WISC 2012 Hyderabad, India 6-9 December
2012 WAO International Scientific Conference
A World Federation of Allergy Asthma and Clinical Immunology Societies

ATOPIC DERMATITIS:PATHOPHYSIOLOGY, DIAGNSOSIS AND MANAGEMENT

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FAAAAI, FACAAI, SLAAI 2010-2012

CENTRO REGIONAL DE ALERGIA E INMUNOLOGIA CLINICA

December 2012

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- Current President of the Latin American Society of Asthma, Allergy and Clinical Immunology (SLAAI) 2010-2012
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- Professor of Regional Centre of Allergy and Clinical Immunology, University Hospital, Monterrey, NL since 1990
- Director of Fundraising Department, University Hospital since 2007
- Director General, Department Fundraising at the Autonomous University of Nuevo Leon
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- Past President Chapter of the Latin American Society Mesoamerica Asthma, Allergy and Clinical Immunology (SLAAI) 1997-1999
- Past president UNASMA (International Asthma Foundation) M2007-2011
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- Faculty of Medicine, U.A.N.L 1977-1983. Monterrey, NL Mexico
- Specialty of Internal Medicine, University Hospital, UANL Monterrey, N.L.1986 – 1988
- Fellowship in Pediatric Allergy and Immunology Clinica, UCSD, University of San Diego, California, USA, 1987-1988
- Subspecialty in Allergy and Clinical Immunology, University Hospital UANL , Monterrey, N. L.1988 – 1990
- Doctor of Medicine, Hospital Universitario UANL , Monterey, N.L.1991 - 1997

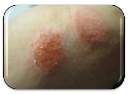
MEDICAL TEAM CRAIC 2012

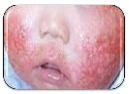
FELLOW IN TRAINING CRAIC 2012

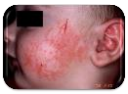
ATOPIC DERMATITIS

CRHONIC SKIN DISEASE


ERYTEMA

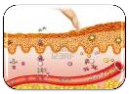

ECCEMA


INFECTIONS


PRURITUS MARKS

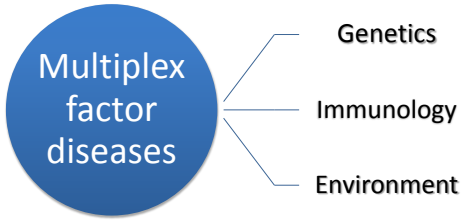

BODY LOCALIZATION


ITCHING


CUTANEOUS HIPERREACTIVITY

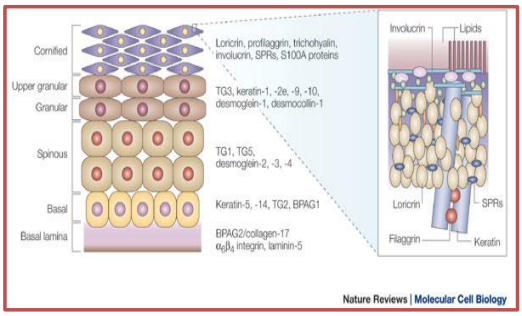
Donald Y. M. Leung, MD, PhD Denver, Colo, Atopic dermatitis: New insights and opportunities for therapeutic intervention, J Allergy Clin Immunol 2000;105:860-76.

AD PATHOPHYSIOLOGY



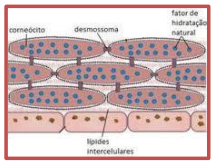
Natalija Novak. New insights into the mechanism and management of allergic diseases: atopic dermatitis. Allergy 2009: 64: 265–275

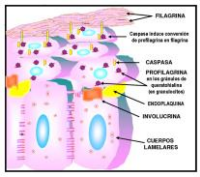
PATHOGENESIS



Emma Guttman-Yassky. Contrasting pathogenesis of atopic dermatitis and psoriasis—Part I: Clinical and pathologic concepts. J Allergy Clin Immunol 2011;127:1110-8.

PATHOGENESIS





Emma Guttman-Yassky. Contrasting pathogenesis of atopic dermatitis and psoriasis—Part I: Clinical and pathologic concepts. J Allergy Clin Immunol 2011;127:1110-8.

*DEFECTS IN CUTANEOUS BARRIER

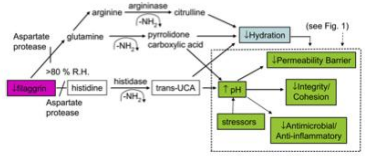
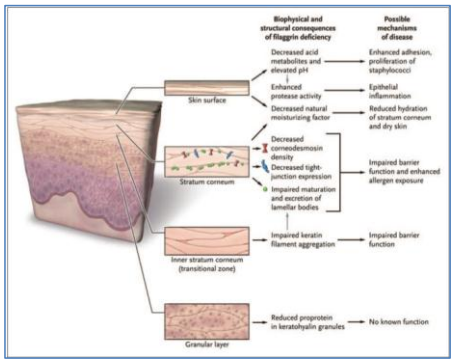


FIG 2. *FLG* proteolytic pathway affects multiple SC functions: potential implications for pathogenesis of AD. *R.H.*, Relative humidity; *trans-UCA*, trans-urocanic acid.

Peter M. Elias. Basis for the barrier abnormality in atopic dermatitis: Outside-inside-outside pathogenic mechanisms. J Allergy Clin Immunol 2008;121:1337-43.



Alan D. Irvine et al. Filaggrin Mutations Associated with Skin and Allergic Diseases. N Engl J Med 2011;365:1315-27.

