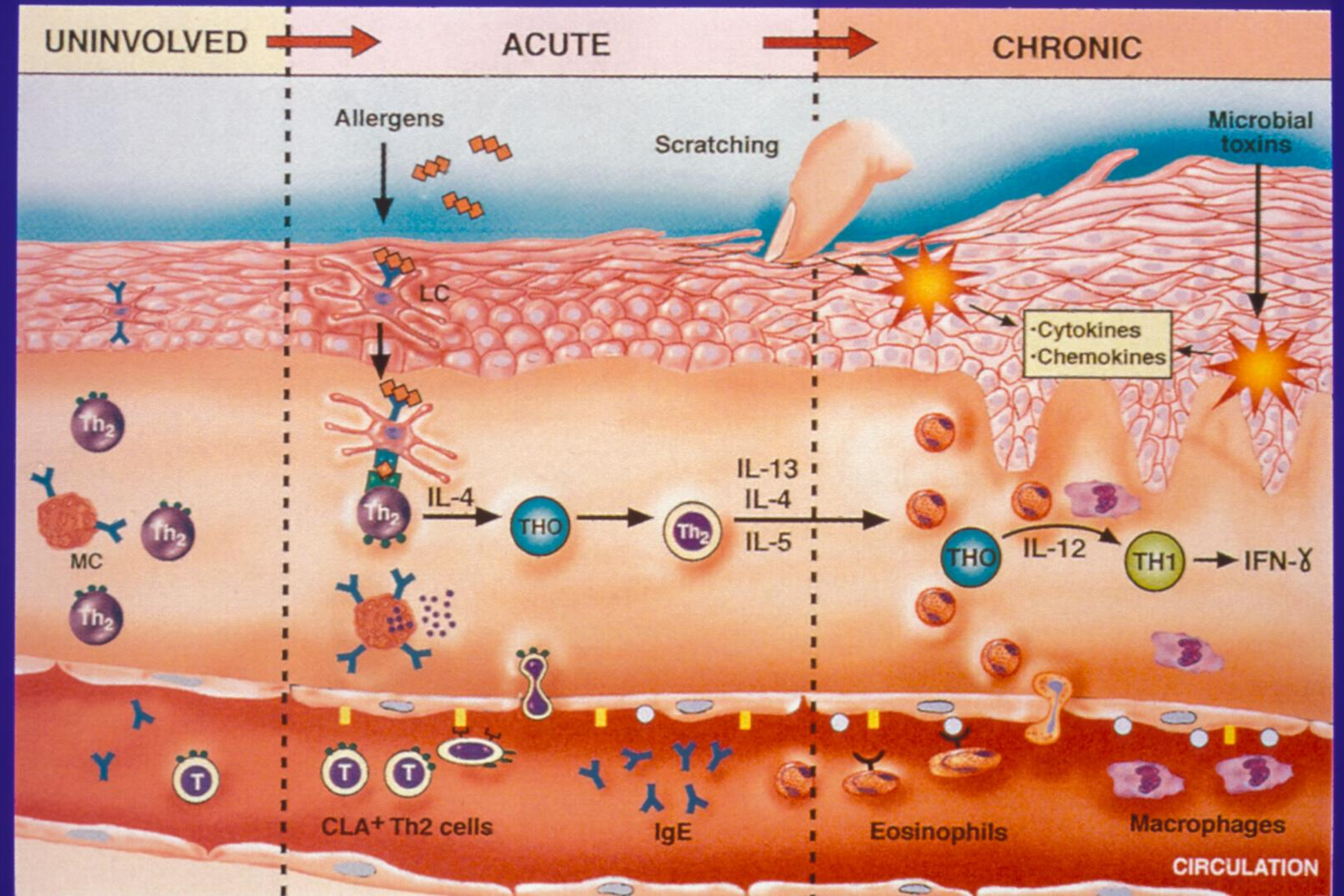
- reduced content of water and fat
- disturbed sweat regulation
- hyperreractivity to mechanical and chemical irritants
- reduced resistance to infection
- susceptibility to inflammation

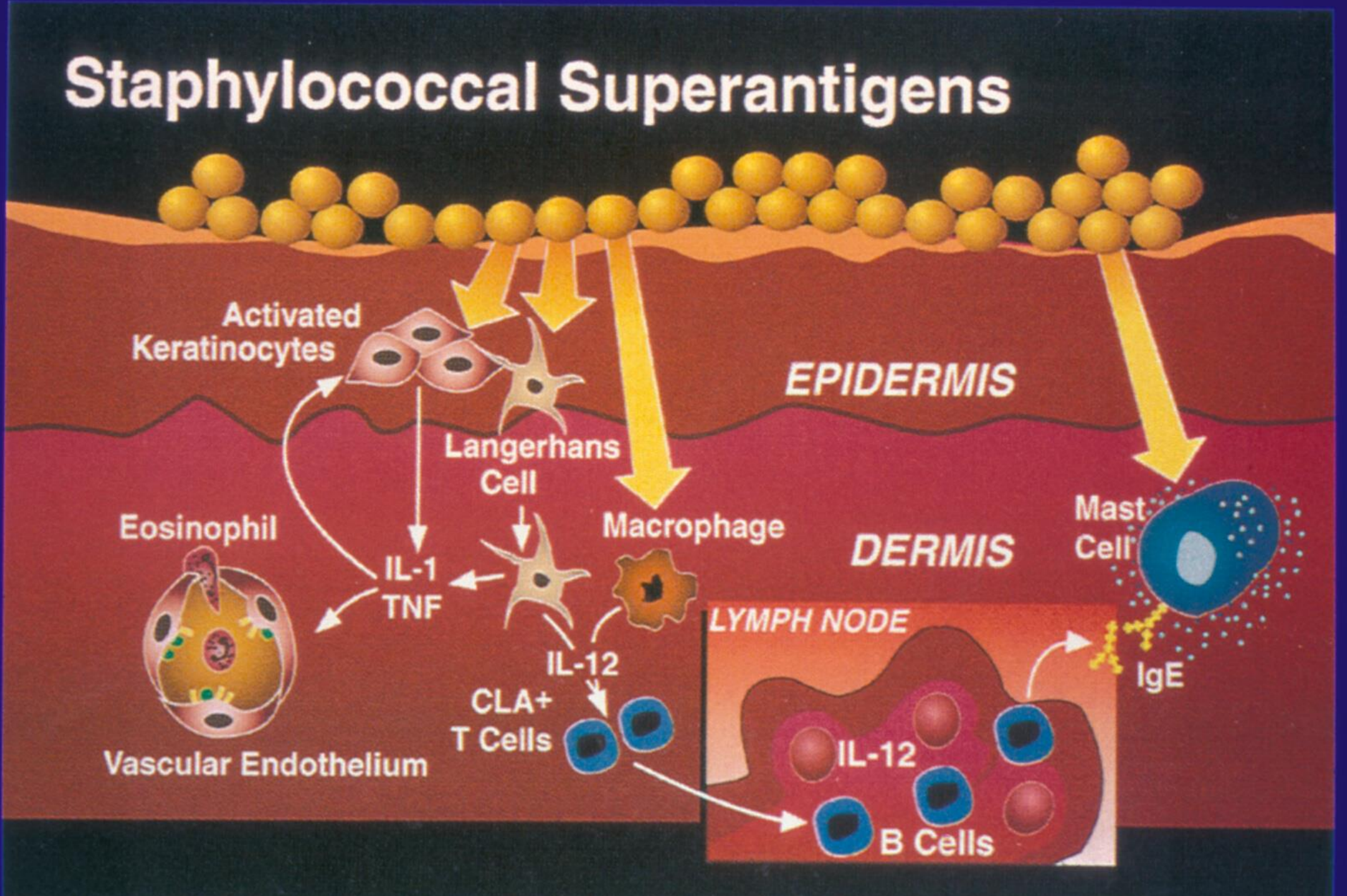
Palmer, CN et al, Nat Genetics, 2006, 38, 441-446

