

ATOPIC DERMATITIS

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Skin Diseases with an Allergic Background

Atopic dermatitis

Allergic contact dermatitis

Urticaria

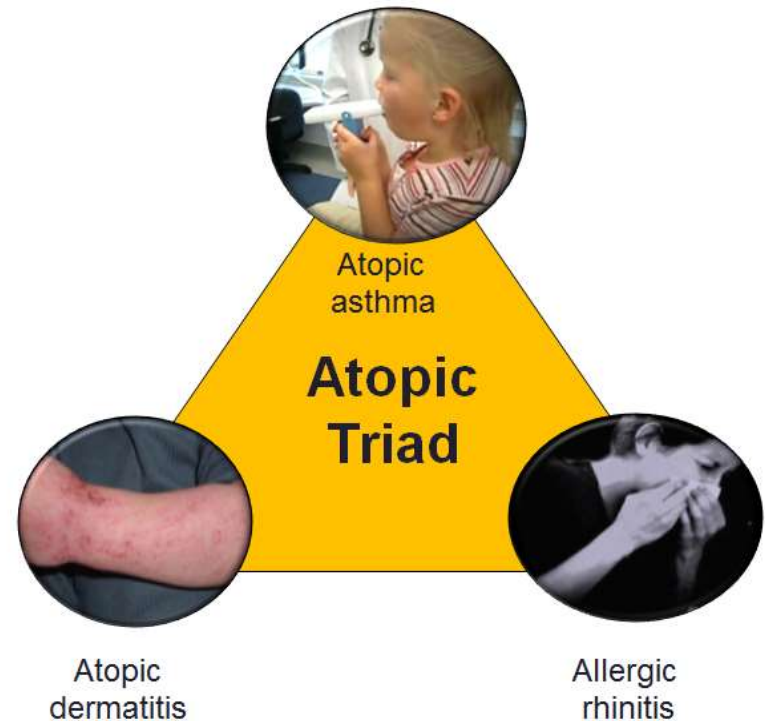
Link between skin barrier dysfunction and allergic sensitization initiating the atopic march

Atopic triad

Atopic asthma

Allergic rhinitis

Atopic dermatitis



Definition

Atopic dermatitis (Eczema) is a chronic highly pruritic
Inflammatory skin disease

It is called also “endogenous eczema” and “neurodermitis”

Atopy is common finding in these patients

Etiology

Intrinsic factors:

Genetic predisposition

Family history of allergic diseases

Psychosomatic factors

Extrinsic factors:

Most common sensitization to food allergens and house dust mites

Irritants

Pathophysiology

Skin barrier abnormalities- mutations within the filaggrin gene

Defective innate immune responses contribute to increased bacterial and viral infections

T-cell responses - initially a predominantly T helper-2 response and later a predominantly Th1 response

Pathophysiology

Increased serum IgE levels

Specific IgE amount is lower than expected

Greater prevalence rates of contact allergy

Pathogenesis

Impaired skin lipid and barrier function - filaggrin mutations

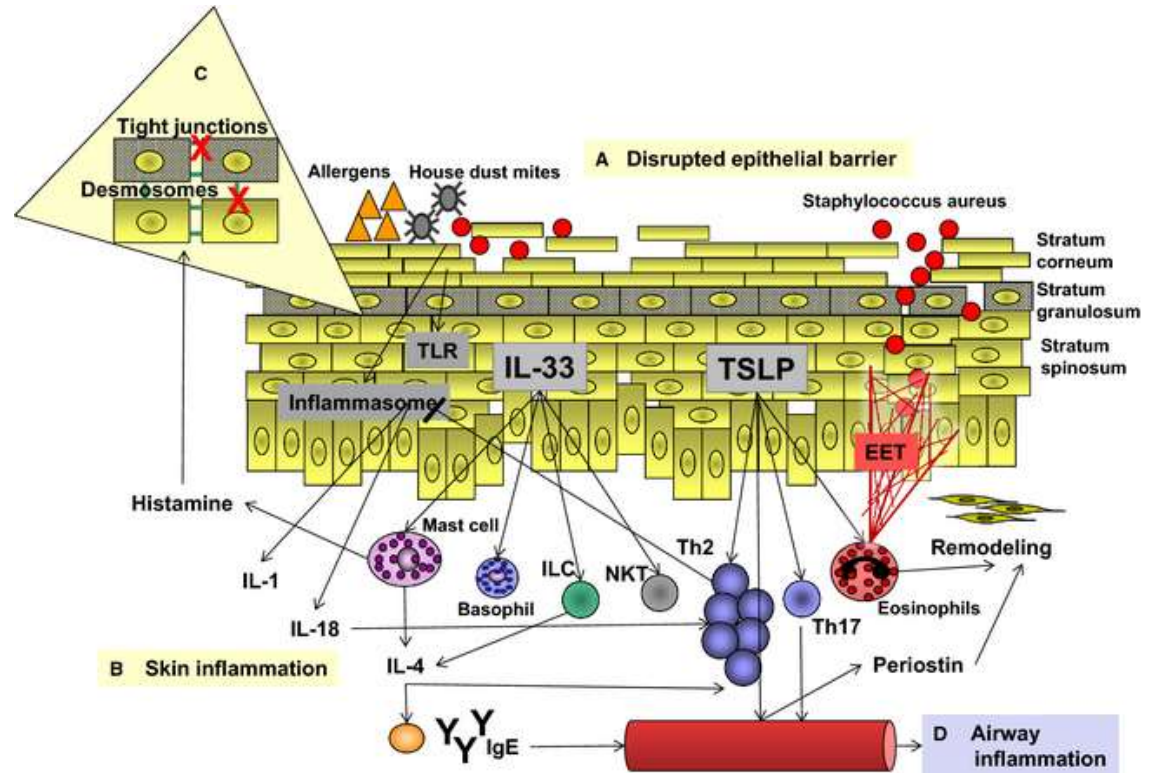
Transepidermal water loss (TEWL)

