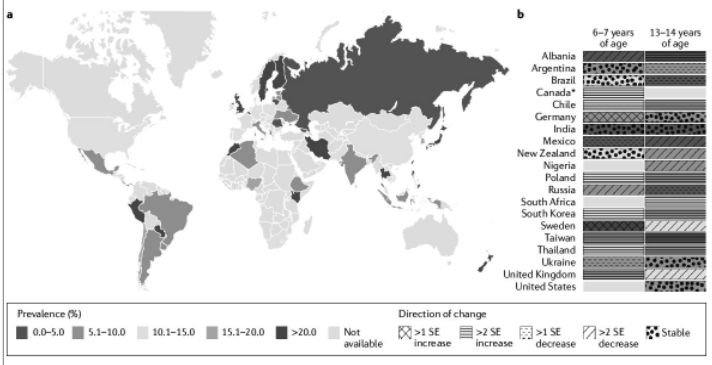
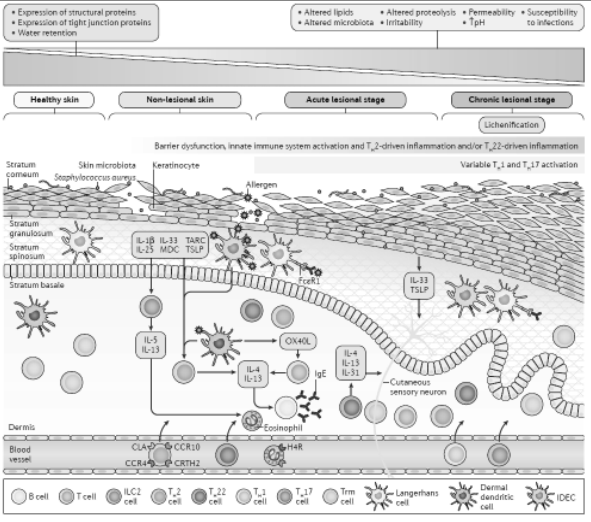
아토피피부염
기본관리부터 최신 치료까지 전문가 되기

최미라
일산백병원 피부과

Global prevalence of atopic dermatitis symptoms

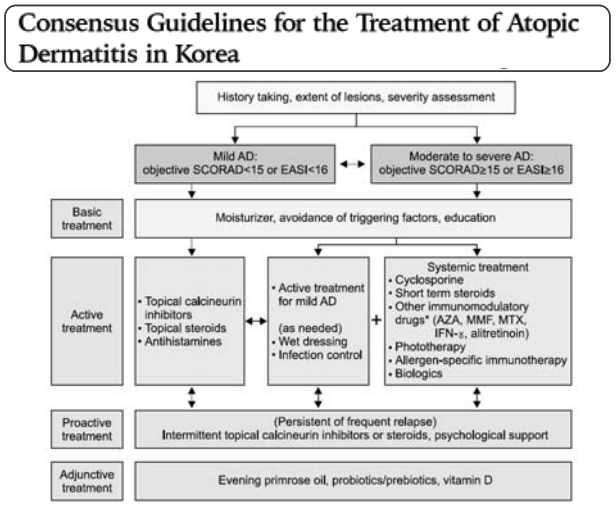


Nat Rev Dis Primers 2018;4:1

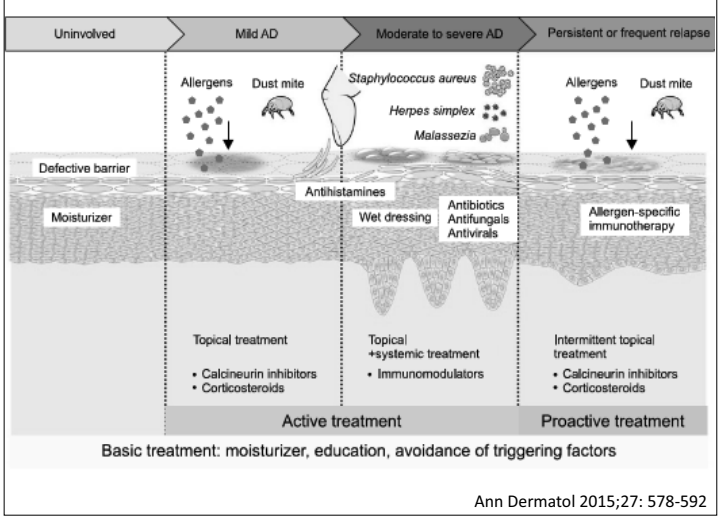


Nat Rev Dis Primers 2018;4:1

Ann Dermatol 2015;27: 578-592
J Eur Acad Dermatol Venereol 2018;32:657–682
Allergology International 2017;66:230-247
J Am Acad Dermatol 2014;70:338-51



Ann Dermatol 2015;27: 578-592



Ann Dermatol 2015;27: 578-592

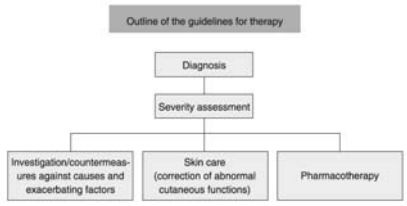
Invited review article

Japanese guidelines for atopic dermatitis 2017☆

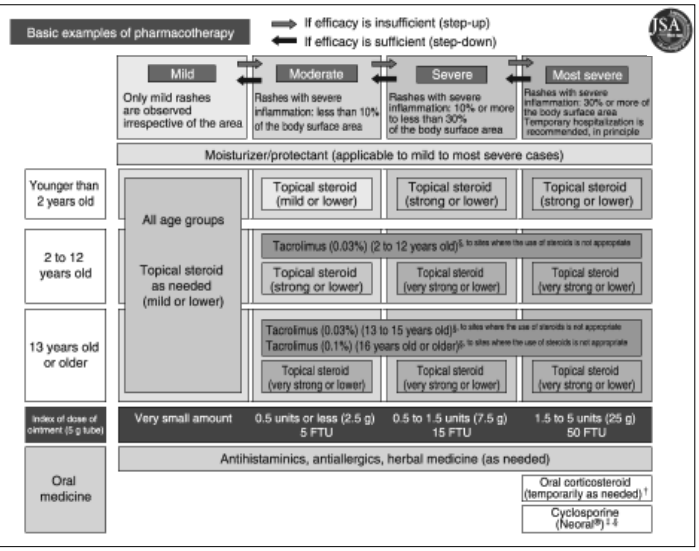
1. Diagnosis
Appropriate diagnosis should be ensured by discriminating them from other diseases with similar symptoms, such as eczema and dermatitis, in accordance with the abovementioned concept.

