Atopic Dermatitis
(Atopic Eczema)

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1402. 7. 27

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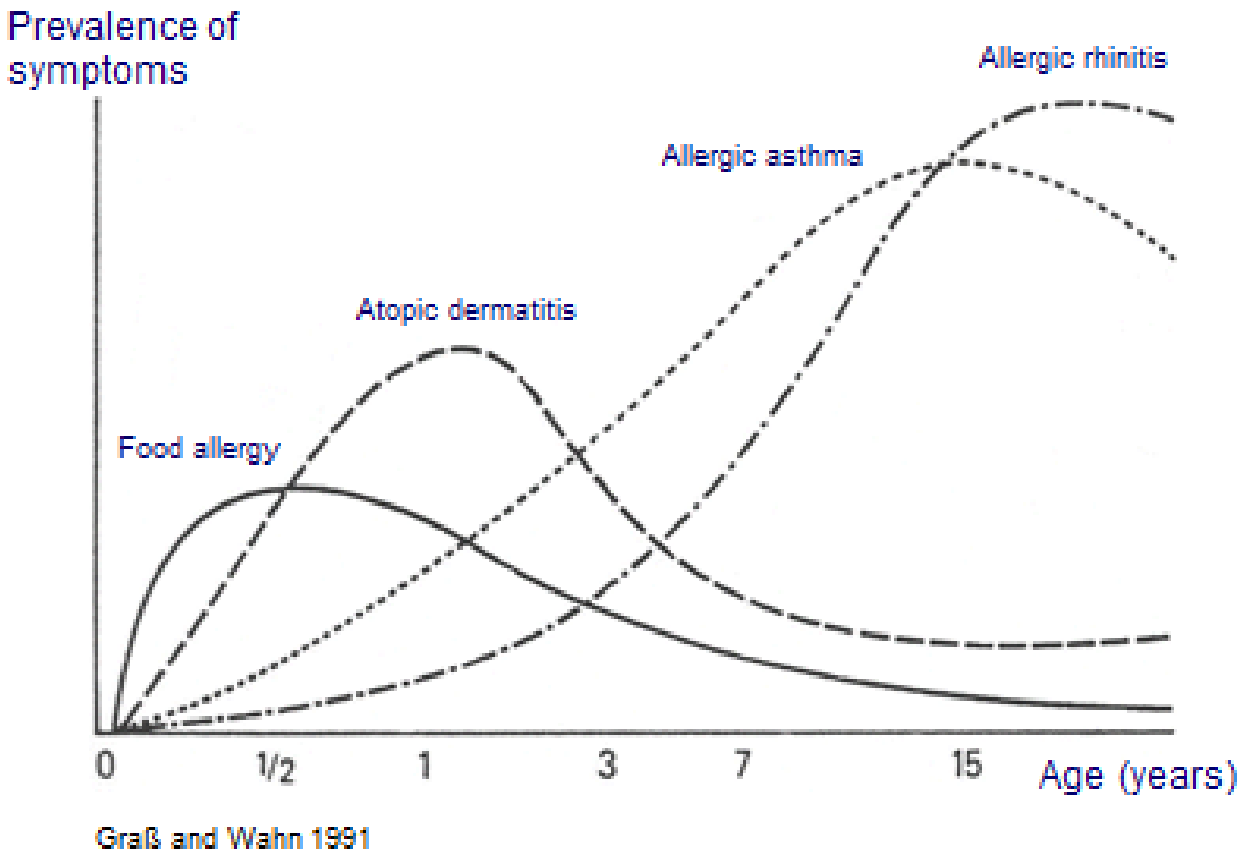
- affects 10–30% of children frequently occurs in families with other atopic diseases.

- 66% had asthma and/or allergic rhinitis

- Infants with AD are predisposed to development of food allergy, allergic rhinitis, and asthma later in childhood(atopic march.)

Course of Atopic Diseases in Childhood



Graß and Wahn 1991

the **skin acts as** a barrier against :

external irritants, moisture loss, and **infection.**

- In **AD** Excess transepidermal water loss, allergen penetration, and microbial colonization.

- **Filaggrin** : critical to **skin barrier function**, including skin moisturization

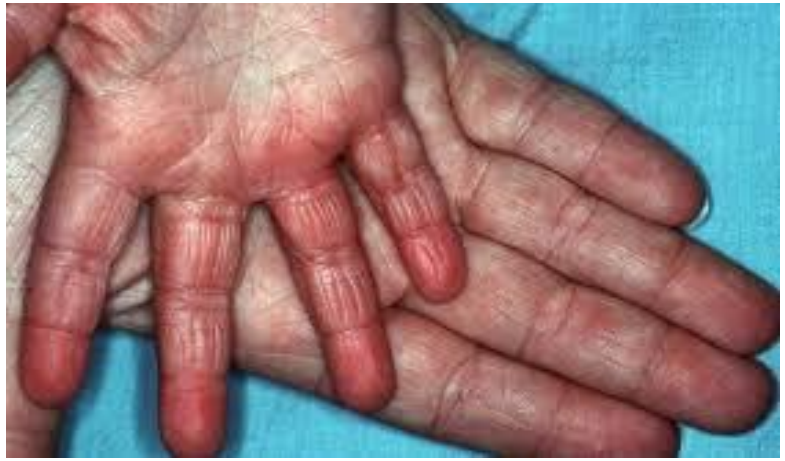
Mutations in the filaggrin gene (FLG) family have been identified in patients with ichthyosis vulgaris (dry skin, palmar hyperlinearity) and in up to 50% of patients with severe AD.

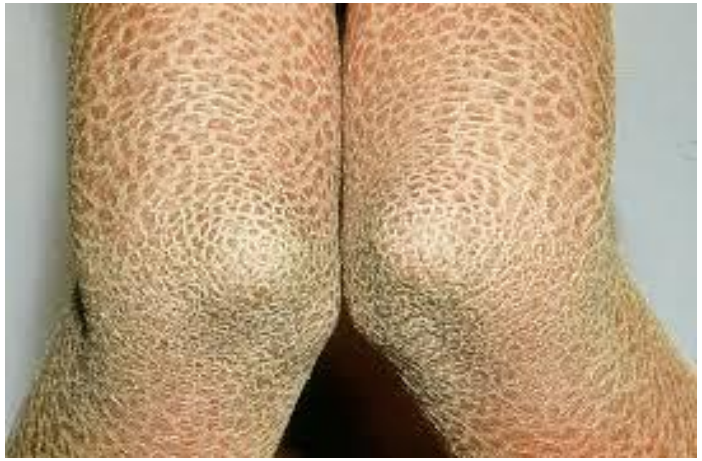
AD Patients with FLG gene mutations, have early-onset, severe, and persistent

reduction in claudin-1 potein: barrier dysfunction and immune dysregulation observed in AD patients

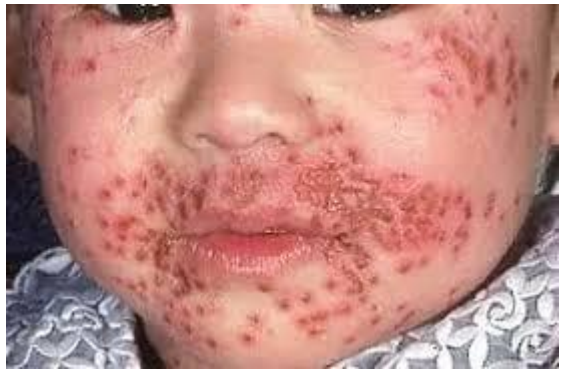
FLG mutation is strongly associated with development of food allergy and eczema herpeticum.

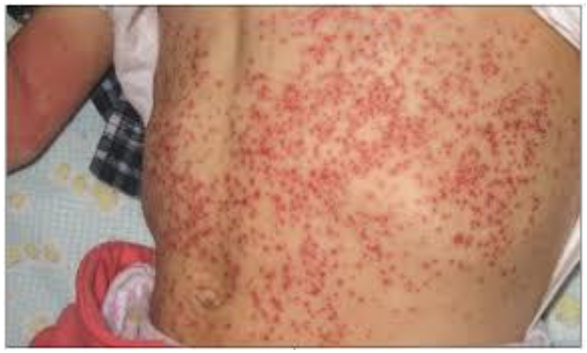
- **ichthyosis vulgaris**

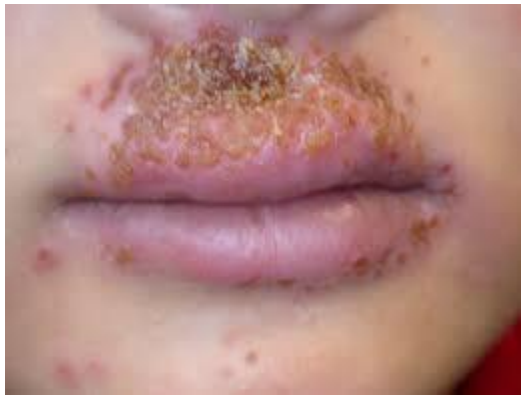




FLG mutation is strongly associated with : development of food allergy and eczema herpeticum.







- Cytokines found in allergic inflammation, such as IL-4,IL-13, IL-22, IL-25, tumor necrosis factor, can also reduce filaggrin and other epidermal proteins and lipids.

