Eczema

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Eczema can be defined as

- cutaneous, itching, polymorphic, inflammatory syndrome involving the epidermis and dermis,
- which may be provoked by a number of external or internal factors,
- with an acute or chronic, continuous or relapsing, course,
- characterized by a succession of distinct phases – erythema, vesiculation, weeping, crusting, desquamation and, in chronic form, lichenification, and
- with a mechanism of type IV hypersensitivity (Th1 response).

Histologically defined as

- Spongiosis in str. spinosus
- Interstitial vesicles
- Vesicles clinically observed in vesiculation stage
- Spongiosis histologically revealed in all stages.

histologically

Extent of allergic risk

- Eczema – the most frequent among allergic dermatoses; 2-10% of world population are eczema sufferers.
- 20-30% prevalence of inpatient dermatological diseases and one third of outpatient dermatological visits.
- Allergic risk increases with a positive family history mainly with an autosomal dominant transmission pattern.

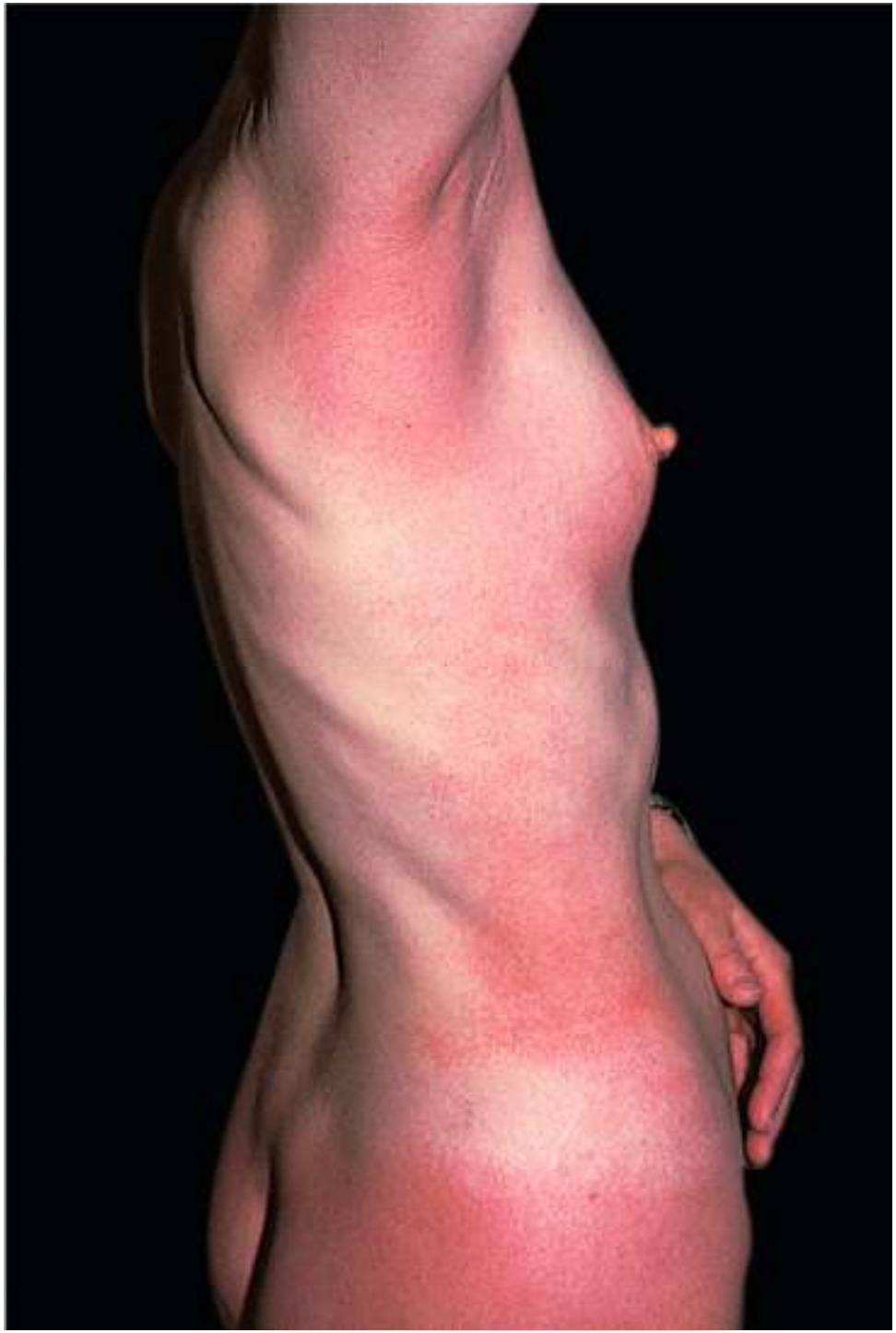
Dermatitis=Eczema

Eczema's clinical stages

- **erythematous** (dermatitis)
- **vesiculous** (papulovesicular eczema)
- **exudative** (oozing, weeping eczema)
- **crustification** (crusted eczema)
- **descuamative** (scaling eczema)
- **lichenification** (lichenoid eczema)

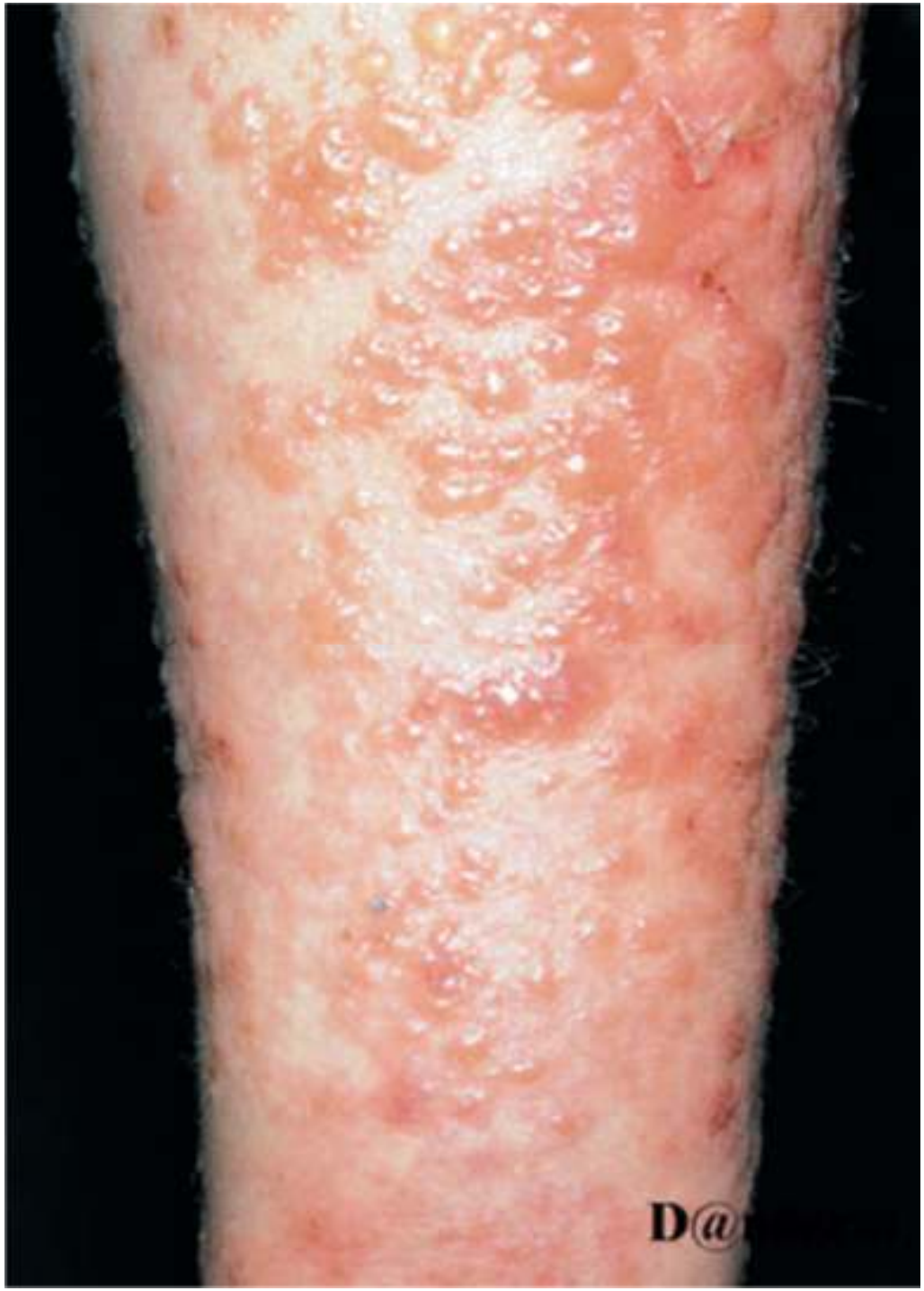
Erythematous stage –

itching erythema patch with discrete edema

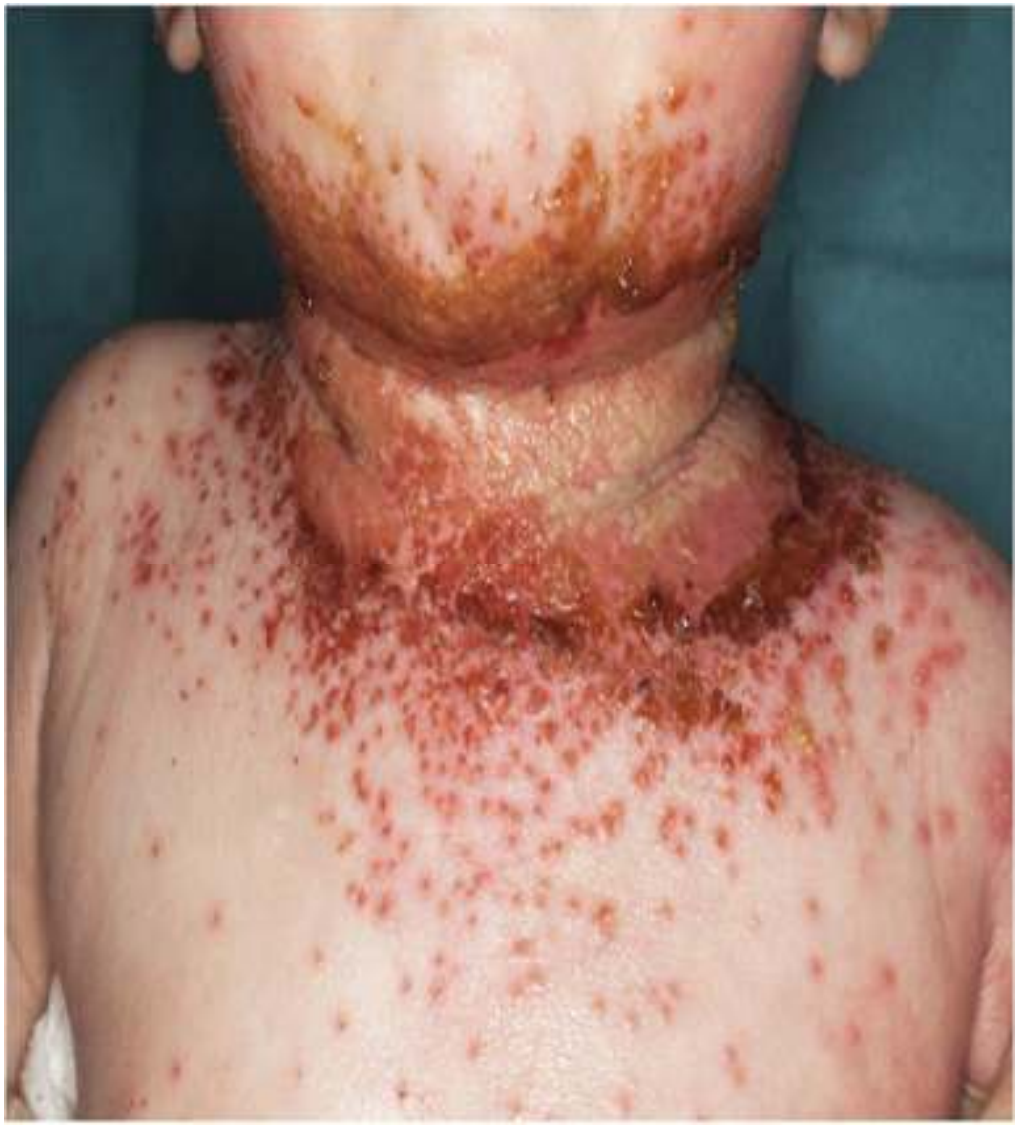


Vesiculation stage –

Vesicles with serous content gradually covering the erythematous patch.

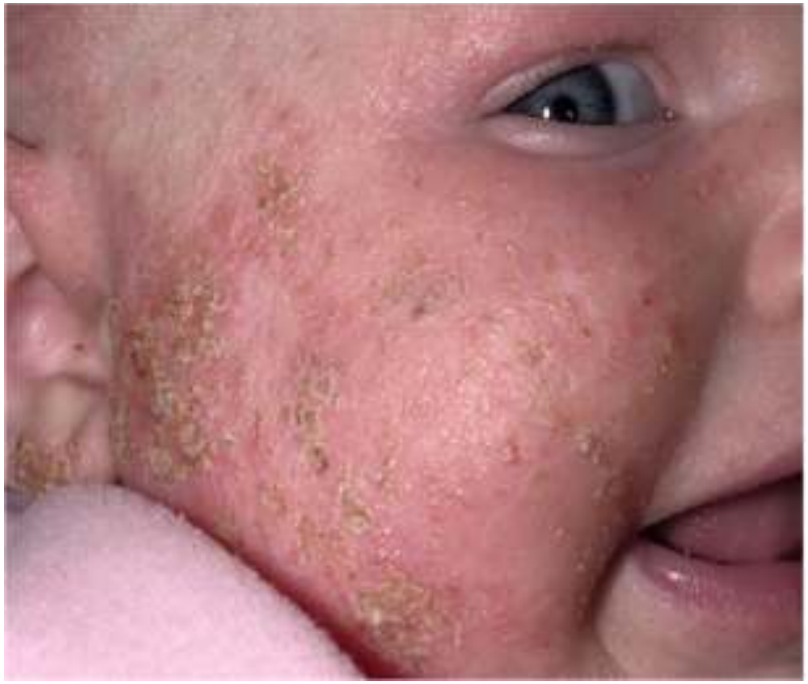


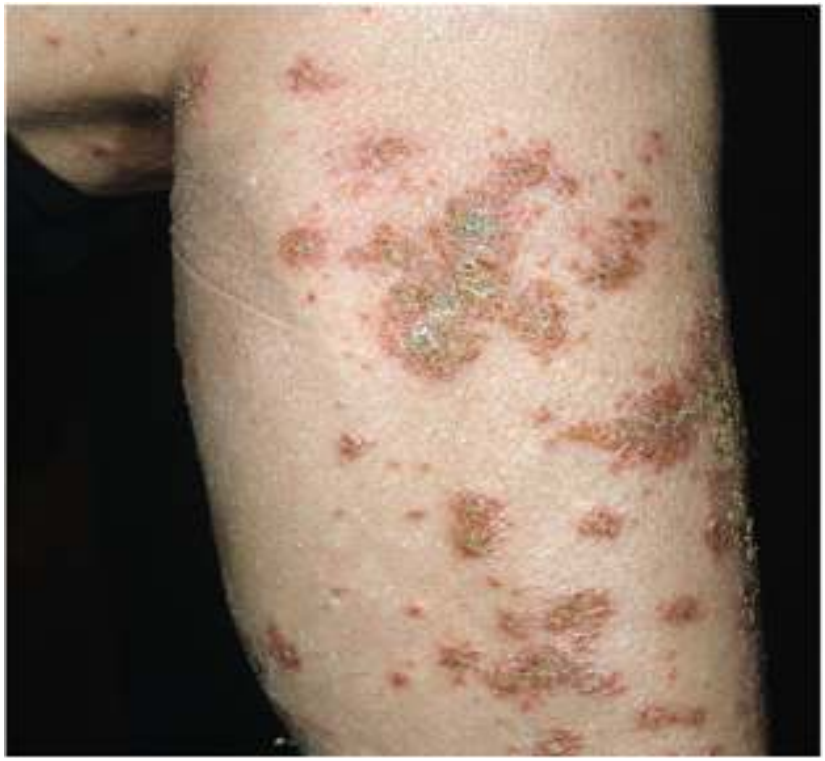
Weeping (oozing) stage – vesicles erupt forming erosive surface with serous exudates



Crusting stage – serous exudates dry into serous crusts;

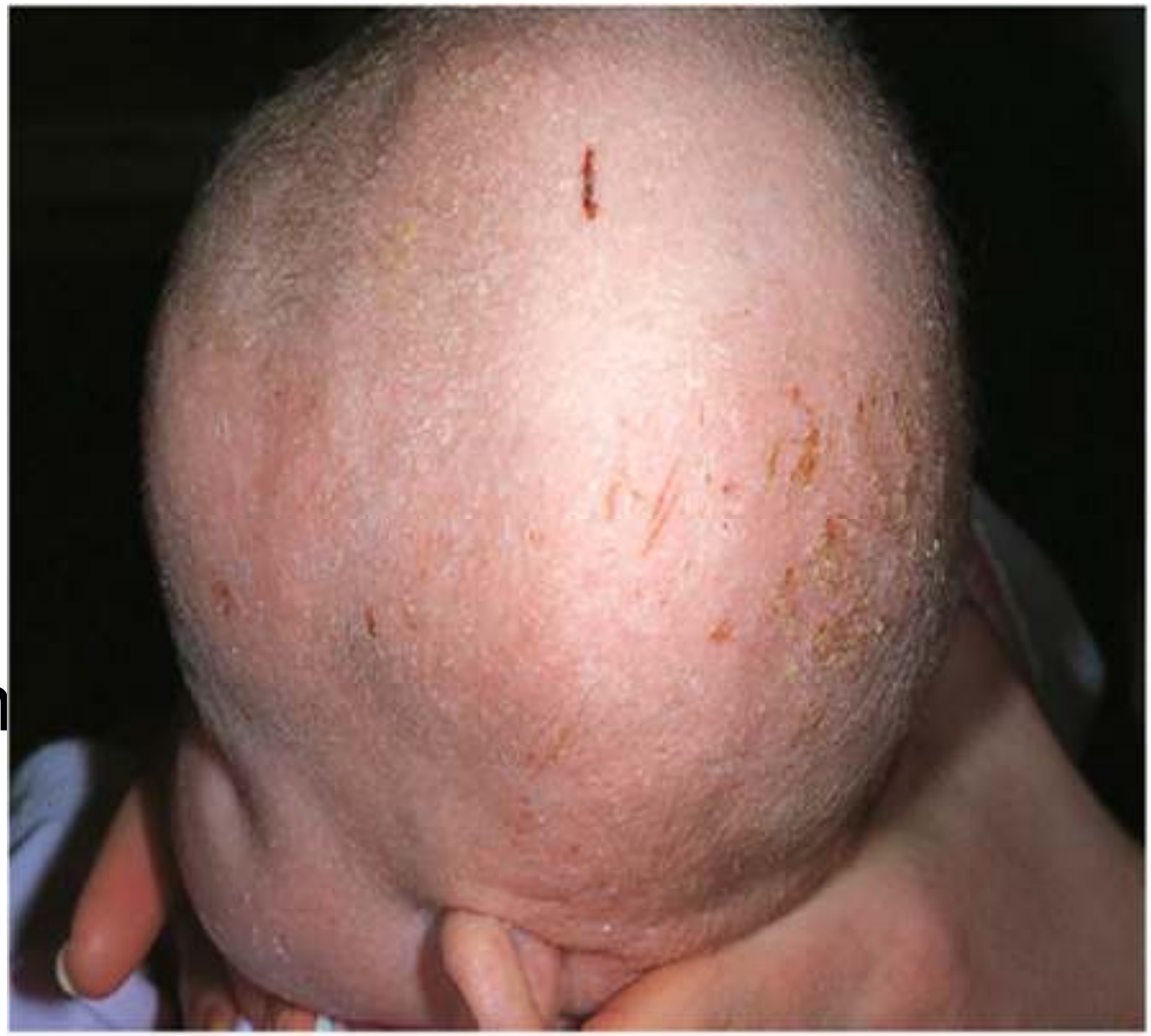
possibility of impetigo complication!!!





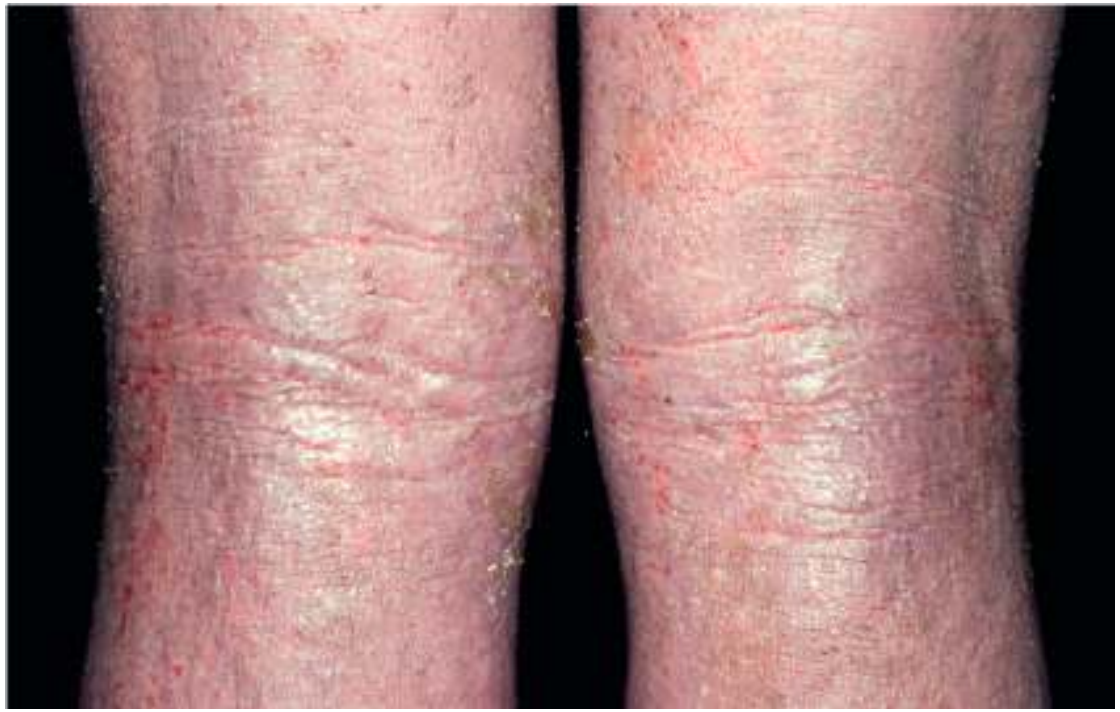
Desquamative stage –

after erosions undergo epithelialization scaling installs with white grayish scales, easily removable, covering a red, smooth and glossy skin.