T cells in skin lesions of atopic dermatitis

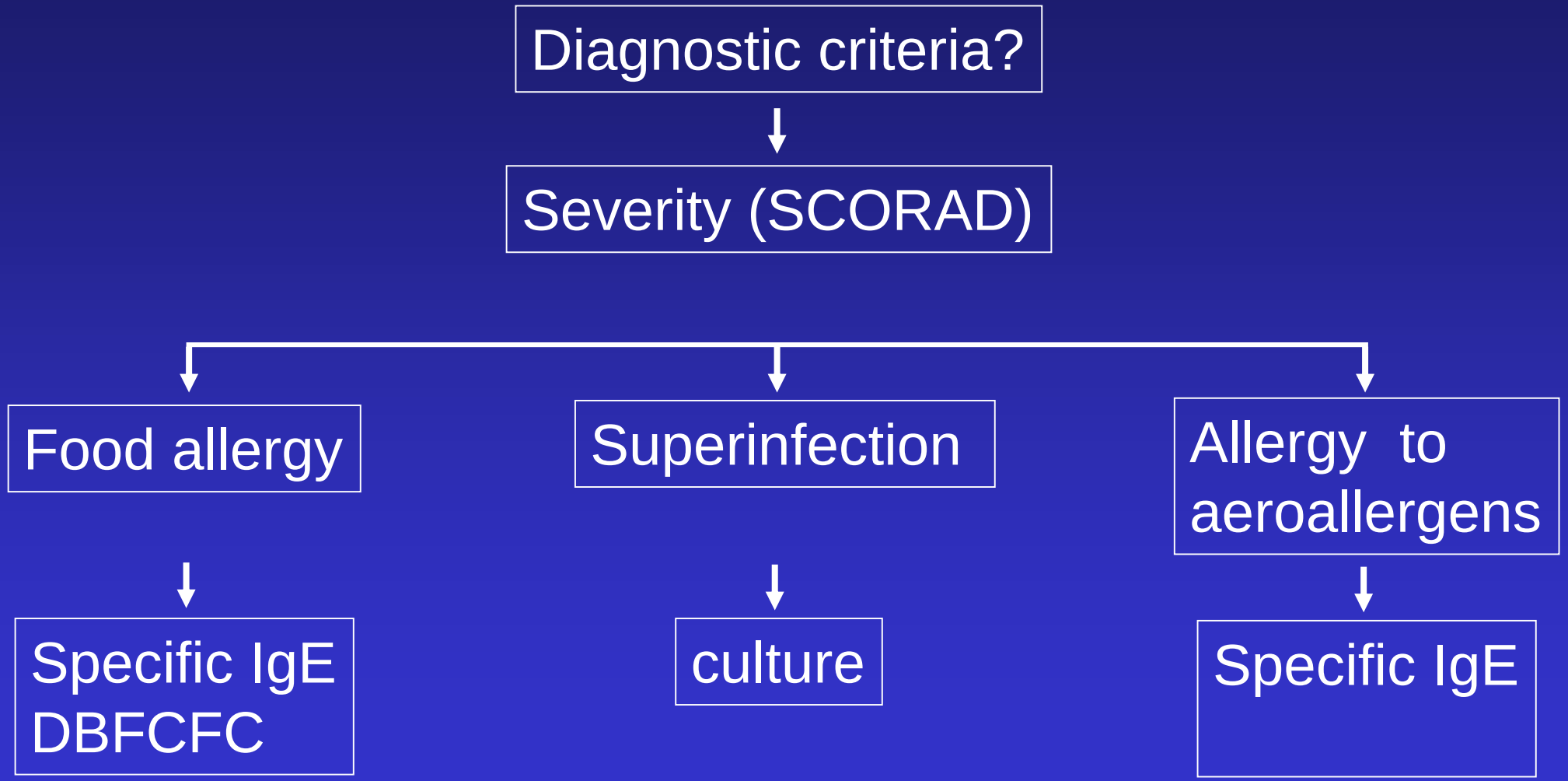


Kindly provided by Professor G Stingl, Vienna, Austria

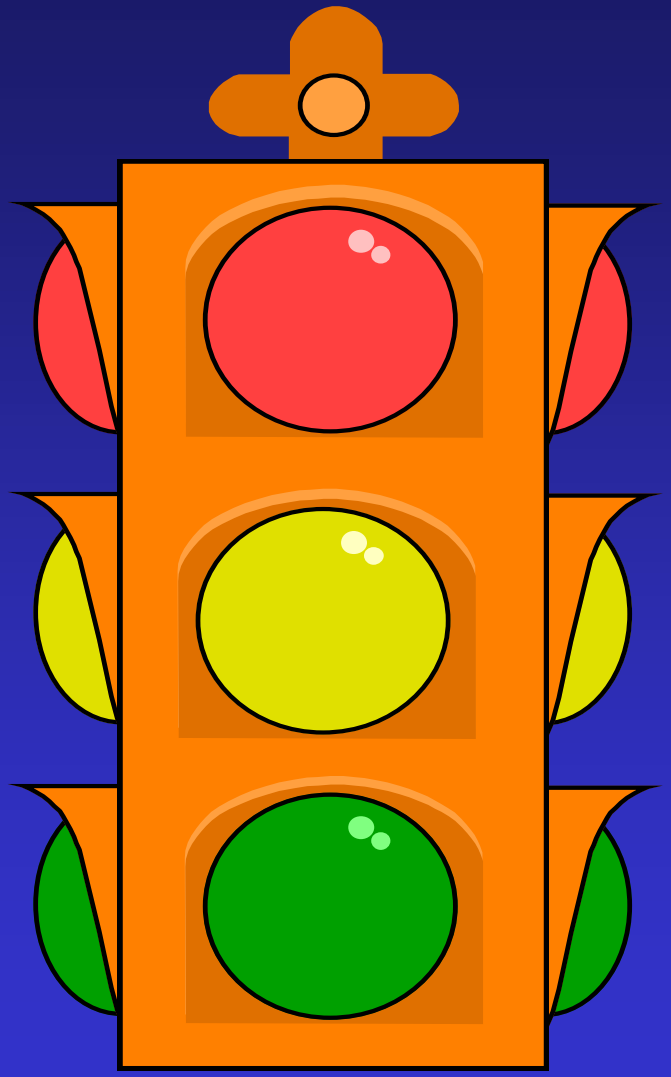

UNINVOLVED
ACUTE
CHRONIC
Allergens
Scratching
Microbial toxins
LC
·Cytokines
·Chemokines
Th2
MC
IL-4
THO
IL-13
IL-4
IL-5
IL-12
TH1
IFN-γ
T
CLA+ Th2 cells
IgE
Eosinophils
Macrophages
CIRCULATION


Staphylococcal Superantigens
Activated Keratinocytes
EPIDERMIS
Langerhans Cell
Eosinophil
Macrophage
DERMIS
Mast Cell
IL-1
TNF
LYMPH NODE
IL-12
IgE
CLA+ T Cells
IL-12
Vascular Endothelium
B Cells