- Immune responses to environmental allergens and microbes that lead to chronic skin inflammation

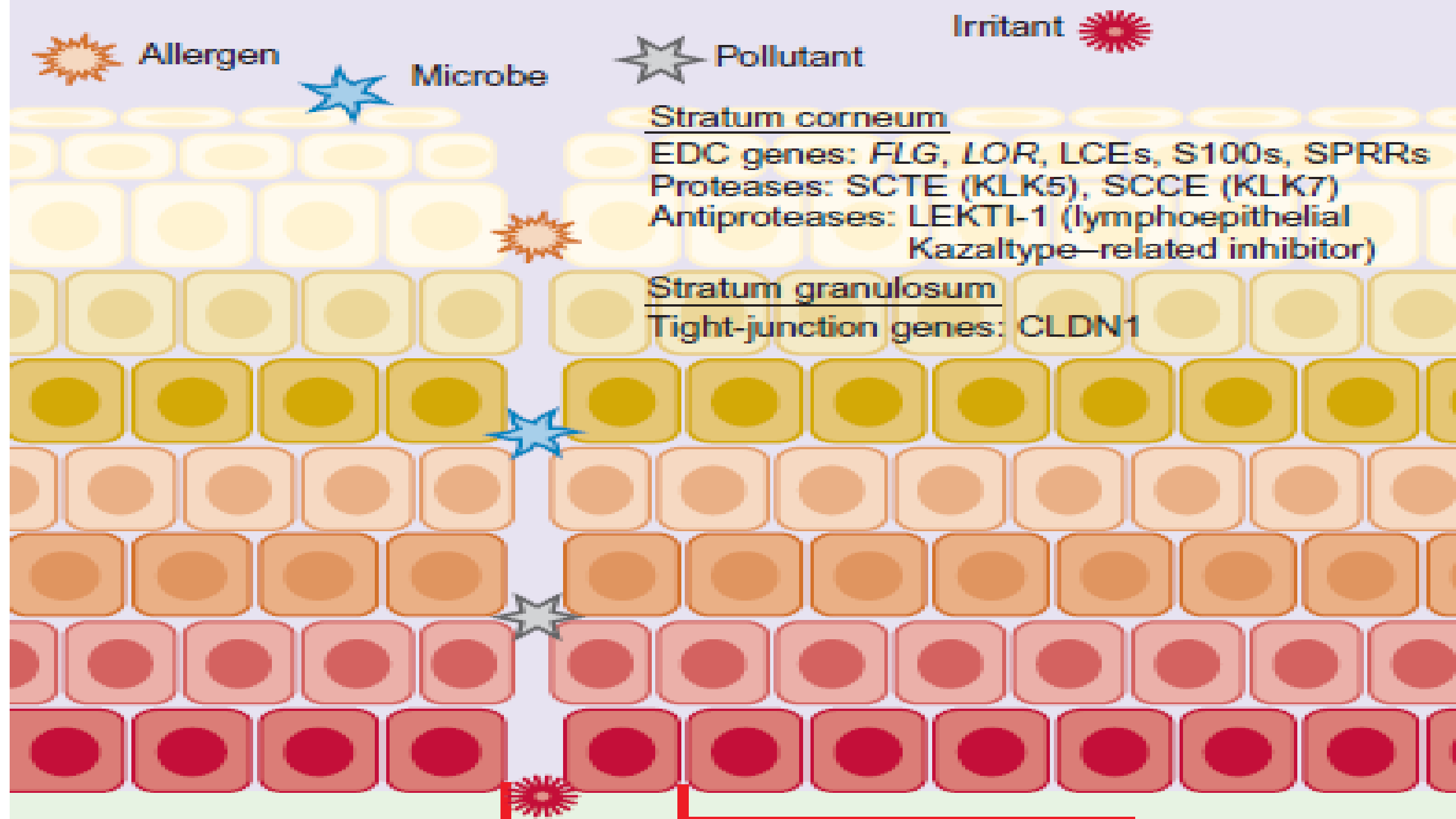
- S. aureus skin colonization and reduction in commensal bacteria (e.g., S. hominis).

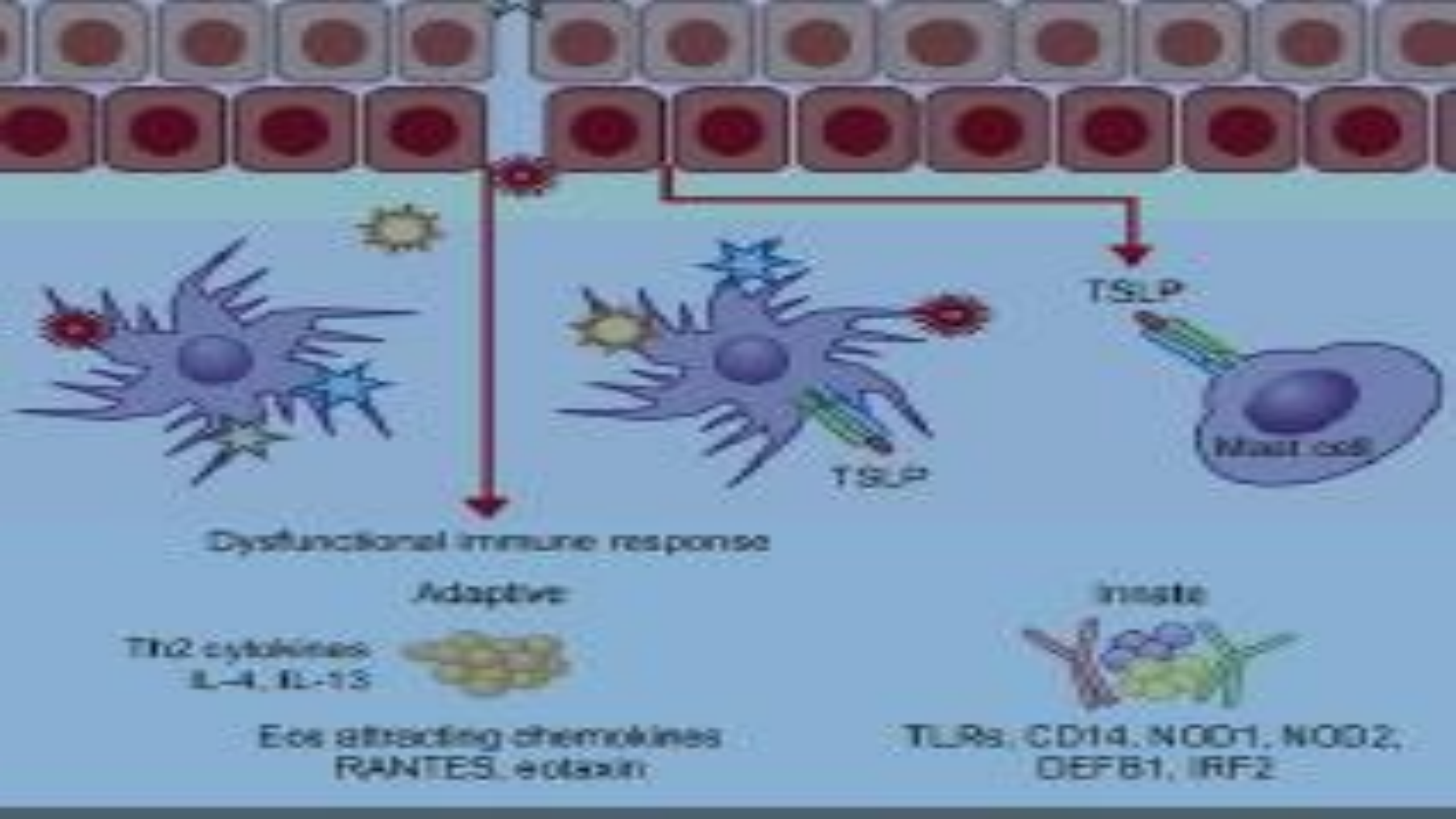
- S. hominis can produce antimicrobial peptides that suppress growth of S. aureus.

- AD patients with EH have reduced interferon γ (IFN-γ) production, and that IFN-γ and receptor (IFN-γR1)

- single-nucleotide polymorphisms (SNPs) are significantly associated with AD and EH and impaired immune response to HSV.

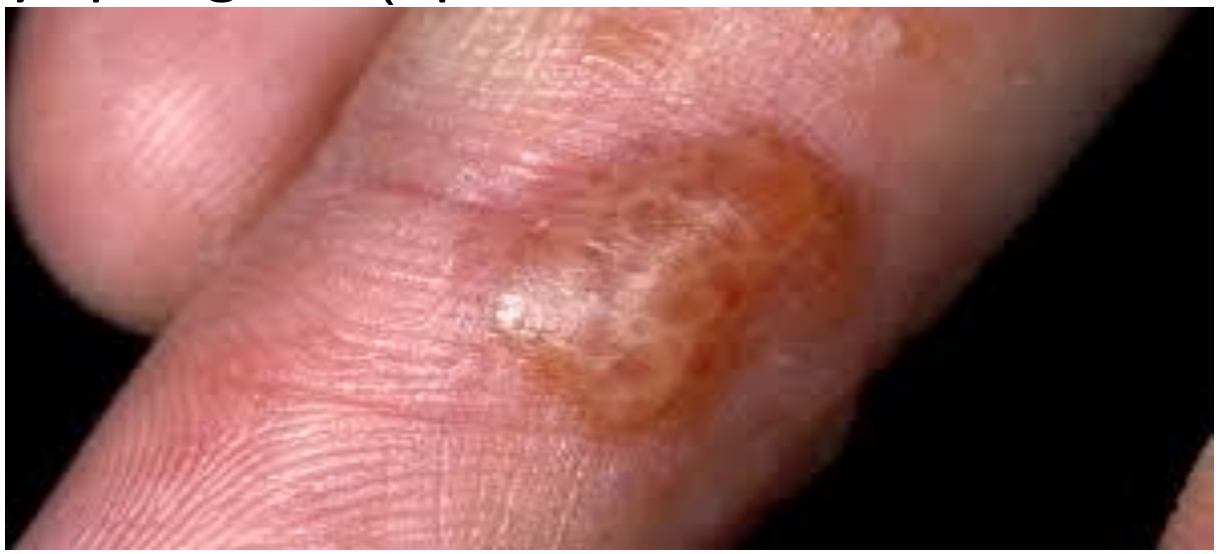
- EH is more than 10 in patients with FLG gene mutations


Allergen
Microbe
Pollutant
Irritant
Stratum corneum
EDC genes: FLG, LOR, LCEs, S100s, SPRRs
Proteases: SCTE (KLK5), SCCE (KLK7)
Antiproteases: LEKTI-1 (lymphoepithelial Kazaltype–related inhibitor)
Stratum granulosum
Tight-junction genes: CLDN1

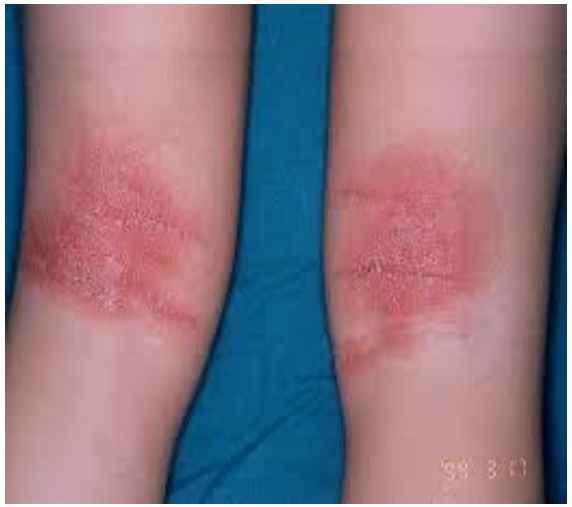

TSLP
TSLP
Dysfunctional immune response
Adaptive
Th2 cytokines
IL-4, IL-13
Eos attracting chemokines
RANTES, eotaxin
Innate
TLRs, CD14, NOD1, NOD2,
DEFB1, IRF2

In acute AD lesions:

- characterized by spongiosis(epidermis intercellular edema).