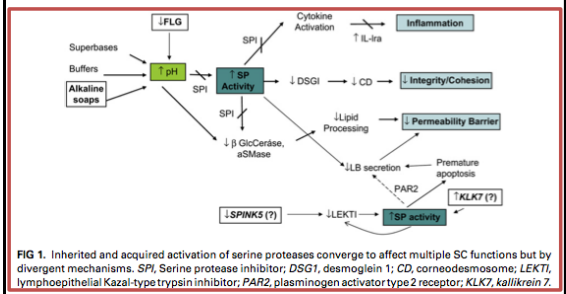


FIG 1. Inherited and acquired activation of serine proteases converge to affect multiple SC functions but by divergent mechanisms. *SPI*, Serine protease inhibitor; *DSG1*, desmoglein 1; *CD*, corneodesmosome; *LEKTI*, lymphoepithelial Kazal-type trypsin inhibitor; *PAR2*, plasminogen activator type 2 receptor; *KLK7*, *kallikrein 7*.

Peter M. Elias. Basis for the barrier abnormality in atopic dermatitis: Outside-inside-outside pathogenic mechanisms. J Allergy Clin Immunol 2008;121:1337-43.

Antimicrobial barrier

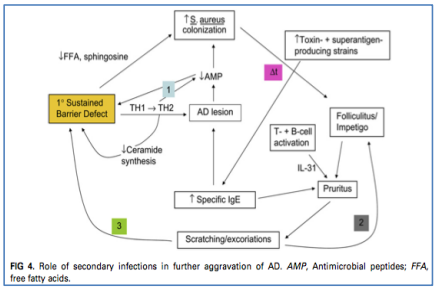
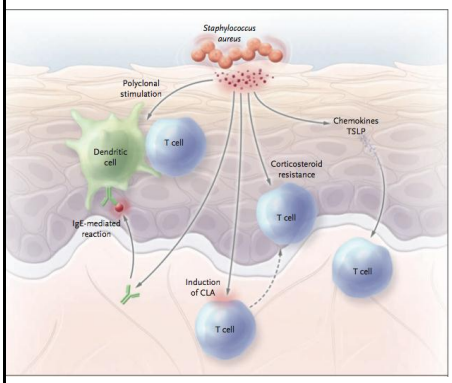


FIG 4. Role of secondary infections in further aggravation of AD. *AMP*, Antimicrobial peptides; *FFA*, free fatty acids.

Boguniewicz M, Schmid-Grendelmeier P, Leung DY. Atopic dermatitis. J Allergy Clin Immunol 2006;118:40-3.



Thomas Bieber. Atopic Dermatitis. N Engl J Med 2008;358:14 83-94.

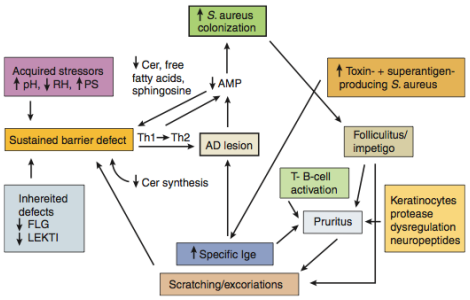


Figure 1. Secondary infections can further aggravate barrier abnormality in atopic dermatitis.
AD, atopic dermatitis; AMP, adenosine monophosphate; Cer, ceramide; FLG, filaggrin; LEKTI, lymphoepithelial Kazal-type related trypsin inhibitor; PS, psychological stress; RH, relative humidity; Th1, T-helper 1; Th2, T-helper 2 (Modified from Elias *et al.*, in press.)

Outside-Inside model

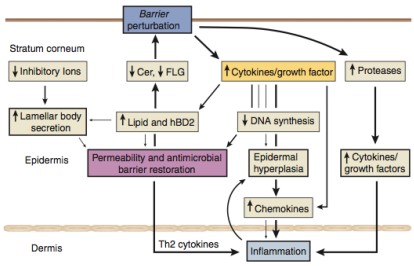


Figure 2. "Outside–inside–outside" model of AD. Cer, ceramide; FLG, filaggrin; hBD2, human β-defensin-2; Th2, T-helper 2. (From Figure 2. Cer, ceramide; FLG, filaggrin; hBD2, human β-defensin-2; Th2, T-helper 2. (From Steinhoff *et al.*, 2005; modified from Elias *et al.*, in press.)

Peter M. Elias, Martin Steinhof. Outside-to-Inside" (and Now Back to "Outside") Pathogenic Mechanisms in Atopic Dermatitis. *Journal of Investigative Dermatology* (2008), 128, 1067–1070.

IMMUNE SYSTEM

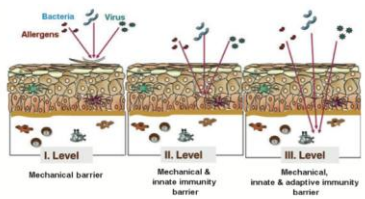
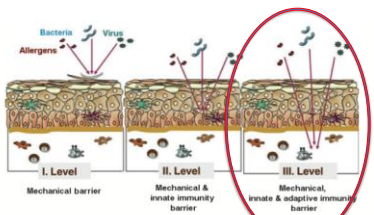


Figure 1. Deficiencies on the level of the skin barrier function as well as the innate and adaptive immune system contribute to the pathophysiological puzzle of atopic dermatitis (AD). The first level of the barrier is the mechanical skin barrier represented by the stratum corneum and the upper part of the skin. The second level of the skin barrier is represented by structures of the innate immune system such as pattern recognition receptors expressed by skin cells or antimicrobial peptides. The third level of the skin barrier is represented by the cellular defense of components of the adaptive immune system. DC, dendritic cell; M, mast cell; MC, macrophage; T, T cell.