2. Assessment of cutaneous symptoms
In selecting a therapy, cutaneous symptoms need to be properly assessed.

3. Basics of treatment
Based on the above assessment, investigation/countermeasures against causes and exacerbating factors, skin care, and pharmacotherapy should be implemented by being optimally combined for each patient. Sufficient information about the treatment should be transmitted to the patient to build a favorable partnership.



Allergology International 2017;66:230-247



GUIDELINES

Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children:

- **General measures and avoidance strategies**
- **Basic emollient treatment and bathing**
- **Dietary intervention**
- **Topical anti-inflammatory therapy**
- **Phototherapy**
- **Antipruritic therapy**
- **Antimicrobial therapy**
- **Systemic anti-inflammatory treatment**
- **Other systemic treatment**
- **Allergen-specific immunotherapy**
- **Complementary medicine**
- **Psychosomatic counselling**

J Eur Acad Dermatol Venereol 2018;32:657–682

EADV

(a) **Treatment recommendation for atopic eczema: adult**

- For every phase, *additional* therapeutic options should be considered
- Add antiseptics / antibiotics in cases of superinfection
- Consider compliance and diagnosis, if therapy has insufficient effect
- Refer to guideline text for restrictions, especially for treatment marked with [1]
- Licensed indication are marked with [2], off-label treatment options are marked with [3]

SEVERE: **SCORAD >50 / or persistent eczema**	Hospitalization; systemic immunosuppression: cyclosporine A [2], short course of oral glucocorticosteroids[3], dupilumab [1,2], methotrexate[3], azathioprin [3], mycophenolate mofetil [3]; PUVA [1]; alitretinoin [1,3]
MODERATE: **SCORAD 25-50 / or recurrent eczema**	Proactive therapy with topical tacrolimus [2] or class II or class III topical glucocorticosteroids [3], wet wrap therapy, UV therapy (UVB 311 nm, medium dose UVA1), psychosomatic counseling, climate therapy
MILD: **SCORAD <25 / or transient eczema**	Reactive therapy with topical glucocorticosteroids class II [2] or depending on local cofactors: topical calcineurin inhibitors [2], antiseptics incl. silver [2], silver coated textiles [1]
BASELINE: **Basic therapy**	Educational programmes, emollients, bath oils, avoidance of clinically relevant allergens (encasings, if diagnosed by allergy tests)

J Eur Acad Dermatol Venereol 2018;32:657-682

EADV

(b) **Treatment recommendation for atopic eczema: children**

- For every phase, *additional* therapeutic options should be considered
- Add antiseptics / antibiotics in cases of superinfection
- Consider compliance and diagnosis, if therapy has insufficient effect
- Refer to guideline text for restrictions, especially for treatment marked with [1]
- Licensed indication are marked with [2], off-label treatment options are marked with [3]

SEVERE: **SCORAD >50 / or persistent eczema**	Hospitalization, systemic immunosuppression: cyclosporine A [2], methotrexate[3], azathioprin[3], mycophenolate mofetil [1,3]
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J Eur Acad Dermatol Venereol 2018;32:657-682

Diagnosis

Severity Assessment
SCORAD, EASI

Basic treatment	Active treatment	Other treatment
Emollient & bathing	**Topical therapy** • Corticosteroid • Calcineurin inhibitor	• Immunotherapy • Pro/prebiotics • Vitamin D
Avoidance strategy	**Systemic therapy** • Phototherapy • Anti-inflammatory therapy • Immunosuppressant • Antimicrobial therapy	**New targeted treatment** • Biologics • Small molecules
Dietary intervention		

Diagnosis

Korean Dermatological Association (2005)

Major features

1) Pruritus
2) Typical morphology and distribution
 - Under the age of 2 years
  : face, trunk , extensor
 - Over the age of 2 years
  : face, neck, flexural involvement
3) Personal or family history (atopic dermatitis, asthma, allergic rhinitis)

Minor features

1) Xerosis
2) Pityriasis alba
3) Facial erythema/facial pallor
4) Periorbital eczema or orbital darkening
5) Periauricular eczema
6) Cheilitis
7) Tendency towards non-specific hand or foot dermatitis
8) Scalp scale
9) Perifollicular accentuation
10) Itch when sweating
11) White dermographism
12) Skin prick test reactivity
13) Elevated serum IgE
14) Tendency towards cutaneous infections

at least 2 of 3 major features and 4 of 14 minor features

Severity Assessment
SCORAD, EASI

Assessment of clinical signs of atopic dermatitis: A systematic review and recommendation

The **Eczema Area and Severity Index (EASI)** and **Severity Scoring of Atopic Dermatitis Index (SCORAD)** are the best instruments to assess the clinical signs of AD. The other 14 instruments identified are (currently) not recommended because of unclear or inadequate measurement properties.