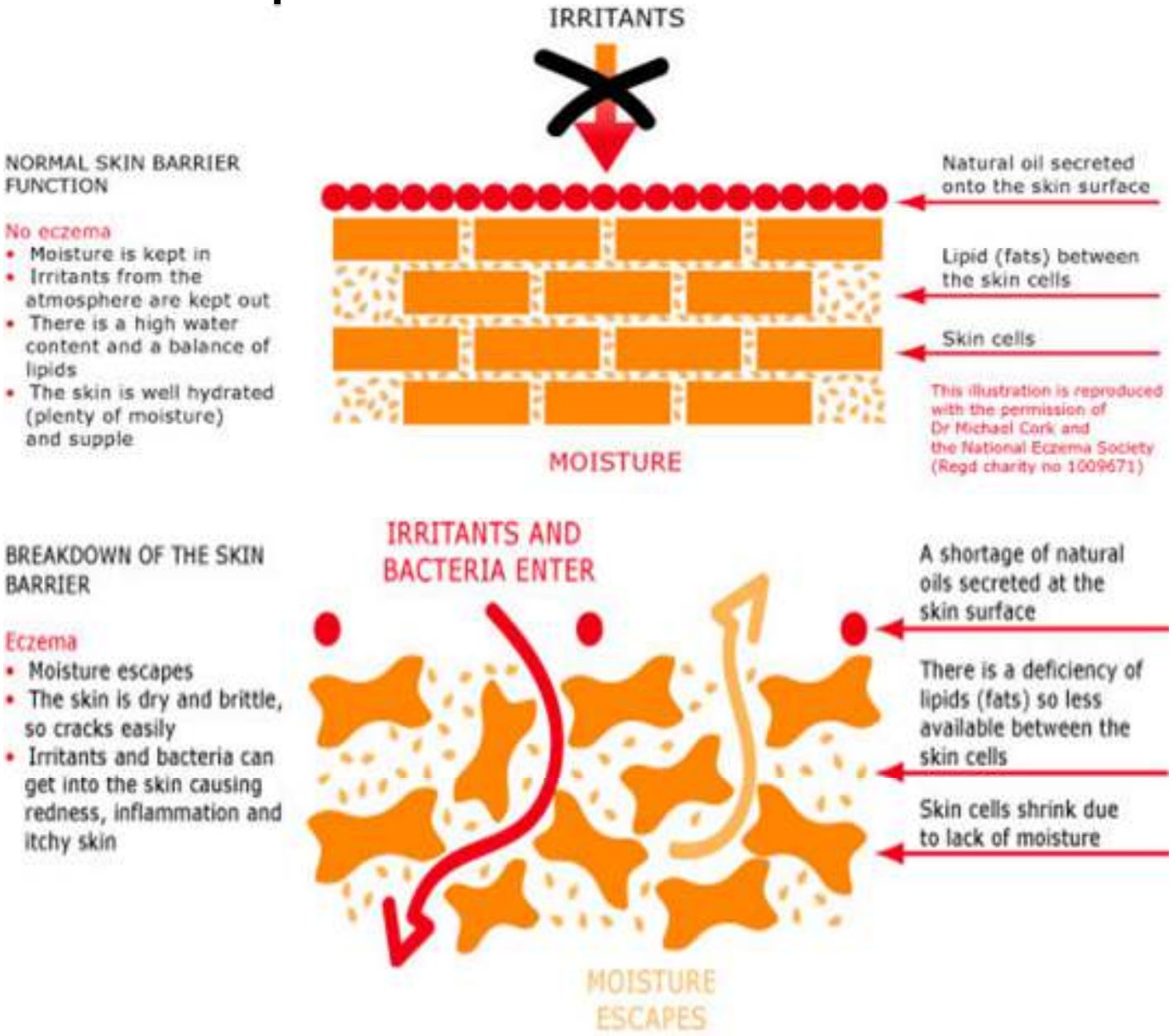


Lichenification stage –

plaques **of** thickened skin, skin lines accentuated (lichenified skin), excoriations, fissuring.



PATHOGENESIS: compromised barrier function



PATHOGENESIS:
MHC classes and immunopathology

- **MHC class I**

- presents intracellular antigens (viral, bacterial, lipid, tumoral antigens) to lymphocytes Tc CD8+ (cytotoxic)
- expressed on the surface of all nucleated cells

- **MHC class II**

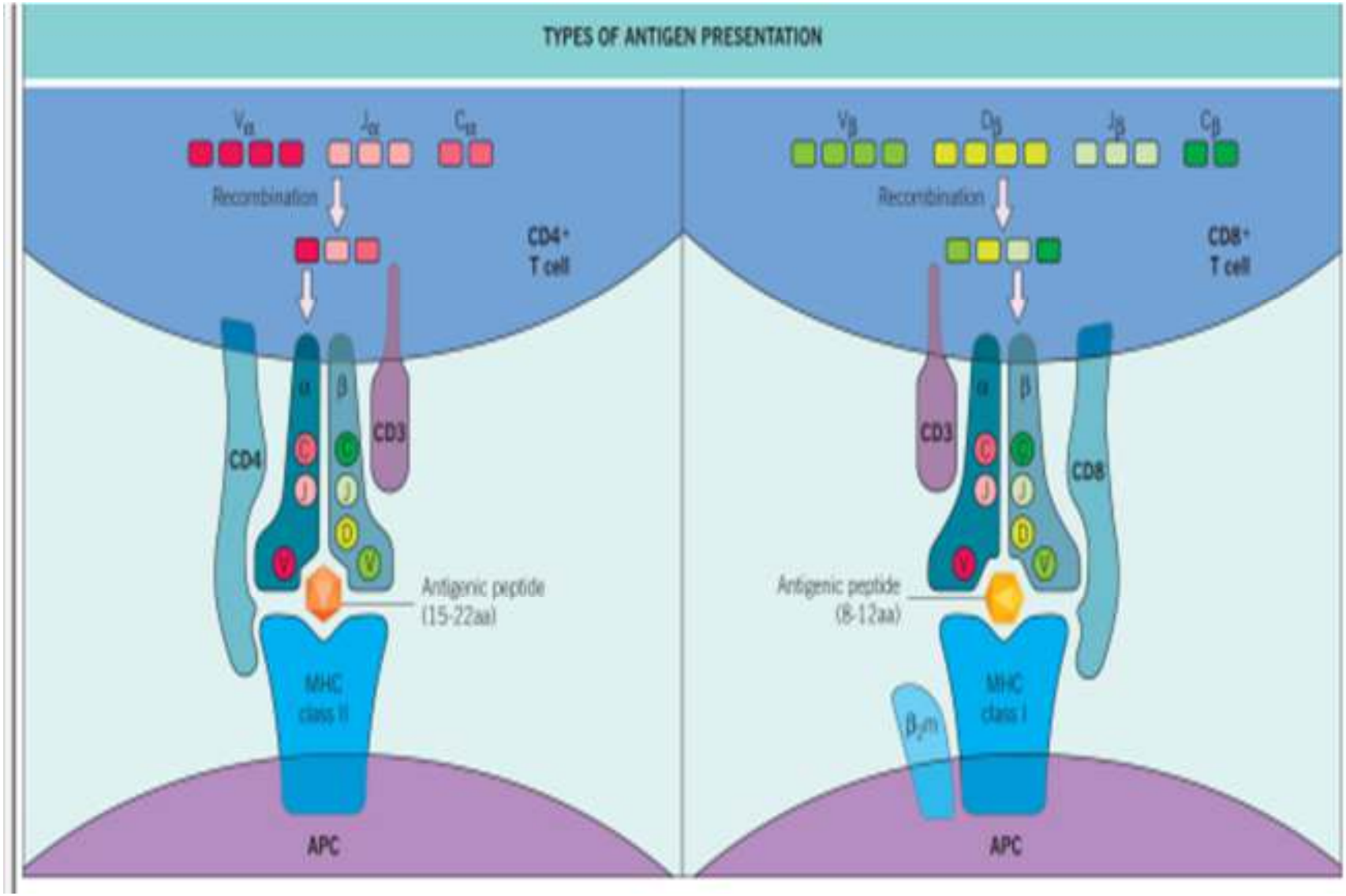
- presents extracellular antigens (contact allergens, bacteria, fungi, parasites) to lymphocytes T_H CD4+ (helper)
- expressed on the surface of antigen presenting cells (APC).

Human MHC – complex HLA (**H**uman **L**eukocitary **A**ntigen).

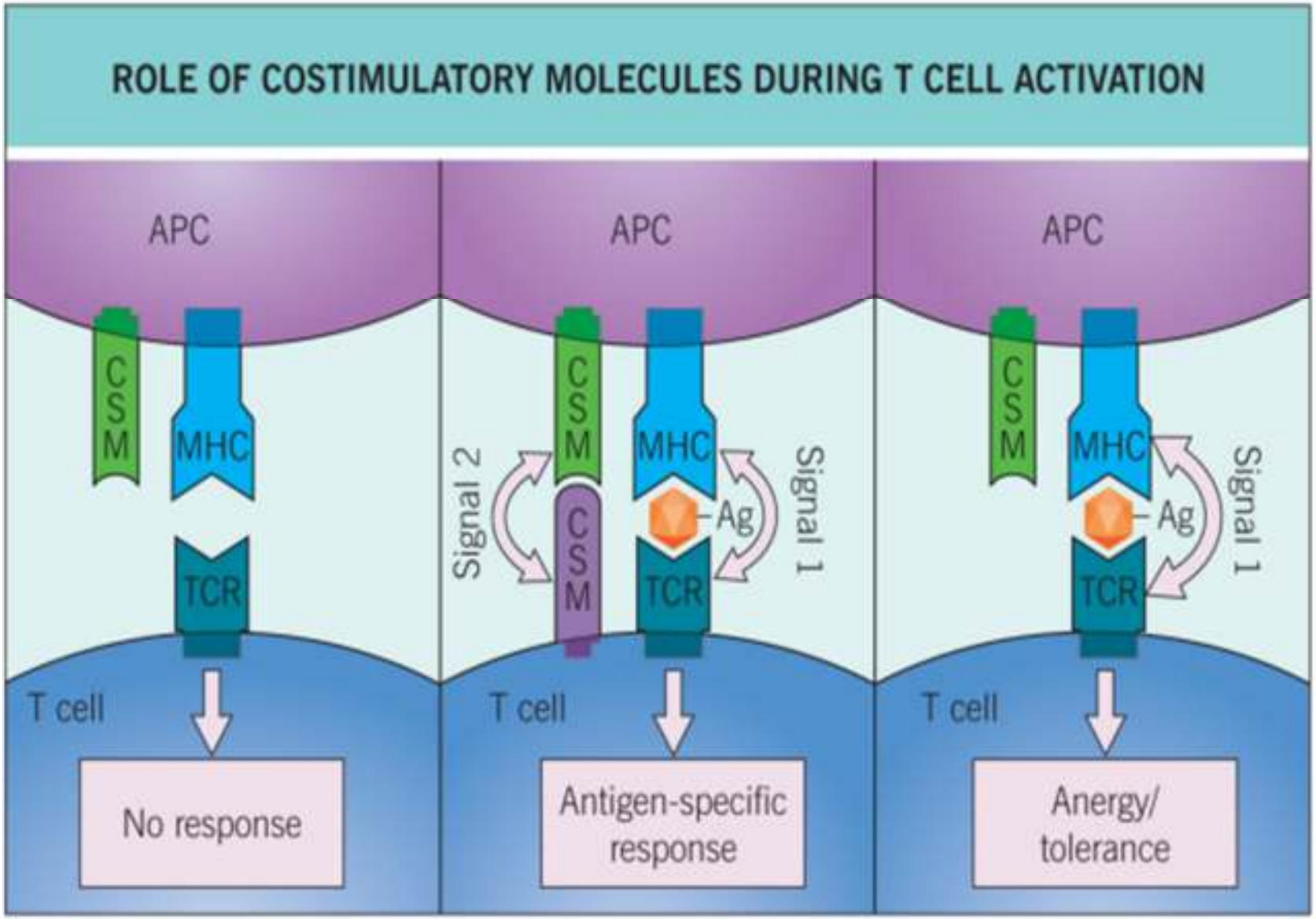
Clasa I = genes A, B şi C ⇒ HLA-A, HLA-B and HLA-C