N. Novak. New insights into the mechanism and management of allergic diseases: atopic dermatitis. Allergy 2009: 64: 265–275

IMMUNE SYSTEM



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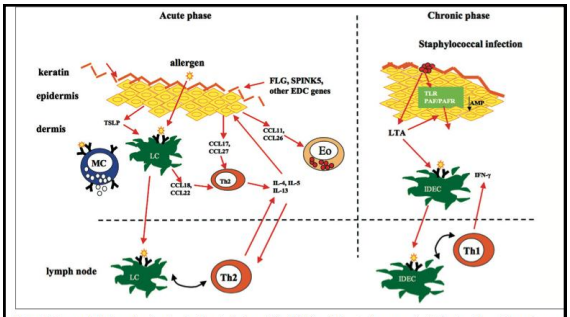
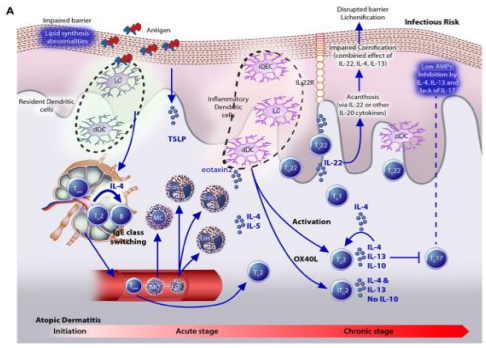


FIGURE 2: Immunological mechanisms involved in atopic dermatitis. Initiation of the atopic response in AD involves the uptake and proces ing of allergens by LCs after penetration through the compromised epithelial barrier. The activated LCs then migrate to skin draining LN ar with IL-4 promote Th2 differentiation. Keratinocytes produce chemokines including CCL17, CCL27, CCL11, CCL26. Chemokines CCL and CCL27 recruit Th2 cells to the skin whereas CCL11 and CCL26 recruit eosinophils. TSLP activates DCs to prime naïve T helper cells Th2 cells and promote Th2 memory. The potentiation of the inflammatory response involves the complication of AD with bacterial infection Staphylococcal exotoxins activate LCs and IDECs to produce inflammatory mediators including **IL-1β** and TNF-α. The mediators lead increased expression of chemokines which recruit T cells. Th2 cytokines in AD decrease AMPs making lesions susceptible to infection. P receptor can also bind to LTA in addition to PAF. LTA activated IDECs migrate to draining lymph nodes of skin to promote Th1 responses

Sarita Sehra . Clinical correlations of recent developments in the pathogenesis of atopic dermatitis. *An Bras Dermatol. 2008;83(1):57-73.*



Emma Guttman-Yassky. Contrasting pathogenesis of atopic dermatitis and psoriasis— Part II: Immune cell subsets and therapeutic concepts. J Allergy Clin Immunol 2011;127:1420-32.

ALLERGIC AND NON-ALLERGIC

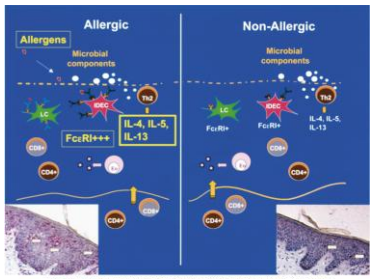


FIG 1. The pathophysiologic puzzle of AD. The differences between the allergic subtype of AD (left) and the nonallergic subtype of AD (right) are indicated in yellow. In addition, immunohistochemical stainings of FcεRI on CD1a+ LCs and IDECs (indicated by arrows) are shown on the bottom of each figure. as, Eosinophils.

Novak N, Tepel C, Koch S, Brix K, Bieber T, Kraft S. Evidence for a differential expression of the FcepsilonRIgamma chain in dendritic cells of atopic and nonatopic donors. J Clin Invest 2003;111:1047-56.

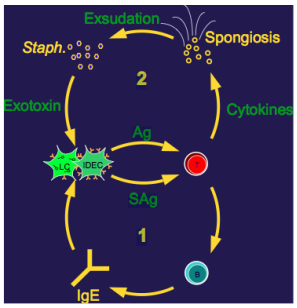
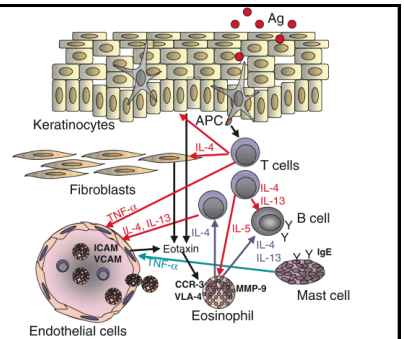


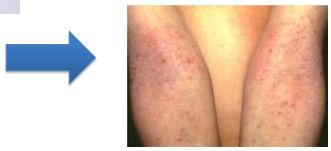
Fig. 3 The vicious circles of immunoactivation in atopic dermatitis lesions. This model demonstrates the two vicious circles of (1) antigen-specific and (2) superantigen-driven T cell activation in atopic dermatitis lesions. 1 Epidermal antigen presenting dendritic cells such as Langerhans cells (LC) and inflammatory dendritic epidermal cells (IDEC) present antigen to T lymphocytes (T), which will activate B cells (B) to produce antigen-specific IgE that in turn may bind to high affinity IgE receptors expressed on dendritic cells and mast cells. In the presence of antigen specific IgE on the dendritic cell surface, the antigen focusing effect of IgE-mediated antigen presentation yields about 100-fold higher T cell activation than a presentation without IgE present. 2 In addition, proinflammatory cytokines produced by T cells induce spongiosis, exsudation, and enhanced Staphylococcus aureus colonization of atopic dermatitis lesions. Staphylococcal exotoxins with superantigenic properties bypass the antigen-specificity of T cell activation, stimulating all T cells sharing the same T cell receptor family. Both mechanisms lead in synergy to profound activation of the skin immune system in the atopic dermatitis lesion

Andreas Wollenberg, Elisabeth Klein. Current Aspects of Innate and Adaptive Immunity in Atopic Dermatitis. Clinic Rev Allerg Immunol (2007) 33:35–44



Simon D, Braathen LR, Simon HU. Eosinophils and atopic dermatitis. Allergy 2004;59:561-70.