Diagnostic steps in atopic dermatitis



Patient's self-management action plan



Exacerbation strategy

Mid-potency topical steroids
Uncontrolled disease:
↑ Potency of topical steroid

Early intervention strategy

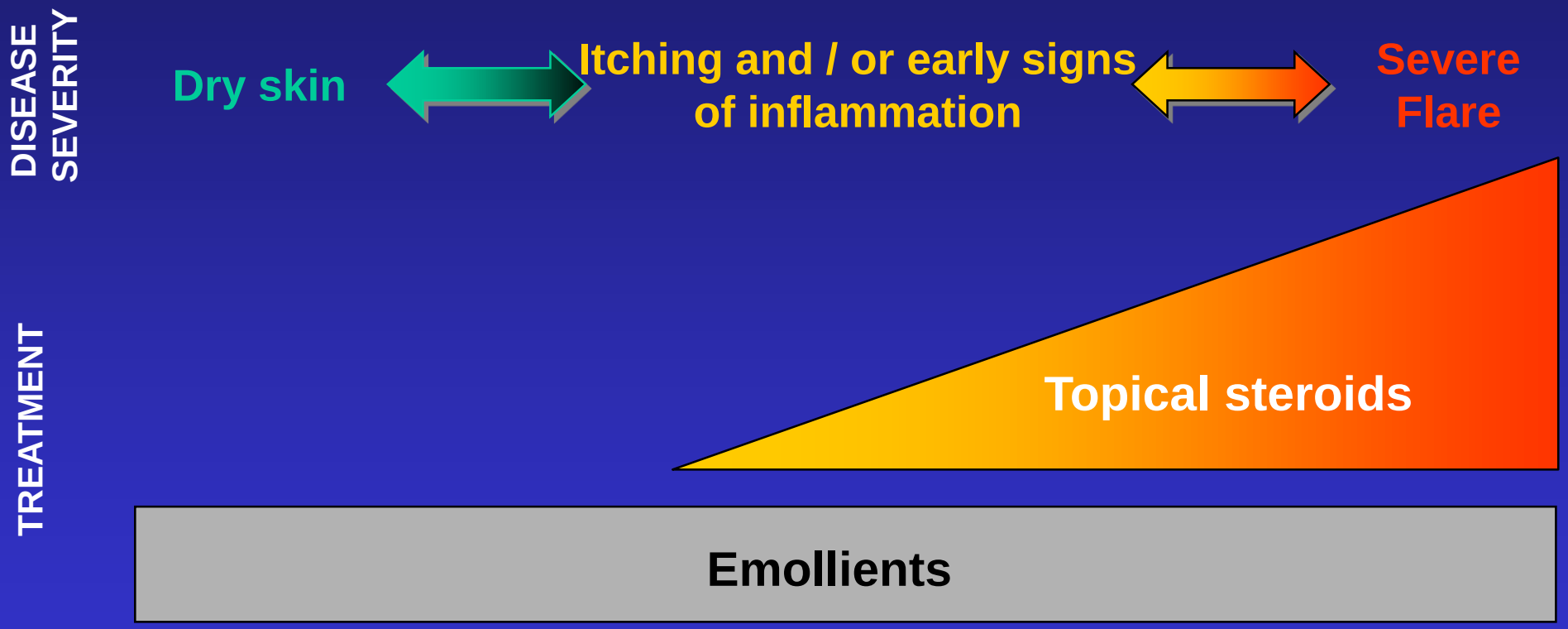
Elidel bid

at first signs or symptoms

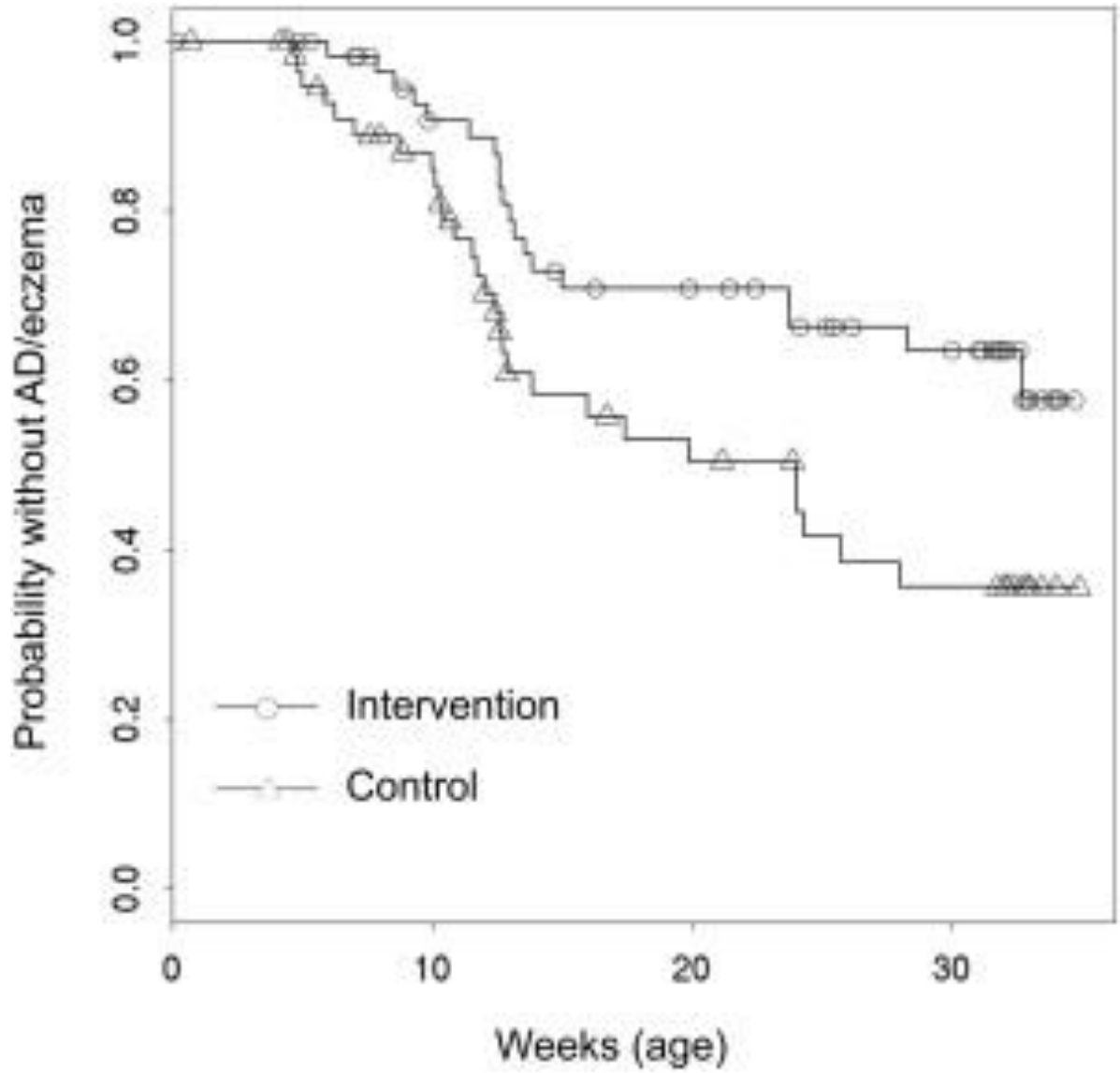
Maintenance strategy

Avoidance/emollients

Conventional Treatment Strategy



Proportions of infants who did not have AD/eczema



Horimukai.K, Morita.K et al, JACI, 134, 4, 2014, 824 - 830.