Class II = genes DP, DQ şi DR ⇒ HLA-DP, HLA-DQ and HLA-DR

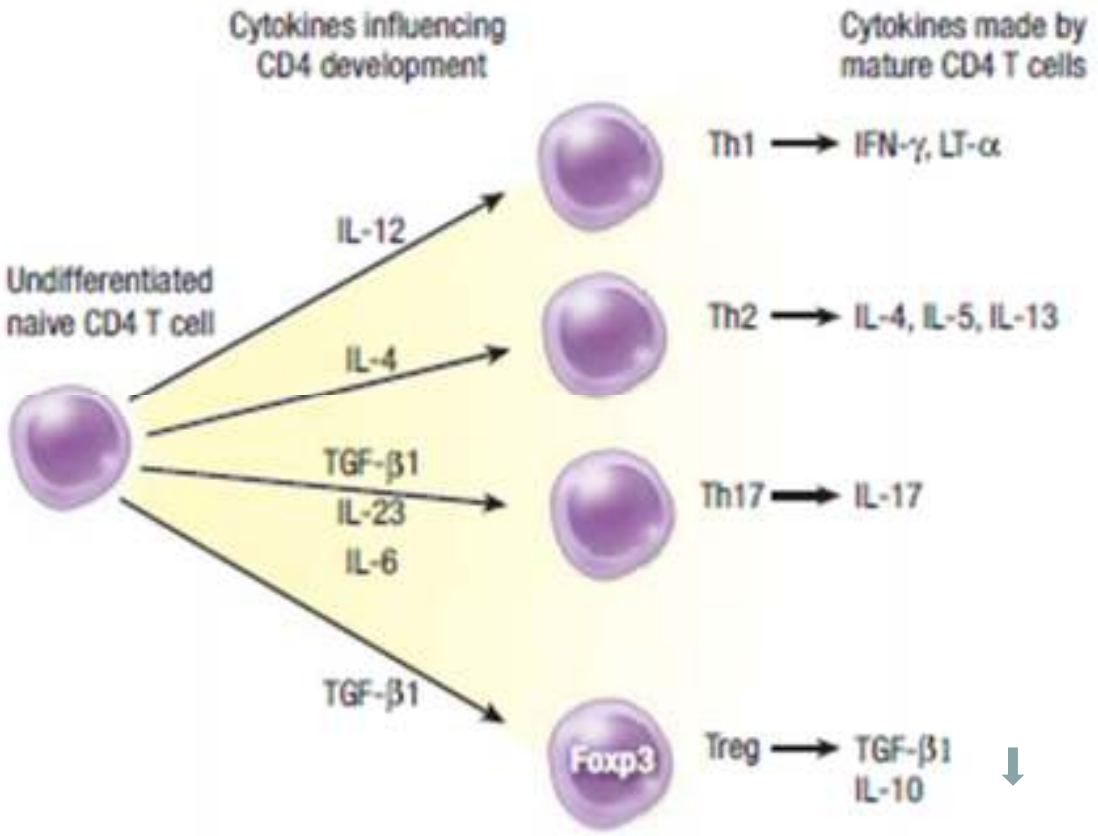
Antigen presentation



Co-stimulation and T-cell responce



Cytokin profile of CD4 lymphocytes

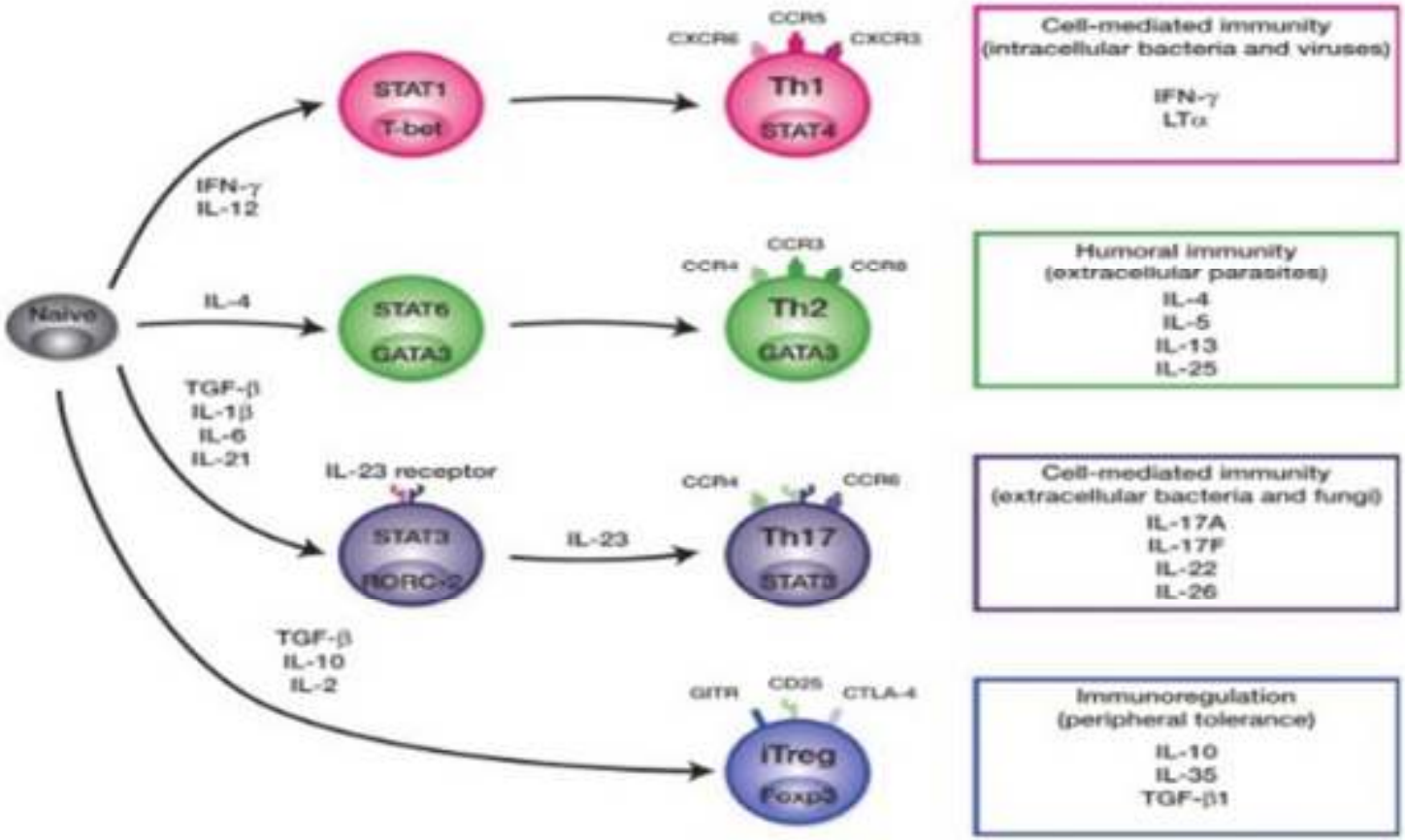


ACD

URTICARIA/ HAY FEVER/ASTHMA / ACUTE ATOPIC ECZEMA

PSORIASIS

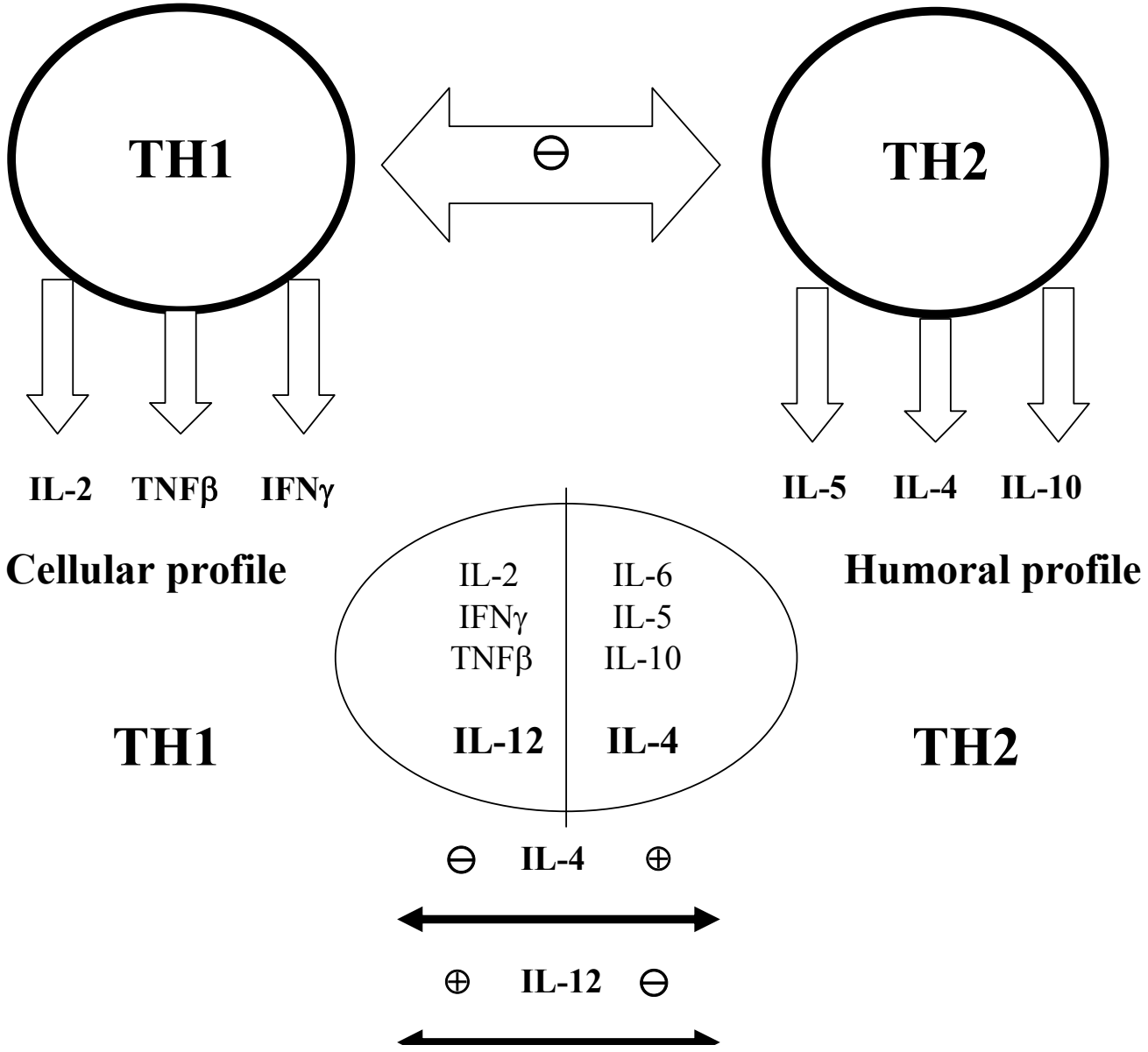
AUTOIMMUNE DERMATOSES

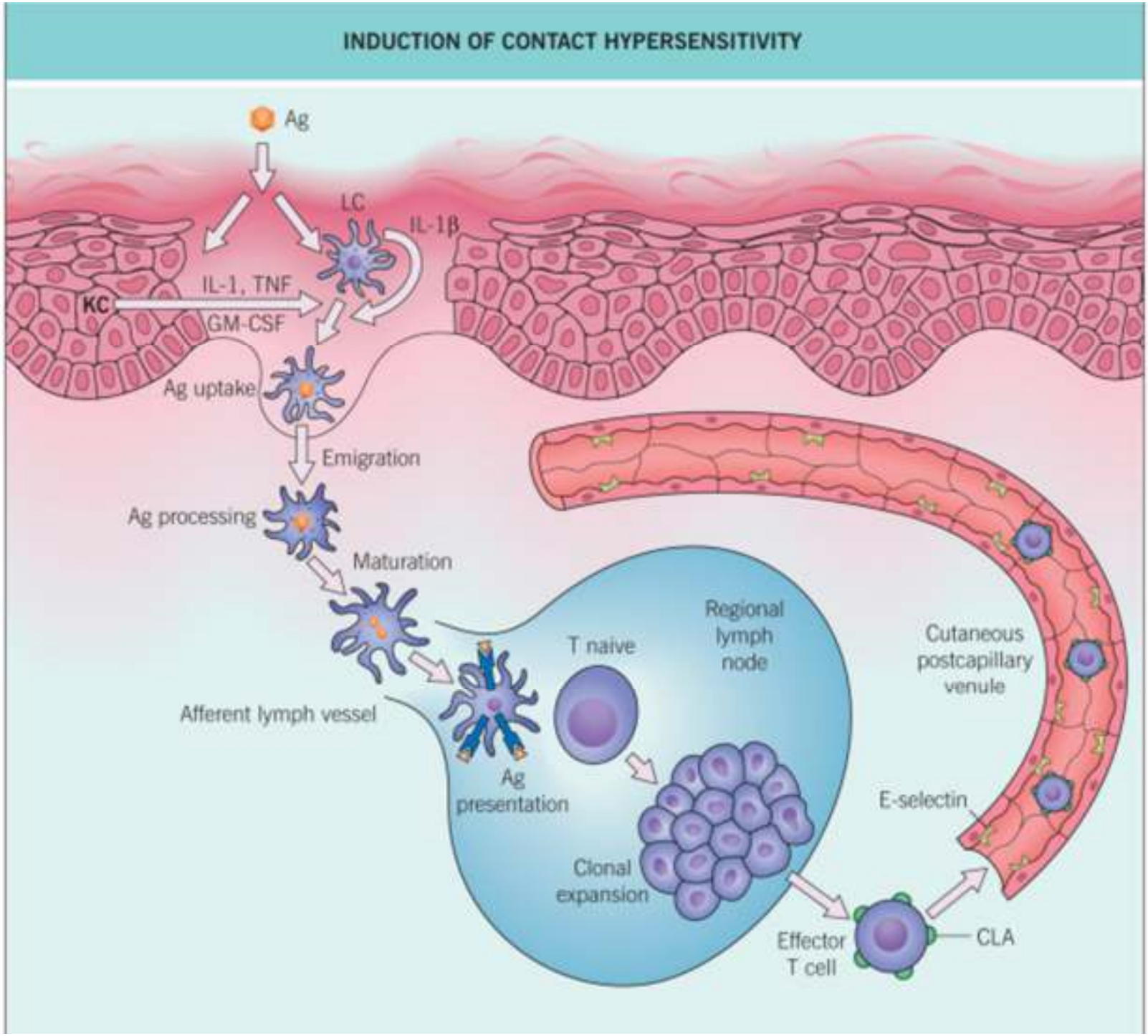


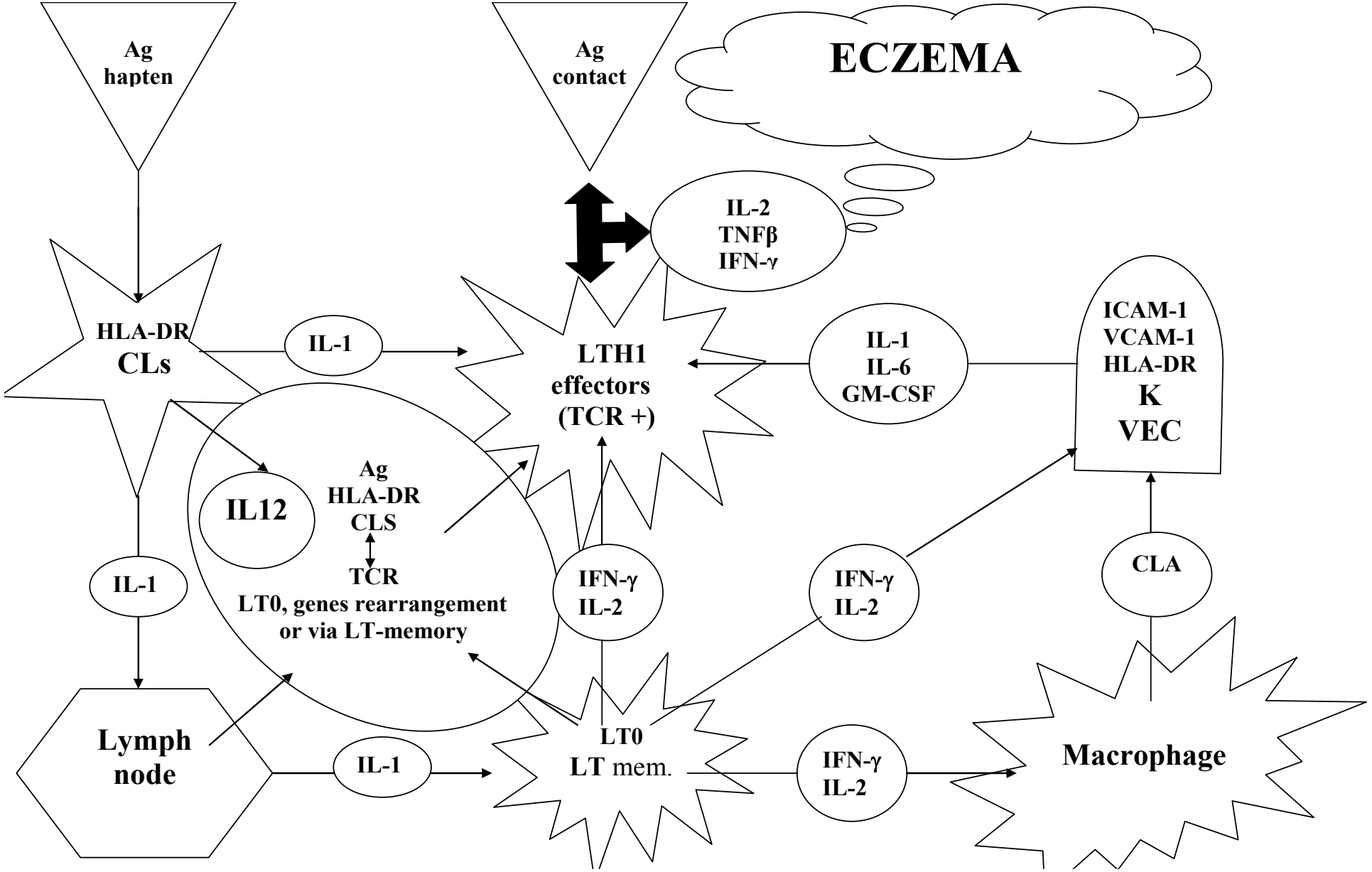
- Interleukin-23 (IL-23) helps to maintain the lesion by leading to the development of Th17 cells.
- These in turn produce necrosis factor-alpha (TNF-a), IL-17 and IL-22.
- IL-22 is believed to drive many of the epidermal changes in psoriasis.
- Many autoimmune diseases, including psoriasis, are characterized by high levels of Th17.

Journal of Investigative Dermatology 2009;129:1339–1350.

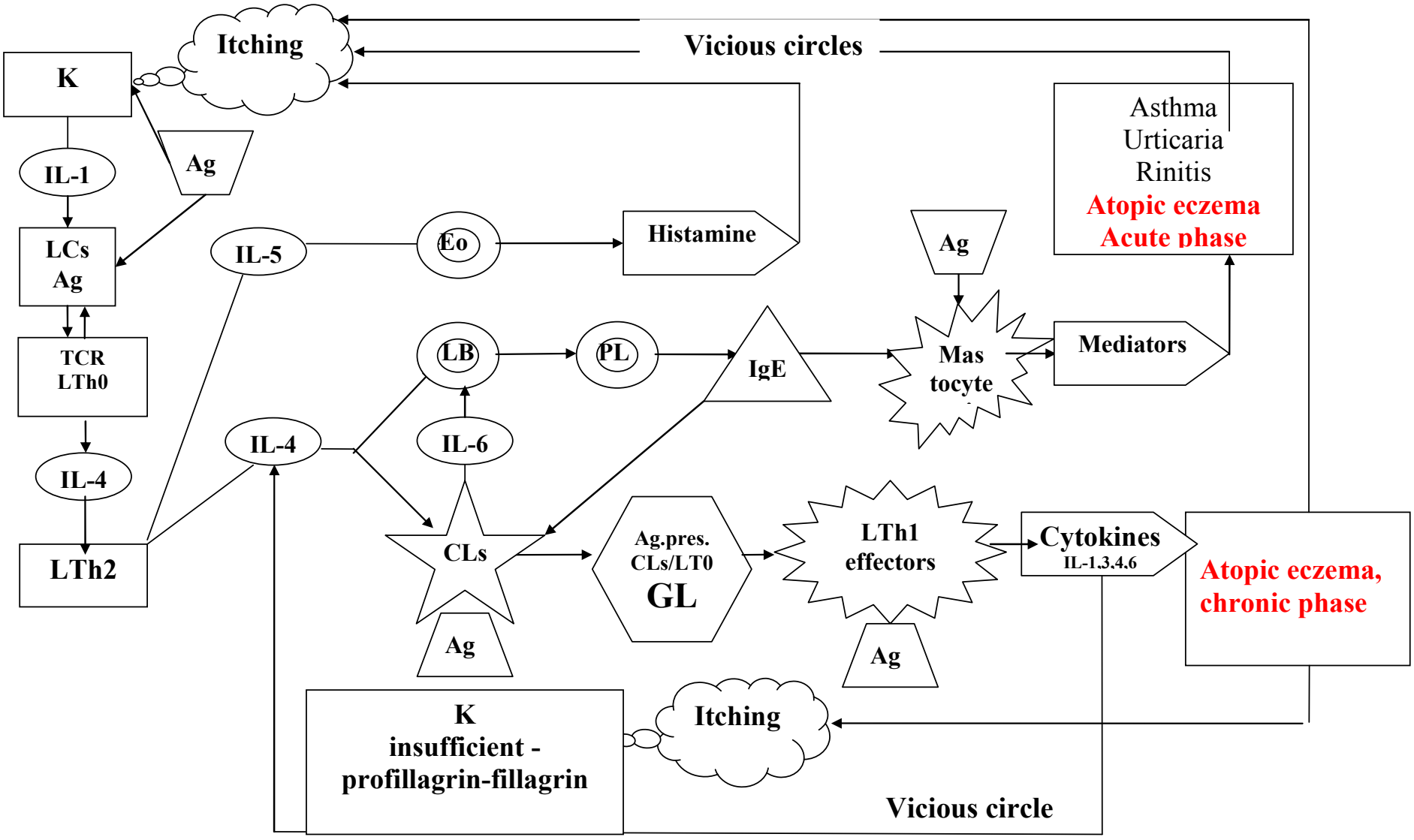
INTERACTION TH1/TH2



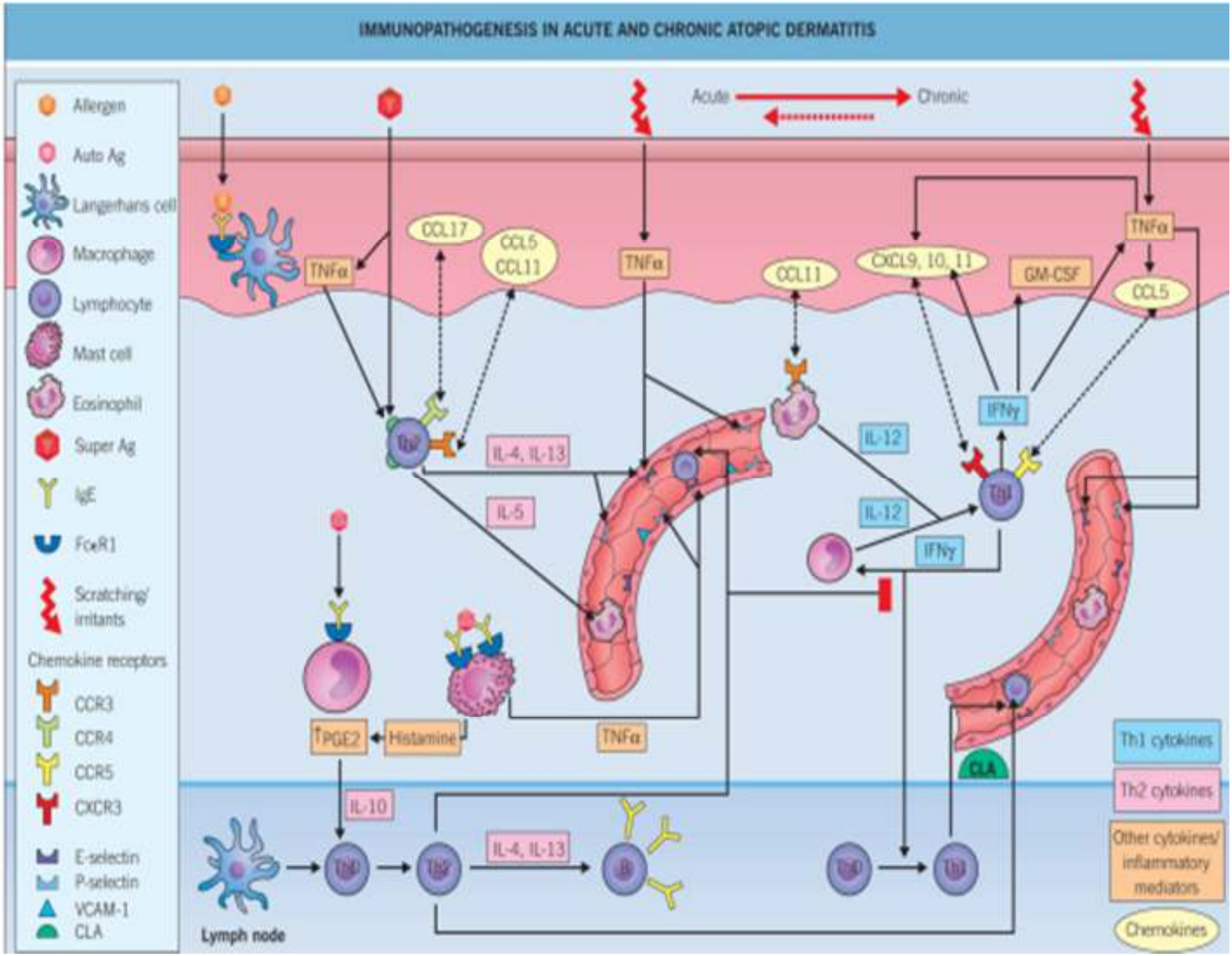

INDUCTION OF CONTACT HYPERSENSITIVITY
Ag
LC
IL-1β
KC
IL-1, TNF
GM-CSF
Ag uptake
Emigration
Ag processing
Maturation
Afferent lymph vessel
Regional lymph node
T naive
Ag presentation
Clonal expansion
Cutaneous postcapillary venule
E-selectin
Effector T cell
CLA



TH1 RESPONSE / TYPE 4 GELL-COOMBS



ATOPIC IMMUNOPATHOLOGY: CONCURRENT TYPE1/TYPE4 GELL-COOMBS, CONCURRENT RESPONCE PROFILE TH1/TH2


IMMUNOPATHOGENESIS IN ACUTE AND CHRONIC ATOPIC DERMATITIS
Allergen
Auto Ag
Langerhans cell
Macrophage
Lymphocyte
Mast cell
Eosinophil
Super Ag
IgE
FcεR1
Scratching/ irritants
Chemokine receptors
CCR3
CCR4
CCR5
CXCR3
E-selectin
P-selectin
VCAM-1
CLA
Acute
Chronic
TNFα
CCL17
CCL5
CCL11
CXCL9, 10, 11
GM-CSF
IL-4, IL-13
IL-5
IL-12
IFNγ
↑PGE2
Histamine
IL-10
Lymph node
Th1 cytokines
Th2 cytokines
Other cytokines/ inflammatory mediators
Chemokines

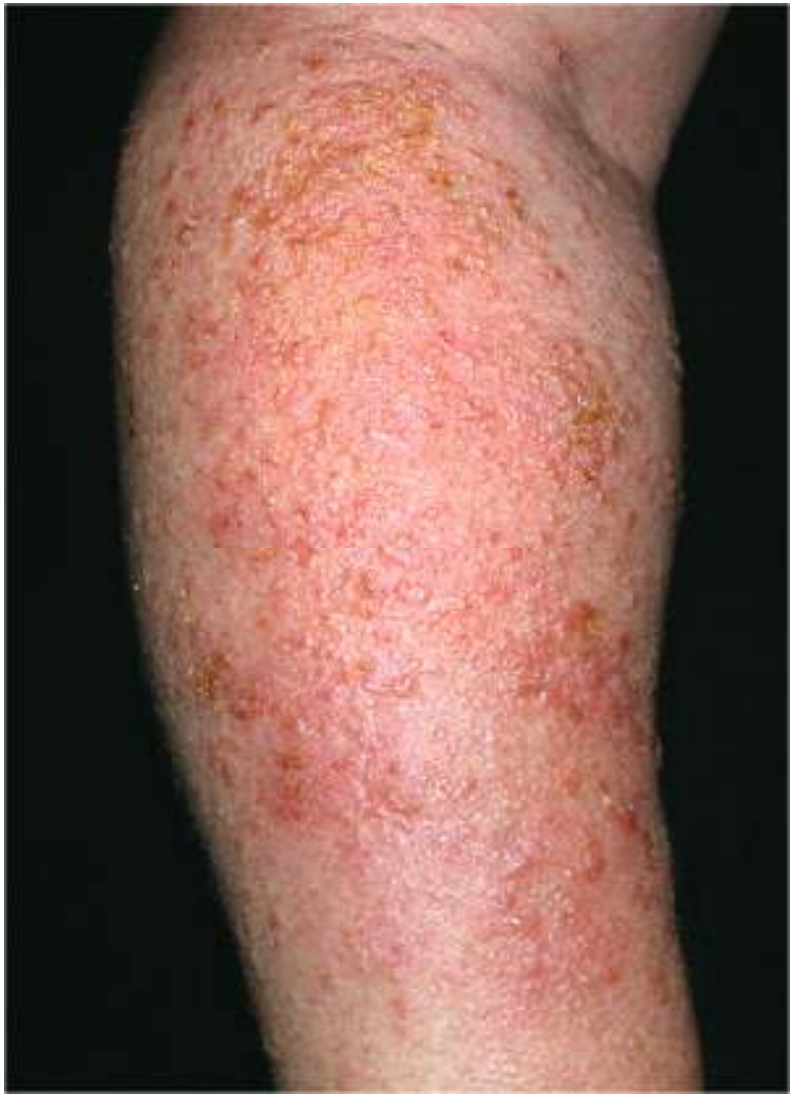
Pathogenesis of atopic eczema

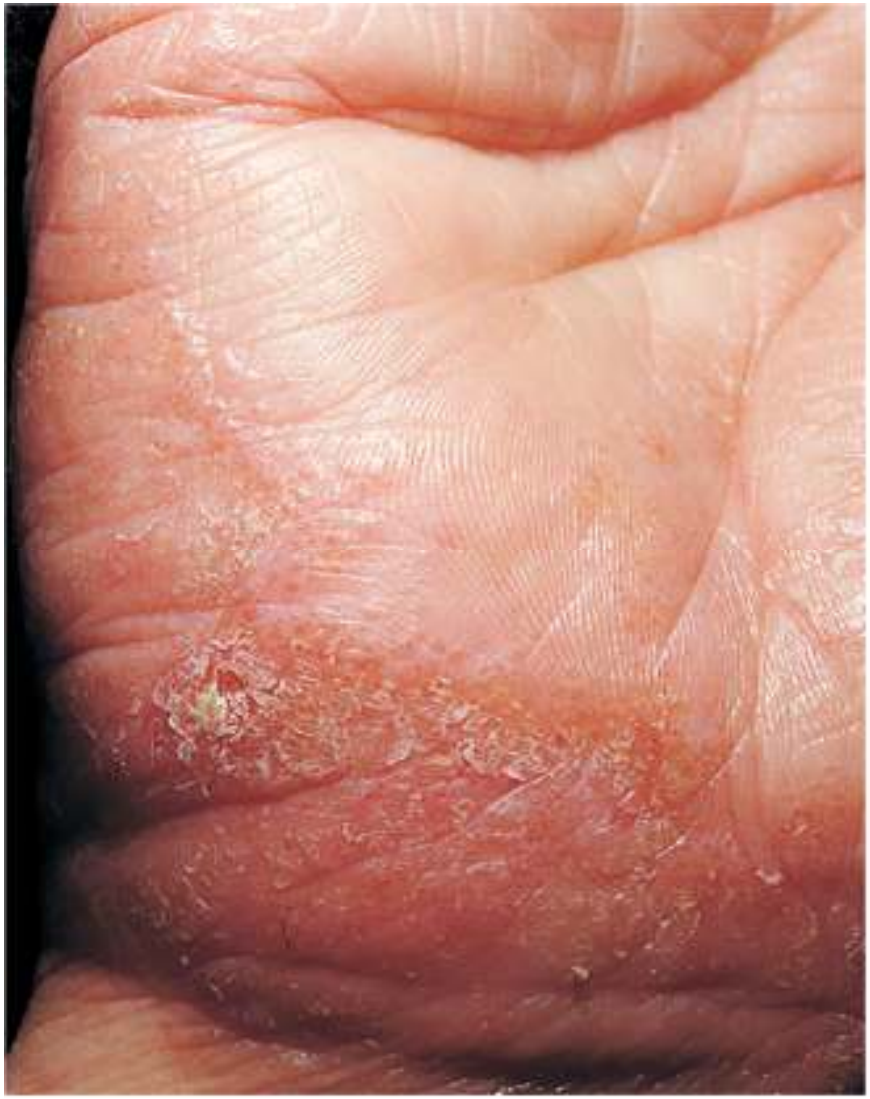
- The pathogenesis of atopic eczema is complex, but involves immunological abnormalities, environmental factors and emotional influence
- Immunological abnormalities in the atopic state include increased serum total IgE and specific IgE antibodies to ingested or inhaled antigens, and preferential activation of the Th2 phenotype CD4 T-cells, which form IL-4 and IL-5.
- The interleukins stimulate IgE synthesis by B-cells / plasmocytes (type I hypersensitivity)
- Staphylococci colonize the skin of patients with atopic eczema, and staphylococcal exotoxins with superantigen properties are also thought to play a pathogenic role in T- an B-cell abnormal activity.
- It has been shown that epidermal Langerhans cells possess high affinity IgE receptors through which an eczema-like reaction (type IV hypersensitivity) could be mediated.
- Both, type I and IV, hypersensitivities maintain and mutual amplify vicious course of atopic eczema.