Figure 1. Mechanisms of eosinophil recruitment and activation in atopic dermatitis. T cells are activated by antigens and/or super-antigens with the help of antigen-presenting cells and subsequently produce T helper 2 cytokines. In particular interleukin (IL)-4 stimulates keratinocytes, fibroblasts, and endothelial cells to produce eotaxin, which attracts CCR-3 positive eosinophils. The expression of the adhesion molecules vascular cell adhesion molecule (VCAM) and intercellular adhesion molecule on endothelial cells is induced by IL-4, IL-13, and tumor necrosis factor-α. In particular, molecular interactions between VCAM and VLA-4 are important for preferential eosinophil recruitment. Interleukin-5 specifically acts on eosinophils and is involved in recruitment, activation, and life-span regulation of these cells. Eosinophils play an important immunoregulatory role because of the production of cytokines. For example, they generate IL-4 and IL-13, two important regulators of T and B cell functions, respectively.



PRURITUS

J. Buddenkotte. Pathophysiology and therapy of pruritus in allergic and atopic diseases. Allergy 65 (2010) 805–821.

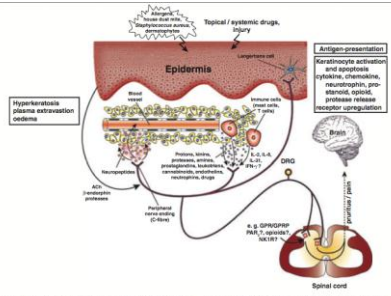


Figure 1 General neuroanatomical and neurophysiological pathways activated during pruritus (pruritogenic itch). Exogenous or endogenous mediators stimulate selective subtypes of peripheral C fibre nerve endings of primary afferent neurons in the epidermis or dermis. High-affinity receptors for various pruritogenic mediators transmit the stimulus, via not completely understood intracellular signaling pathways, from the periphery to the dorsal root ganglia (DRG), and the spinal cord. DRGs can modulate this stimulus on the transcriptional and posttranscriptional level, thereby modulating peripheral and central nerve endings. Within the spinal cord, itch signals can be also modulated. From lamina 1, a selective area within the ipsi dorsal horn of spinal cord, the signal will be transmitted to the CNS after crossing to the contralateral side. Activation of specific areas in the CNS results in the perception of itch leading to 'discomfort' and an acute or chronic scratch response. Additionally, the associated peripheral axon reflex may lead to the release of mast cell-stimulating neuropeptides (e.g. substance P) thereby amplifying pruritus via release of histamine, tryptase and IL-31, for example. This figure does not consider the complex interaction between pain and itch fibres on the spinal cord level where GRPR, opioid receptors, NK1R (post-synaptic), PAR2 (pre-synaptic primary afferents) and probably other mediators/ receptors can exert excitatory or inhibitory influences.

Table 1 Mediators of itch in atopic dermatitis

Substrate	Provocation of itch	Mechanism
Spinal inductor of itch		
GRP	+	Binding to GRPR of the spinal cord
Cutaneous inductors of itch		
Histamine	(+)	Binding to histamine receptors on sensory nerve fibres
Neuropeptides (e.g. substance P)	+	Mast cell degranulation, increased concentration in lesional skin
Acetylcholine	+	Central sensitization?
Tryptase kallikreins, cathepsin S	+	Binding to PAR_2 on sensory nerve fibres
Cytokines: Interleukin 2	+	Possible release of various mediators
Interleukin 8	–	
Interleukin 31	+	
Neurotrophin-4	+	m.n.n.
Eosinophils	+/?	Release mediators like PAF, leucotriens; histamine, proteinase liberation
Platelet activating factor	+	Histamine liberator
Leukotriens	+	m.n.n. (LTB4?)
Cutaneous suppressors of itch		
Cannabinoids	Interruption of itch transmission	Binding to CB1 and CB2 on cutaneous sensory nerve fibres
Opioid peptides	Induction of itch-inhibiting neurons on spinal level; suppression in the skin?	Binding to opioid receptors
TRP channels (Vanilloids)	Suppression of itch transmission	TRPV1, TRPV3 involved in itch Direct or indirect effects on sensory nerves suppressing itch
Interferon gamma	Suppression of pruritus	m.n.n. (IFN-γ receptor on nerves?)
Calcineurin inhibitors	Interruption of itch transmission	Downregulation of pruritic cytokines by effecting T cells Binding to TRPV1 on cutaneous sensory nerve fibres Ameliorating neuropeptide release Decreasing effects of neuropeptides on mast cells?

–, no induction of itch; (+), induction of weak itch; +, clear induction of itch; m.n.n., mechanism not known.

J. Buddenkotte. Pathophysiology and therapy of pruritus in allergic and atopic diseases. Allergy 65 (2010) 805–821.

AMPLIFICATION CIRCLE

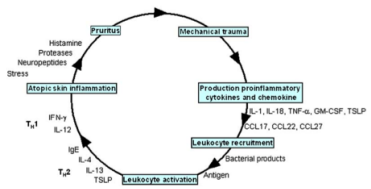


FIG 1. The amplification circle of atopic skin inflammation. Pruritus, the major symptom, induces scratching that enhances inflammation through leukocyte recruitment and activation. Among the molecules acting at each step, a key role is devoted to chemokines. Adapted from B. Homey's communication. *TSLP*, Thymic stromal lymphopoietin.