New pathogenic insights

Impaired skin lipid and barrier function

- activated keratinocytes to produce cytokines
- released mediators further impair skin barrier

Cells and mediators derived from skin may cause airway inflammation



A different look at histamine

- Reducing the expression of tight junction proteins and desmosomal proteins
- Significant suppression of differentiation of epidermal keratinocytes
- Thinning of the epidermis and stratum corneum

Increased expression of interleukins in AD lesions

IL-33 - Activation of

- innate lymphoid cells (ILC)
- invariant natural killer T cells (iNKT)
- basophils and mast cells
- dendritic cell maturation and migration and T helper 2 (Th2) differentiation
- enhance eosinophil survival
- amplify IgE synthesis independent of the allergen via IL-4 produced by mast cells and eosinophils

Thymic stromal lymphopoietin (TSLP)

- promotes Th2 inflammation
- regulates Th17 responses
- enhance allergen sensitization and trigger allergic asthma by inducing IL-17 responses in the airways
- stimulate eosinophils to generate eosinophil extracellular traps (EETs)

IL-17 from Th17 and IL-22 expressions in the skin are associated with remodeling in eczematous lesions

Periostin is a cytokine that has been linked to remodeling and tissue fibrosis

Periostin production by microvascular endothelial cells and fibroblasts has been shown to be refractory to corticosteroids

Symptoms and signs

Eczematous skin lesions

Dry and itchy skin-Xerosis cutis

Hyperlinearity of palms and soles

Pruritus

Skin secondary infections

White dermatographism

Symptoms and signs

Skin thickening

Lichenification, fissures

Hyperpigmentation

Irritability of environment irritants: wool, synthetics, dust, worm and dry air

AD in Infants

0-2 years

Localization of lesions: face (forehead, cheeks, chin), scalp, neck, extensor surfaces of extremities, trunk

Typical rash: erythema with papules, exudation, excoriations

Skin infections, common due to rubbing and scratching



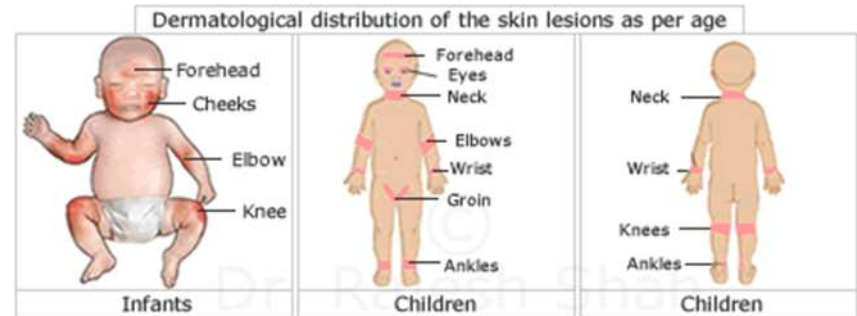
AD in Children

Childhood - 2 years to puberty

Localization of lesions: flexural surfaces of extremities, neck, wrists, ankles

Typical rash: lesions are lichenified, skin is thickened, itch all the time

Itchy, scaly patches where the rash appeared



AD in Adults

Adolescence/adulthood

Localization of lesions: Flexural surfaces of extremities, hands, feet

Typical rash: pink to red papules and plaques, hand eczema, thick and dark patches of skin, scaly skin