J Allergy Clin Immunol 2013;132:1337-47

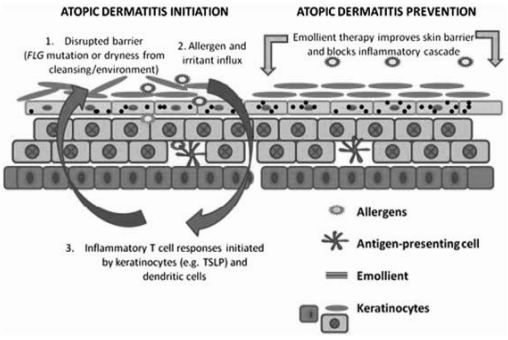
Diagnosis

Severity Assessment
SCORAD, EASI

Basic treatment	Active treatment	Other treatment
Emollient & bathing	**Topical therapy** • Corticosteroid • Calcineurin inhibitor	• Immunotherapy • Pro/prebiotics • Vitamin D
Avoidance strategy	**Systemic therapy** • Phototherapy • Anti-inflammatory therapy • Immunosuppressant • Antimicrobial therapy	**New targeted treatment** • Biologics • Small molecules
Dietary intervention		

Basic treatment

Emollient & bathing



Emollient therapy from birth represents
a novel approach to atopic dermatitis primary prevention !

J Allergy Clin Immunol 2014;134:818-23

Basic treatment

Emollient & bathing

- **Must be cleansed thoroughly, but gently and carefully**
  - Get rid of crusts
  - Mechanically eliminate bacterial contaminants in the case of bacterial superinfection
- **Cleansers ± antiseptics**
  - Non-irritant and low-allergen formulas
  - Bath additives (from peanut or colloidal oat..)
    - Should be *avoided* esp. < 2yrs
- **Rapid rinse in the bath (27–30˚C)**
  - Short duration of the bath (only 5 min)
  - Use of bath oils (2 last minutes of bathing)
  - Topical emollients directly after a bath or a shower

Basic treatment

Emollient & bathing

- **Regular use of emollient**
  - Short- and long-term steroid sparing effect in mild-to-moderate AE
  - Induction of remission with topical corticosteroids or topical calcineurin inhibitors is required first
- **Emollients should be**
  - Adequate amounts
  - Used liberally and frequently
  - In a minimum amount of 250 g per week for adults
    - Up to 100 g per week in young children, up to even 500 g in adults
  - Higher lipid content are preferable in wintertime

Basic treatment

Emollient & bathing

When choosing a moisturizer

- Use of pure oil products (coconut oil..) instead of emulsions
  - Dry out the skin → TEWL ↑ : NOT RECOMMENDED
- Propylene glycol
  - Irritating (<2 yrs) , toxicity↑
- Emollients containing intact proteins (peanut allergen, colloidal oat meal..)
  - Risk of skin sensitization and allergy ↑
- Proteinaceous allergens, haptens (lanolin/wool wax alcohol, methylisothiazolinone)
  - Contact allergy ↑ (esp. < 2yrs)

Basic treatment

Avoidance strategy

- Pollen avoidance measures can be recommended during pollen season.

- House dust mite avoidance measures (encasing) may be tried in selected cases.

- Cat epithelia should be avoided!
- Dogs might even protect from AE, possibly due to exposure to non-pathogenic microbes.

- All children diagnosed with AE should be vaccinated according to the national vaccination plan.

Basic treatment

Dietary intervention

- **Primary prevention of food allergy-associated AD**
  - Exclusive breast milk feeding until 4 months of age
  - If breast milk is lacking
    - Low-risk children: conventional cow's milk formula
    - High-risk children : documented hypoallergenic formula
- **Introduction of complementary foods**
  - Between 4 ~6 months of age in low- and high-risk children irrespective of an atopic heredity
- Patients with moderate-to-severe AD should observe a therapeutic diet eliminating those foods that elicitated clinical early or late reactions upon *controlled oral provocation tests*.

Diagnosis

Severity Assessment
SCORAD, EASI

Basic treatment	Active treatment	Other treatment
Emollient & bathing	**Topical therapy** • Corticosteroid • Calcineurin inhibitor	• Immunotherapy • Pro/prebiotics • Vitamin D
Avoidance strategy	**Systemic therapy** • Phototherapy • Anti-inflammatory therapy • Immunosuppressant • Antimicrobial therapy	**New targeted treatment** • Biologics • Small molecules
Dietary intervention		

Active treatment

Topical therapy
- Corticosteroid
- Calcineurin inhibitor

	TCS class II	TCS class III	Tacrolimus	Pimecrolimus
Overall recommendation	default treatment	short-term flare treatment	long-term maintenance	children, facial lesions
Most important side-effects	Skin atrophy Telangiectasia Striae distensae	Skin atrophy Telangiectasia Striae distensae	Initial burning/stinging	Initial burning/stinging
Suitable for long-term treatment	Sometimes	No	Yes	Yes
Suitable for proactive therapy	Yes†	Yes†	Yes‡	No
Suitable for children >2 years of age	Yes	Sometimes, see text	Yes‡	Yes‡
Suitable for babies <2 years of age	Yes	Diluted use	Yes†	Yes†
Suitable during pregnancy	Yes	Yes	Possible with strict indication†	Possible with strict indication†
Suitable during lactation	Yes	Yes	Possible with strict indication†	Possible with strict indication†

†Off label use; ‡Licensed use.

J Eur Acad Dermatol Venereol 2018;32:850-878

Active treatment

Topical therapy : Corticosteroid

	TCS class II	TCS class III	Tacrolimus	Pimecrolimus
Overall recommendation	default treatment	short-term flare treatment	long-term maintenance	children, facial lesions
Most important side-effects	Skin atrophy Telangiectasia Striae distensae	Skin atrophy Telangiectasia Striae distensae	Initial burning/stinging	Initial burning/stinging
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Suitable during pregnancy	Yes	Yes	Possible with strict indication†	Possible with strict indication†
Suitable during lactation	Yes	Yes	Possible with strict indication†	Possible with strict indication†

†Off label use; ‡Licensed use.