AD: Regular treatment with emoillients

- **Improvement of barrier function**

  Breternitz et al, Skin Pharmacol Physiol 2008, 21, 39-45

  Verallo-Rowell et al, Dermatitis 2008, 19, 308-15

- **Steroid sparing effect**

  Grimali et al. Dermatology 2007, 214, 611-67

  Szczepanowska et al. PAI 2008, 19, 614-8

Antiinflammatory Treatment:

Steroids: Different potencies- different risks

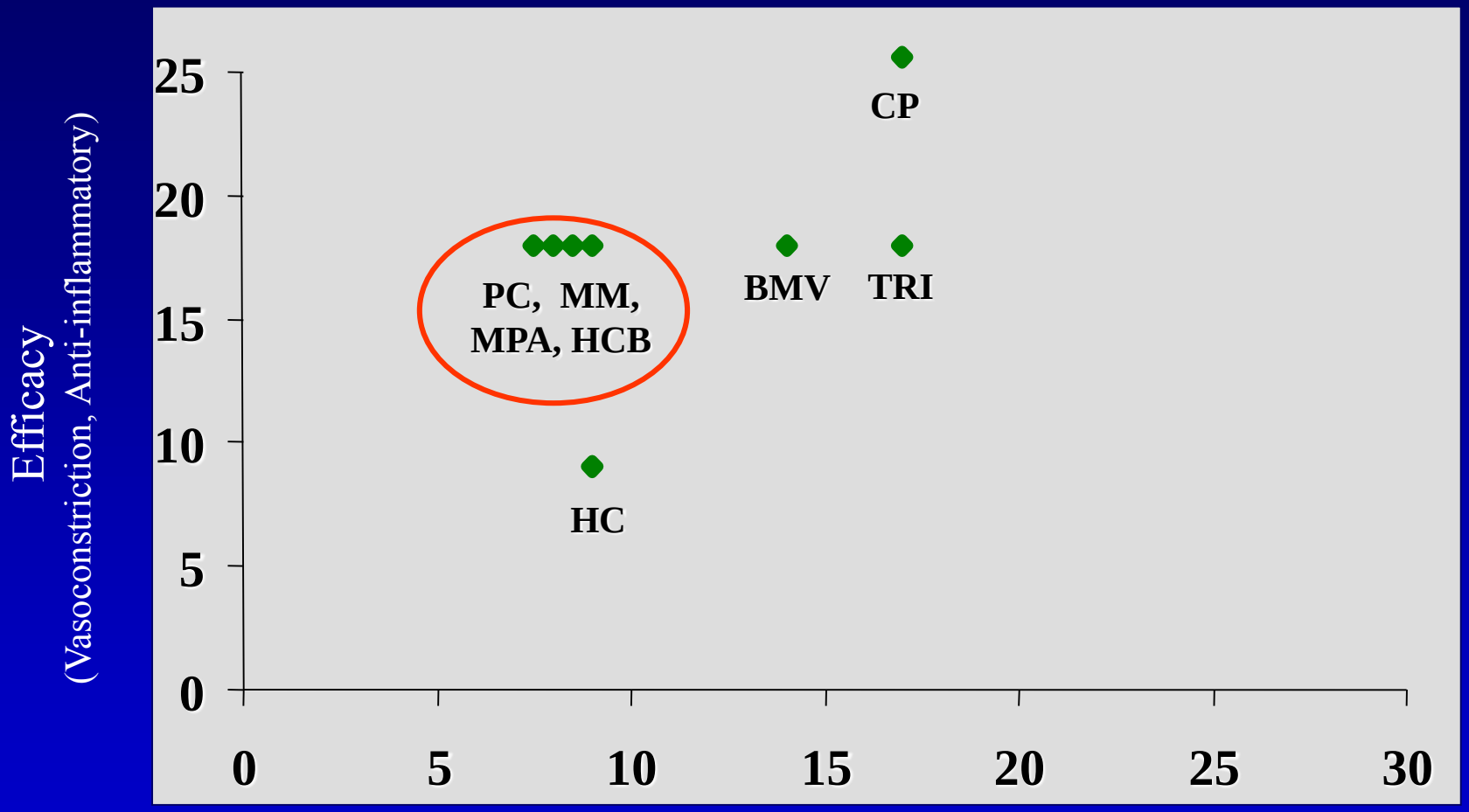
Calcineurin-Inhibitors: Tacrolimus, Pimecrolimus

Topical Corticosteroids
Potency Ranking (Miller & Munro)

Generic Name / Trade Name	Concentration	
Clobetasol-17-propionat	0,05%	Dermoxin
Diflucortolon-21-valerat	0,3%	Temetex forte Roche
I Very High Potency		
Amcinonid	0,1%	Amciderm
Betamethason-17,21-dipropionat	0,05%	Diprosone
Betamethason-17-valerat	0,1%	Betnesol, Celestan
Desoximetason	0,25%	Topisolon
Diflucortolon-21-valerat	0,1%	Nerisona
Fluocinolonacetonid	0,025%	Jellin
Fluocinonid	0,05%	Topsym
Fluocortolon	0,5%	Ultralan
Flupredniden-21-acetat	0,1%	Decoderm
Halcinonid	0,1%	Halog
Hydrocortisonaceponat	0,1%	Retef
Hydrocortisonbuteprat	0,1%	Pandel
Hydrocortison-17-butyrat	0,1%	Alfason
6-Methylprednisolonaceponat	0,1%	Advantan
Mometason	0,1	Ecural
Prednicarbat	0,25%	Dermatop
Triamcinolonacetonid	0,1%	Delphicort, Volon A
Clobetasonbutyrat	0,05%	Emovate
Clocortolon-21-pivalat	0,1%	Kaban
Fluocortinbutyl	0,75%	Vaspit
Flumetason-21-pivalat	0,02%	Locacorten
Hydrocortison	0,1-1%	Ficortril