Eczema evolutive forms

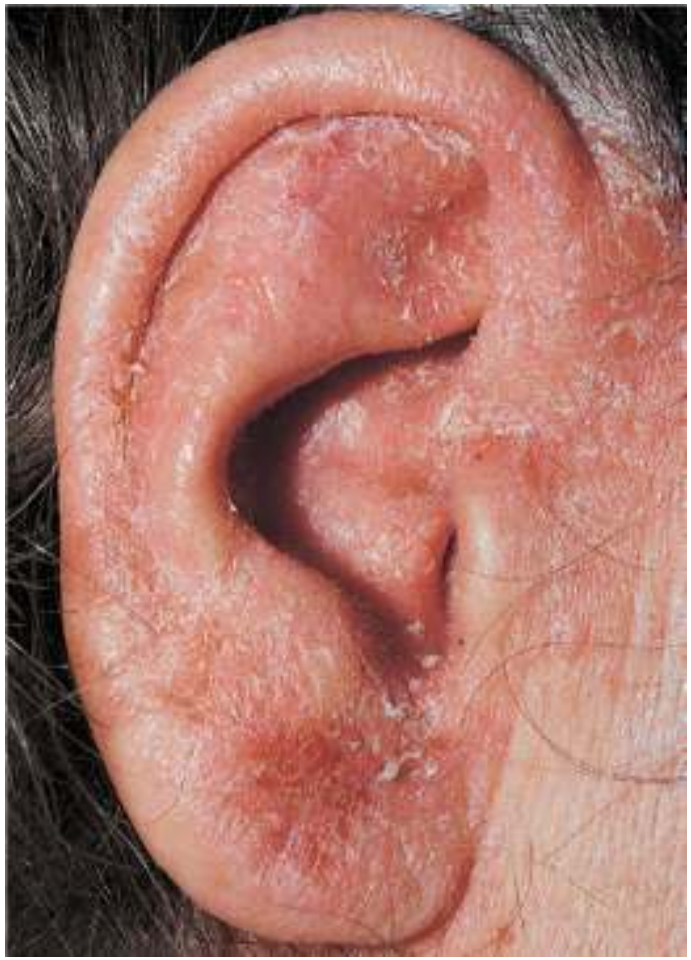
- **Acute eczema:** pain, burning, tingles, edema, erythema with ill-defined borders, acute exudation, vesicles and crusting; histo – spongiosis and vesicles prevail; eczema passes rapidly during several days through all stages.
- **Subacute eczema:** itching, crusting and scaling; histo – acanthosis and perivascular infiltrates prevail, decreasing spongiosis and vesiculation; eczema retains in crusting and desquamative stages for several weeks.
- **Chronic eczema:** well defined, thickened, hypo- or hyperpigmented plaques with intense itching and descuamation, severe lichenification; histo – predominance of hyperkeratosis, acanthosis, papillomatosis, focal parakeratosis, diffuse deep cellular infiltrate in dermis, spongiosis and vesicles are minimal; eczema retains in desquamative and lichenification stages for months and years.

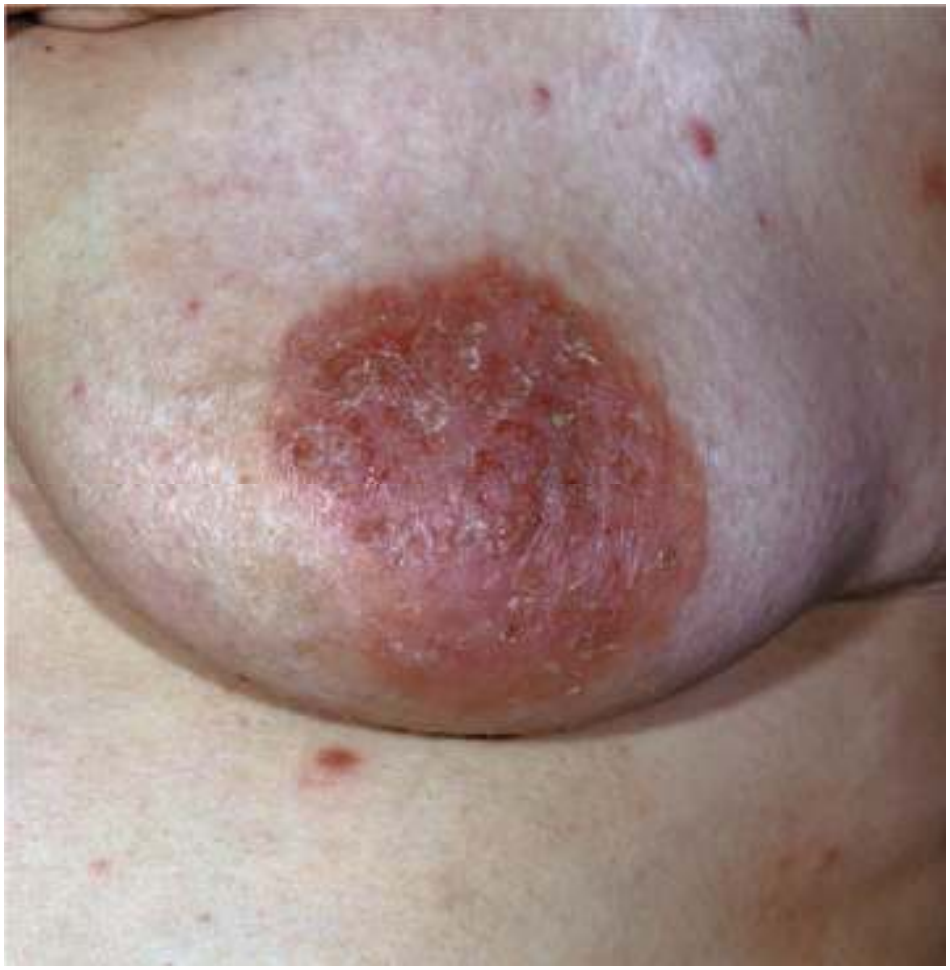
Acute eczema



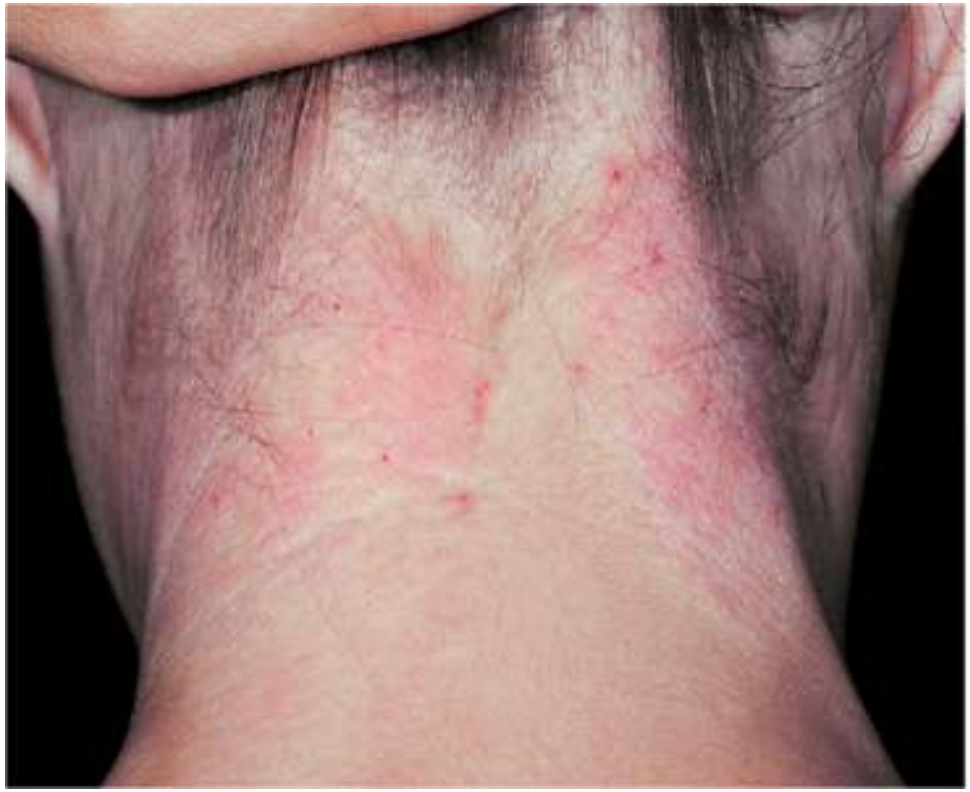


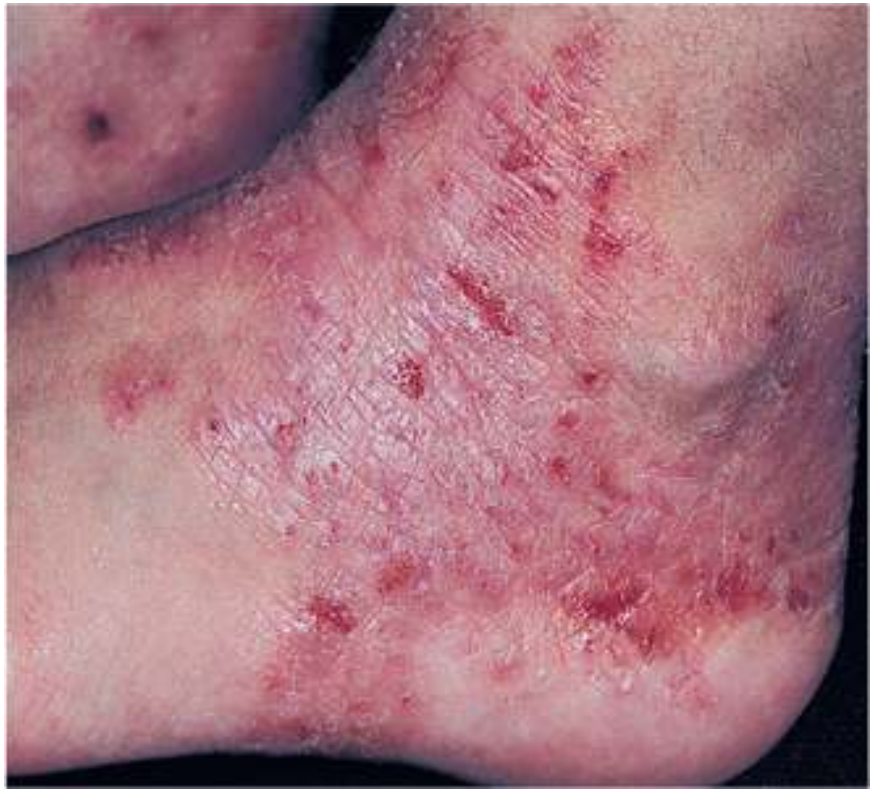
Subacute eczema





Chronic eczema (lichenified)





Eczema
etiological forms

- **Exogenous eczema –** irritative eczema (dermatitis), allergic eczema (dermatitis), systemic allergic eczema (dermatitis);
- **Endogenous eczema (constitutional)** – atopic dermatitis (eczema);
- **Exo-endogenous eczema (mixed)** – nummular (discoid) eczema; dyshidrotic (pompholyx) eczema; microbial eczema; stasis (varicose) eczema; seborrheic eczema; asteatotic (xerotic) eczema; eczema associated with malabsorbtion; id (autoeczematization).

Irritant contact dermatitis - ICD

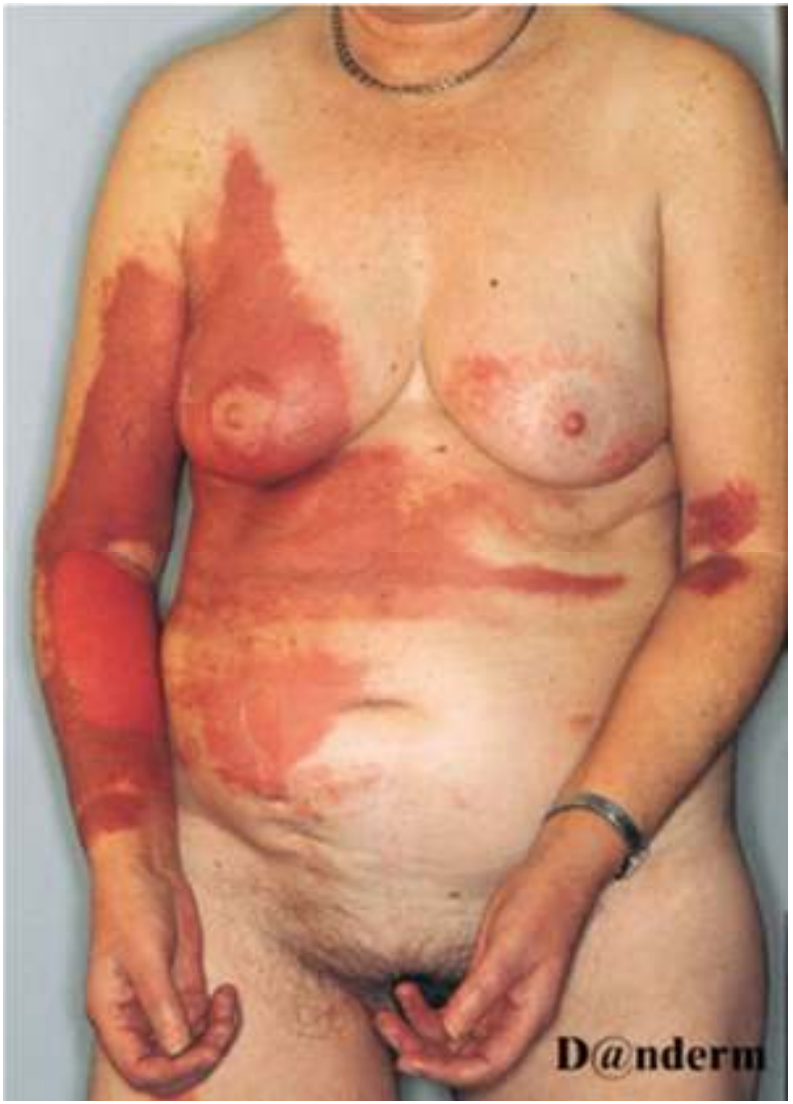
- Irritant contact dermatitis occurs when chemicals or physical agents damage the surface of the skin faster than the skin is able to repair the damage.
- The dermatitis or eczema is often well demarcated with a glazed surface but there may be erythema, itching, swelling, blistering and scaling of the damaged area.

ICD examples

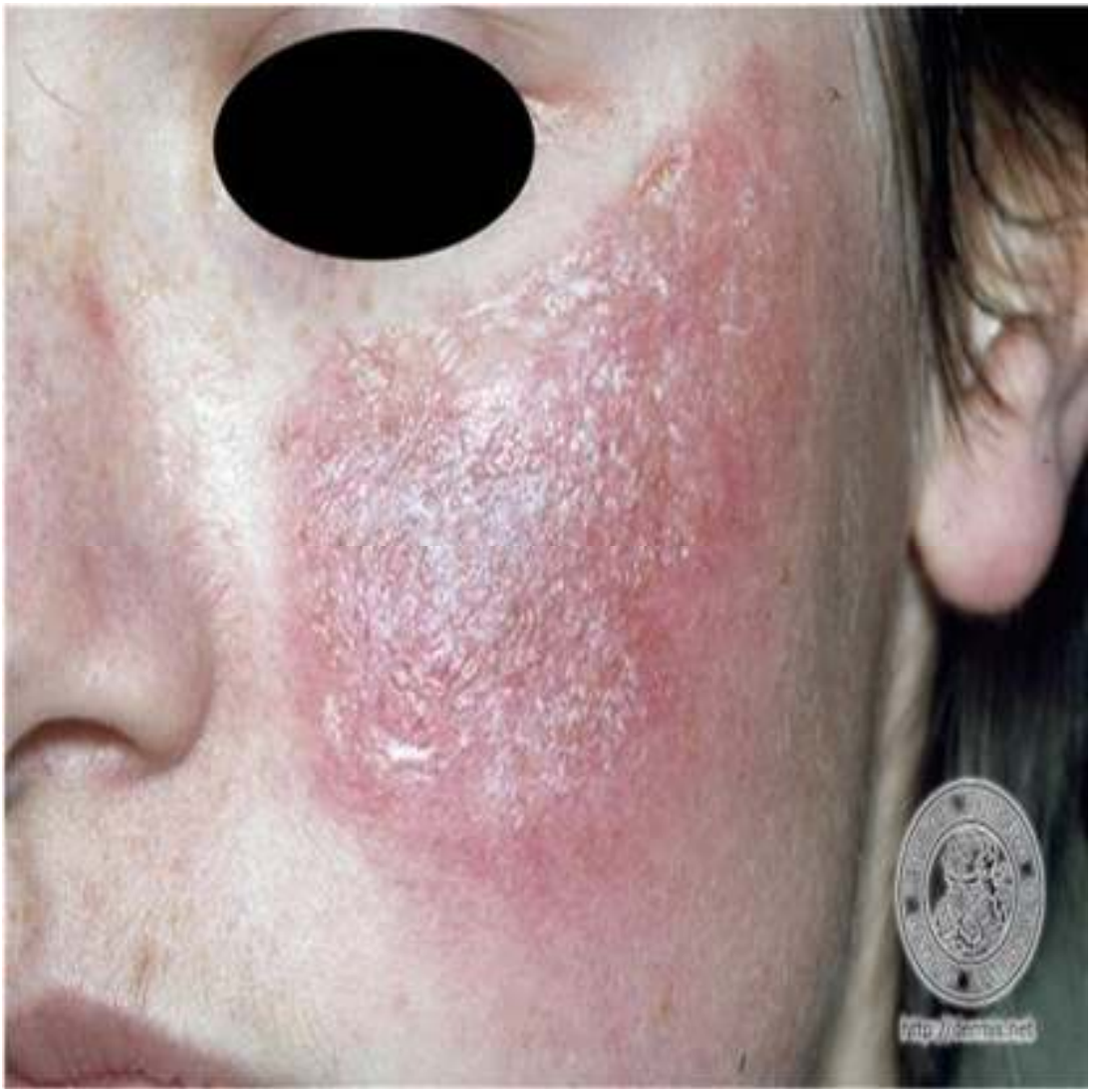
- Dribble rash around the mouth or on the chin in a baby, or in older children due to licking; the cause is saliva, which is alkaline.
- Napkin dermatitis due to urine and faeces.
- Chemical burns from strong acids (eg. hydrochloric acid) and particularly alkalis (eg. sodium or calcium hydroxide).
- Housewife's eczema is hand dermatitis caused by excessive exposure to water, soaps, detergents, bleaches and polishes.
- Dermatitis on a finger underneath a ring due to accumulation of irritants.
- Rubber gloves or the powder or sweat or tiny quantities of chemicals that have been occluded inside them may have a direct irritant action on hands.
- Fiberglass may cause direct mechanical/frictional damage.
- Dry cold air may cause dry irritable skin (winter itch)
- Cosmetics may irritate sensitive facial skin (especially in rosacea) resulting in immediate stinging, burning and redness followed by itching and dryness.