- Most important anti-inflammatory drugs
  - Esp. in the acute phase
  - Wet wraps with diluted topical corticosteroid for short-term
- Proactive therapy with TCS
  - Twice-weekly application in long-term follow-up → Relapses ↓
  - May be used safely for at least 20 weeks
- Patient fear of side-effects of corticosteroids (corticophobia)

J Eur Acad Dermatol Venereol 2018;32:850-878

Active treatment

Topical therapy : Calcineurin inhibitor

	TCS class II	TCS class III	Tacrolimus	Pimecrolimus
Overall recommendation	default treatment	short-term flare treatment	long-term maintenance	children, facial lesions
Most important side-effects	Skin atrophy Telangiectasia Striae distensae	Skin atrophy Telangiectasia Striae distensae	Initial burning/stinging	Initial burning/stinging
Suitable for long-term treatment	Sometimes	No	Yes	Yes
Suitable for proactive therapy	Yes†	Yes†	Yes‡	No
Suitable for children >2 years of age	Yes	Sometimes, see text	Yes‡	Yes‡
Suitable for babies <2 years of age	Yes	Diluted use	Yes†	Yes†
Suitable during pregnancy	Yes	Yes	Possible with strict indication†	Possible with strict indication†
Suitable during lactation	Yes	Yes	Possible with strict indication†	Possible with strict indication†

†Off label use; ‡Licensed use.

- Important anti-inflammatory drugs
- Treating acute flares with TCI (X)
- Initial treatment with TCS before switching to TCI (O)
- Esp. sensitive skin areas (face, intertriginous sites, anogenital area)
- Proactive therapy
  - Twice-weekly application of tacrolimus ointment may reduce relapses.
- Effective sun protection should be recommended in patients treated with TCI

J Eur Acad Dermatol Venereol 2018;32:850-878

Active treatment

Topical therapy
- Corticosteroid
- Calcineurin inhibitor

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Suitable for babies <2 years of age	Yes	Diluted use	Yes†	Yes†
Suitable during pregnancy	Yes	Yes	Possible with strict indication†	Possible with strict indication†
Suitable during lactation	Yes	Yes	Possible with strict indication†	Possible with strict indication†

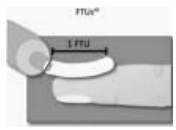
†Off label use; ‡Licensed use.

★ *Effective topical therapy* ★
- Sufficient strength
- Sufficient dosage
- Correct application

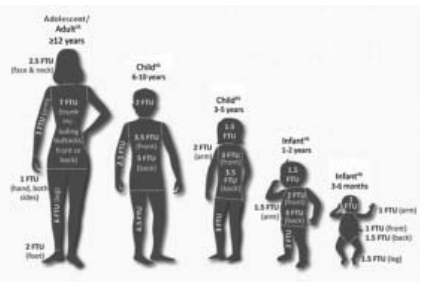
J Eur Acad Dermatol Venereol 2018;32:850-878

Active treatment

Topical therapy
- Corticosteroid
- Calcineurin inhibitor



Fingertip unit (FTU)
- Adult patient's index finger
- ≈ 0.5 g
- 1 FTU = 2 palms



- *Moisturizers first? Or topical drug first?*
  - Lotion type : 10 ~15 minutes before topical steroid application
  - Ointment type: After topical steroid application

Pediatrics 2015;136:554-65

Active treatment

Topical therapy
- Corticosteroid
- Calcineurin inhibitor

Weekly/Monthly Quantities by Age Group (Whole Body Application)[a]

Moisturizer[c]	Basic Management
Infant	100 g/week
Child	150–200 g/week[g]
Adolescent/Adult	500 g/week[g]

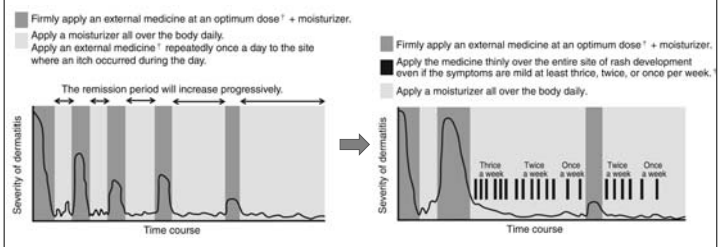
Ointment	Acute Treatment[f,5,46] 2-times daily	Maintenance Treatment 1-2–times weekly[d]	2-3–times weekly[d]	1-2–times daily[d]
Infant	60–100 g/week	10 g/month	15 g/month	75 g/month
Child	125–250 g/week	20 g/month	30 g/month	150 g/month
Adolescent/Adult	260–300 g/week	40–60 g/month	60–90 g/month	300–450 g/month

Cream[b]	Acute Treatment 2-times daily	Maintenance Treatment 1-2–times weekly	2-3–times weekly	1-2–times daily
Infant	66–110 g/week	15 g /month	20 g/month	100 g/month
Child	140–275 g/week	25 g/month	35 g/month	175 g/month
Adolescent/Adult	290–330 g/week	45–70 g/month	70–100 g/month	350–500 g/month

Pediatrics 2015;136:554-65

Active treatment

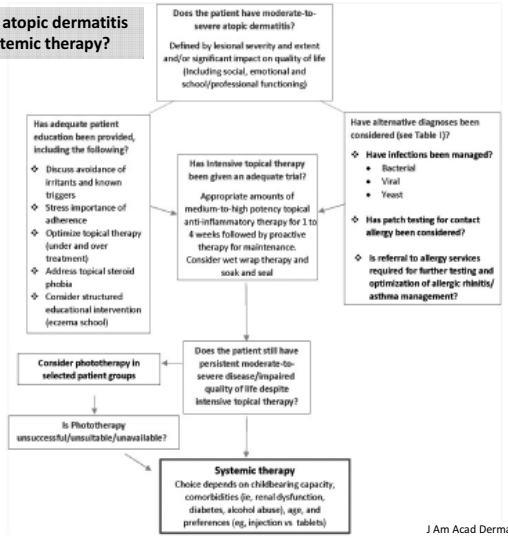
Topical therapy
- Corticosteroid
- Calcineurin inhibitor



Reactive therapy **Proactive therapy**

Allergology International 2017;66:230-247

When does atopic dermatitis warrant systemic therapy?