Taieb, et al. Proceedings of the 4th Georg Rajka International Symposium on Atopic Dermatitis, Arcachon, France, September 15-17, 2005. J Allergy Clin Immunol 2006;117:378-90.

Diagnosis Criteria in AD

- Diagnosis
  - Hanifin & Rajka
  - UK
  - American Academy of Dermatology

	Hanifin & Rajka	AAD
Sensitivity	96%	86%
Espe	93%	95%

M. S. de Bruin Weller. Evaluation of the child with atopic dermatitis. Clinical and experimental Allergy 2011

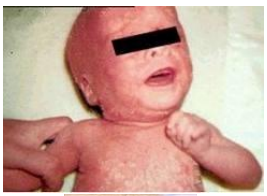
UK Diagnostic criteria

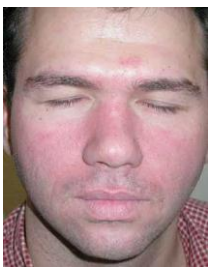
Table 1. UK diagnostic criteria

UK diagnostic criteria
child must have itchy skin conditions in the past 12 months
PLUS three or more of:
History of involvement of skin creases
Personal history of asthma or hayfever*
History of generally dry skin in the past year
Visible flexural dermatitis#
Onset below age 2**

*history of atopic disease in 1st degree relative if age < 4 years.
#as defined by photographic protocol.
**not used in children < 4 years.

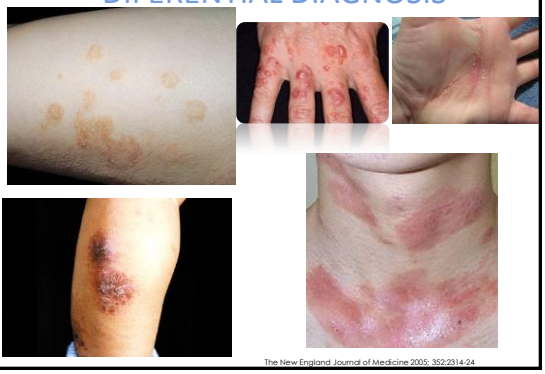
DIFERENTIAL DIAGNOSIS





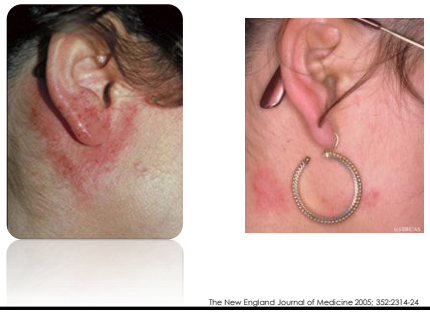
The New England Journal of Medicine 2005; 352:2314-24

DIFERENTIAL DIAGNOSIS



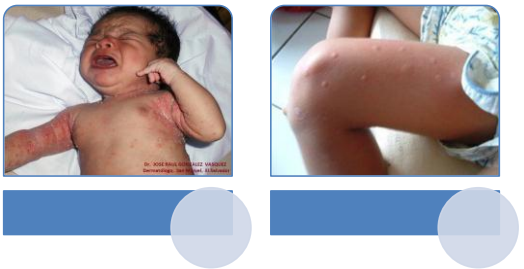
The New England Journal of Medicine 2005; 352:2314-24

DIFERENTIAL DIAGNOSIS



The New England Journal of Medicine 2005; 352:2314-24

DIAGNÓSTICO DIFERENCIAL



The New England Journal of Medicine 2005; 352:2314-24

DIAGNOSTIC APPROACH

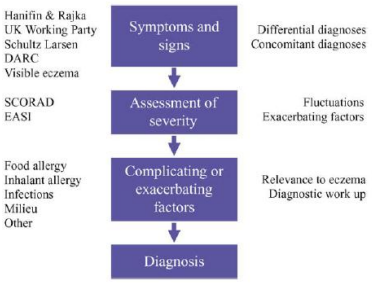
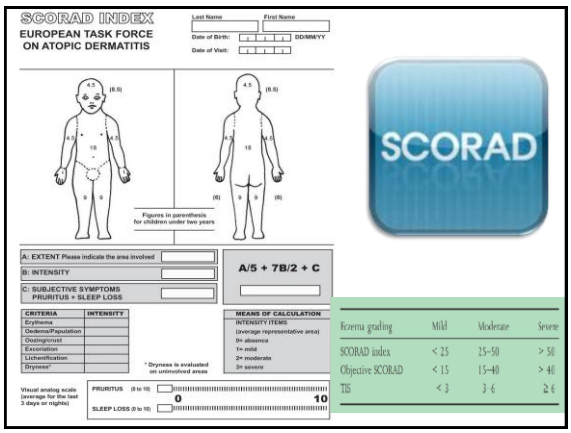
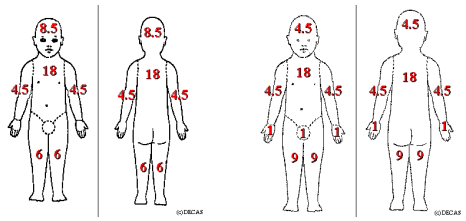


FIG 3. Diagnostic approach to patients presenting with symptoms and signs of atopic dermatitis.