ICD

Turpentine

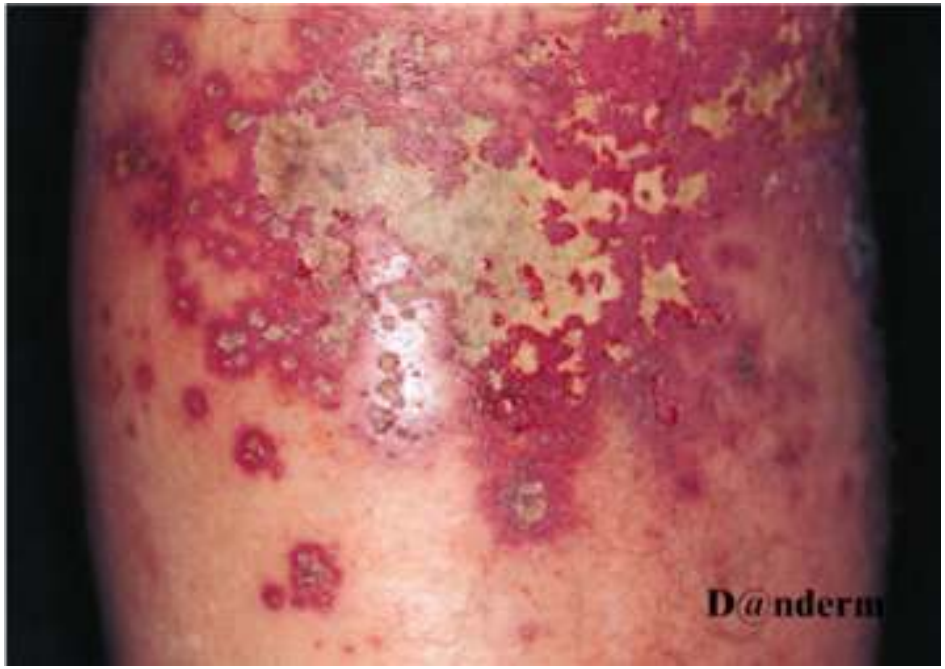


Glycolic acid

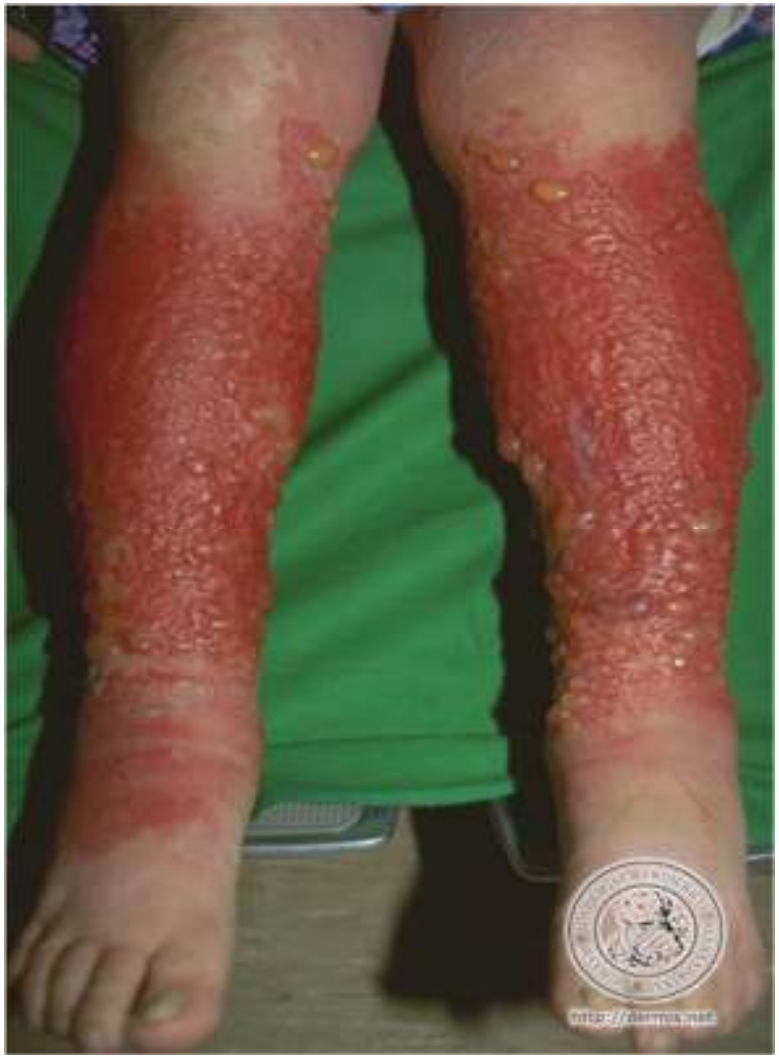


ICD

Alkali

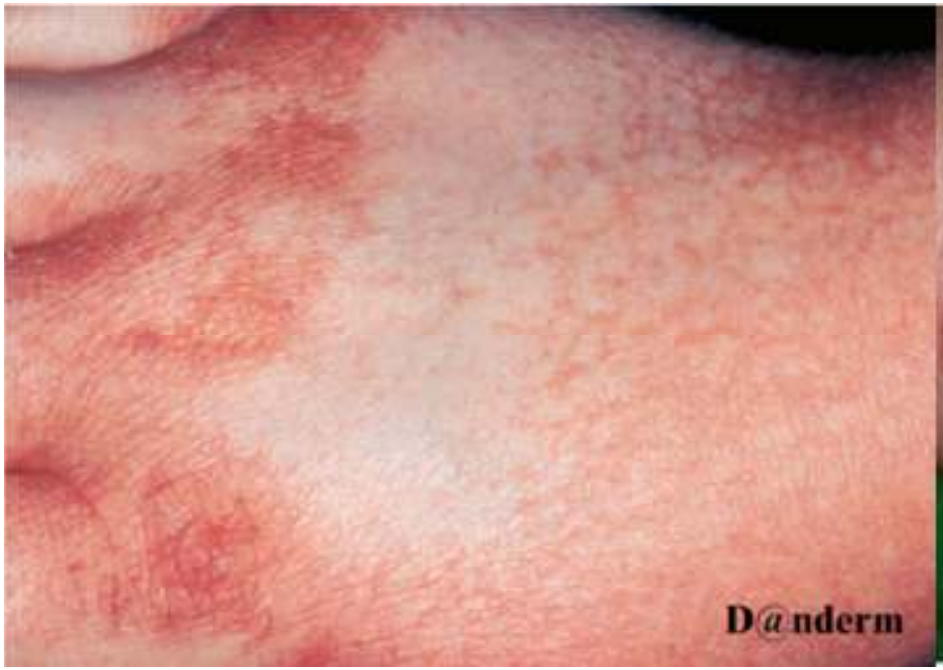


Acid

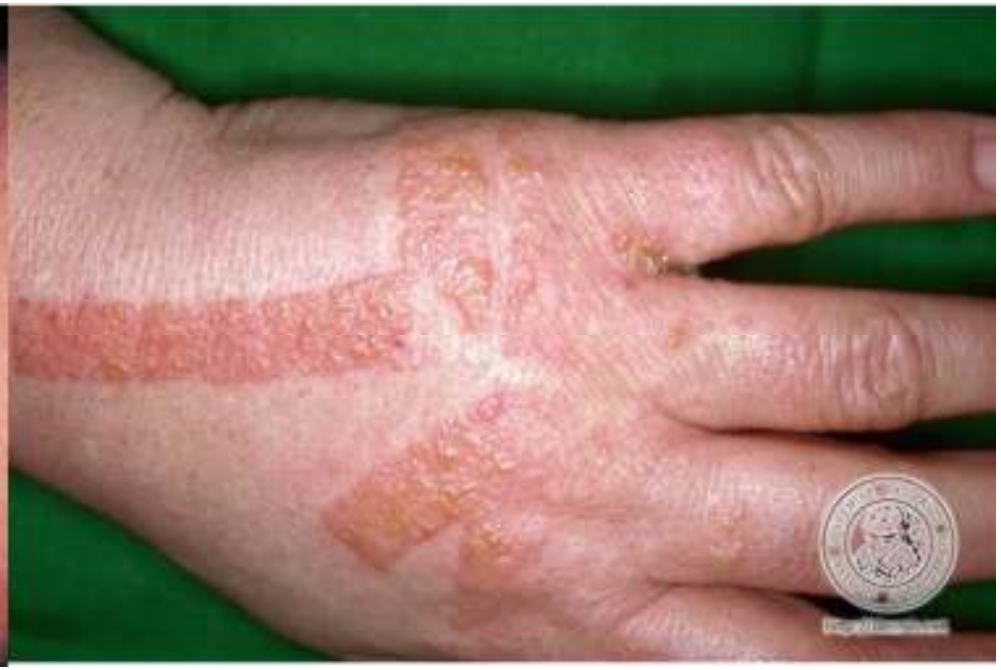


ICD

Hadwashing



Adhesive band



Allergic contact dermatitis – ACD

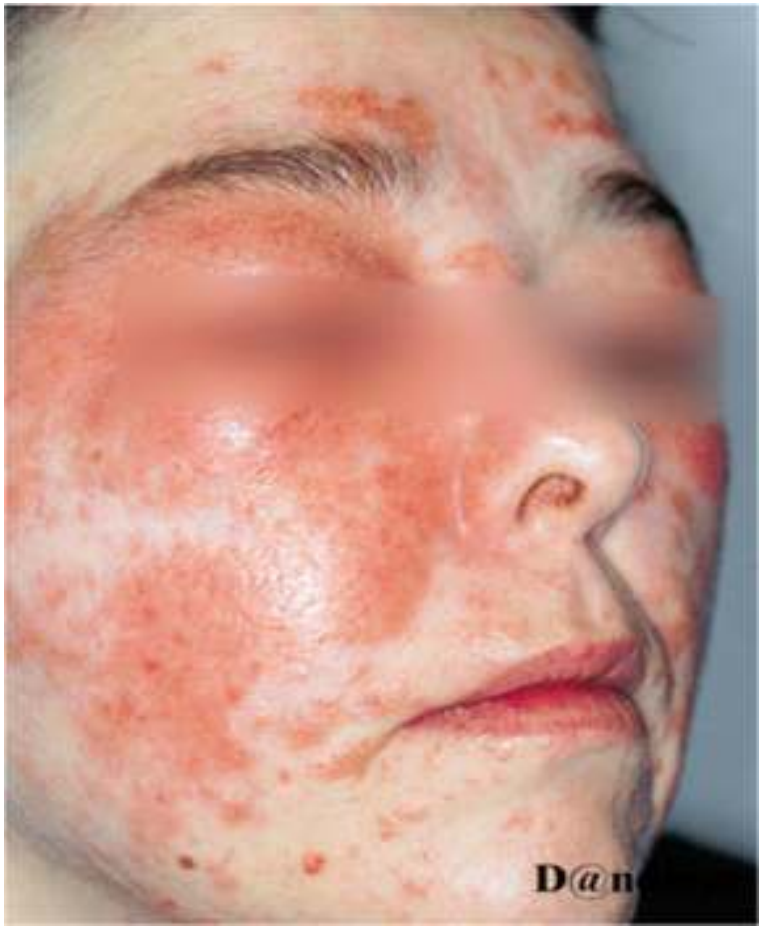
- Allergic contact dermatitis is an itchy skin condition caused by an allergic reaction to the allergen in contact with the skin.
- It arises in 24-72 hours after contact with the responsible material, and settles down over some days if the skin is no longer in contact with it.
- In severe cases contact allergic dermatitis may be followed by generalised autoeczematisation (id reaction).
- Ingestion of a contact allergen is usually safe, but rarely may lead to baboon syndrome or generalised systemic contact dermatitis.

Common allergens in ACD

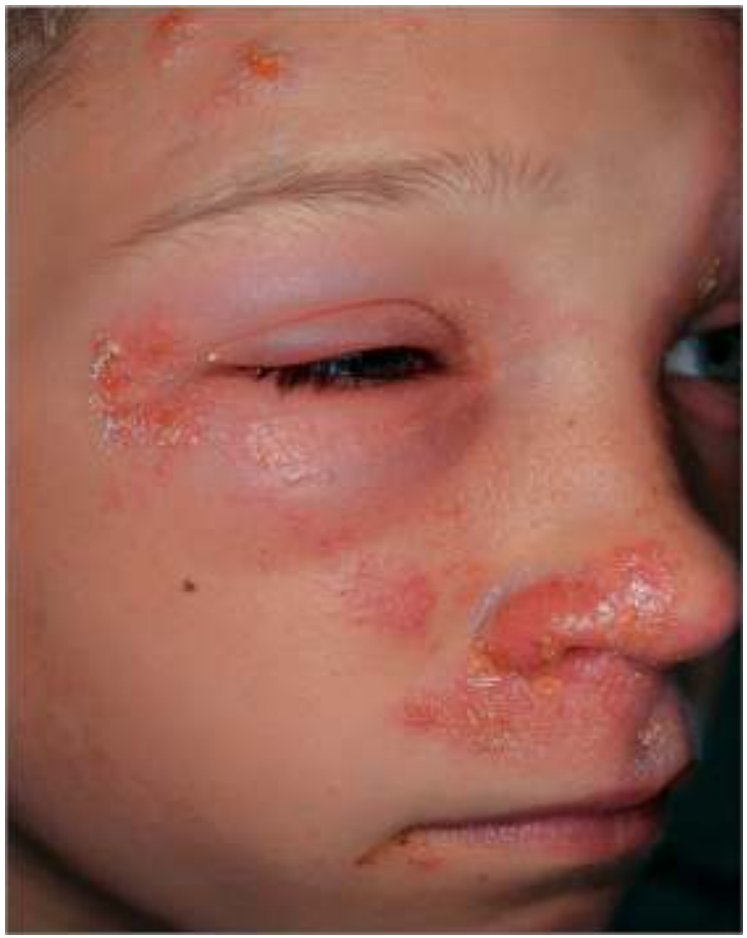
- Adhesives, including those used for false eyelashes or toupees
- Antibiotics such as neomycin rubbed on the surface of the skin
- Balsam of Peru (used in many personal products and cosmetics, as well as in many foods and drinks)
- Fabrics and clothing
- Fragrances in perfumes, cosmetics, soaps, and moisturizers
- Nail polish, hair dyes, and permanent wave solutions
- Nickel or other metals (found in jewelry, watch straps, metal zips, bra hooks, buttons, pocketknives, lipstick holders, and powder compacts)
- Poison ivy, poison oak, poison sumac, and other plants
- Rubber or latex gloves or shoes