Chronic AD : lichenified hyperkeratosis and ,minimal spongiosis



.***Atopic eczema(dermatitis)***:

- IgE-mediated sensitization, occurs in 70–80% of patients with AD.

- increased levels IL-4 and IL-13(induce isotype IgE synthesis), IL-5 (eosinophil development and survival).

Non atopic eczema

is not associated with IgE-mediated sensitization and is seen in 20–30% of patients with AD.

lower IL-4 and IL-13 but increased IL-17 and IL-23 , **IL-5, GMCSF, IL-12, and (IFN)-γ**.

Both forms of AD are associated with **eosinophilia.**

increased risk of infection(bacterial, viral, and fungal) is related to impairment of:

- ❖innate immunity
- ❖ disturbances in the microbiome
- ❖ skine epithelial dysfunction
- ❖dampen of host antimicrobial (defensin)responses.

- **CLINICAL MANIFESTATIONS:**

- 50% experience symptoms in the 1st yr of life
- 30% are diagnosed between 1 and 5 yr of age.

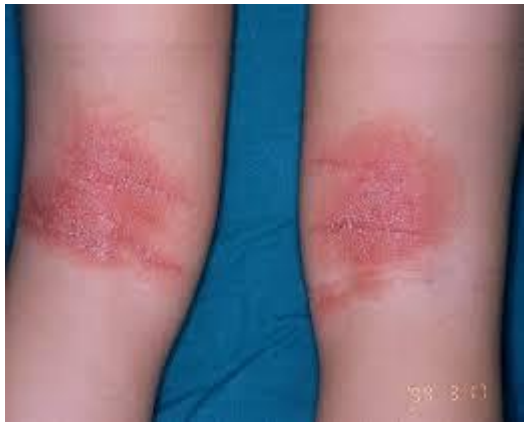
- Intense pruritus, especially at night

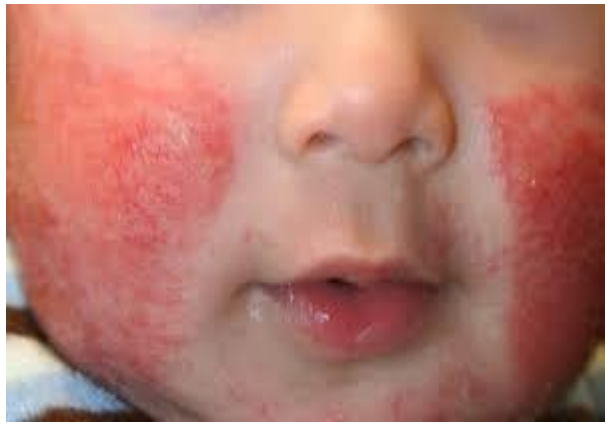
- Scratching and excoriation cause increased skin inflammation that contributes to the development of more pronounced eczematous skin lesions.

pruritus and scratching triggers:

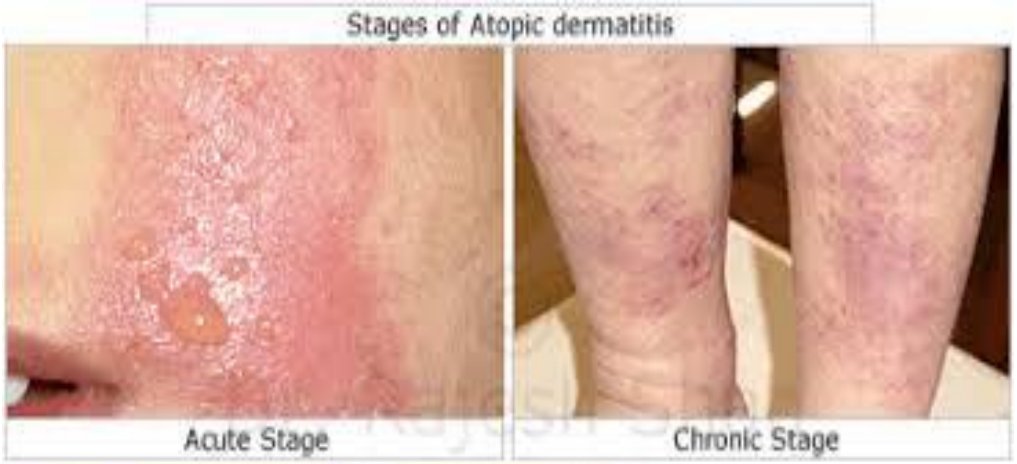
- Foods (cow's milk, egg, peanut, tree nuts, soy, wheat, fish, shellfish), aeroallergens (pollen, grass, animal dander, dust mites)
- infection :Staphylococcus aureus, herpes simplex, coxsackievirus, molluscum
- reduced humidity,excessive sweating, and irritants (wool, acrylic, soaps,, fragrances, detergents).

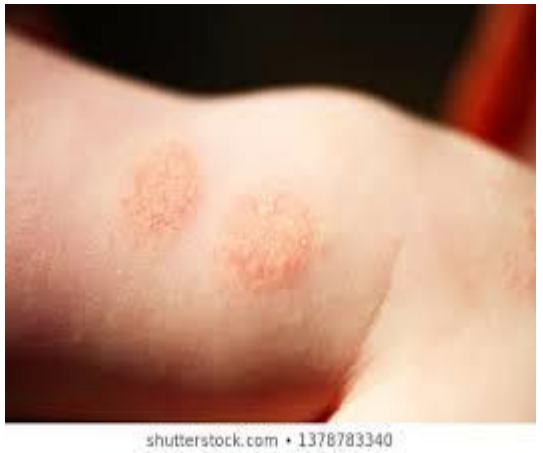
- Acute AD skin lesions : are intensely pruritic with erythematous papules

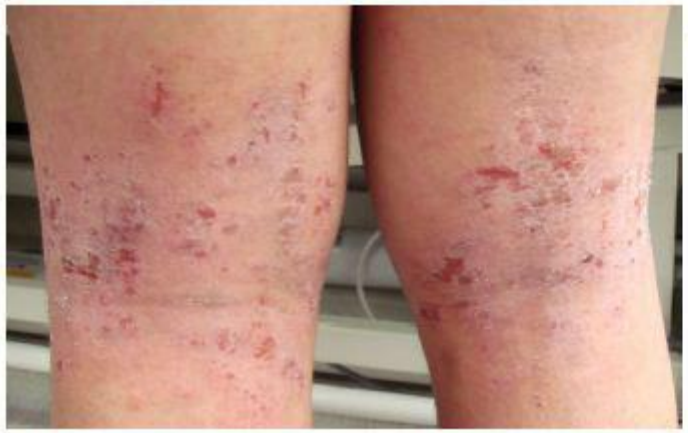


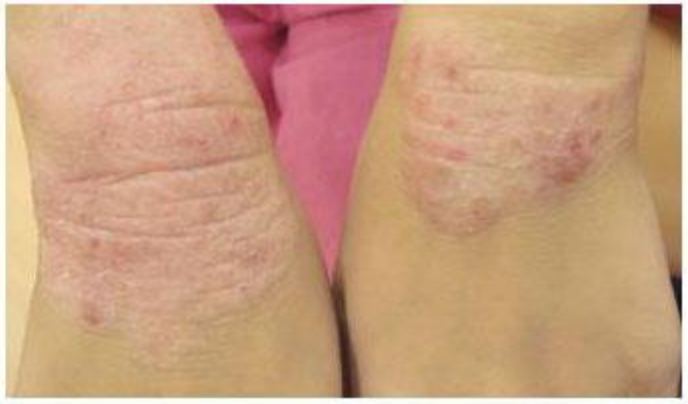


- Subacute dermatitis manifests as erythematous, excoriated, scaling papules.
- chronic AD is characterized by lichenification or thickening of the skin with accentuated surface markings, and fibrotic papules.






Acute Atopic Dermatitis


Chronic Atopic Dermatitis

- In chronic AD, all 3 types of skin reactions may coexist.
- AD is generally more acute in infancy and involves the face, scalp, and extensor surfaces of the extremities.
- The diaper area is usually spared. (Seborrheic dermatitis)
- Older children and children with chronic AD have: lichenification

and localization of the rash to the flexural folds of the extremities.

remission as the patient grows older

persistent eczema as In adult.

- LABORATORY FINDINGS:
- ***No specific laboratory*** tests to diagnose AD.

- Many patients have ***peripheral blood eosinophilia*** and increased *serum IgE levels.*

Serum **specific *IgE measurement or skin-prick*** testing can identify the allergens (***foods, inhalant/microbial allergens***) to which patients are sensitized.