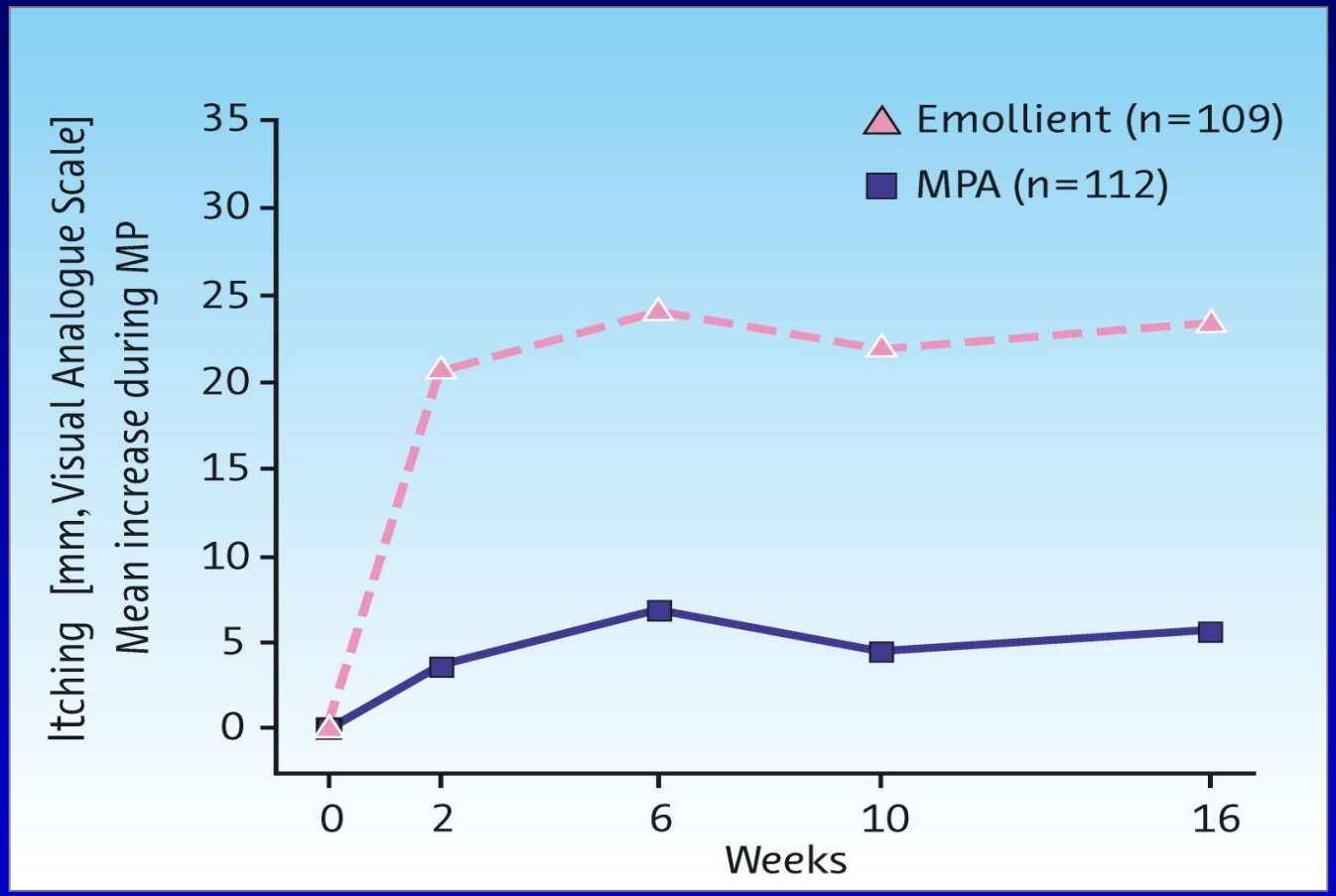
Corticosteroids: Therapeutic Index (TIX)

(Quotient: Efficacy/Adverse Events)



Luger TA et al JDDG 2, 629, 2004.

MPA leads to a significantly lower intensity of itch during the maintenance phase



- Intensity of itch remained stable over the course of the maintenance phase

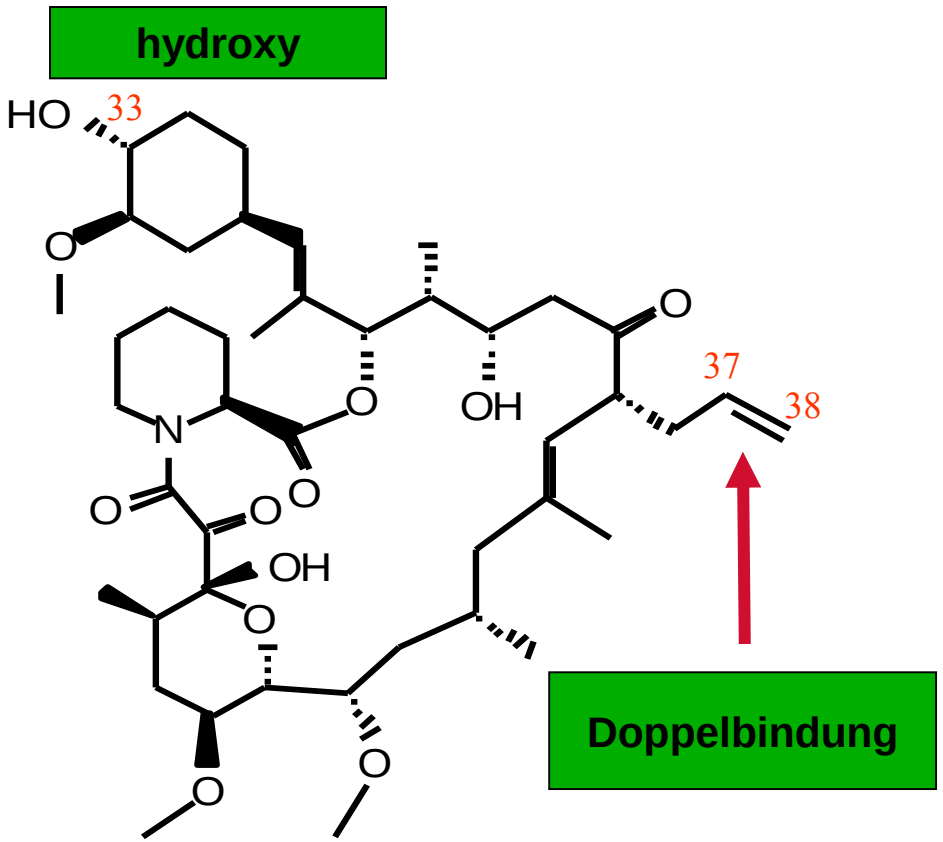
Peserico A et al, Br J Dermatol 2008;158:801-7

Short-Term Efficacy of MPA

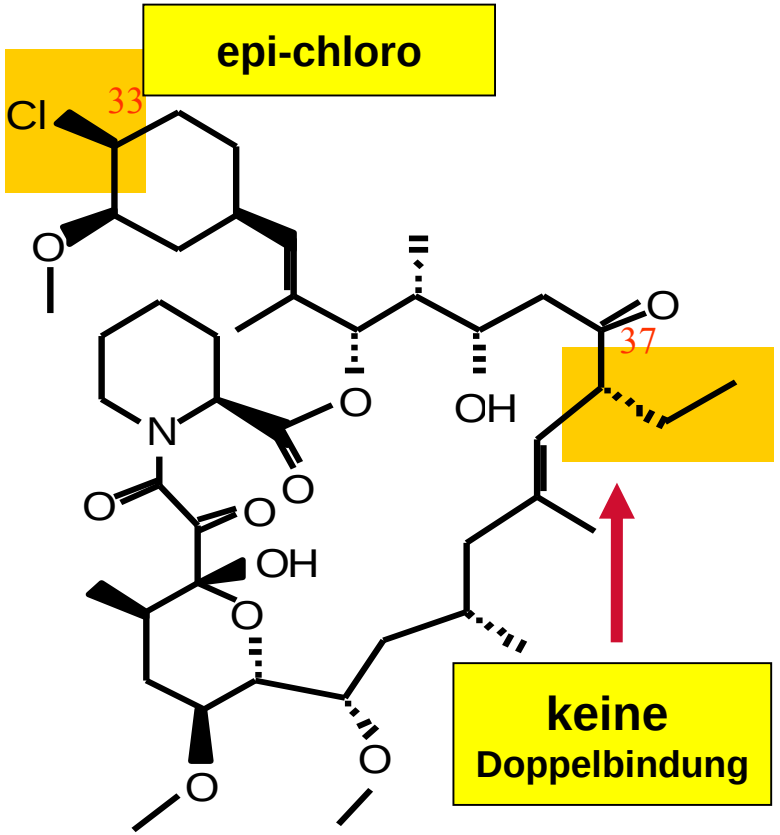
- MPA leads to rapid relief of symptoms: complete or near complete clearing of atopic dermatitis lesions occurred in 2/3 of patients.
- Both treatment groups were efficacious, nevertheless more patients treated with MPA had completely cleared symptoms by the end of treatment (37.2% MPA vs 29.4% tacrolimus).
- MPA was superior to tacrolimus for EASI, itch relief and quality of sleep.
- MPA shows excellent tolerability.