ACD

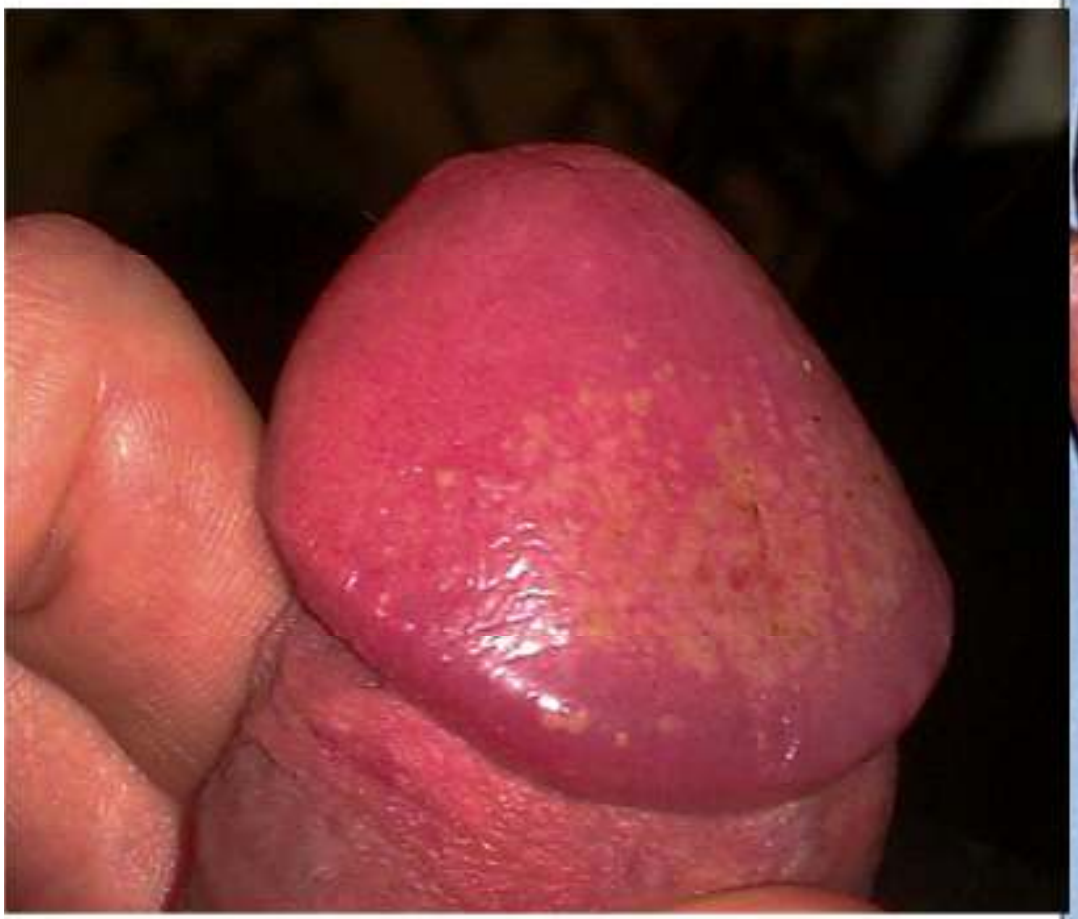
parabens

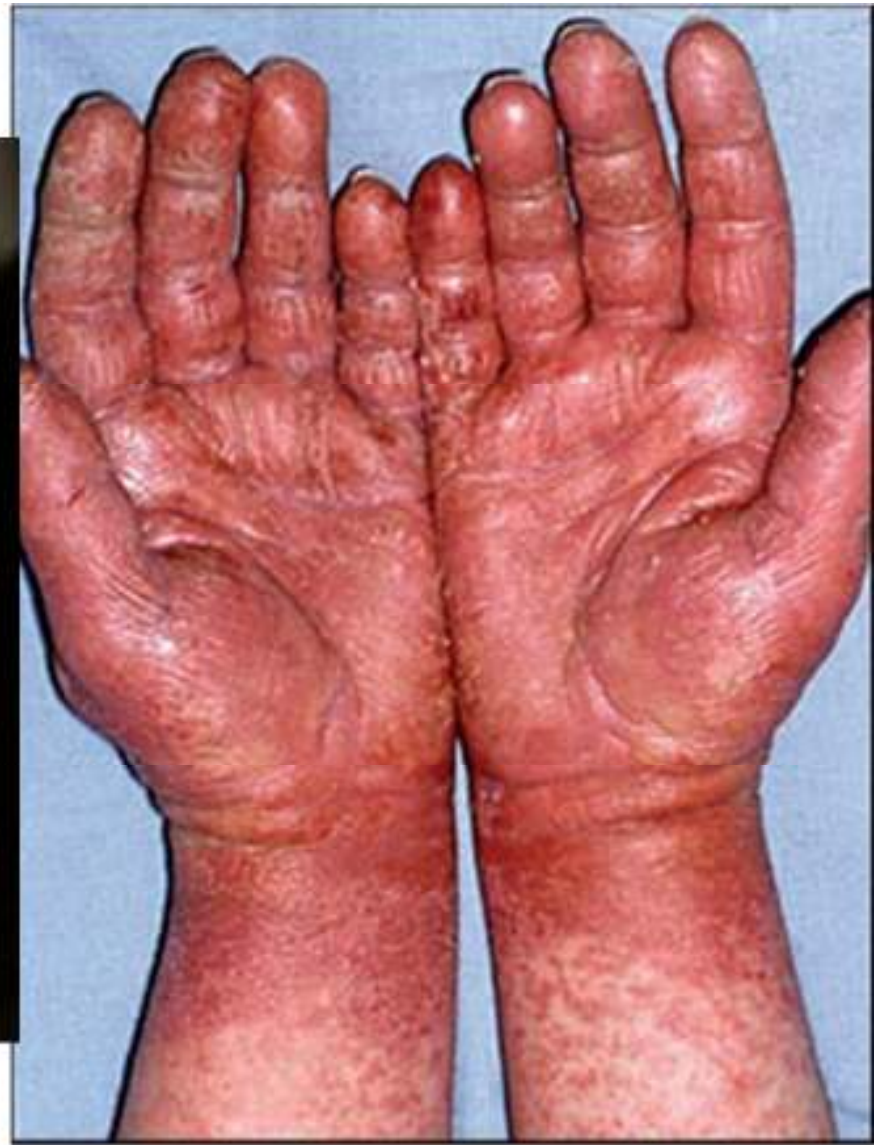


poison ivy

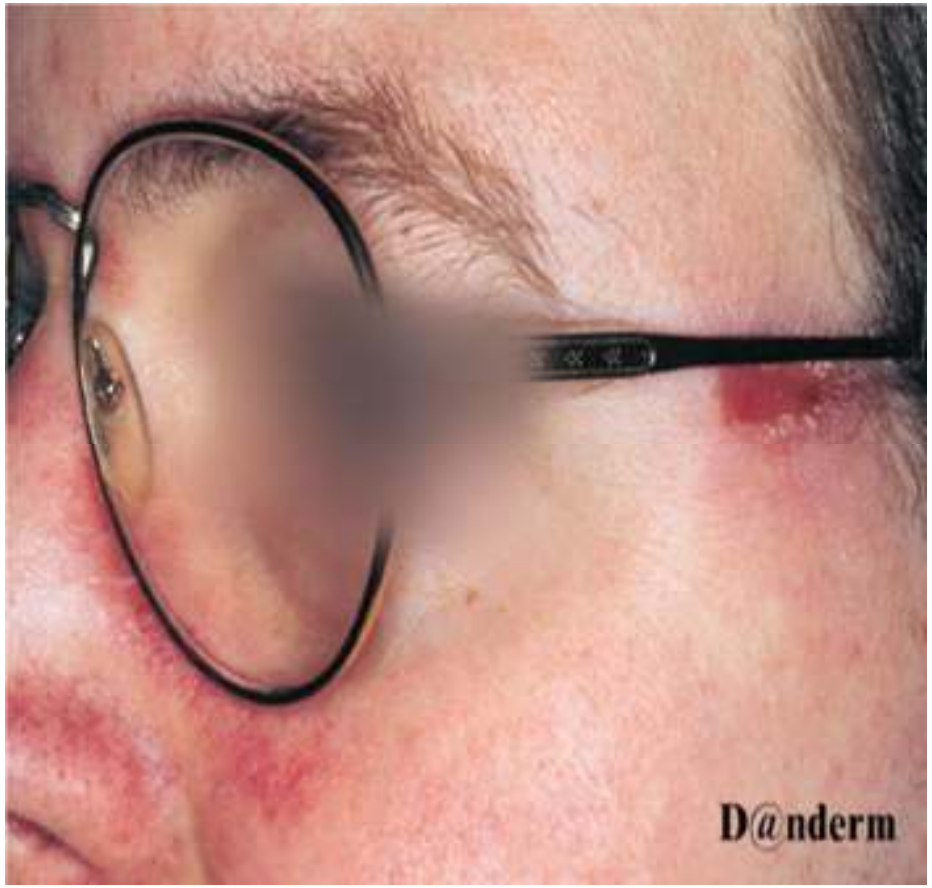


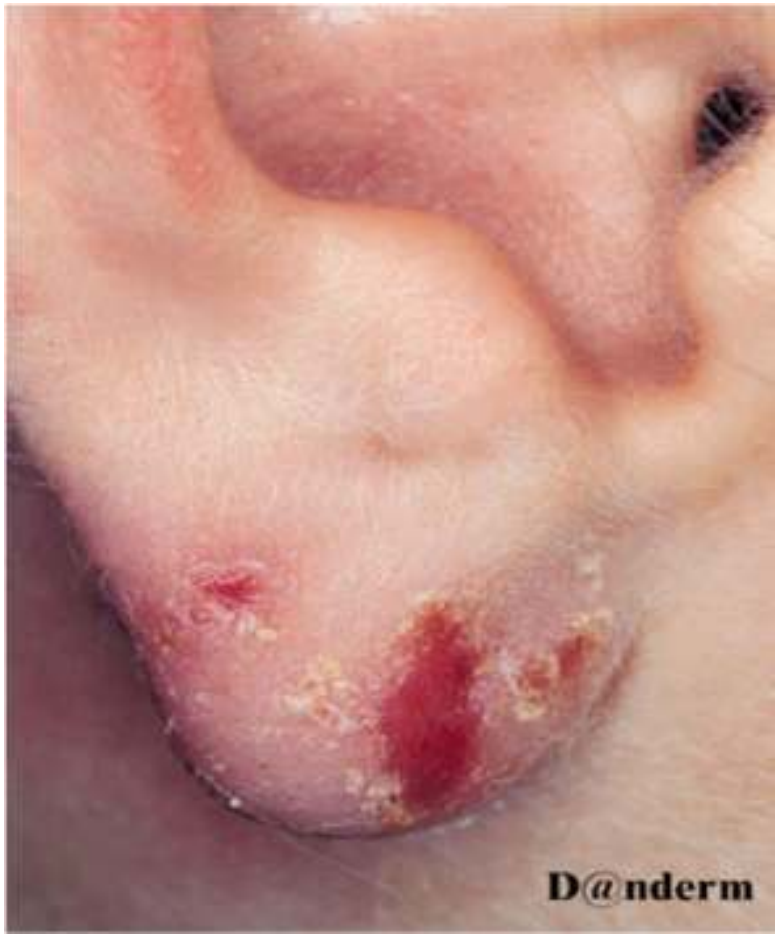
ACD latex



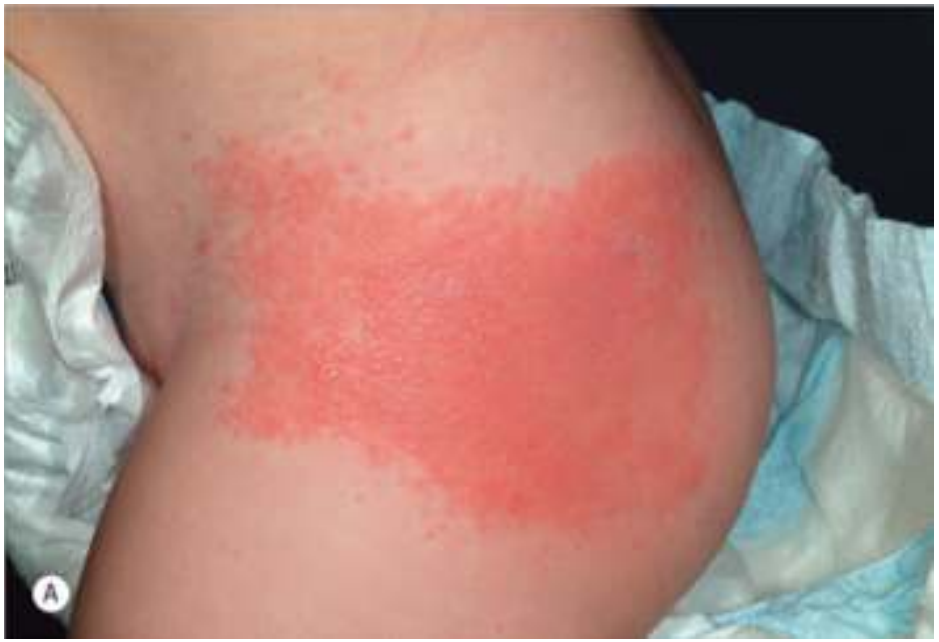


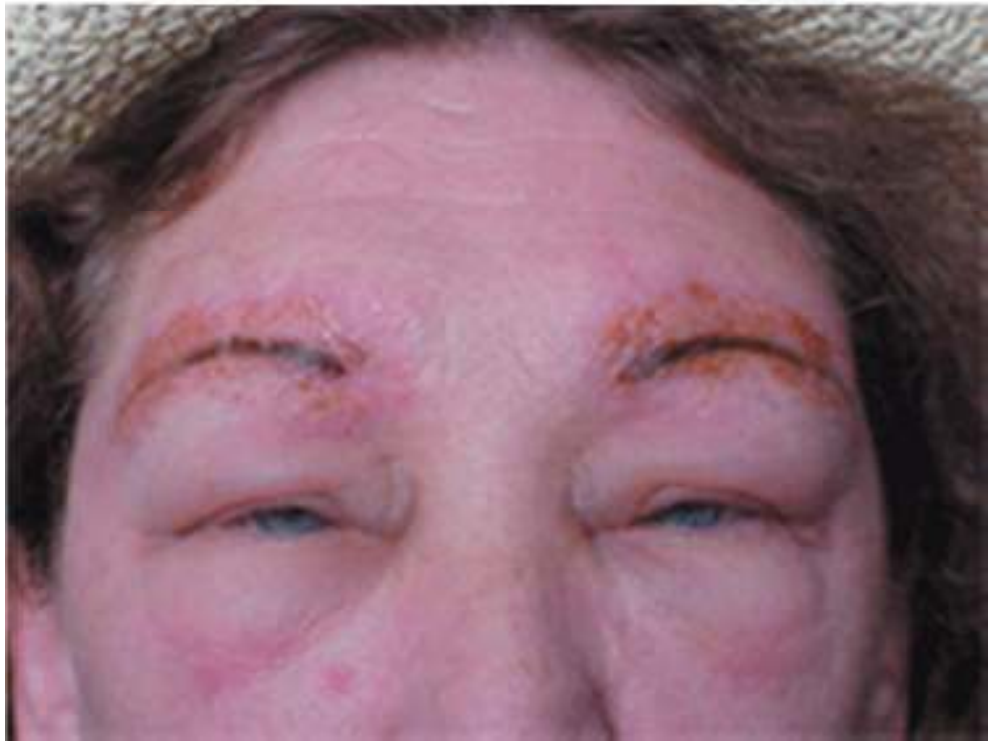
ACD – nickel



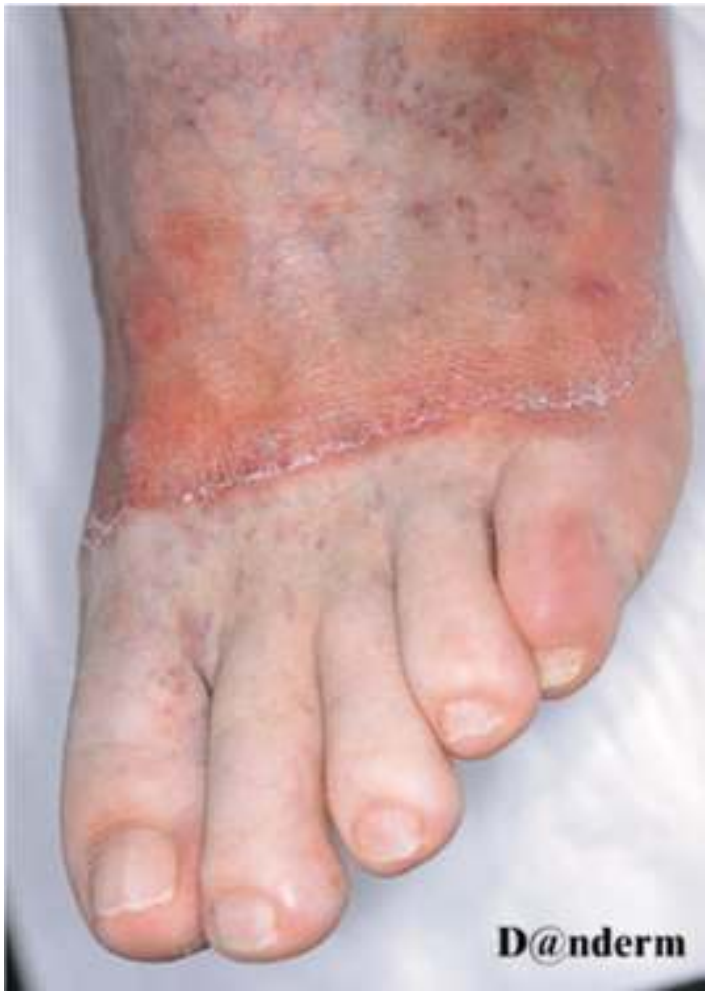


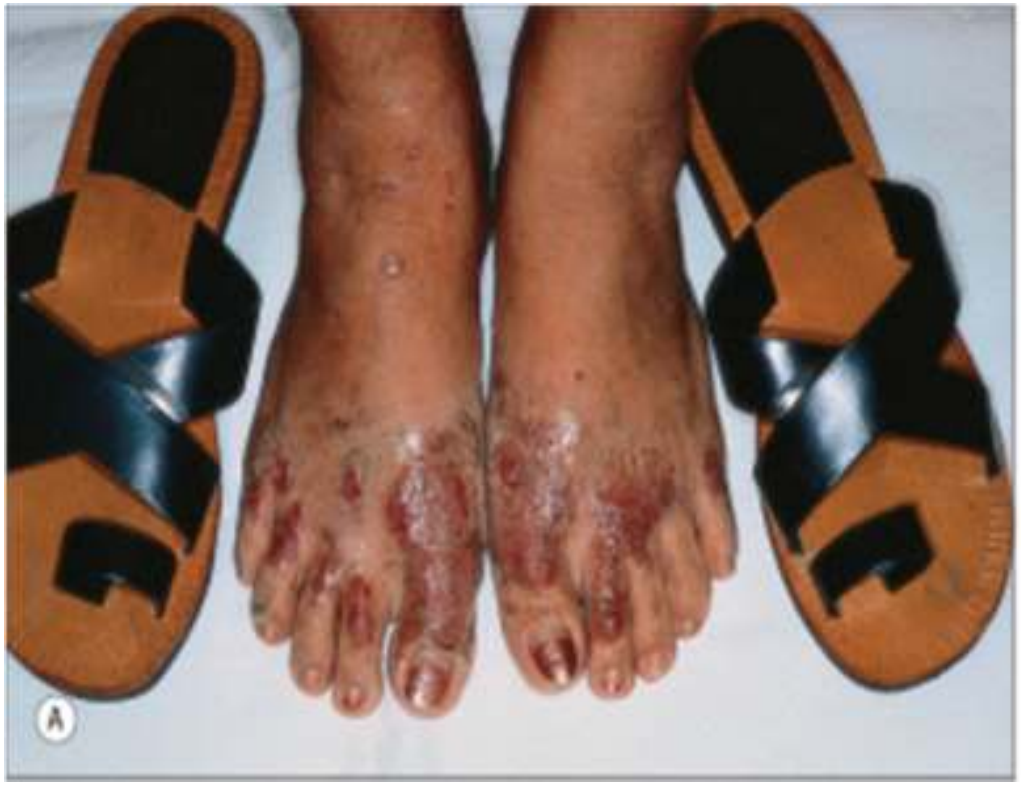
ACD – antibiotics





ACD - paraphenilendiamine



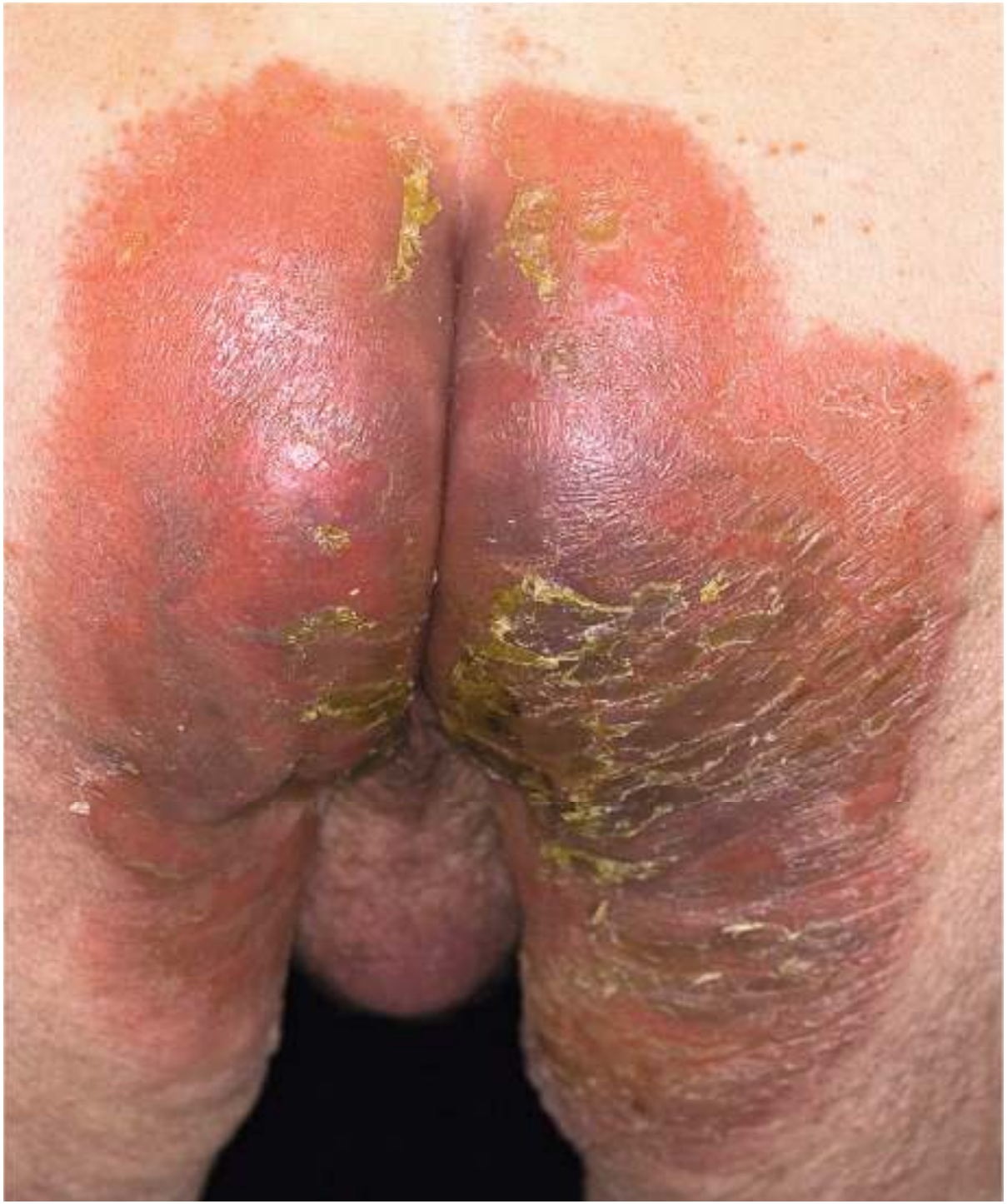


Systemic contact dermatitis -SCD

- Systemic contact dermatitis (SCD) or systemically reactivated allergic contact dermatitis is dermatitis/eczema that occurs when a person who is already sensitized to a substance through skin contact is exposed to that substance (allergen) via a systemic route.
- Exposure may be through oral, inhalational, injectable, and trans-mucosal routes.

SCD: common allergens

Allergen causing ACD after topical exposure	Allergen causing SCD after systemic exposure
Topical cream containing sorbic acid	Foods containing sorbic acid such as strawberries, candies, margarine and cheeses
Jewelry, zippers or buckles containing nickel	Food containing nickel such as cocoa, beans, tinned foods. Nickel alloy on an intratubal birth control device.
Balsam of Peru in cosmetics and perfumes	Spices such as cinnamon, vanilla, cloves that are used to flavor foods, drinks and medicines
Formaldehyde in fabrics, cosmetics and paints	Artificial sweetener aspartame used as a sugar substitute in many drinks and foods is metabolized in the body to formaldehyde
Parabens in cosmetics and pharmaceutical/self-hygiene products	Paraben-containing foods such as marinated fish products, jams and jellies, pickles and preserves
Propylene glycol in topical corticosteroid cream	Propylene glycol in oral antihistamine tablets
Direct contact with plants or pollens from the Compositae group of plants	Vegetable and herbs such as lettuce, endive, chamomile and echinacea
Ethylenediamine in topical antibiotic/steroid creams	Intravenous or oral administration of aminophylline
Neomycin in over-the-counter antiseptic preparations	Intravenous or sub-conjunctival administration of neomycin



Baboon syndrome: ingestion of nickel

SCD

Nickel ingested

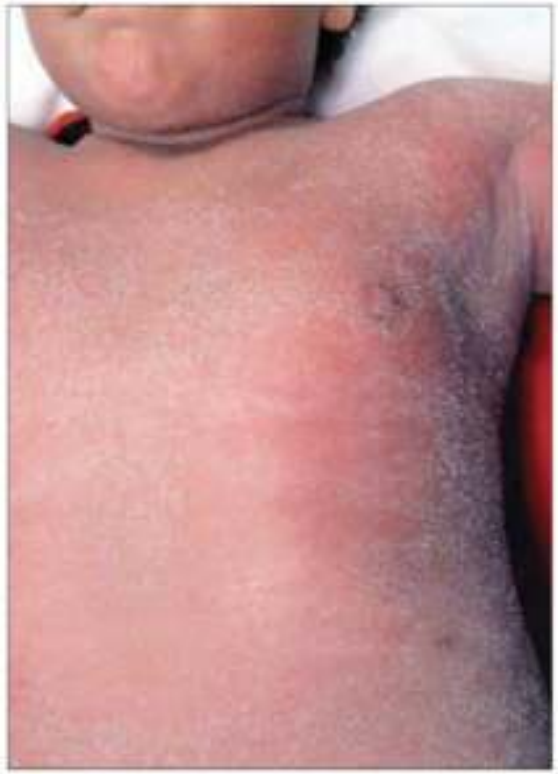
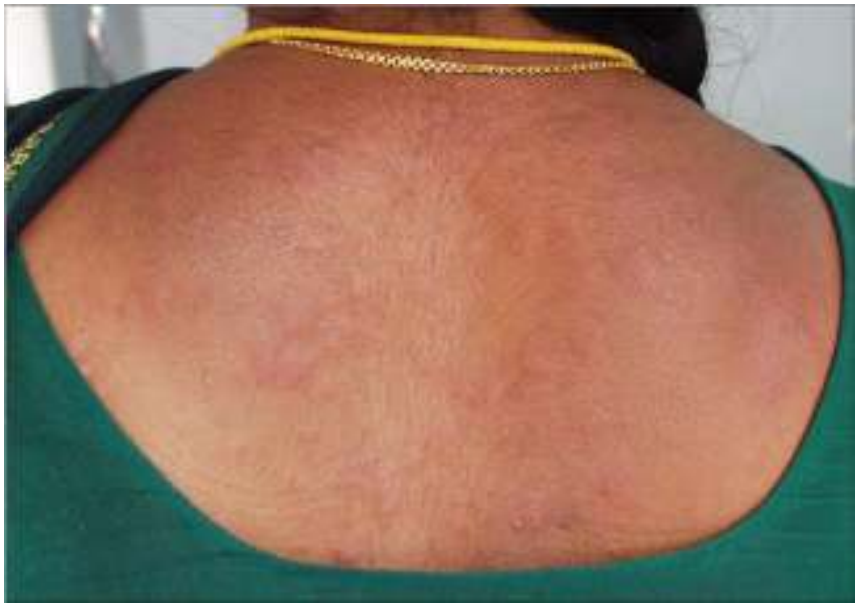


Figure 1 – Desquamative erythroderma on the trunk of a young boy is a manifestation of systemic contact dermatitis from nickel exposure.

Diclofenac im



Atopic eczema: definition

- Atopic eczema (dermatitis) is an acute, subacute or chronic relapsing skin disorder that usually begins in infancy (after first 2 months) and is characterized principally by marked pruritus, which with rubbing and scratching leads to lichenification (hyperplasia of the skin).
- The serum IgE level is usually elevated.
- A personal or family history of atopic eczema, allergic rhinitis and asthma is often associated.

Atopic eczema: genetic aspects

- The inheritance pattern is probably autosomal-dominant
- 60% of adults with atopic eczema have children with atopic eczema
- The prevalence in children is 80-85% when both parents had atopic eczema
- HLA haplotype associations (HLA B9); mutations in loricrin and filaggrin gene (1q21); str.corneaum serine proteases gene SPINK5; cytokine IL-3, IL-4, IL-5, IL-13 genes on 5q31-33, etc.

Atopic eczema: eliciting factors

- Foods: eggs, milk, peanuts, soybeans, fish, and wheat
- Inhalants: specific aeroallergens, especially dust mites
- Microbial agents: exotoxins of Staphylococcus aureus may act as superantigens; group A streptococcus, herpes simplex virus, fungus (candidiasis and dermatophytosis)
- Skin dehydration: frequent bathing and hand washing
- Hormonal: pregnancy, menstruation, thyroid
- Season: in temperate climates, usually improves in summer, flares in winter
- Clothing: pruritus flares after taking of clothing; wool clothing or blankets directly in contact with skin
- Emotional stress: primary or secondary resulting from the disease

Atopic eczema: major clinical features (by Hanifin and Rajka)

- Pruritus (if there is no scratching, there is no eruption) - **itch→scratch→rash→itch;**
- Typical morphology and distribution of lesions for age: on face and extensor extremities up to 2 years, then flexural or linear distribution after 2 years;
- Chronic or chronically relapsing course;
- Personal or family history of asthma, allergic rhinitis, or atopic eczema.