The diagnosis of clinical allergy to these allergens requires confirmation by history and environmental ***challenges***(Doul Blind Placebo Control Food Challenge Test)

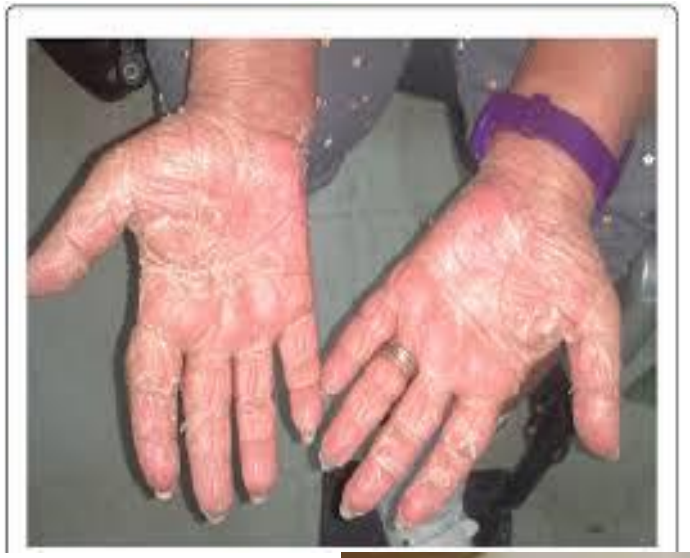
DIAGNOSIS of AD:

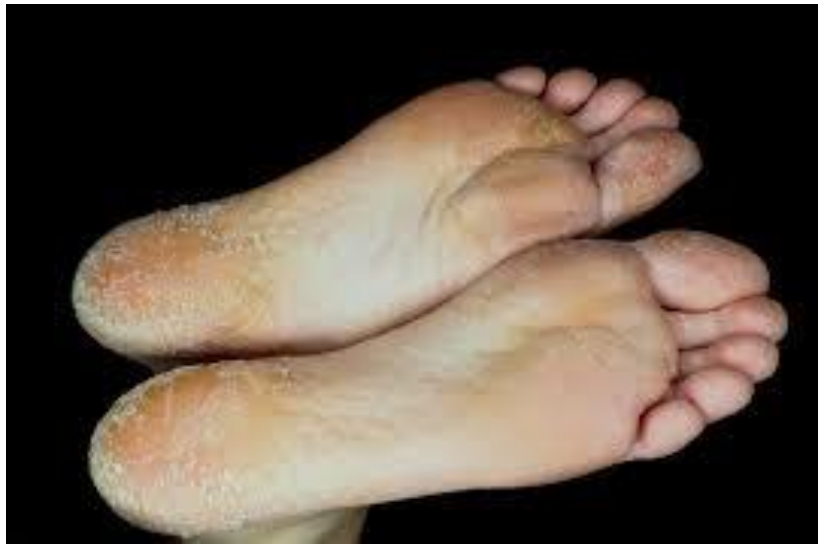
MAJOR FEATURES

- Pruritus
- Facial and extensor eczema in infants and children
- Flexural eczema in adolescents
- Chronic or relapsing dermatitis
- Personal or family history of atopic disease

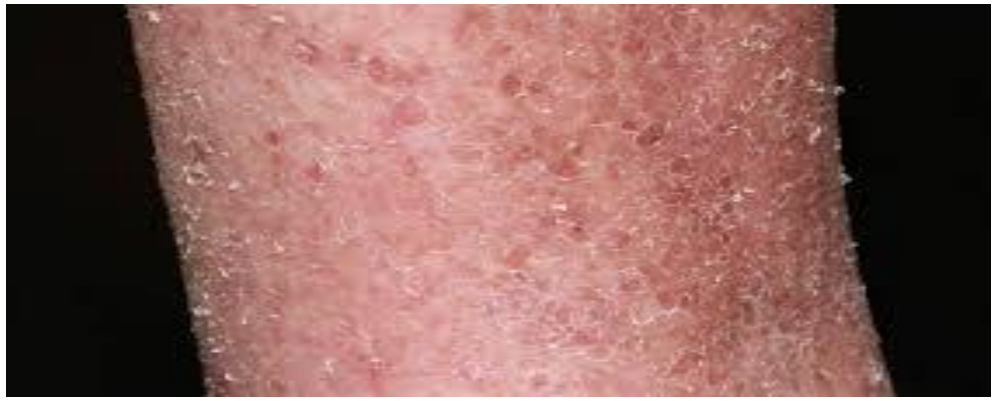
- ***ASSOCIATED FEATURES***

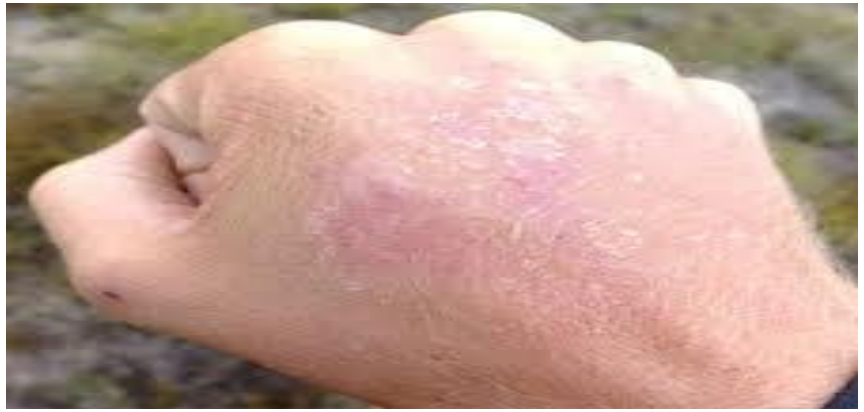
- Ichthyosis(exrem dry,thick skin thus interfere dead skin sheding ability)





xerosis(extrem dry ,scaly skin)

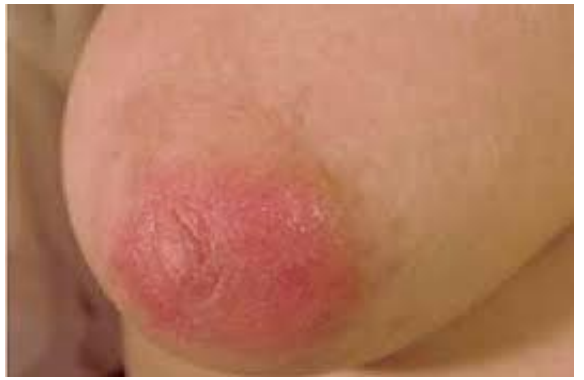




- Cutaneous infections (Staphylococcus aureus, group A Strept ococcus, herpes simplex, coxsackievirus, vaccinia, molluscum, warts)

- Nonspecific dermatitis of the hands or feet

- palmar hyperlinearity, keratosis pilaris
- Nipple eczema
- White dermatographism(cap vaso cons)
- Anterior subcapsular cataracts,keratoconus
- Elevated serum IgE levels
- immediate-type allergy skin tests
- Dennie-Morgan infraorbital folds
- Facial erythema or pallor
- Course influenced by environmental and/or emotional factors



- DDXs :

Primary *Immuno deficiencies*

skin malignancies

genetic disorders

infectious diseases

- Primary *Immuno deficiencies:*

SCID&leaky SCID: first yr of life with diarrhea,FTT, generalized scaling rash, and recurrent cutaneous and/or systemic infection

- Wiskott-Aldrich syndrome, an X-linked,thrombocytopenia, immune defects, infections, is characterized by a rash almost indistinguishable from that in AD.

- hyper-IgE synd elevated serum IgE(AR inheritance ,Dock8 mutations) bacterial infections, chronic dermatitis, and refractory dermatophytosis , increased susceptibility to viral infections, young children with severe eczema, food allergy, disseminated skin viral infections.

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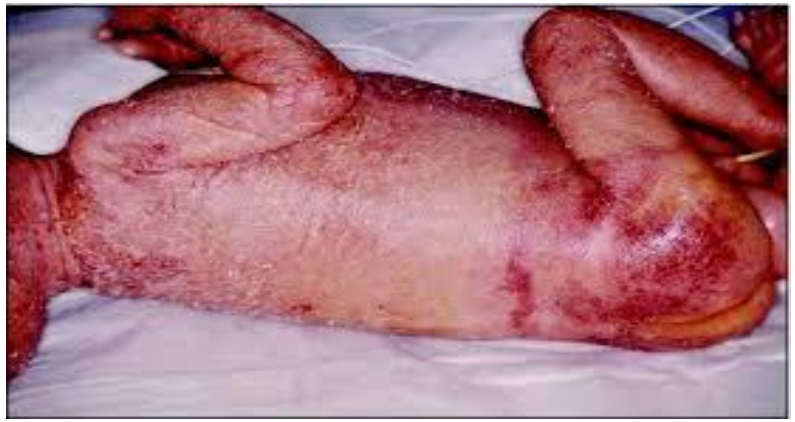
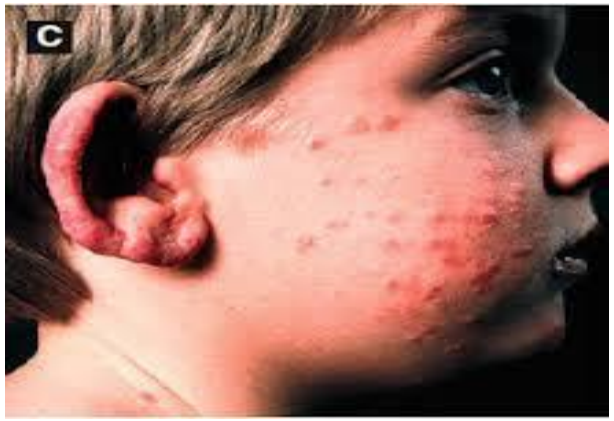
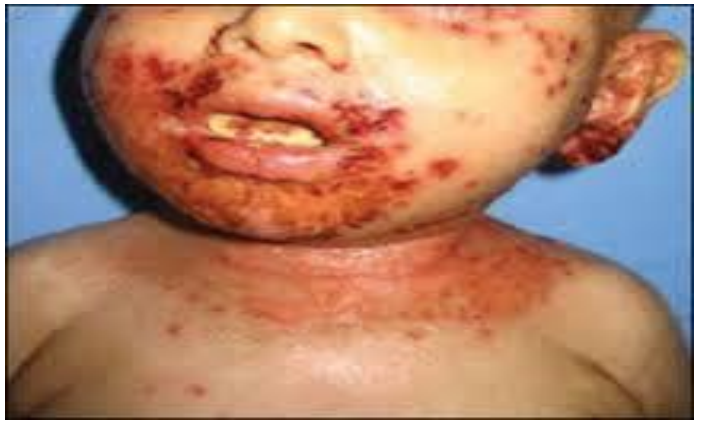
Omenn,synd .