Bieber T et al, Allergy 2007;62:184-9

Structural differences between Pimecrolimus und Tacrolimus



Tacrolimus

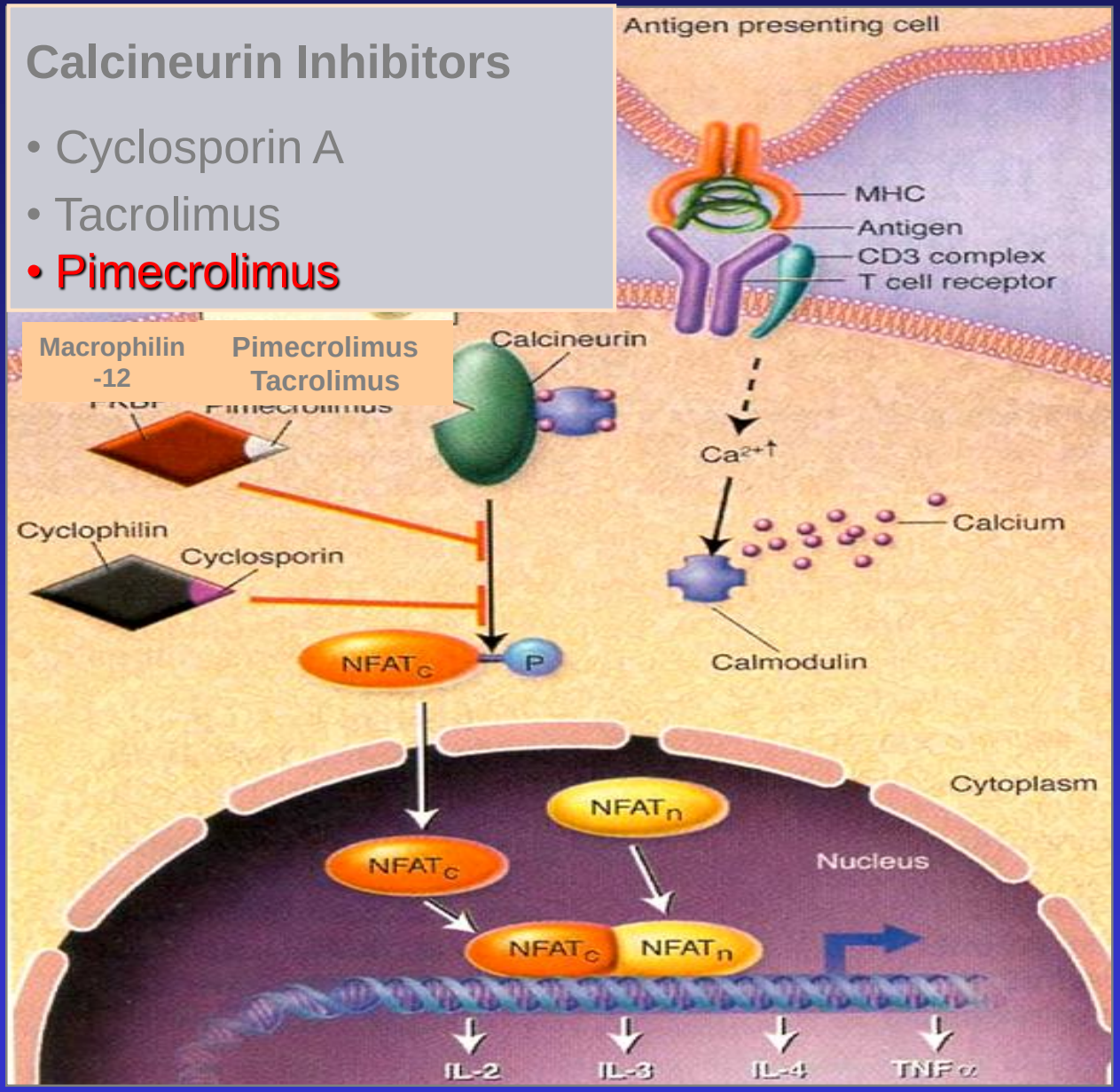


Pimecrolimus

Calcineurin inhibitors - mechanism of action

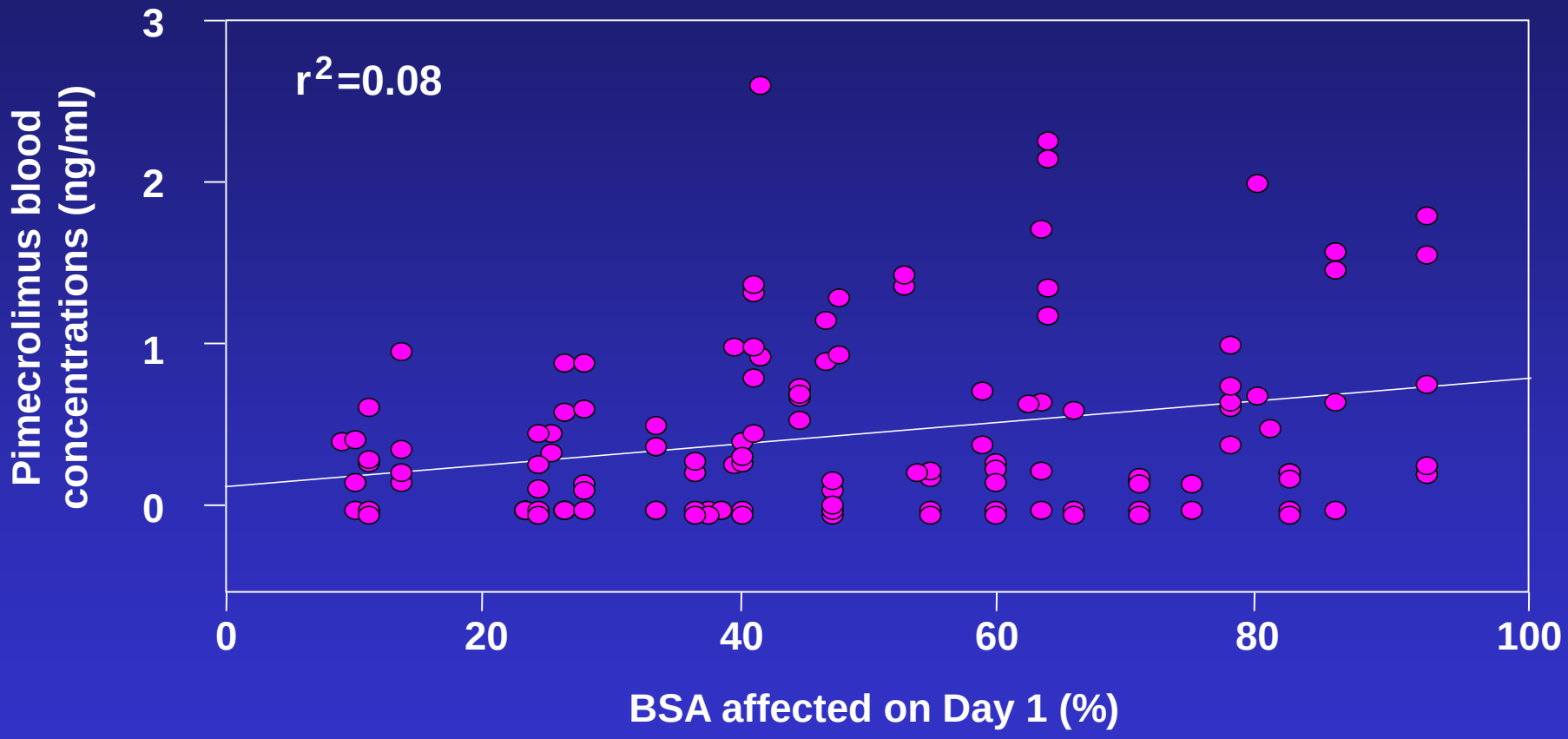
Calcineurin Inhibitors

- Cyclosporin A
- Tacrolimus
- Pimecrolimus



Nghiem P et al.J Am Acad Dermatol 46: 228-241 (2002)