Atopic eczema: minor clinical features

- Dry skin
- Keratosis pilaris (follicular horny plugs)
- Hyperlinear palms and soles
- Periorbital bluish discoloration
- Dennie-Morgan lines (double infraorbital fold)
- Pityriasis alba (dry streptococcal skin infection)
- Vascular abnormalities (skin pallor)
- Cataracts
- White dermatographism

Atopic dermatitis standardization: diagnostic threshold

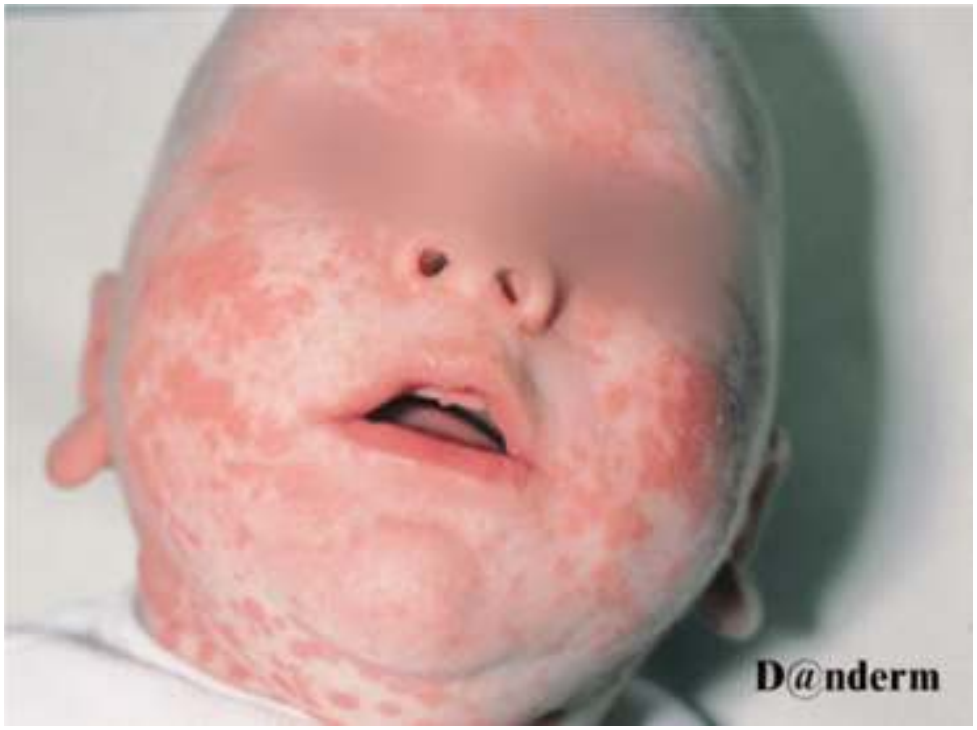
3 major (**pruritus is compulsory**), plus

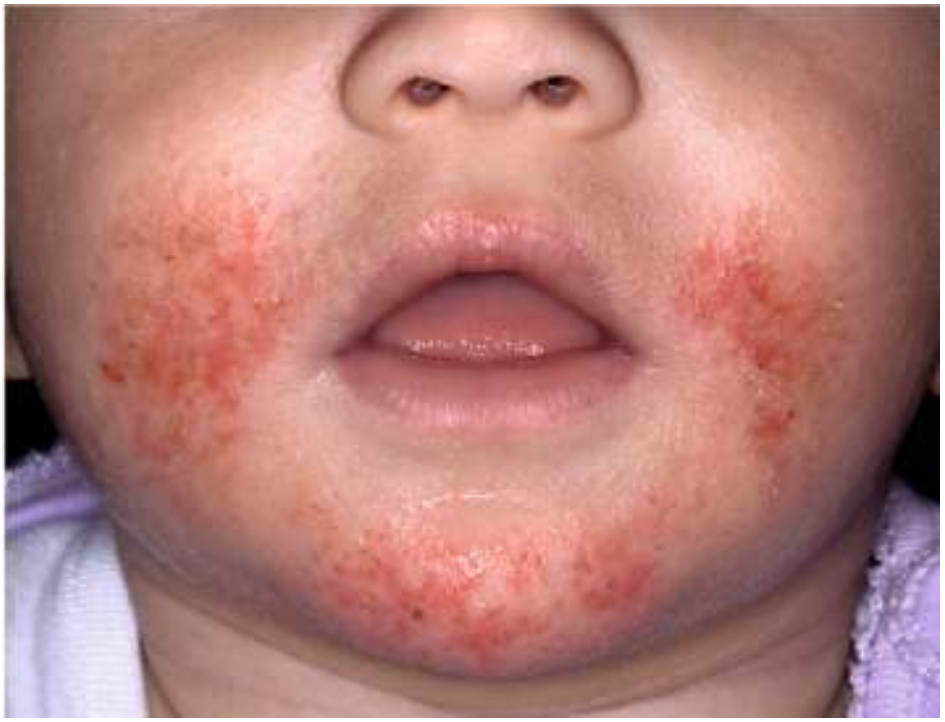
3 minor criteria

Atopic eczema at different ages

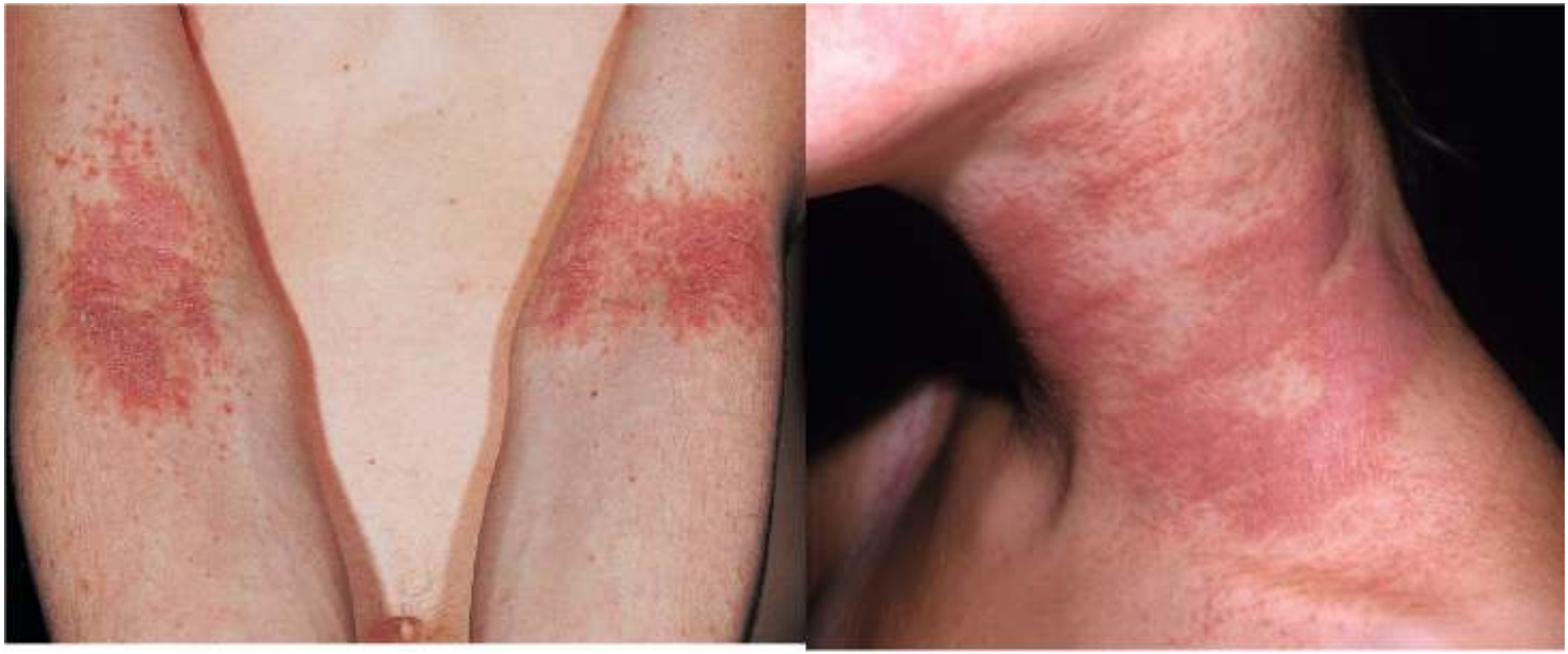
- Infantile phase (2 mo – 2 yrs): characterized by intense itching, erythema, papules, vesicles, oozing and crusting; typically location on cheeks, forehead, and scalp (acute eczema).
- Childhood phase (3-11 yrs): more chronic, lichenified scaly patches and plaques that may have crusting and oozing; classic areas include the wrists, ankles, backs of the thighs, buttocks, and antecubital and popliteal fossae (subacute eczema).
- Adolescent/young adult phase (12-20 yrs): thick, dry, lichenified plaques that involve the face, neck, upper arms, back, and flexures (chronic or lichenified eczema).
- Adult phase (>20 yrs): most commonly involves the hands, sometimes the neck and face, and rarely diffuse areas (lichenified eczema, nummular eczema, neurodermitis); only 10% of infantile or childhood cases of atopic eczema persist into adulthood.

Atopic dermatitis – infantile eczema, under 2 years

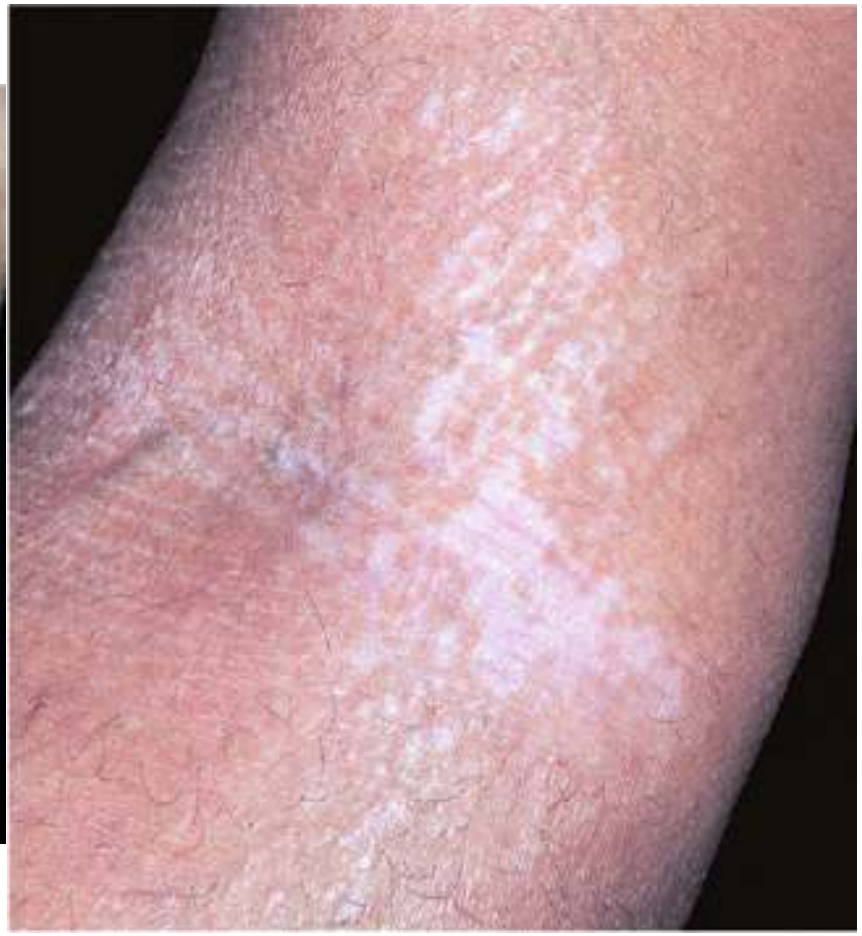




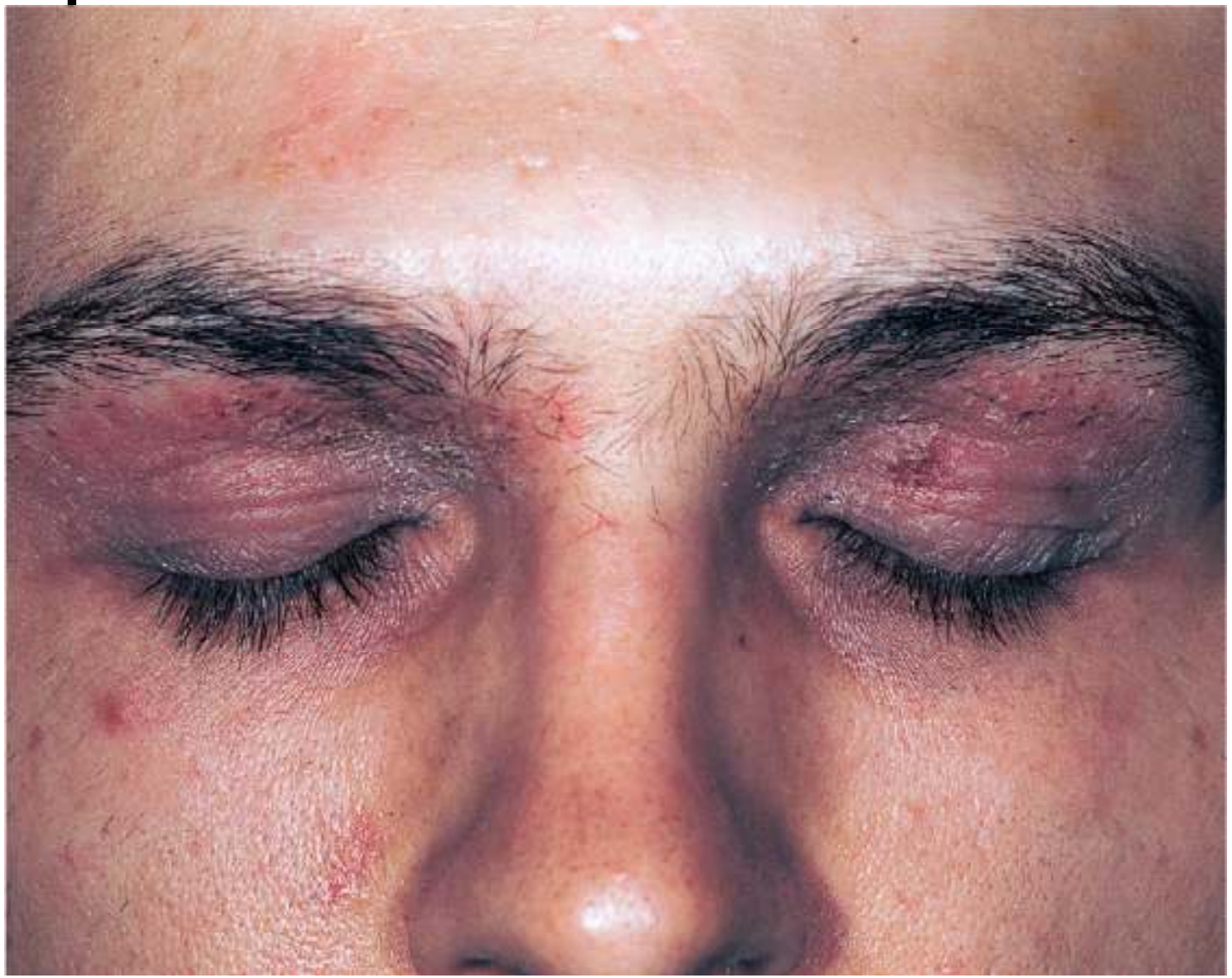
Atopic dermatitis of childhood – flexural eczema, 2-12 years



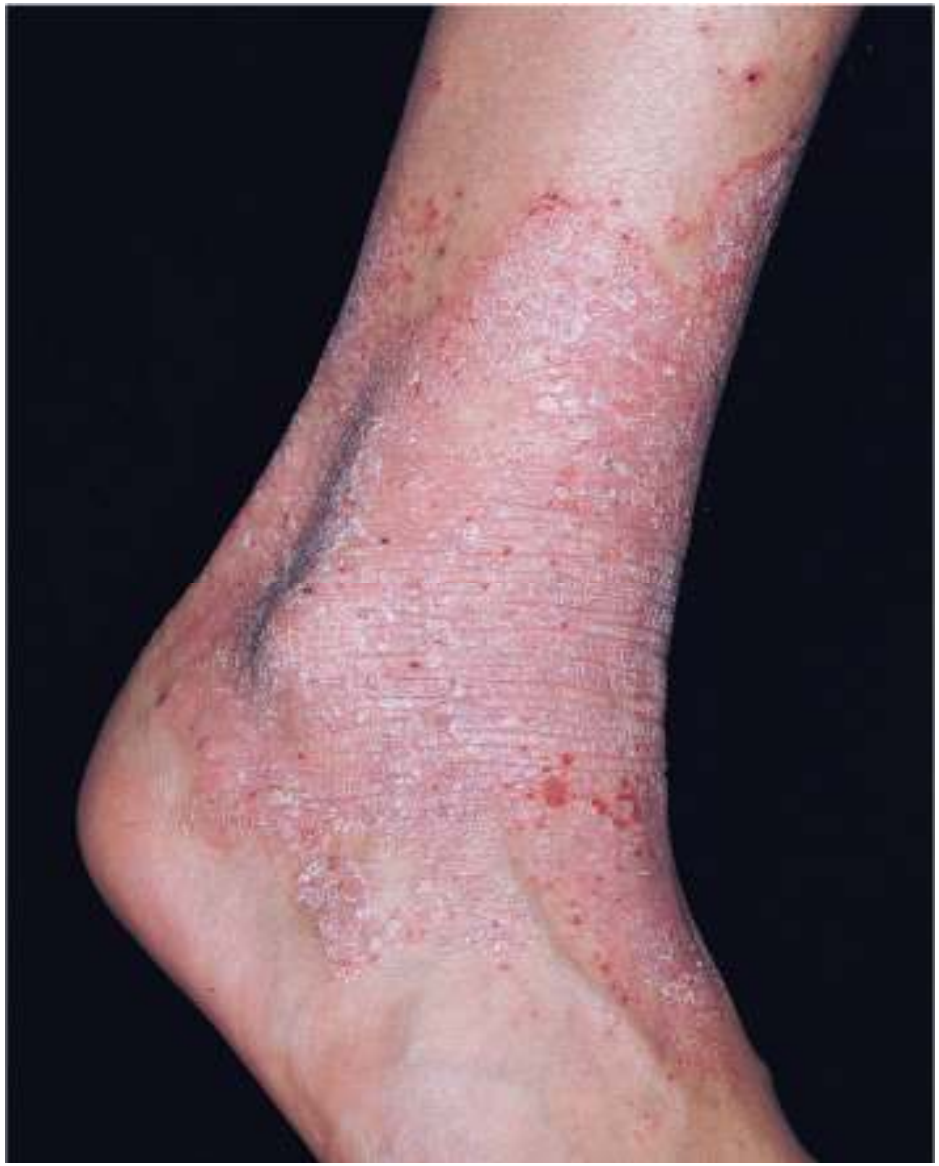
Dermatita atopica a adultului (peste 2 ani) - eczemă lichenificată