Hyper IgE synd

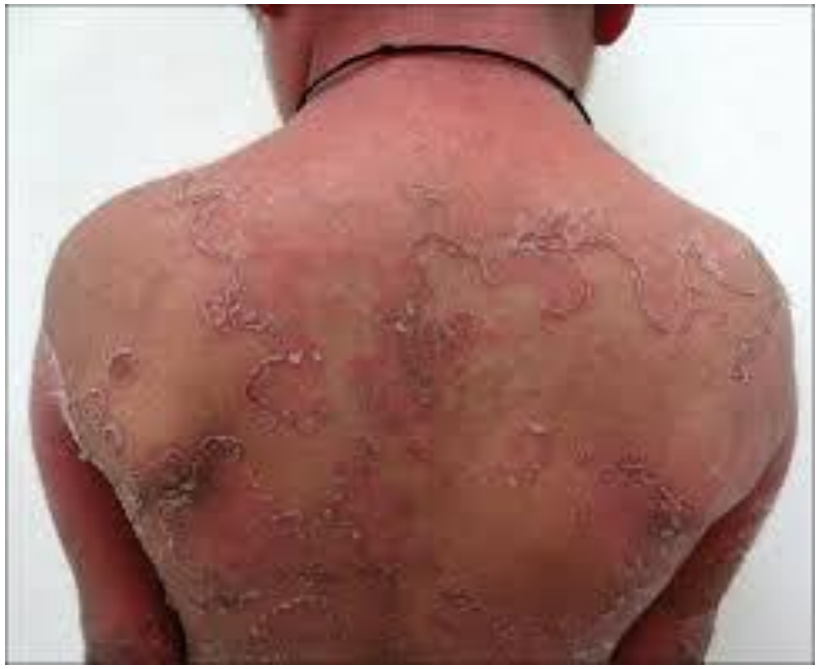


wiskott- Aldrich



- Histiocytosis should be excluded in any infant with AD and failure to thrive .

Netherton syndrome



Erythroderma in infancy, Ichthyosis, poor hair growth (bamboo hair) , FTT and atopy

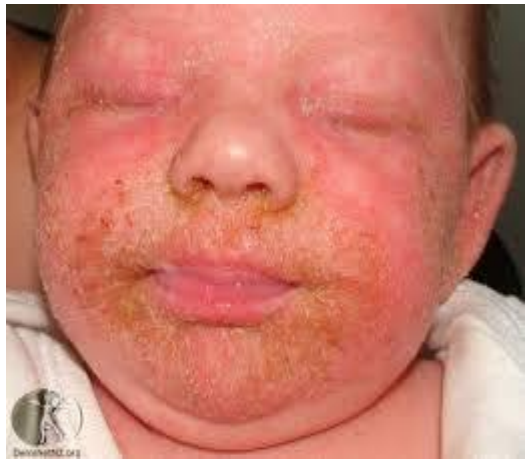
allergic contact dermatitis(any AD does not respond to appropriate therapy):

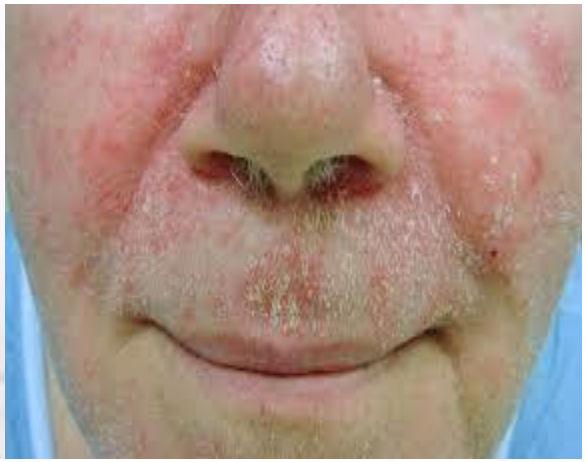
Adolescents who present with an eczematous dermatitis but no history of childhood eczema, respiratory allergy, or atopic family history

Sensitizing chemicals, such as parabens and lanolin (irritants as vehicles in therapeutic topical agents).

Topical glucocorticoid contact allergy (In Topical corticosteroid therapy)

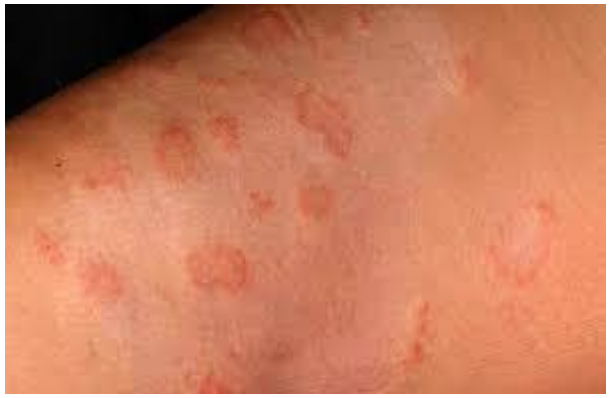
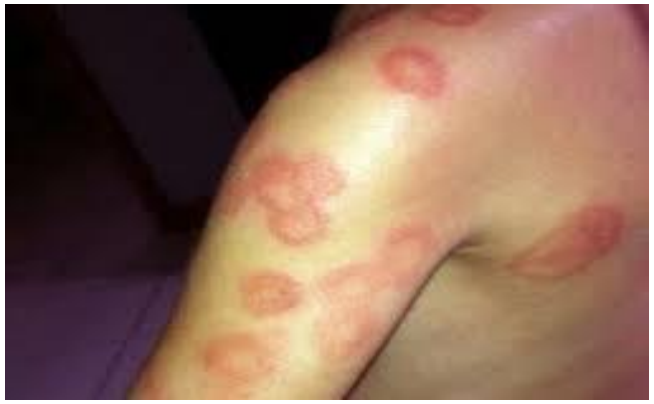
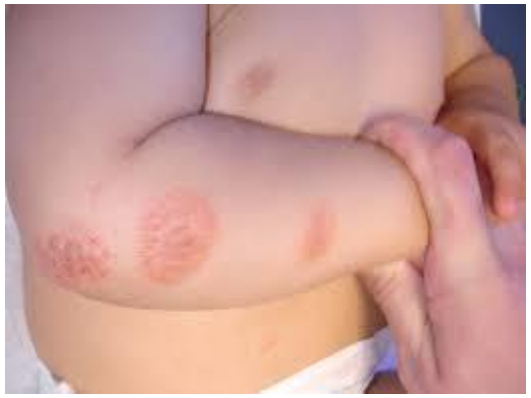
❖**<u>Infantile</u>** Seborrheic dermatitis : Salmon-red greasy scaly lesions, often on the scalp (cradle cap) and napkin area; generally presents in the 1st 6 wk of life; typically clears within weeks



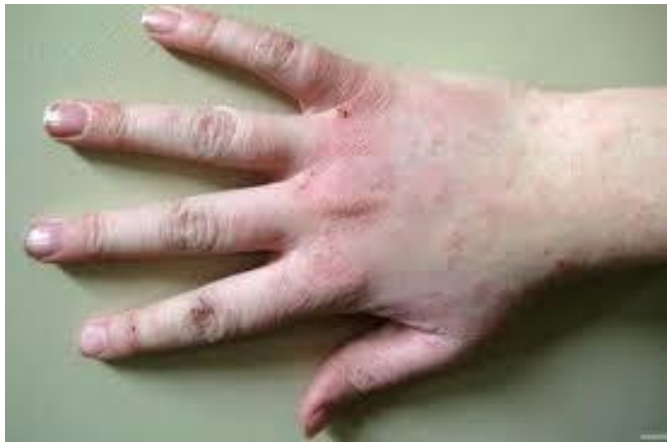



❖<u>Adult</u> Seborrheic dermatitis: Erythematous patches with yellow, white, or grayish scales in seborrheic areas, particularly the scalp, central face, and anterior chest

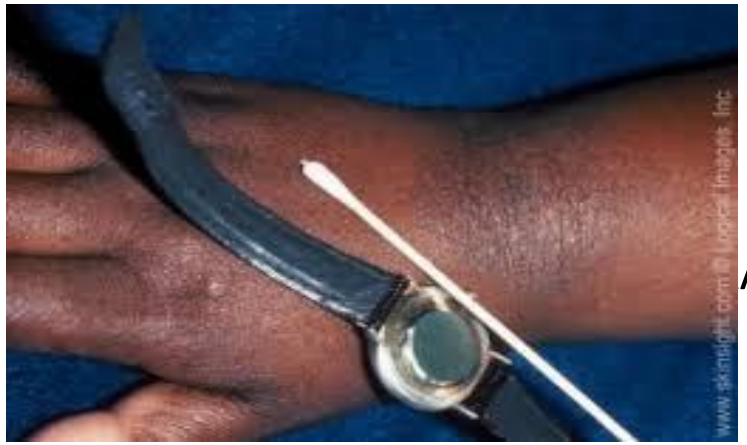
- Nummular dermatitis(unknown and likely multi factorial dry skin,trauma,bites,chemicals,aberasions,…) Children and adults Common Coin-shaped scaly patches, mostly on legs and buttocks; ***usually no itch***