SCORAD

CHILDREN **ADULTS**



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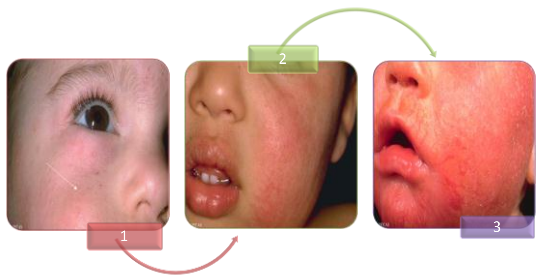

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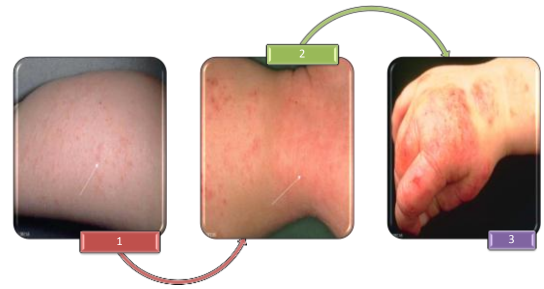

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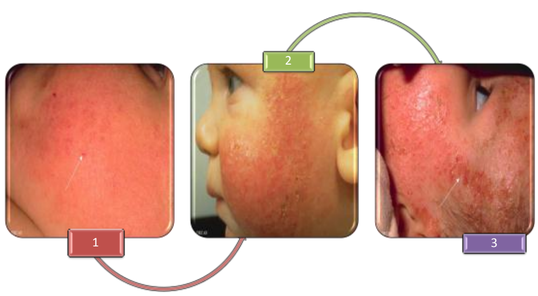

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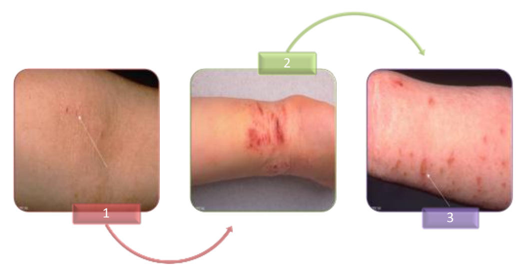

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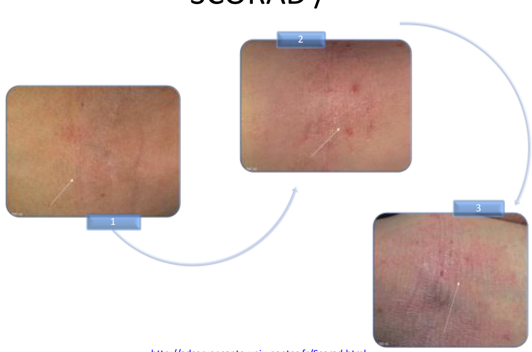

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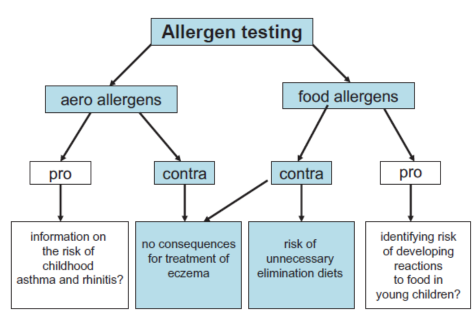
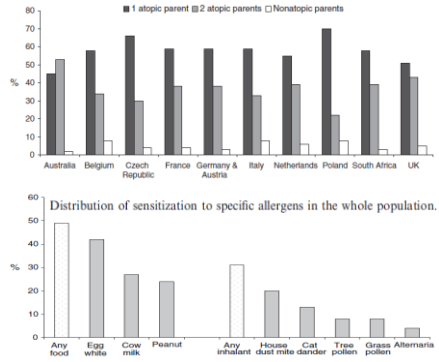


Fig. 1. Pro's and contra's of allergen testing in children with AD.

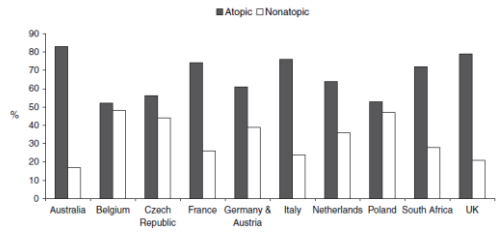
The allergic sensitization in infants with atopic eczema from different countries

Benedictis et al. The allergic sensitization in infants with atopic eczema from different countries. Allergy 2009; 64:295–303.



Benedictis et al. The allergic sensitization in infants with atopic eczema from different countries. Allergy 2009; 64:295–303.

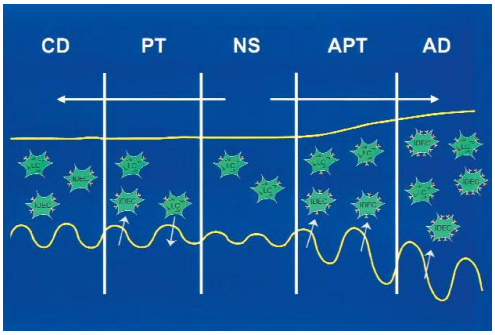
The allergic sensitization in infants with atopic eczema from different countries



Benedictis et al. The allergic sensitization in infants with atopic eczema from different countries. Allergy 2009; 64:295–303.