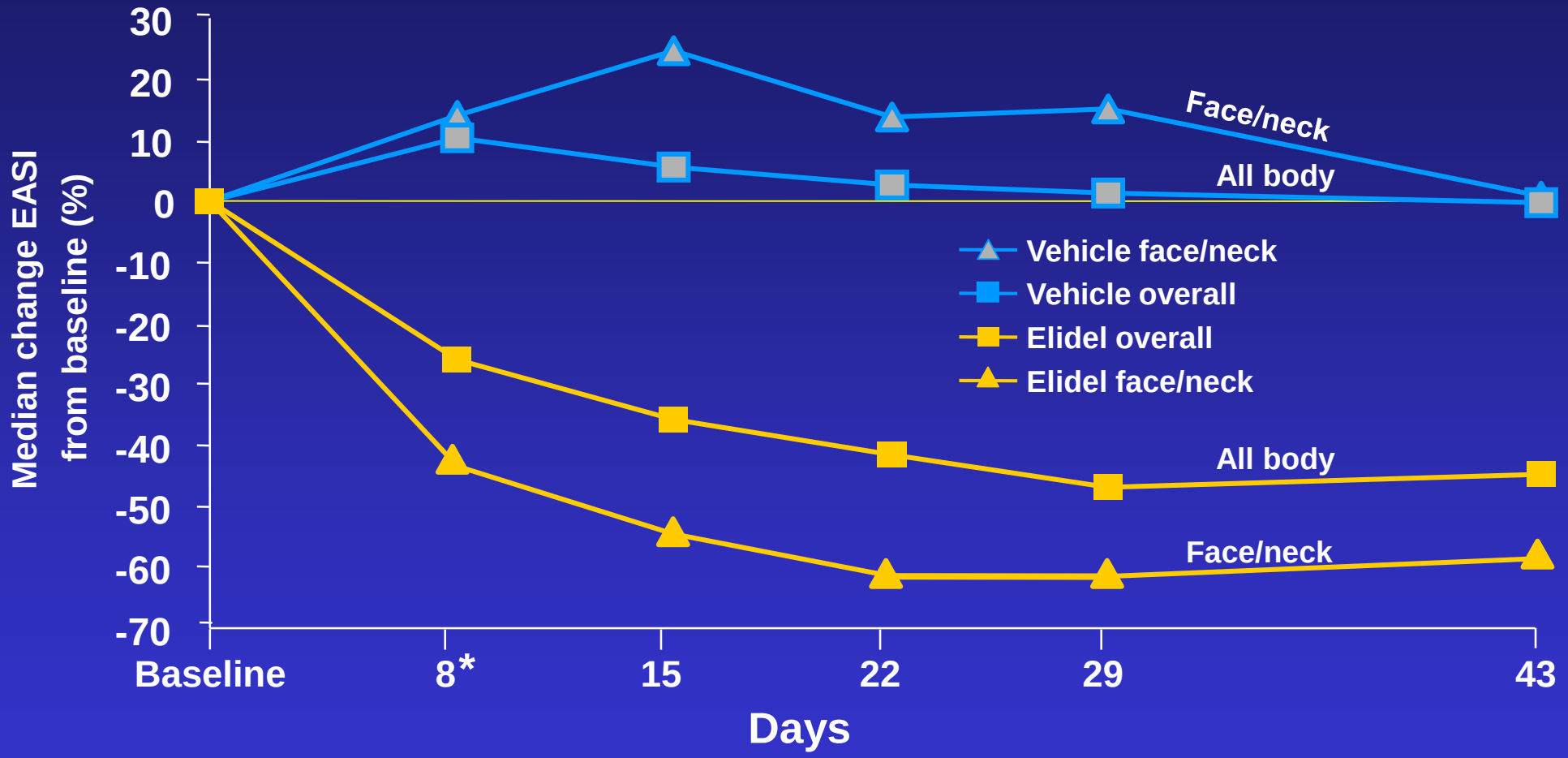
Minimal Increase in Blood Concentrations with Rising % BSA Treated



Difference in mean blood concentration for infants with 90% BSA and 10% BSA is 0.5 ng/ml

Lakhanpaul *et al.* AAD*2002*

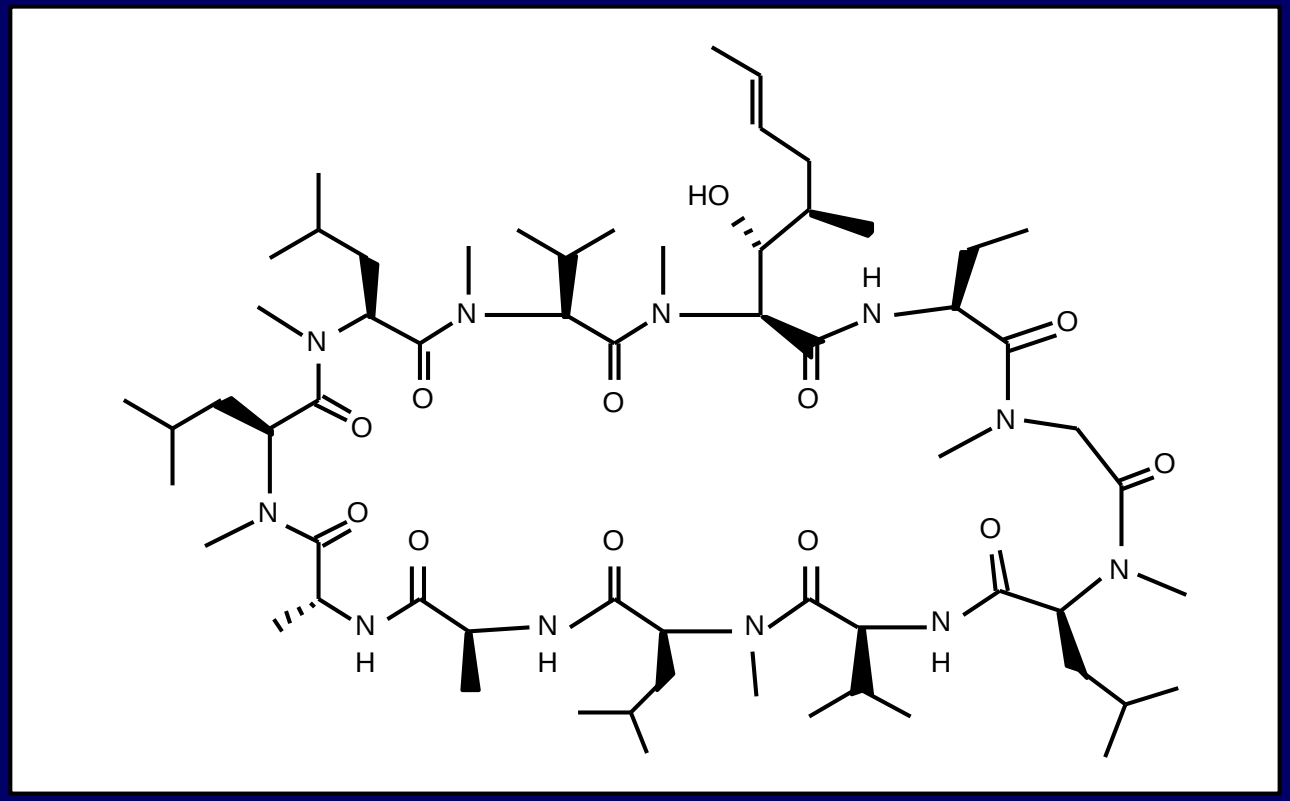
In children pimecrolimus is particularly effective in treating AD of face and neck