AD in Adults

Extremely dry skin

Skin infections

Non-stop itch

Eye problems

Some adults may have primarily
chronic hand involvement

Areas with infection can develop
thick crusts



Co-Factors

Food allergies and intolerance

Microbial colonization: Staphylococcus aureus in 95%, Malassezia furfur

Eczema herpeticum

Moluscum contagiosum

Verrucae vulgares

Candida, Trichophyton

Environmental triggers: cold weather, emotional stress, wool clothing, harsh detergents

Psychosomatic factors

Diagnosis

There are no specific diagnostic tests

Medical history

Clinical manifestations

High levels of IgE

Exacerbating factors: inhalant allergens, irritants, foods, emotional stress

Diagnosis

Major criteria

Pruritus

Family history for atopy

Minor criteria

Older children/adults:

History of itchiness in skin creases (e.g., folds of elbows, behind the knees, front of ankles, around the neck)

Personal history of asthma or allergic rhinitis

Personal history of general dry skin in the last year

Visible flexural dermatitis (i.e., in the bends or folds of the skin at the elbow, knees, wrists, etc.)

Onset under age 2 years

Children <4 years:

History of itching of the cheeks

History of atopic disease in a first-degree relative

Eczema of cheeks, forehead and limbs

Differential Diagnosis

Other skin conditions

Contact dermatitis

Seborrheic dermatitis

Psoriasis

Infections

Scabies

Impetigo

Metabolic and nutritional deficiencies

Phenylketonuria

Zinc deficiency

Differential Diagnosis

Immunodeficiency syndromes with skin manifestations

Wiskott-Aldrich syndrome

Severe combined immunodeficiency syndrome with Omenn's syndrome

Immune dysregulation, polyendocrinopathy, enteropathy, X-linked Graft vs. host disease

Dermatitis herpetiformis

Malignancies

T-cell lymphoma

Management

From

avoidance strategies

Toward

induction of tolerance and restoring skin barrier function

Primary prevention with probiotics or neonatal vitamin A supplementation failed to significantly reduce allergic diseases including eczema

The effect of vitamin D on allergy is still under debate

Treatment

MAIN TIPS

Education

Repairing the skin

Treatment of skin infections

Decreasing inflammation

Limiting itching

Patient education

Symptomatic treatment

Emollients with urea:

Children-4%

Adults-10%

Oil baths

Anti-inflammatory treatment: Treatment of skin infections

Topical corticosteroids

Topical calcineurin inhibitors

Systemic corticosteroids

Antihistamines

Other therapies

Topical Corticosteroids

Anti-inflammatory, antiproliferative and immunosuppressive action

Ointment preparations are preferred over creams

Potency of topical CS:

Very potent

Potent

Moderately potent

Mild

The therapy should be stopped for short periods to reduce the risk for:

Local side effects

striae (stretch marks)

petechiae (small, red/purple spots)

telangiectasia, skin thinning

atrophy, acne

Systemic side effects-rare

growth retardation

reduced bone density

hypothalamic –pituitary axis

suppression

Topical Calcineurin Inhibitors

Mechanism of action

Immunosuppression on T lymphocytes

Inhibition of synthesis of calcineurin activating proinflammatory cytokines

Clinical effect

↓ pruritus

↓ continuous topical corticosteroid treatment

↓ systemic absorption

Agents

Pimecrolimus (Elidel)

Tacrolimus (Protopic)

Local side effects

skin burning

irritation

skin malignancy-rare

lymphoma-rare

Topical Calcineurin Inhibitors

Elidel (pimecrolimus) - crème

Protopic (tacrolimus) ointment:

0,03% should be used in children, between the ages of 2 and 16

0.1% in adults over the age of 16.

Antihistamines

First generation are preferred for short-term treatment

hydroxyzine

diphenhydramine

chlorpheniramine

Non-sedating second generation have limited value in AD patients

cetirizine

levocetirizine

loratadine

desloratadine

Treatment of Skin Infections

Oral or topical antibiotic therapy in bacterial infection

Cephalosporins

Penicillins

Fucidin

Intranasal eradication of S. aureus

Mupirocin

Systemic antiviral treatment in viral infections

Acyclovir

Systemic Corticosteroids

Indication: severe AD flare-ups

Reduce inflammation, itching and thickening of skin

hydrocortisone

methylprednisolone

prednisolone

prednisone

Side effects

growth retardation in children

hypertension

myopathy

glaucoma

Cushing`s syndrome

glucose intolerance

osteonecrosis

cataracts

Other Systemic Immunosuppressive Therapy

Cyclosporine-2.5 to 5 mg/kg/d

side effects

nephrotoxicity

hypertension

gingival hyperplasia

hyperlipidemia

hypertrichosis

rebound flare

Azathioprine-2.5 mg/kg/d

side effects

vasculitis

hepatotoxicity

erythema nodosum

nephritis

Monoclonal Anti-IgE and Immunotherapy

Omalizumab - Xolair

House dust mites allergens – SCIT; SLIT

Thank You!