The diagnostic value of atopy patch testing and prick testing in atopic dermatitis: facts and controversies. Clinics in Dermatology (2010) 28, 38–44

Test	Sensitivity	Specificity
Prick tests	69%-82%	44%-52%
Specific IgE	65%-94%	42%-64%
APT	42%-56%	69%-92%



Karin Kerschenlohr. Atopy patch test reactions show a rapid influx of inflammatory dendritic epidermal cells in patients with extrinsic atopic dermatitis and patients with intrinsic atopic dermatitis . JACI 2003

Comparison of irritatant reactions between using lyophilized and commercial food allergen extracts in atopy patch tests in a normal population

Onsuree Boonyaviwat, Punchama Pacharn, Orathai Piboonpocanun, Pakit Vichyanond and Nualanong Visitsunthorn

IgE antibody responses in young children with atopic dermatitis.
Wahn U, Warner J, Simons FE, de Benedictis FM, Diepgen TL, Naspitz CK, de Longueville M, Bauchau V; EPAAC Study Group

Pediatr Allergy Immunol. 2008

The Relationship Between Serum Levels of Total IgE, IL-18, IL-12, IFN-γ and Disease Severity in Children With Atopic Dermatitis

Relationship between serum levels of interleukin-18, IgE and disease severity in patients withatopic dermatitis.
Trzeciak M
Department of Dermatology, Venereology and Allergology, Medical University of Gdańsk, Gdańsk, Poland.

Advances in Management of Atopic Dermatitis: New Therapies and Novel Uses of Existing Treatments

Elizabeth P. Chase, MD, and April W. Armstrong, MD, MPH

Seminars in Cutaneous Medicine and Surgery

Treatment with a barrier-strengthening moisturizing cream delays relapse of atopic dermatitis: a prospective and randomized controlled clinical trial

K Wirén,[†] C Nohlgård,[‡] F Nyberg,[§] L Holm,[¶] M Svensson,[**] A Johannesson,[††] P Wallberg,[††] B Berne,[‡‡] F Edlund,[†] M Lodén[†,*]

	Group using moisturizer ($n = 22$)	Group using no treatment ($n = 22$)
No. (%) of patients having a relapse	7 (32%)	15 (68%)
Median time to relapse (days)	> 180	30
Hazard ratio (no treatment:moisturizer)	3.2 (95% CI 1.3 to 7.8 $P = 0.01$)	
Absolute risk reduction (%)	36%	
Number needed to treat (NNT)	2.8	
Relative risk reduction (%)	53%	

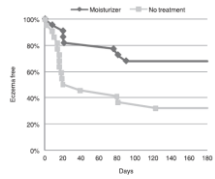


Figure 2 Kaplan-Meier plot of time to recurrence of eczema in the moisturizer and no treatment groups.

Wirén K, Nohlgård C, Nyberg F, et al: Treatment with a barrierstrengthening moisturizing cream delays relapse of atopic dermatitis: A prospective and randomized controlled clinical trial. J Eur Acad Dermatol Venereol 2009

Treatment of *Staphylococcus aureus* Colonization in Atopic Dermatitis Decreases Disease Severity

Jennifer T. Huang, Melissa Abrams, Brook Tlougan, Alfred Rademaker and Amy S. Paller

Pediatrics 2009;123;e808

TABLE 2 Changes in EASI Scores According to Location

Group	*n*	Change in EASI Score, Mean ± SE	*P*
Exposed sites: head and neck			
Change from baseline to 1 mo			
Treatment	11	−0.98 ± 0.86	.32
Placebo	14	−0.16 ± 0.80	
Change from baseline to 3 mo			
Treatment	9	−1.06 ± 1.04	.62
Placebo	13	−0.57 ± 0.86	
Bath-submerged sites: upper limbs, trunk, and lower limbs			
Change from baseline to 1 mo			
Treatment	11	−2.61 ± 0.60	.03
Placebo	14	−0.78 ± 0.55	
Change from baseline to 3 mo			
Treatment	9	−4.94 ± 0.74	.0005
Placebo	13	−0.88 ± 0.62	

Silver-loaded seaweed-based cellulosic fiber improves epidermal skin physiology in atopic dermatitis: safety assessment, mode of action and controlled, randomized single-blinded exploratory *in vivo* study

Joachim W. Fluhr[1,2], Maria Breternitz[1], Doreen Kowatzki[1], Andrea Bauer[1], Joerg Bossert[3], Peter Elsner[1] and Uta-Christina Hipler[1]

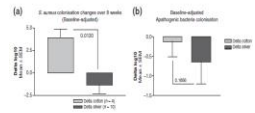


Figure 2. *Staphyloccocus aureus* reduced but not significant changes for apathogenic bacteria. (a) Comparing the two groups of patients with atopic dermatitis a significant reduction of *S. aureus* was detectable for baseline adjusted bacterial counts ($P = 0.0120$; cotton $n = 4$, silver $n = 10$). (b) Apathogenic bacterial colonization showed no change in the cotton group and a slight but not significant decrease was observed in the silver T-shirt group; however, the two groups did not show a significant difference (cotton $n = 18$, silver $n = 19$).

Table 1 Recent Prospective Studies Examining Recombinant Monoclonal Antibodies or Fusion Proteins in the Treatment of AD

Agent	MOA	Rationale	Study	Study Design
Infliximab	Antibody against TNF-α	TNF-α is increased in AD lesions	Jacobi et al[37]	Open-label
Omalizumab	Antibody against IgE	Blocks IgE from binding to receptor on mast cells	Sheinkopf et al[38]	Open-label
			Heil et al[39]	Randomized, doubleblind, placebocontrolled
Efalizumab	Antibody against CD11a	Disrupts recruitment of T cells	Takiguchi et al[40]	Open-label
Alefacept	Fusion protein, which interferes with LFA-3/CD2 interaction	Impairs T cell activation	Moul et al[41]	Open-label
			Simon et al[42]	Open-label
Mepolizumab	Antibody against IL-5	IL-5 stimulates eosinophil differentiation, growth, and release from bone marrow	Oldhoff et al[43]	Randomized, placebo-controlled, parallel group
			Oldhoff et al[44]	Double-blind, placebo-controlled
Rituximab	Antibody against CD20 on B cells acts to destroy the B cells	Loss of the antigen-presenting and immunomodulatory functions of B cells	Simon et al[45]	Open-label

AD, atopic dermatitis; TNF-α, tumor necrosis factor alpha; EASI, Eczema Area and Severity Index; IgE, immunoglobulin E; IGA, investigator's global assessment; SCORAD, SCORing Atopic Dermatitis; CD11a, cluster of differentiation 11a; LFA3/CD2, lymphocyte function-associated antigen 3/cluster of differentiation 2; IM, intramuscular; IL-5, interleukin 5; PGA, Physician's Global Assessment; CD20, cluster of differentiation 20.