Irritant contact dermatitis :Acute to chronic eczematous lesions, mostly confined to the site of exposure; history of locally applied irritants might coexist with AD



Irritant contact dermatitis



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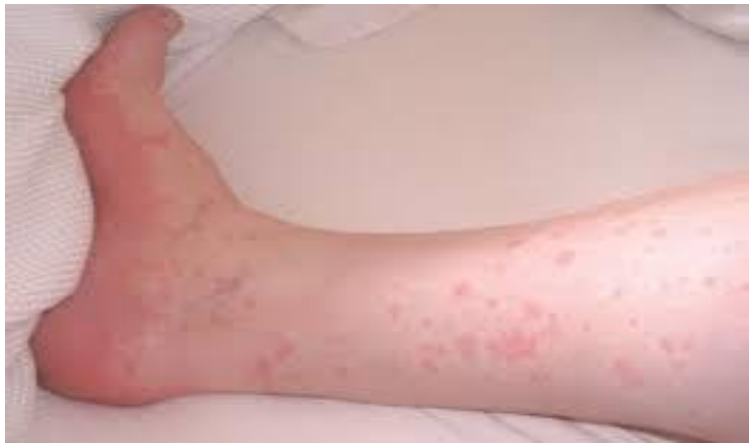
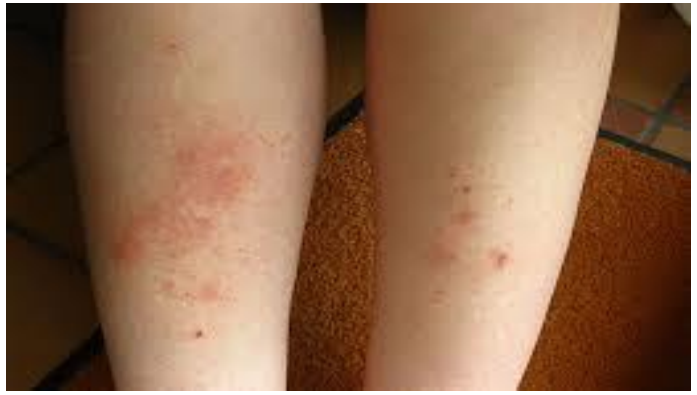
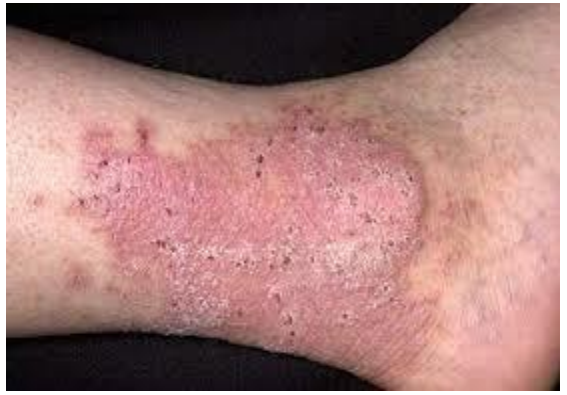


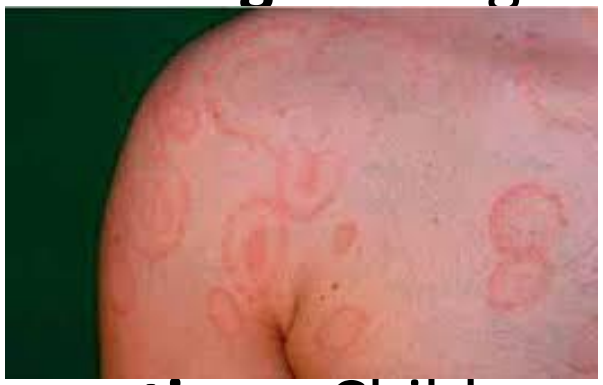
Alergic .c .d

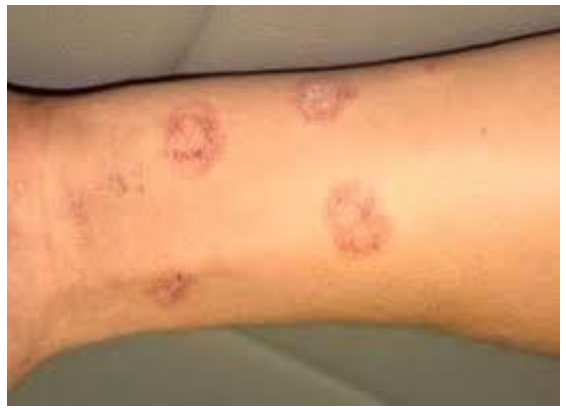
❖Lichen simplex chronicus Adults, Uncommon, One or more localized, circumscribed, lichenified plaques that result from repetitive scratching or rubbing because of intense itch(underlying pathophysiology is unknown).





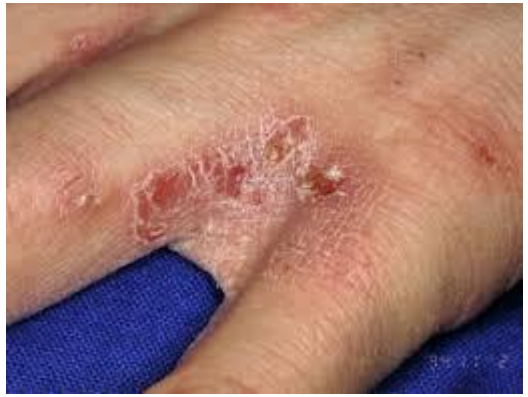
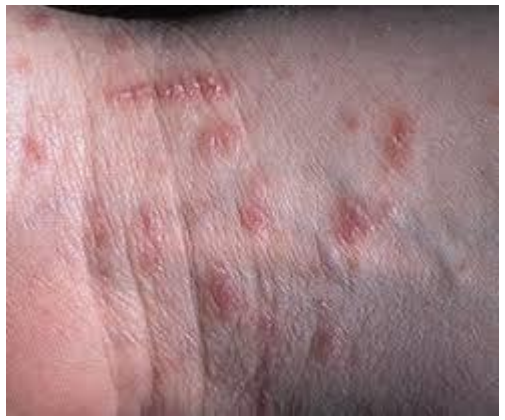
- **Dermatophyte infection** One or more demarcated **scaly plaques with central clearing** and slightly **raised reddened edge**; variable **itch**



Impetigo Children Demarcated **erythematous patches with blisters** or honey-yellow crusting

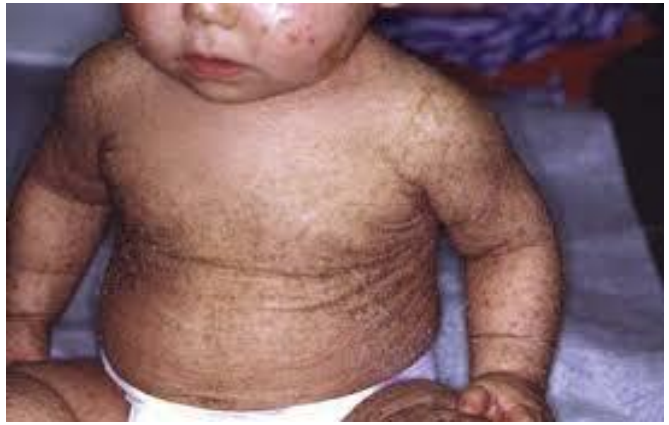
Scabies Children Common† Itchy superficial burrows and pustules on palms and soles, between fingers, and on genitalia; might produce secondary eczematous changes

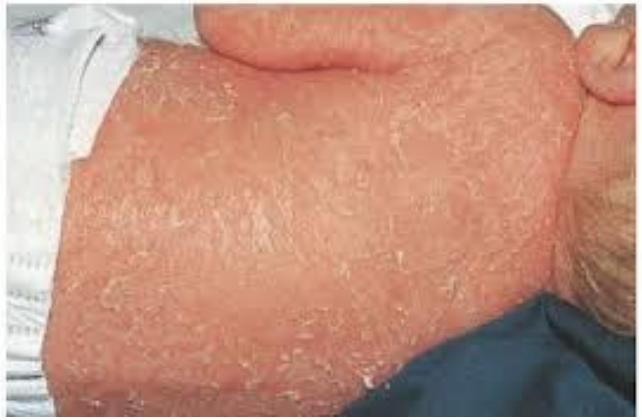




HIV: Children and adults Uncommon Seborrhea-like rash

Keratinization Disorders:

Ichthyosis vulgaris Infants and adults Uncommon Dry skin with fine scaling, particularly on the lower abdomen and extensor; **often coexists with AD**





- **Zinc deficiency**(acrodermatitis enteropathica) Children Uncommon Erythematous scaly patches and plaques, most often **around the mouth ananus**; rare congenital form accompanied by **diarrhea and alopecia**

- **Biotin deficiency** (nutritional or biotinidase deficiency) Infants ,Scaly periorofacial dermatitis, alopecia, conjunctivitis, lethargy, hypotonia

- **Pellagra** (niacin deficiency) all ages ,Scaly crusted epidermis, desquamation, ***sun-exposed areas***, diarrhea

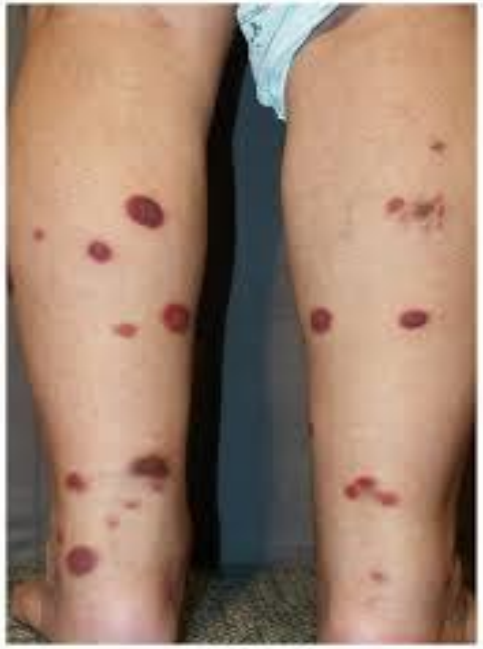
- **Kwashiorkor** Infants and children Geographic dependent Flaky scaly dermatitis, swollen limbs with cracked peeling patches