J Am Acad Dermatol 2017;77:623-33

Active treatment

Systemic therapy

	Cyclosporine	Methotrexate	Azathioprine	Mycophenolic acid	Corticosteroids
Overall recommendation	++ acute flare intervention	++ long-term maintenance	Can be used long term	++ little toxicity	Outdated‡
Time to respond (weeks)§	2	8–12	8–12	8–12	1–2
Time to relapse (weeks)	<2	>12	>12	>12	<2
Most important side-effects	Serum creatinine ↑ blood pressure ↑	Haematological liver enzymes ↑ gastrointestinal	Haematological liver enzymes ↑ gastro-intestinal	Haematological skin infections gastro-intestinal	Cushing's osteoporosis diabetes
Starting dose adult	4–5 mg/kg/day‡	5–15 mg/week	50 mg/day‡	MMF 1–2 g/day (EC-MPA 1.44 g/day)	0.2–0.5 mg/kg/day
Maintenance dose adult	2.5–3 mg/kg/day	Most often 15/week; can increase to max 25 mg/week	2–3 mg/kg/day†	MMF 2–3 g/day (EC-MPA 1.44 g/day)	Not for maintenance‡
Starting dose children	5 mg/kg/day	10–15 mg/m²/week	25–50 mg/day	MMF 20–50 mg/kg/day	0.2–0.5 mg/kg/day
Maintenance dose children	2.5–3 mg/kg/day	Increase 2.5–5 mg/ week, decrease 2.5 mg/week to effective/lowest effective dose	2–3 mg/kg/day†	Increase daily total dose by 500 mg every 2–4 weeks up to 30–50 mg/kg/day	Not for maintenance‡
Pregnancy	Possible	Teratogenic, absolutely contraindicated	Conflicting data, possible with strict indication	Teratogenic, absolutely contraindicated	Possible
Fathering	Possible	Little information, conflicting data, contra-indicated	Little information, possible with strict indication	Conflicting data	Possible

†TPMT heterozygote 1–1.5 mg/kg/day. ‡See full text. §Time to reach most of expected full response.
EC-MPS, enteric-coated mycophenolic sodium; MMF, mycophenolate mofetil.

J Eur Acad Dermatol Venereol 2018;32:850-878

Active treatment

Systemic therapy

human monoclonal antibody against IL-4Rα

	Cyclosporine	Methotrexate	Azathioprine	Mycophenolic acid	Corticosteroids	Dupilumab
Overall recommendation	++ acute flare intervention	++ long-term maintenance	Can be used long term	++ little toxicity	Outdated‡	Long-term maintenance
Time to respond (weeks)§	2	8–12	8–12	8–12	1–2	4–6
Time to relapse (weeks)	<2	>12	>12	>12	<2	>8
Most important side-effects	Serum creatinine ↑ blood pressure ↑	Haematological liver enzymes ↑ gastrointestinal	Haematological liver enzymes ↑ gastro-intestinal	Haematological skin infections gastro-intestinal	Cushing's osteoporosis diabetes	Conjunctivitis
Starting dose adult	4–5 mg/kg/day‡	5–15 mg/week	50 mg/day‡	MMF 1–2 g/day (EC-MPA 1.44 g/day)	0.2–0.5 mg/kg/day	600 mg loading dose
Maintenance dose adult	2.5–3 mg/kg/day	Most often 15/week; can increase to max 25 mg/week	2–3 mg/kg/day†	MMF 2–3 g/day (EC-MPA 1.44 g/day)	Not for maintenance‡	300 mg/2 weeks
Starting dose children	5 mg/kg/day	10–15 mg/m²/week	25–50 mg/day	MMF 20–50 mg/kg/day	0.2–0.5 mg/kg/day	No data yet
Maintenance dose children	2.5–3 mg/kg/day	Increase 2.5–5 mg/ week, decrease 2.5 mg/week to effective/lowest effective dose	2–3 mg/kg/day†	Increase daily total dose by 500 mg every 2–4 weeks up to 30–50 mg/kg/day	Not for maintenance‡	No data yet
Pregnancy	Possible	Teratogenic, absolutely contraindicated	Conflicting data, possible with strict indication	Teratogenic, absolutely contraindicated	Possible	No data yet
Fathering	Possible	Little information, conflicting data, contra-indicated	Little information, possible with strict indication	Conflicting data	Possible	No data yet

†TPMT heterozygote 1–1.5 mg/kg/day. ‡See full text. §Time to reach most of expected full response.
EC-MPS, enteric-coated mycophenolic sodium; MMF, mycophenolate mofetil.

J Eur Acad Dermatol Venereol 2018;32:850-878

ORIGINAL ARTICLE

Dupilumab Treatment in Adults with Moderate-to-Severe Atopic Dermatitis

N Engl J Med 2014;371:130-9

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Two Phase 3 Trials of Dupilumab versus Placebo in Atopic Dermatitis

N Engl J Med 2016; 375:2335-2348

Long-term management of moderate-to-severe atopic dermatitis with dupilumab and concomitant topical corticosteroids (LIBERTY AD CHRONOS): a 1-year, randomised, double-blinded, placebo-controlled, phase 3 trial