Table 1 (Cont'd)

No. Subjects	Dose/Timing	Primary End Point Measure
9	5 mg/kg given at weeks 0, 2, 6 and then every 8 wks for 4 additional doses	Reduction of EASI score at week 10 by >50% (excellent), 30%–49% (moderate), <29% (nonsignificant)
21	150 mg or 300 mg dosed every 2 wks based on pretreatment IgE levels and body weight	IGA based on modified SCORAD
Intervention: 13 Control: 7	0.016 mg/kg/IgE [IU/mL] per 4 wks for 16 wks	Immunological disease parameters: flow cytometry, immunohistology, and serum IgE levels
10	0.7 mg/kg conditioning dose, followed by 1.0 mg/kg weekly for 11 additional weeks	Change in EASI at week 12 from baseline
9	30-mg IM injection weekly ×8 wks; at week (9) (a) those with ≥50% reduction in EASI received 15 mg IM weekly × 8 additional weeks (b) those without EASI 50% reduction received 30 mg IM weekly × 8 additional weeks	50% reduction in EASI at week 18
10	15-mg IM injection weekly for 12 wks	EASI, pruritus score, differential white blood cell analysis, skin histology, immunofluorescence, and cytokine expression analysis
Intervention: 18 Control: 22	2 single 750-mg doses given 1 wk apart***	Percentage of patients with at least "marked improvement" in PGA of improvement after 2 wks
Intervention: 20 Control: 23	2 single 750-mg doses given 1 wk apart	Clinical evaluation of atopy patch test and number of eosinophils in skin biopsy
6	Two 1000-mg infusions given 2 wks apart	EASI score, pruritus score

Chase et al. Advances in Management of Atopic Dermatitis: New Therapies and Novel Uses of Existing Treatments. Semin Cutan Med Surg 2012

Long-term Efficacy of Intravenous Immunoglobulin Therapy for Moderate to Severe Childhood Atopic Dermatitis

Sue-Jung Jee, Joo-Hwa Kim, Hey-Sung Baek, Ha-Baik Lee, Jae-Won Oh*

Table 2. Comparison of SCORAD index, serum IgE, and eosinophil count between children with IVIg treatment and the controls

Visit	SCORAD index		Serum IgE (IU/mL)		Eosinophil count (/mm³)	
	IVIg	Control	IVIg	Control	IVIg	Control
V1	61.5 ± 13.0*	42.1 ± 9.9	571.2 ± 753.4	615.2 ± 1023.2	529.4 ± 462.6	290 ± 179.3
V4	46.9 ± 17.3*	40.4 ± 6.3	384.9 ± 519.5	598.8 ± 858.4	397.6 ± 342.8	247.1 ± 153.1
V5	32.1 ± 19.4*	35.7 ± 8.9	493.9 ± 620.3	622.0 ± 932.5	470.8 ± 411.7	330 ± 150.5
V6	39.3 ± 18.4	35.9 ± 9.6	548.9 ± 677.2	633.9 ± 946.7	547.6 ± 393.3	270.0 ± 71.3

*There shows significantly differences of SCORAD between IVIg and control at V1 vs. V4 (P=0.005) and V1 vs. V5 (P=0.17).
IVIg, intravenous immunoglobulin; V1, before therapy; V4, during therapy; V5, 3-month follow-up visit; V6, 6-month follow-up visit.

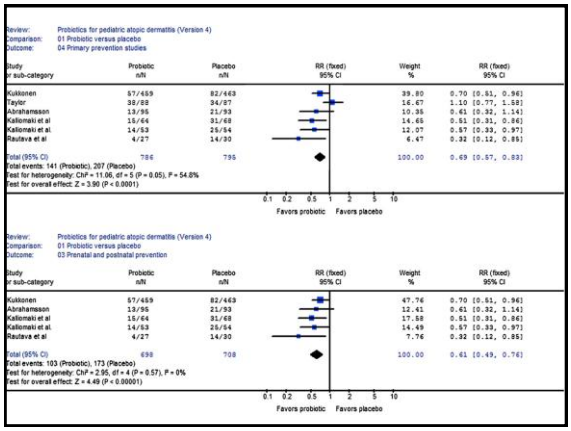
Allergy Asthma Immunol Res. 2011

Treatment of pruritus with topically applied opiate receptor antagonist

Paul L. Bigliardi, MD,[a,b] Holger Stammer, MSc,[a] Gerhard Jost, MD,[c] Theo Rufli, MD,[b] Stanislaw Büchner, MD,[b] and Mei Bigliardi-Qi, PhD[a,b]
Lausanne, Basel, and Egerkingen, Switzerland; and Munich, Germany

Meta-analysis of clinical trials of probiotics for prevention and treatment of pediatric atopic dermatitis

Joohee Lee, AB,b David Seto, BA,b and Leonard Bielory, MDa



Conclusions

- Multidisciplinary management are needed in AD
- Management
  - Pruritus
  - Infections
  - Co-morbidity
- Many therapy in research
- Value Risk /benefits
- Personalized Medicine

Gracias!!!