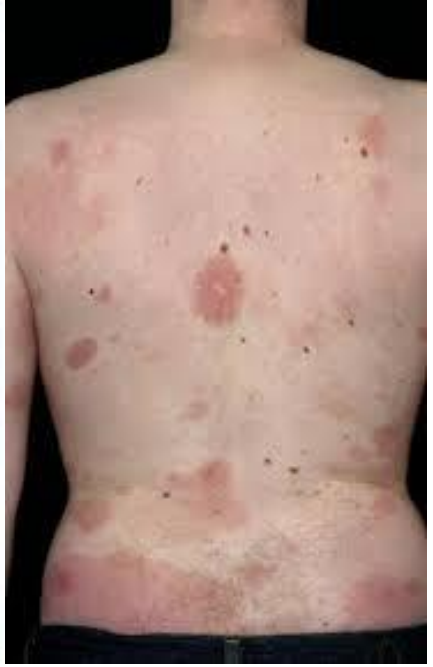
- **Phenylketonuria** Infants eczematous rash, hypopigmentation, **blonde hair**, developmental delay

NEOPLASTIC DISEASE

- **Cutaneous T-cell lymphoma(MF)**:

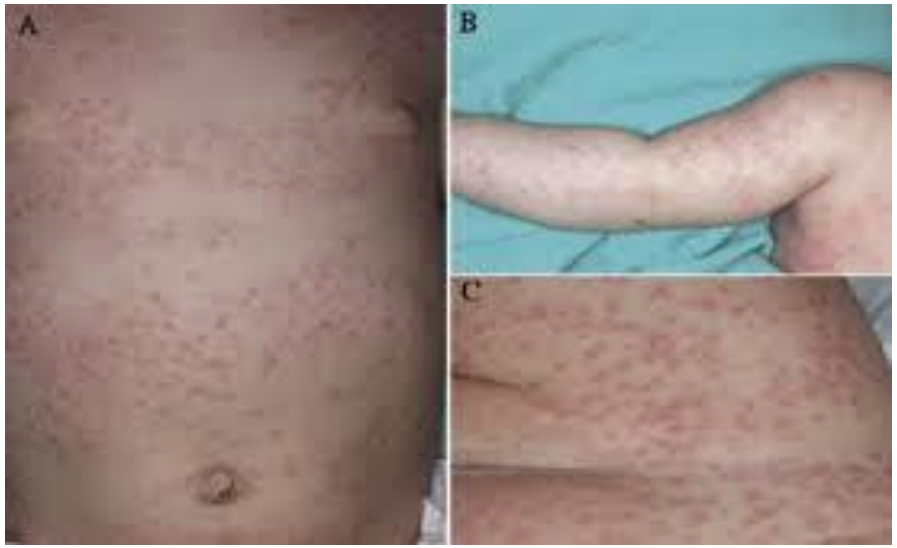
Adults ,Erythematous pink-brown macules and plaques with a fine scale; poorly responsive to topical corticosteroids; variable itch (in early stages)

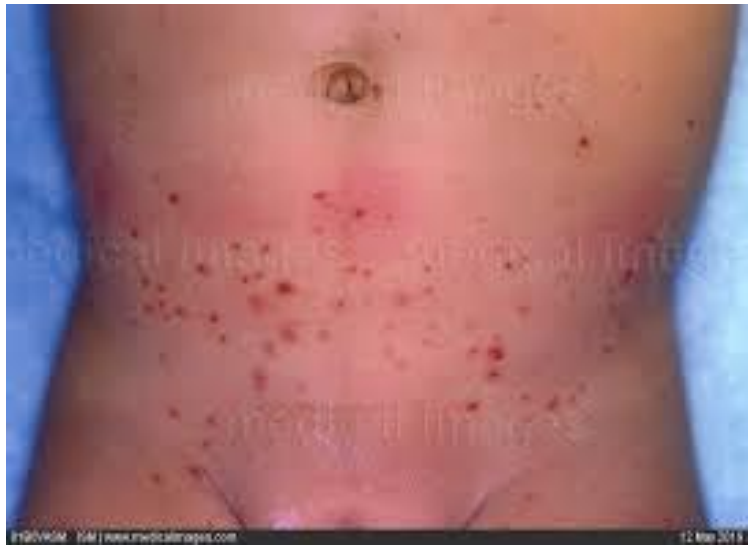




Langerhans cell histiocytosis:

Infants Scaly and purpuric dermatosis, ***<u>hepatosplenomegaly, cytopenias.</u>***





TREATMENT

- **Moisturizers are first-line therapy.**

Lukewarm soaking baths or showers for 15-20 min

followed by an occlusive emollient(folliculitis) and if not well tolerated : ceramides and

filaggrin acid metabolites creams intended to improve skin barrier function

- **Topical Corticosteroids (7 GROUP)** are the cornerstone of antiinflammatory treatment for acute exacerbations of AD.

ultrahigh-potency glucocorticoids:Clobetasol propionate (Temovate) 0.05% ointment/cream

Betamethasone dipropionate (Diprolene) 0.05% ointment/lotion/gel

Midpotency Glucocorticoids (topical fluticasone or mometasone): can be used for longer periods to treat chronic AD involving the trunk and extremities.

Mild est potency: Hydrocortisone (Hytone) 2.5%, 1%, 0.5% ointment/cream/lotion

- **Adverse effects:**
- Systemic: **potency** of the topical corticosteroid, **site** of application, **occlusiveness** of the preparation, **percentage of the body surface** area covered, and length of use (adrenal suppression is greatest in infants and young children)

- Local: striae and skin atrophy

- Compared with creams, ointments have a greater potential to occlude the epidermis, resulting in enhanced systemic absorption.

Topical Calcineurin Inhibitors:

Topical calcineurin inhibitors may be **better than topical corticosteroids** in poorly responsive to topical steroids, steroid phobia, face and neck dermatitis , skin atrophy.

Both are approved for ≥2 yr unresponsive to or intolerant of other conventional therapies or inadvisable because of potential risks.

- **Pimecrolimus cream 1%** (Elidel) is indicated for **mild to moderate** AD.

- **Tacrolimus ointment** 0.1% and 0.03% (Protopic) is indicated for **moderate to severe** AD.

- Phosphodiesterase Inhibitor
- **Crisaborole (Eucrisa**) is an approved topical nonsteroidal anti-inflammatory agent.

- phosphodiesterase-4 (PDE-4) inhibitor indicated for the treatment of mild to moderate AD.
- It may be used as an **alternative** to **topical corticosteroides or calcineurin** inhibitors for patients 2 years and older .

- **Perinatal** administration of the probiotic reduce the incidence of AD in at-risk children during the 1st 2 yr of life.

- Vitamin D deficiency often accompanies severe AD(low baseline vitamin D, as during winter)
- Vitamin D enhances skin barrier function, **reduces corticosteroid requirements to control inflammation**

- Vit D augments skin **antimicrobial function** (defencin production).

Coal tar : antipruritic and antiinflammatory effects on the skin (adverse effects:skin irritation, folliculitis, and photosensitivity).

- Tar shampoos particularly beneficial for scalp dermatitis.

- antihistaminic minimal benefit.(IL31,Staph A super Ag)
- Because pruritus is usually worse at night, sedating antihist (hydroxyzine, diphenhydramine)
- Doxepin (AD and concomitant urticarial)

Melatonin(tab 1 mg) For children may be effective in **promoting sleep** because production is deficient in AD.

Systemic corticosteroids are rarely indicated in the treatment of chronic AD.

- Important to taper the dosage and begin intensified skin care, particularly with topical corticosteroids, and frequent bathing, followed by application of emollients or proactive topical corticosteroids, to prevent rebound

Cyclosporine(5mg/kg /day) acts primarily on T cells by suppressing cytokine gene transcription and effective in the control of severe AD.

DupilumabA monoclonal antibody that binds to the **IL-4 receptor α subunit**, dupilumab (Dupixent) inhibits the signaling of IL-4 and IL-13, cytokines associated with AD.

Indication:

In adults with moderate to severe AD not controlled by standard topical therapy.

Unproven Therapies

IFN-γ is known to suppress Th2-cell function, decrease total circulating eosinophil counts.

Omalizumab(xolair) : monoclonal anti-IgE

- severe AD and elevated serum IgE values with may be considered in those with allergen-induced flares of AD.

- **no published double-blind, placebo-controlled trials of omalizumab's use**.

- **Allergen Immunotherapy**
- **aeroallergens** : treatment is controversial.
- specific immunotherapy in patients with AD sensitized to dust mite allergen showed improvement in severity of skin disease

irritants

- soaps or detergents, chemicals, smoke, abrasive clothing, extremes of temperature.
- 2nd rinse cycle
- **sport** such as **swimming** may be
- U.v may be beneficial, sunscreens should be used to avoid sunburn.