*Day 8 = first scheduled visit

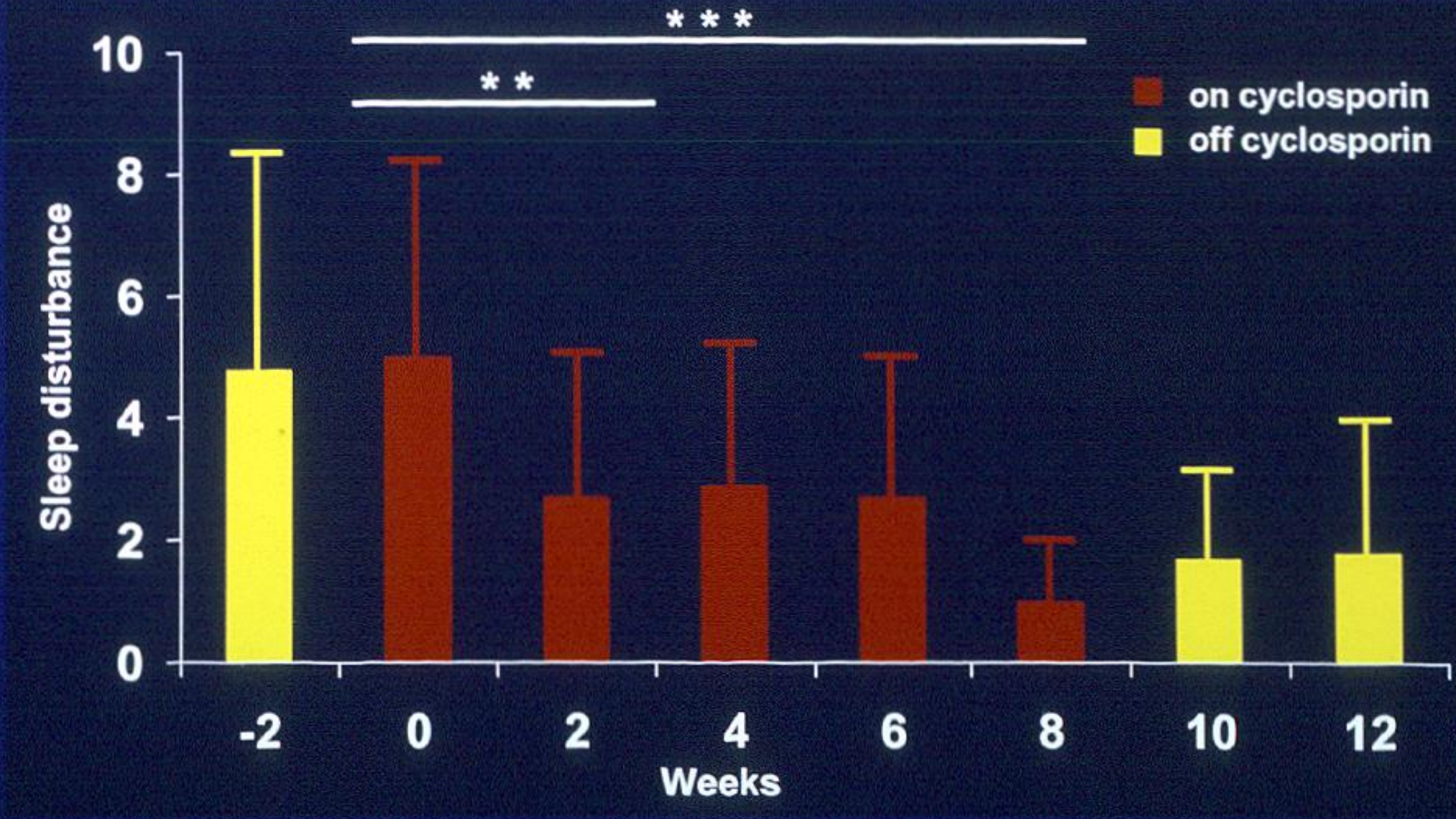
Eichenfield L *et al. J Am Acad Dermatol* 2002;46:495–504

Cyclosporin A (Neoral®, CyA)



- Wirkung: Hemmung der T-Zellaktivierung über Calcineurin/NFAT
- Orales CyA bei entzündlichen Hauterkrankungen hocheffektiv
- Topisches CyA unwirksam

Cyclosporin in Severe Atopic Dermatitis



Education is esssential!

Staab, D; Diepgen,TL et al

„Age related structural educational programmes for the management of atopic dermatitis in children and adolescents: multicentre randomized controlled trial.“

BMJ 2006, 332, 933-8

Neurodermitis Elternschulung



Universitätskinderklinik der Humboldt-Universität zu Berlin

Mead Johnson

Children with atopic dermatitis and their parents need more than emoillients, creams, and drugs!

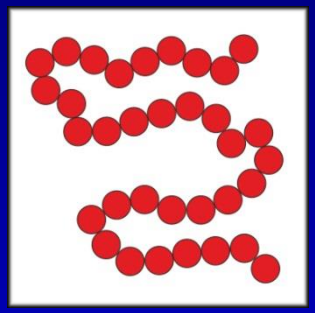
-Instruction by nurses

-structured educational programs for children and caregivers

Thank you for attention!

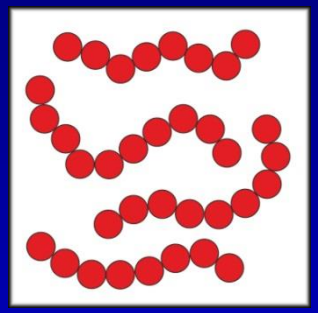
Prevention?

Principles of Reducing Allergenicity



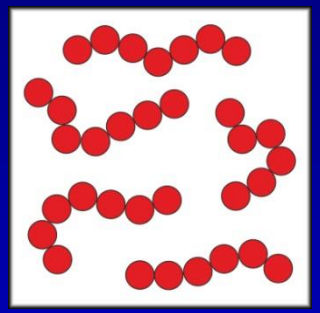
Whole protein

Cows milk protein



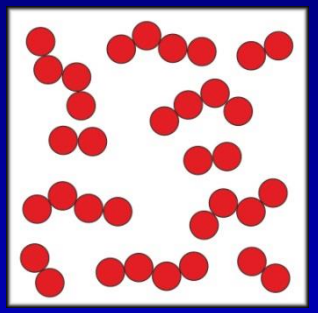
Moderately hydrolyzed

Beba HA
Humana HA
Milumil HA



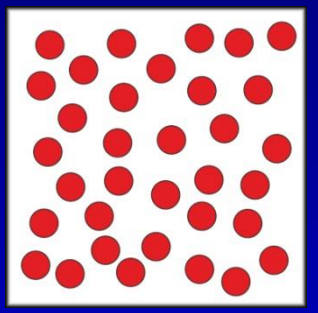
Highly hydrolyzed

Aptamil HA
Hipp HA



Extensively hydrolyzed

Alfaré
Nutramigen
Pregomin
Althera



Amino acids

Neocate
Pregomin AS

Allergenicity

Prebiotic, Probiotic and Synbiotic Food