Lancet 2017; 389: 2287–303

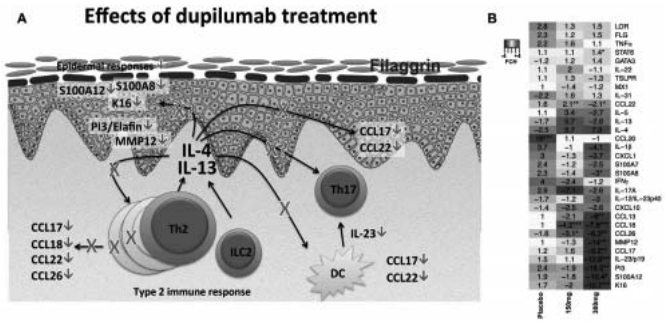
ORIGINAL ARTICLE

Efficacy and Safety of Dupilumab in Glucocorticoid-Dependent Severe Asthma

N Engl J Med 2018;378:2475-85

Active treatment

Systemic therapy : dupilumab



J Allergy Clin Immunol 2017;139:S65-76

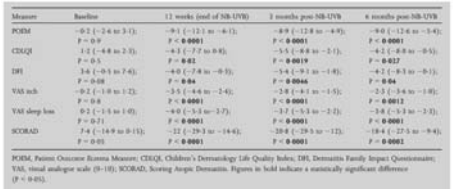
Active treatment

Systemic therapy: Phototherapy

PAEDIATRIC DERMATOLOGY

BJD
British Journal of Dermatology

Narrowband ultraviolet B phototherapy in children with moderate-to-severe eczema: a comparative cohort study*



Measure	Baseline	12 weeks (end of NB-UVB)	2 months post-NB-UVB	6 months post-NB-UVB
POEM	−0·2 (−2·6 to 3·1); P = 0·9	−9·1 (−12·1 to −6·1); P < 0·0001	−8·9 (−12·8 to −4·9); P < 0·0001	−9·0 (−12·6 to −5·4); P < 0·0001
CDLQI	1·2 (−4·8 to 2·3); P = 0·5	−4·3 (−7·7 to 0·8); P = 0·02	−5·5 (−9·8 to −2·1); P = 0·0019	−6·1 (−8·8 to −0·5); P = 0·017
DFI	3·6 (−0·5 to 7·6); P = 0·08	−4·0 (−7·8 to −0·5); P = 0·04	−5·4 (−9·1 to −1·8); P = 0·0046	−4·2 (−9·3 to −0·1); P = 0·04
VAS itch	−0·2 (−1·0 to 1·2); P = 0·8	−3·5 (−4·4 to −2·4); P < 0·0001	−3·8 (−4·1 to −1·5); P < 0·0001	−2·3 (−3·4 to −1·9); P = 0·0012
VAS sleep loss	0·2 (−1·4 to 1·0); P = 0·71	−4·0 (−5·3 to −2·7); P < 0·0001	−3·7 (−5·3 to −2·2); P < 0·0001	−3·6 (−5·3 to −2·1); P < 0·0001
SCORAD	7·4 (−14·9 to 0·15); P = 0·05	−22 (−29·3 to −14·4); P < 0·0001	−20·8 (−29·5 to −12); P < 0·0001	−18·4 (−27·5 to −9·4); P < 0·0001

POEM, Patient Oriscorre Eczema Measure; CDLQI, Children's Dermatology Life Quality Index; DFI, Dermatitis Family Impact Questionnaire; VAS, visual analogue scale (0–10); SCORAD, Scoring Atopic Dermatitis. Figures in bold indicate a statistically significant difference (P < 0·05).

- 2/wk (total Tx: 24)
- Starting dose : 70% MED
- % based dose increments

- QOL, objective score improvement
- Maintained up to 6 months post-treatment
- Relief pruritus!

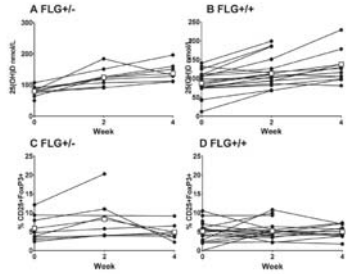
Br J Dermatol 2014;170:150-6

Active treatment

Systemic therapy: Phototherapy

Increase in Vitamin D but not Regulatory T Cells following Ultraviolet B Phototherapy of Patients with Atopic Dermatitis

Stine SIMONSEN[1], Charlotte Menné BONEFELD[2], Jacob Pontoppidan THYSSEN[1], Carsten GEISLER[2] and Lone SKOV[1]
[1]Department of Dermatology and Allergy, Herlev and Gentofte Hospital, University of Copenhagen, Hellerup, [2]Department of Immunology and Microbiology, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark



NBUVB for AD

- Serum 25(OH)D concentrations ↑
- NO changes in immune system

Acta Derm Venereol 2019;99:139-145

Diagnosis

Severity Assessment
SCORAD, EASI

Basic treatment	Active treatment	Other treatment
Emollient & bathing	**Topical therapy** • Corticosteroid • Calcineurin inhibitor	• Immunotherapy • Pro/prebiotics • Vitamin D
Avoidance strategy	**Systemic therapy** • Phototherapy • Anti-inflammatory therapy • Immunosuppressant • Antimicrobial therapy	**New targeted treatment** • Biologics • Small molecules
Dietary intervention		

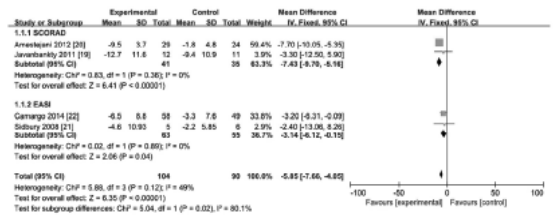
Other treatment

- **Allergen-specific immunotherapy**
  - Currently *not recommended* as a general treatment option for A
  - May be considered for selected patients
    - House dust mite, birch or grass pollen sensitization in severe AD
    - History of clinical exacerbation after exposure to the causative allergen
    - Positive corresponding atopy patch test