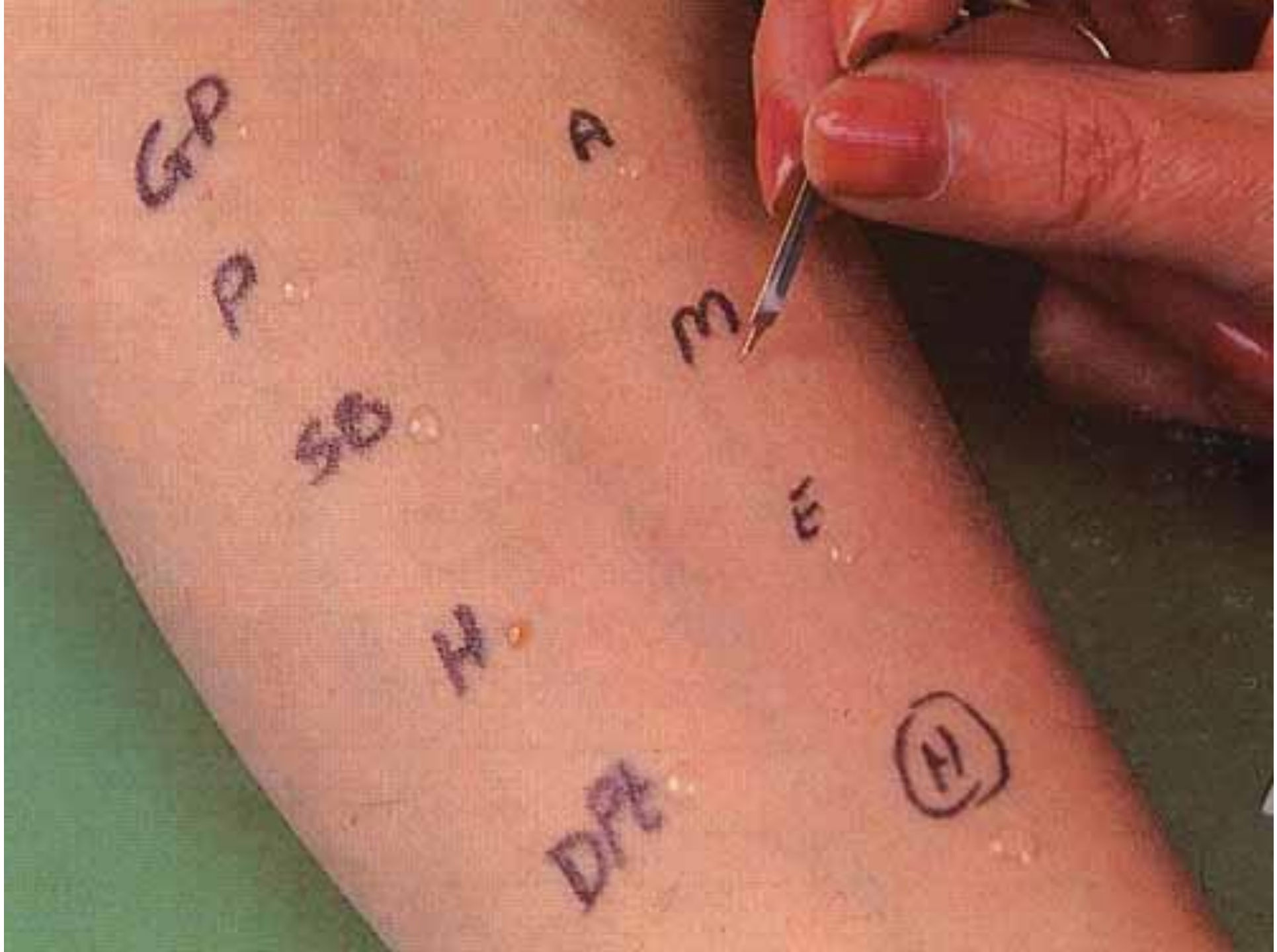
- **food allergies may induce eczematous dermatitis in** 40% of infants and young children with moderate to severe AD

Removal of food allergens : (egg, milk, peanut, wheat, soy) contaminate many foods and are difficult to avoid.

- Potential Food allergens identification : careful history, skin-prick tests **or** in vitro blood testing for allergen-specific IgE.

- **Negative skin and blood test** results for allergen-specific IgE have a **high predictive value for excluding suspected allergens.**

- **Positive results** of skin or blood tests using foods often do not correlate with clinical symptoms and should be confirmed with controlled food challenges and elimination diets.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AD = Food allergy ?!

+ SPT = Sensitization

+ SPT = Allergy ?!

- Extensive elimination diets rarely required : nutritionally deficient

- Even with multiple positive skin test results, the majority of patients react to fewer than 3 foods under controlled challenge conditions

Infections

- Erythromycin ,azithromycin are usually beneficial(if not colonized with a resistant S. aureus strain)
- Cephalosporin

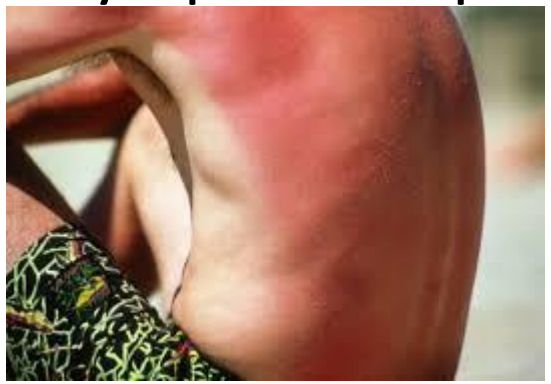
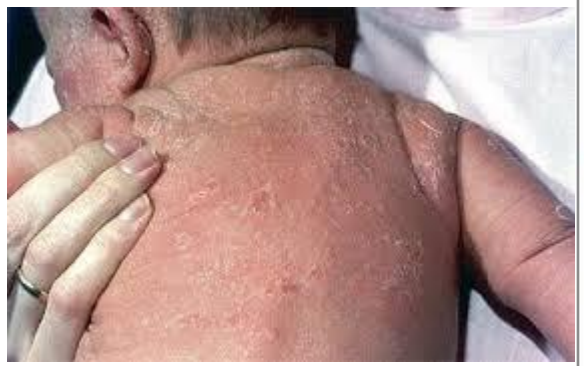
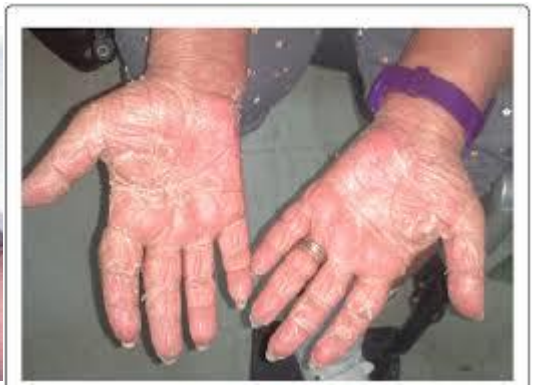
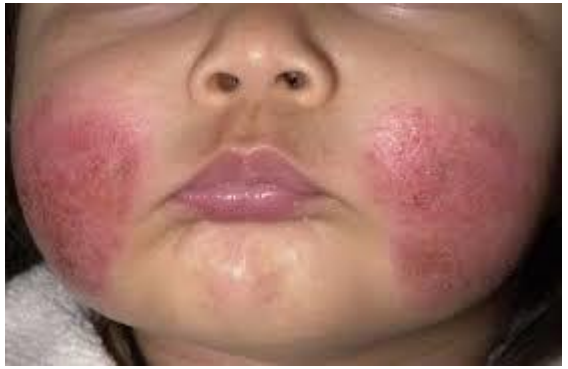
- Topical mupirocin
- Dilute bleach baths {1 /2 cup(236.5 ml) of bleach in 40 gallons of water}

- HSV : can provoke recurrent dermatitis and may be misdiagnosed as S. aureus infection
- Topical corticosteroids should be temporarily discontinued if HSV infection is suspected.

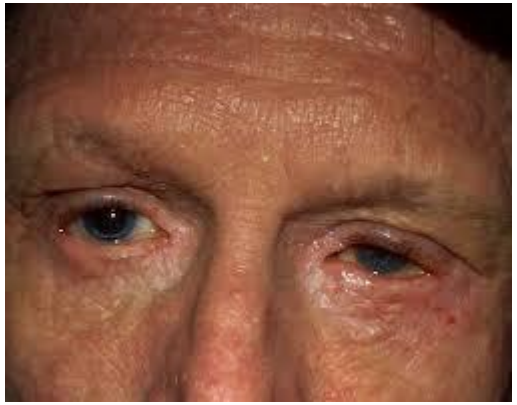
- COMPLICATIONS

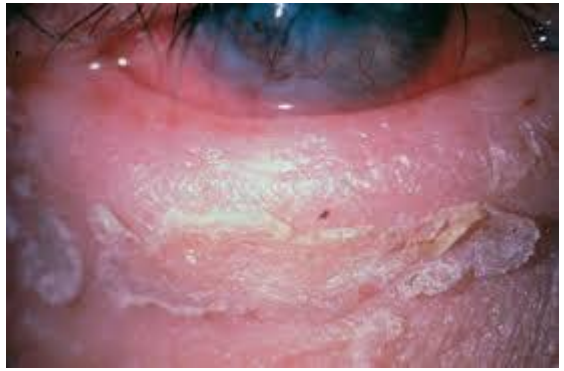
Exfoliative dermatitis:

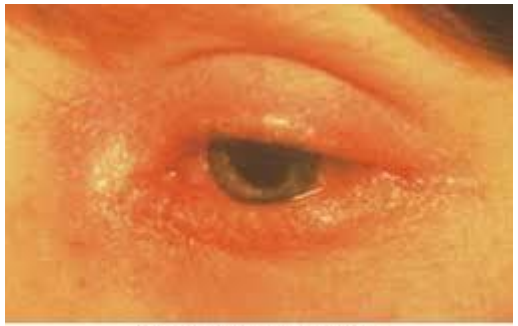
- caused by superinfection (S. aureus or HSV) or inappropriate therapy.
- generalized redness, scaling, weeping, crusting, systemic toxicity, lymphadenopathy

- Atopic keratoconjunctivitis : bilateral and can have disabling symptoms







The eyelids in atopic keratoconjunctivitis.

- Resolution : during infancy, particularly for mild
- >50% a relapse as adults as hand dermatitis(especially if hand wetting)

poor prognosis:

- wide spread AD in childhood
- concomitant allergic rhinitis and asthma,
- AD in parents or siblings,
- early age at onset
- being an only child
- serum IgE levels.


Thank You
For Your Atten


حوا انسار