J Eur Acad Dermatol Venereol 2018;32:657–682

Other treatment

Vitamin D Status and Efficacy of Vitamin D Supplementation in Atopic Dermatitis: A Systematic Review and Meta-Analysis



- **Serum vitamin D level was lower in the AD patients**
- **Vitamin D supplementation could be a new therapeutic option for AD**

Nutrients 2016;8:789-799

Other treatment

Probiotics for the Treatment of Atopic Dermatitis in Children:
A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Front Cell Infect Microbiol 2017;7:392

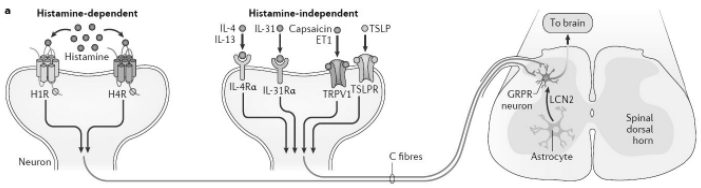
- Research to date has not robustly shown that probiotics are beneficial for children with AD.
- However, caution is needed when generalizing our results, as the populations evaluated were heterogeneous.

Probiotics for treating eczema

Cochrane Database Syst Rev 2018;11:CD006135

- Currently available probiotic strains probably make little or no difference in improving patient-rated eczema symptoms.
- Probiotics may make little or no difference in QoL for people with eczema nor in investigator-rated eczema severity score.

Q. What is the most important clinical symptom in AD ?
A. ITCH !!



Itch pathways in atopic dermatitis

Nat Rev Dis Primers 2018;4:1

Antihistamine?

- There is not enough evidence to support the general use of both first- and second-generation H1R antihistamines for the treatment of pruritus in AD.
  - May be tried for the treatment of pruritus in AE patients, if standard treatment with TCS and emollients is not sufficient.
  - Long-term use of sedative antihistamines in childhood may affect sleep quality and is therefore not recommended.

Is there any other Mx for itching?

- Opioid receptor antagonists
  - Naltrexone, nalmefene
- Selective serotonin reuptake inhibitors
  - Paroxetine, fluvoxamine

→ *NOT recommended for routine treatment of itch in AD*

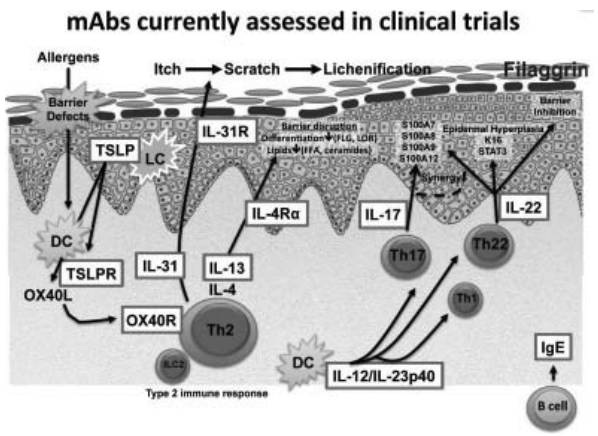
J Eur Acad Dermatol Venereol 2018;32:850-878

Diagnosis

Severity Assessment
SCORAD, EASI

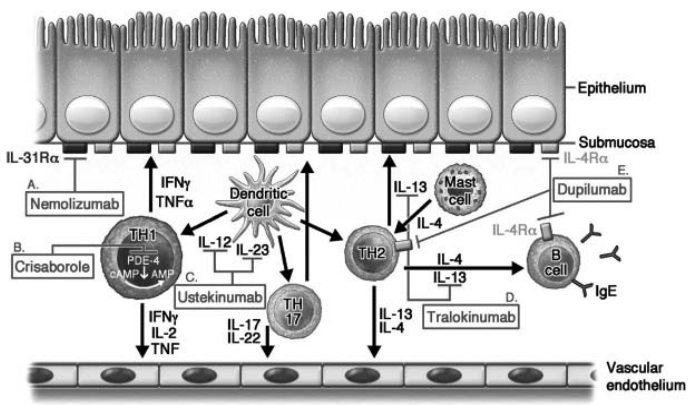
Basic treatment	Active treatment	Other treatment
Emollient & bathing	**Topical therapy** • Corticosteroid • Calcineurin inhibitor	• Immunotherapy • Pro/prebiotics • Vitamin D
Avoidance strategy	**Systemic therapy** • Phototherapy • Anti-inflammatory therapy • Immunosuppressant • Antimicrobial therapy	**New targeted treatment** • Biologics • Small molecules
Dietary intervention		

New targeted treatment



J Allergy Clin Immunol 2017;139:S65-76

New targeted treatment



J Allergy Clin Immunol 2018;142:1740-7

New targeted treatment

TABLE I. New or in the pipeline: Topicals

Target	Compound	Indication	Phase
AhR	Tapinarof/bemitimod	Moderate-severe	2a →
PDE4	Crisaborole (Eucrisa)	Mild-moderate	3 in EU (FDA 2016)
PDE4	Roflumilast	Moderate	2a →?
PDE4	RVT-501	Mild-moderate	2a →
JAK1, JAK3	Tofacitinib	Moderate-severe	2a → STOP
JAK1, JAK2	INCB18424	Mild-moderate	2a →
JAK1, JAK3	LEO 124249/JTE-052	Mild-moderate	2a
S aureus	R mucosa bacteria	Antecubital AD	1/2
S aureus	Coagulase-negative *Staphylococcus*	Moderate-severe on ventral arms	1/2

→, Drug development program is ongoing, phase 3 is planned but not yet running; →?, unknown future of drug development program; → *STOP*, drug development program has been stopped; *EU*, European Union; *FDA*, US Food and Drug Administration.

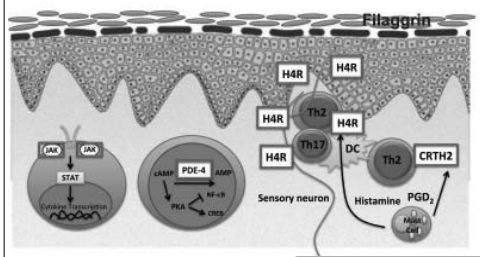
TABLE II. New or in the pipeline: Biologics

Target	Compound	Indication	Phase
TSLP	Tezepelumab	Moderate-severe	2a →
Ora1	Anti-Ora1	Moderate-severe	2a →
IL-4/IL-13R	Dupilumab (Dupixent)	Moderate-severe	Approved by FDA, 2017; approval pending in EU
IL-4	Pitrakinra	Moderate-severe	2a →?
IL-13	Tralokinumab	Moderate-severe	3
IL-13	Lebrikizumab	Moderate-severe	3
IL-5	Mepolizumab	Moderate-severe	2a
IgE	QGE031/ligelizumab	Moderate-severe	2a →?
IL-12/IL-23	Ustekinumab (Stelara)	Moderate-severe	2a →
IL-22	Fezakinumab (intravenous)	Moderate-severe	2a →
IL-17A	Secukinumab (Cosentyx)	Moderate-severe	2a →
IL-31 receptor A	CIM331/nemolizumab	Moderate-severe	2b →
IL-31	BMS-981164	Moderate-severe	1b →?

→, Drug development program is ongoing, phase 3 is planned but not yet running; →?, unknown future of drug development program; *EU*, European Union; *FDA*, US Food and Drug Administration.

J Allergy Clin Immunol 2017;140:633-43

New targeted treatment



Target	Compound	Indication	Phase
CRTH2	OC000459	Moderate-severe	2a → STOP
CRTH2	QAW 039	Moderate-severe	2b → STOP
PDE4	Apremilast (Otezla)	Moderate-severe	2a → STOP
H4R	ZPL389	Moderate-severe	2a →
JAK 1/2	Baricitinib	Moderate-severe	2b →
JAK 1	Pf-04965842	Moderate-severe	2a →
JAK 1	Upadacitinib (ABT 494)	Moderate-severe	2a →
NK1R	VLY-686/tradipitant	Moderate-severe	2a →
NK1R	Serlopitant	Moderate-severe	2a →

→, Drug development program is ongoing, phase 3 is planned but not yet running; → *STOP*, drug development program has been stopped.

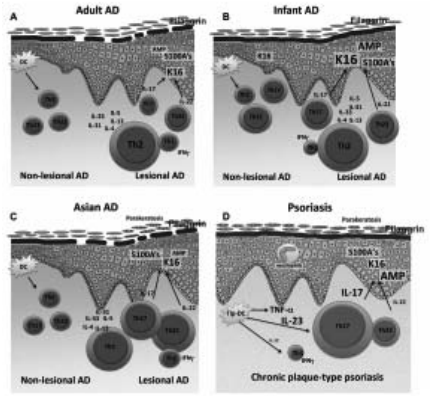
J Allergy Clin Immunol 2017;139:S65-76

New targeted treatment

Drug	Study	Dosage	Effectiveness
Tofacitinib	Topical Bissonnette et al. (2016) (phase 2a trial) Sistemic Levy et al. (2015)	2% ointment twice a day versus placebo ointment Oral 5 mg twice daily	EASI score mean reduction (81.7% vs. 29.9%) Mean SCORAD index decreased of 66.6%
Crisaborole	Paller et al. (2016); FDA approved	2% ointment twice a day	ISGA score (AD-301:32.8% vs. 25.4%; AD-302: 31.4% vs. 18.0%)
Nemolizumab	Ruzicka et al. (2017)	Subcutaneous 0.1 mg/kg, 0.5 mg/kg, and 2 mg/kg dose every 4 weeks	EASI score respectively of −23, −42.3, and −40.9%
Apremilast	No sufficient data, only very small significative studies		
Dupilumab	SOLO1 and SOLO2; FDA approved	Subcutaneous 300 mg weekly/every 2 weeks/placebo	EASI-75 at week 16: 48, 44–51, and 15–26%, respectively
Lebrikizumab	Simpson et al. (2018); phase 2 trial TREBLE	Subcutaneous 125 mg every 4 weeks versus placebo	EASI-50: 82.4% versus 62.3%, respectively
Baricitinib	Guttman-Yassky et al. (2018)	Oral 2 mg, 4 mg, placebo daily	EASI-50: 61% (4 mg) versus 37% (placebo)

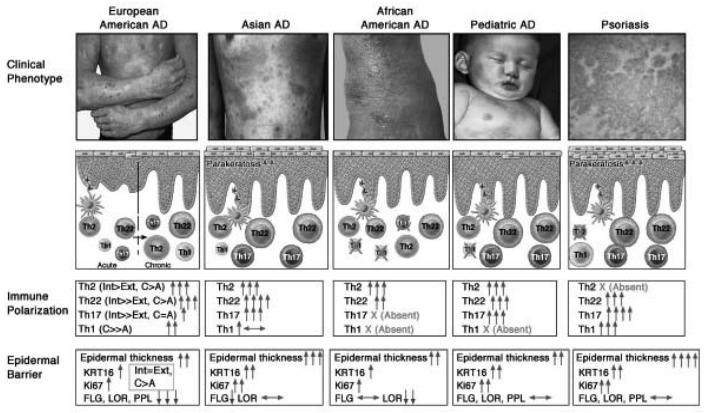
Dermatol Ther 2018 (Epub ahead of print)

AD phenotypes and related endotypes



J Allergy Clin Immunol 2017;139:S65-76

AD phenotypes and related endotypes



J Allergy Clin Immunol 2019;143:1-11

CONCLUSION

Diagnosis

Severity Assessment
SCORAD, EASI

Basic treatment	Active treatment	Other treatment
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Guideline based individualized treatment plan important !