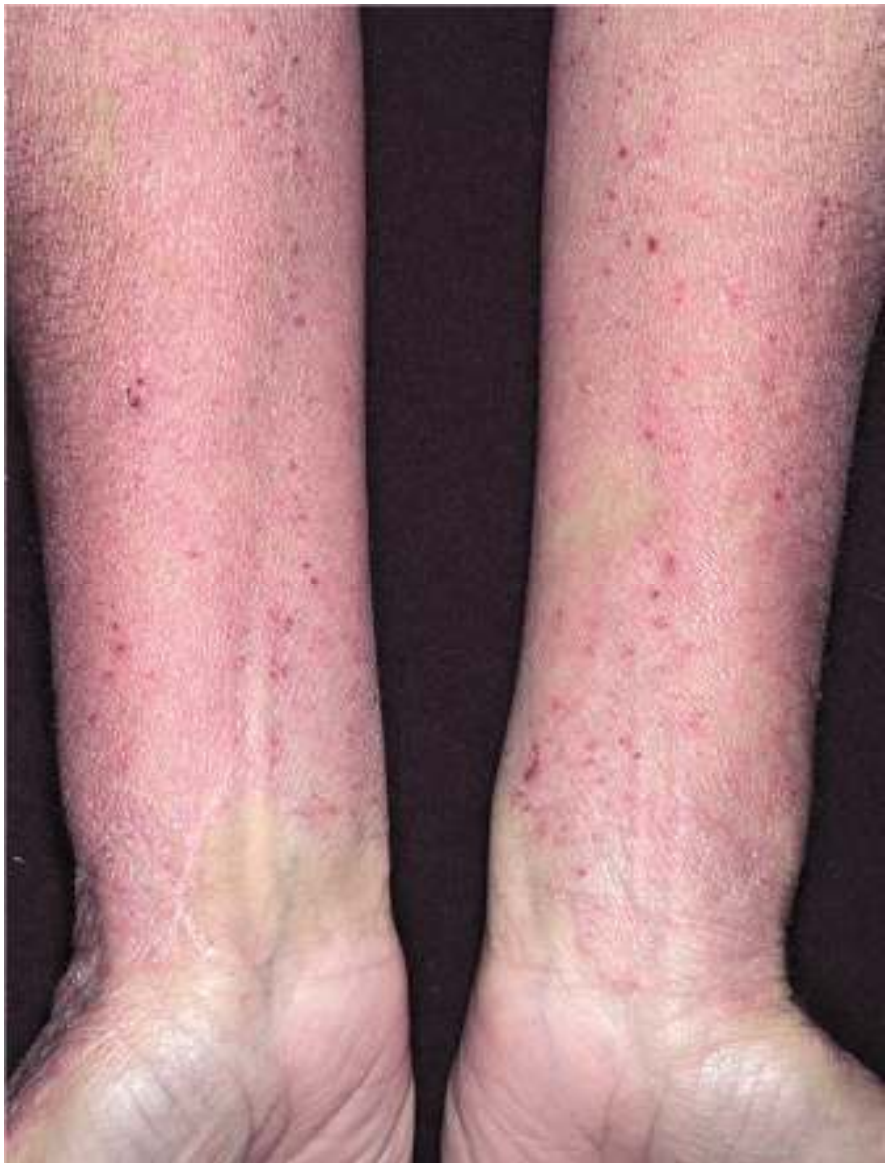


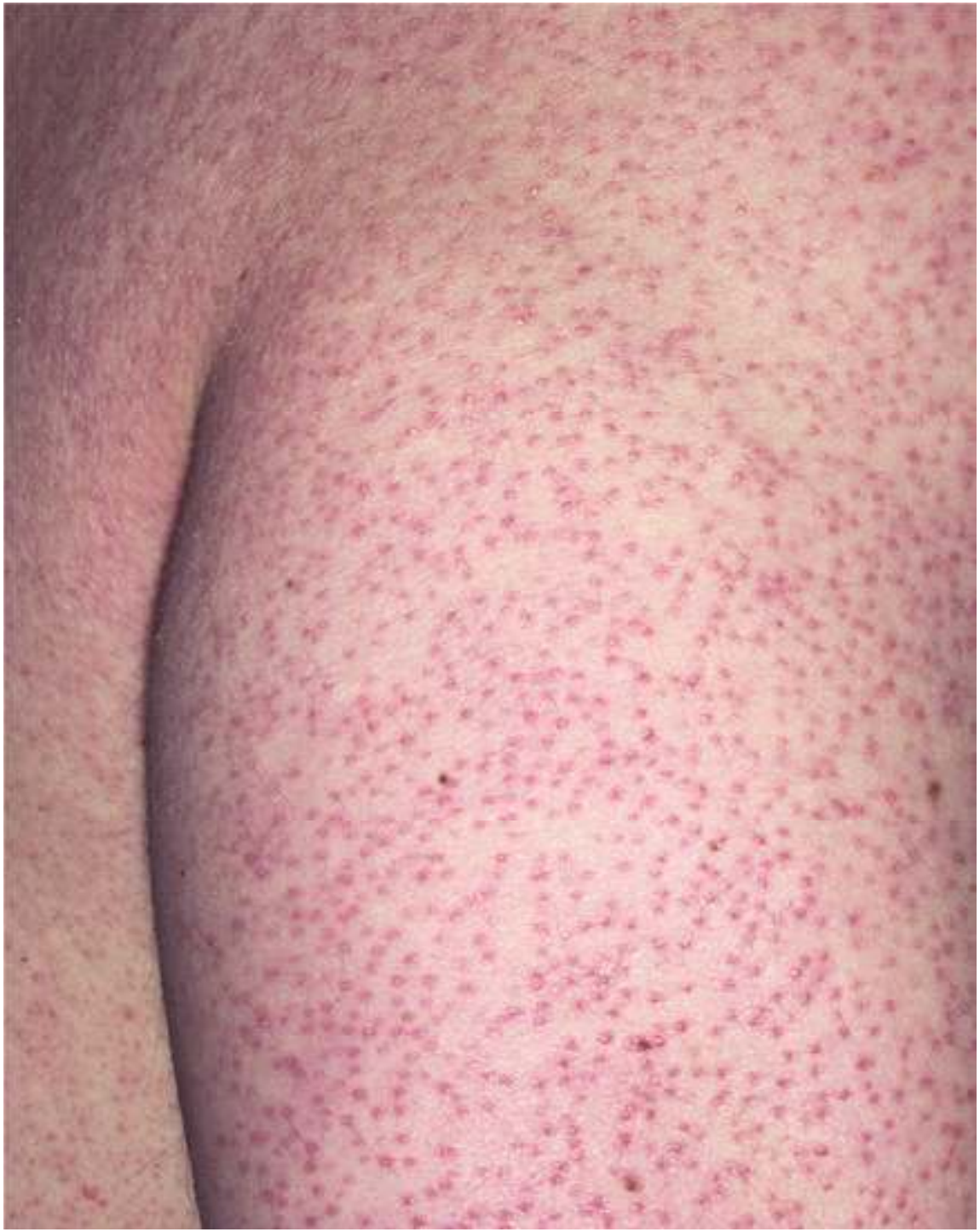
Atopic dermatitis – periorbital eczema in adult



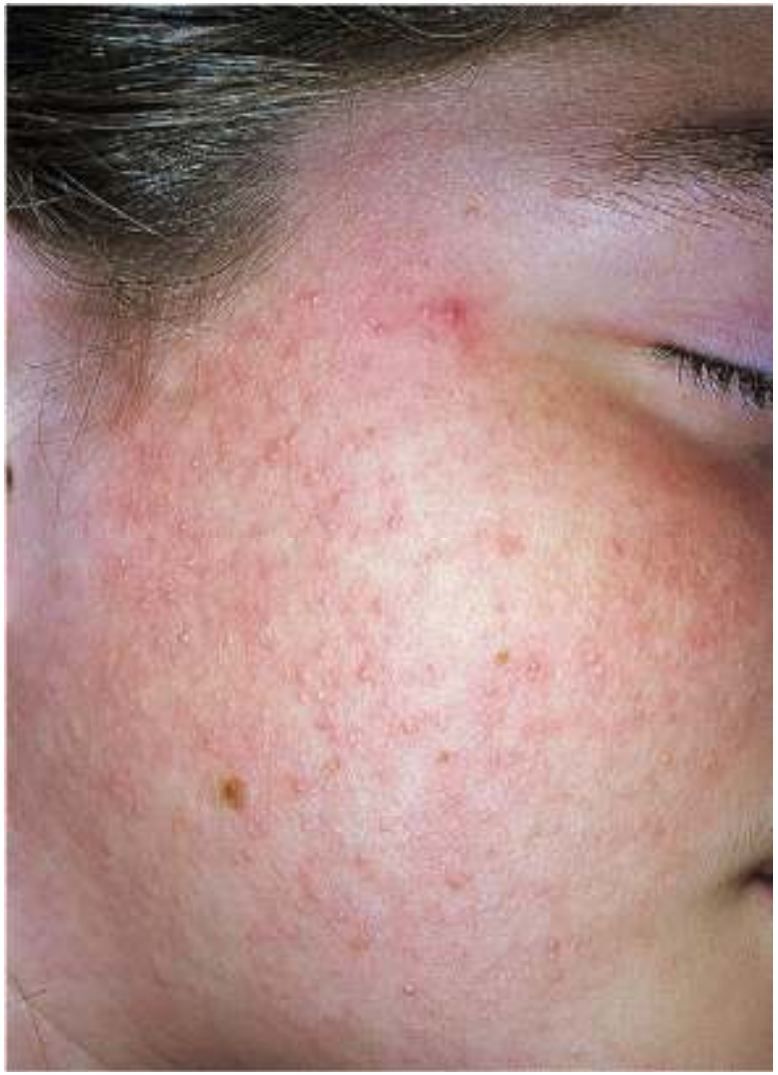
Atopic dermatitis: neurodermitis in adult







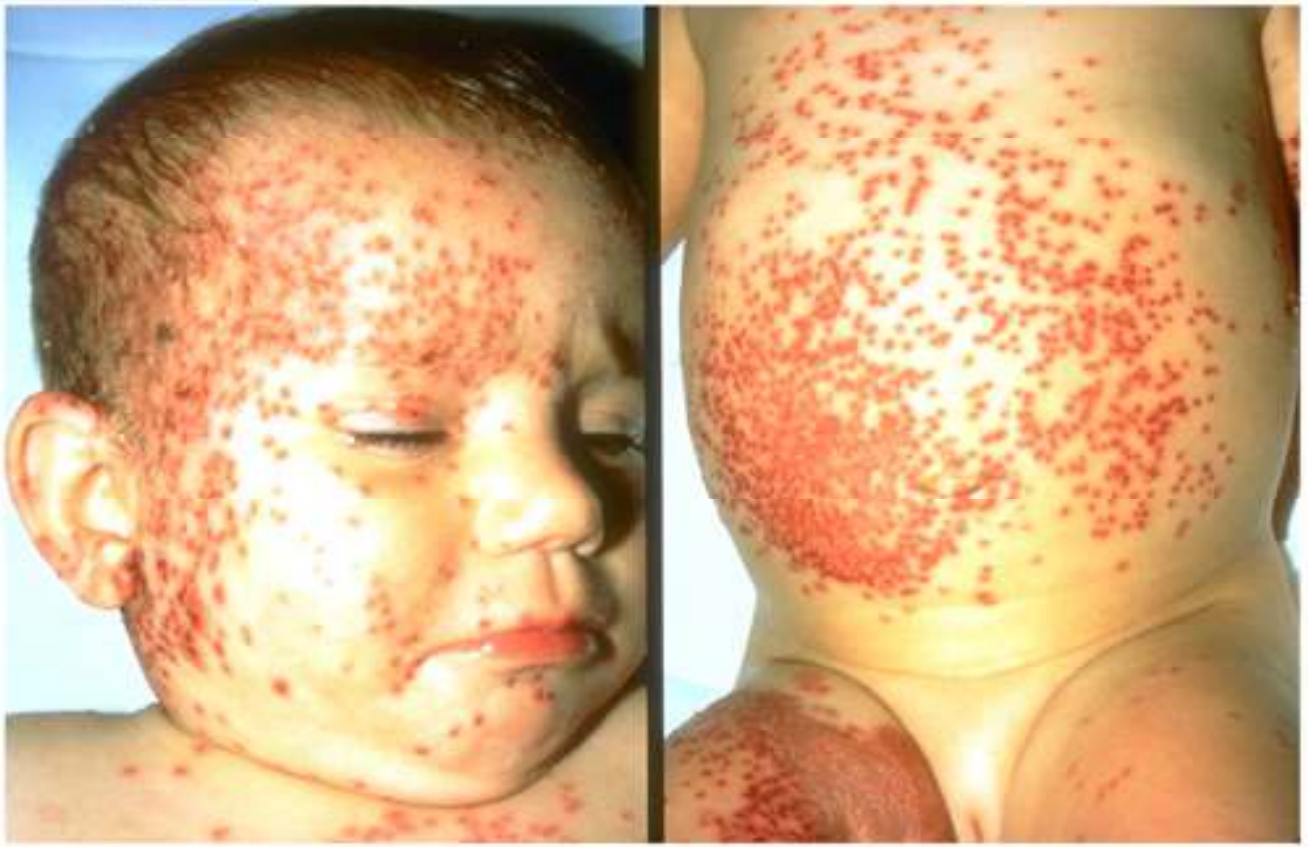
AD:
keratosis pilaris



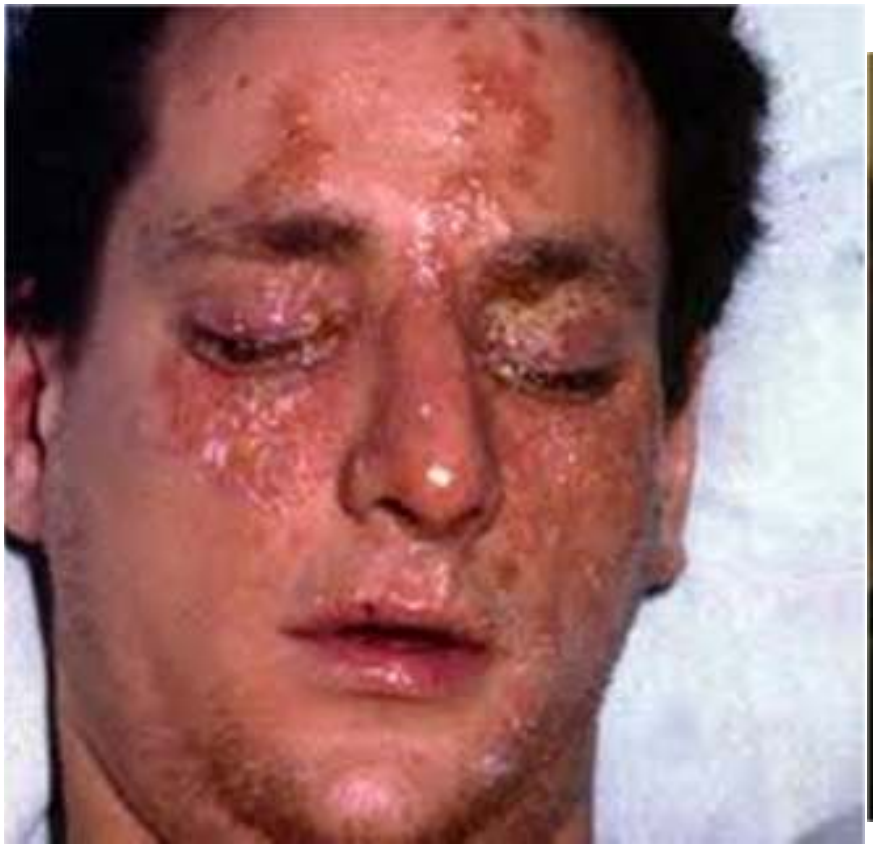
Atopic dermatitis: complications

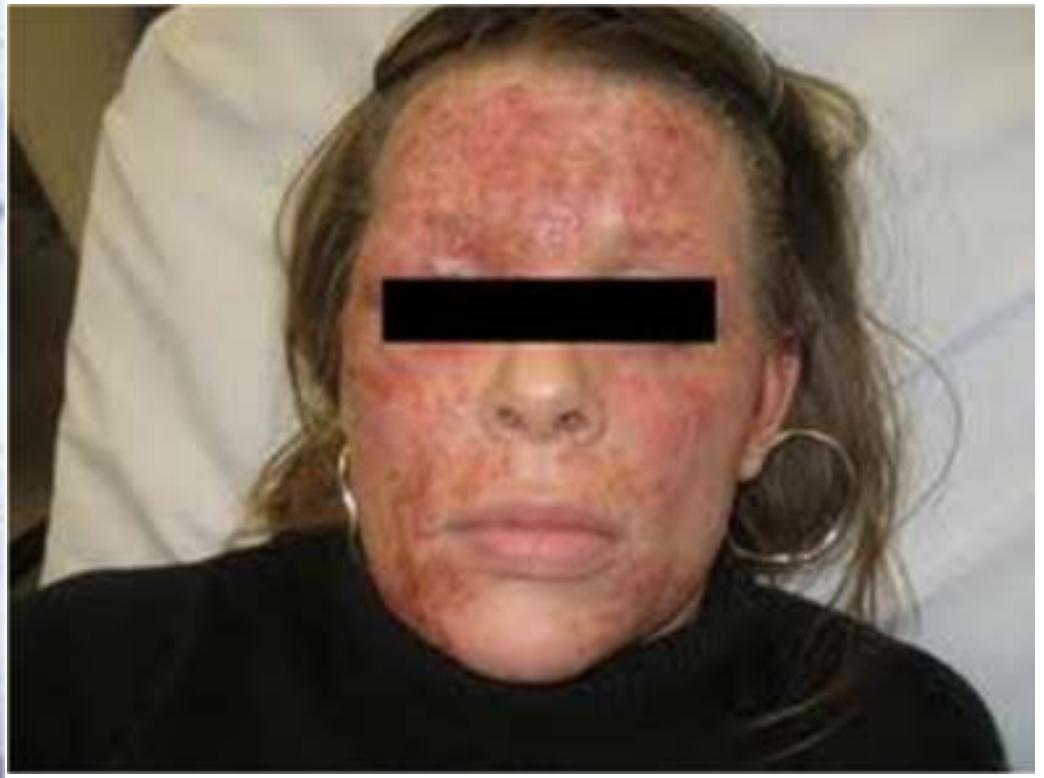
- Strep/staph: secondary pyodermas
- Viral infections: *eczema herpeticum,* Kaposi-Juliusberg's syndrome*; eczema vaccinatum*.
- Fungal infections: candidosis; trychophyton Tinea.
- Erythroderma (Hill).
- Drug sensitization;
- Growth retardation.
- Psychotic disturbances.

Eczema herpeticum

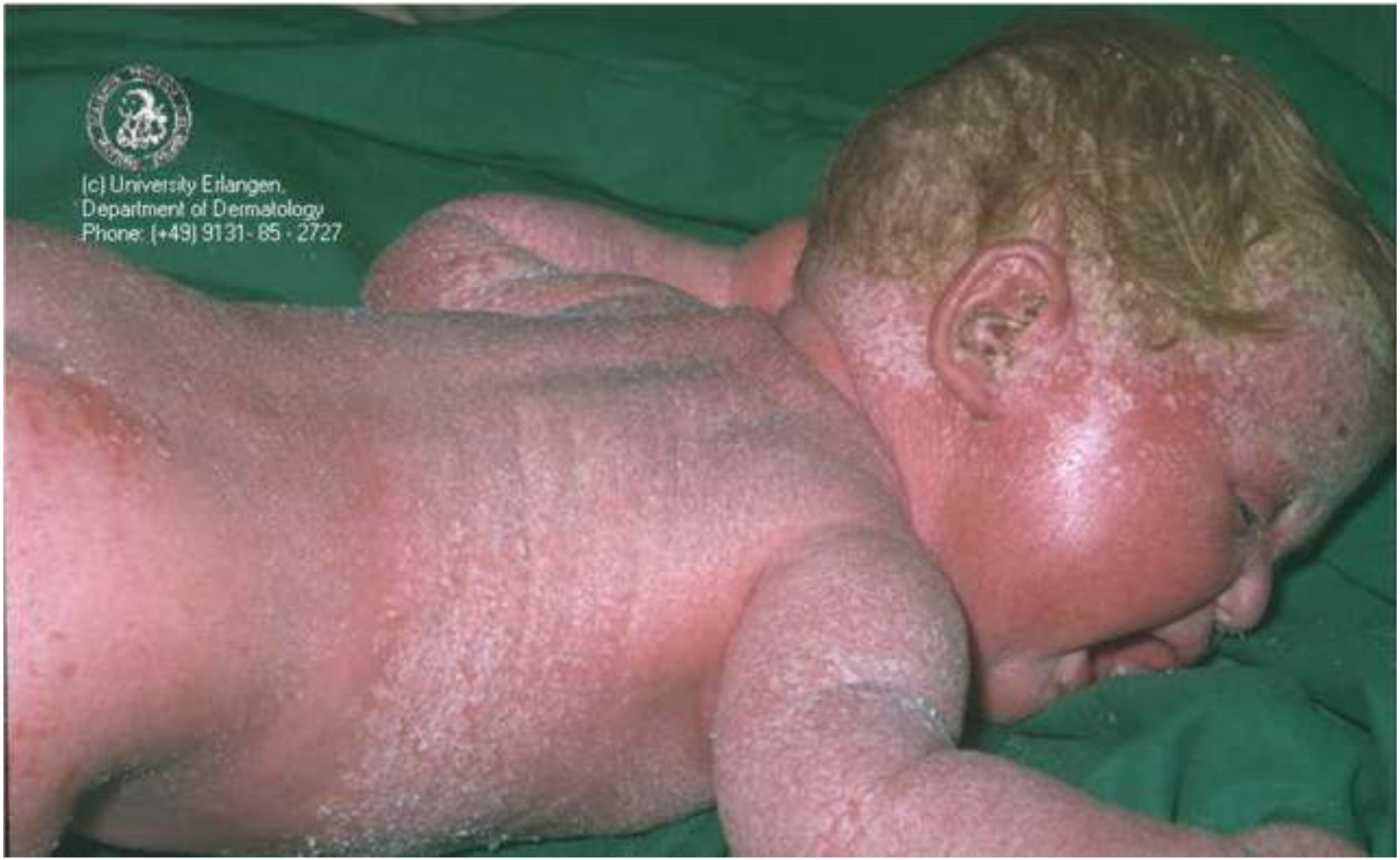


Kaposi-Juliusberg dermatitis





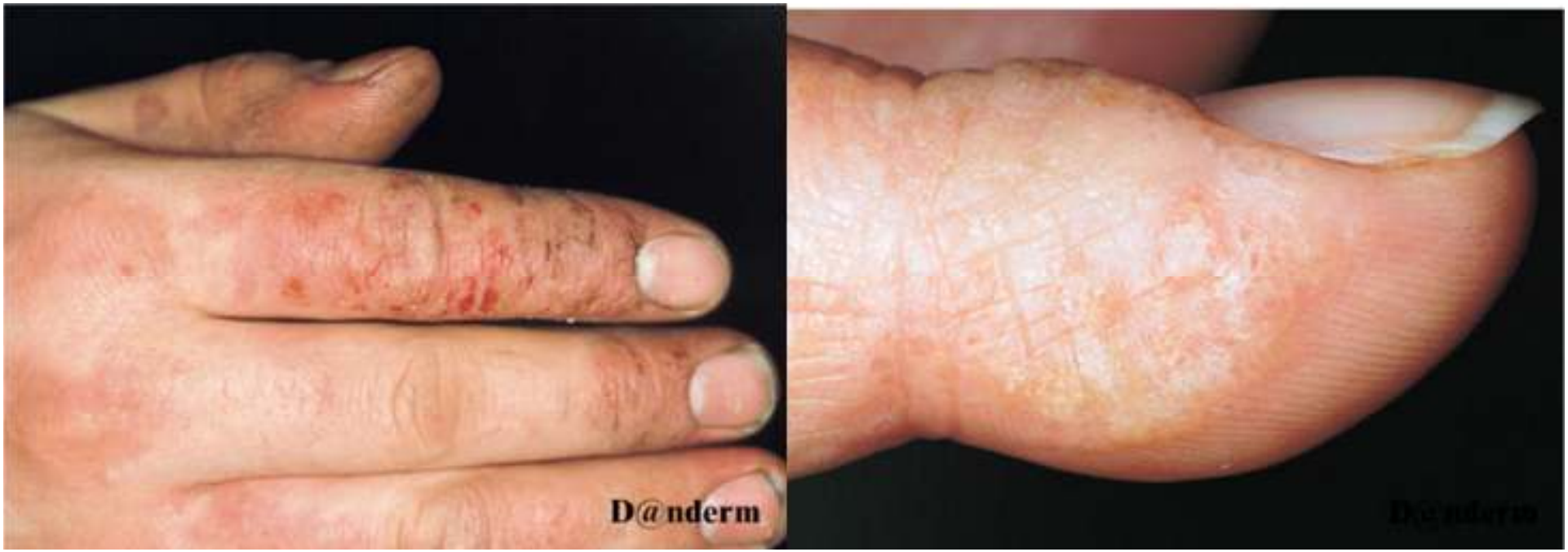
Atopic dermatitis: Hill's erythroderma



Dyshidrotic eczema

- Supposed association with increased sweat gland
- Crops of clear, deep-seated vesicles on the palms and sides of the fingers, rarely present on soles as well
- High prevalence of atopy
- Sensibility to nickel, fungi, oral allergens, etc.

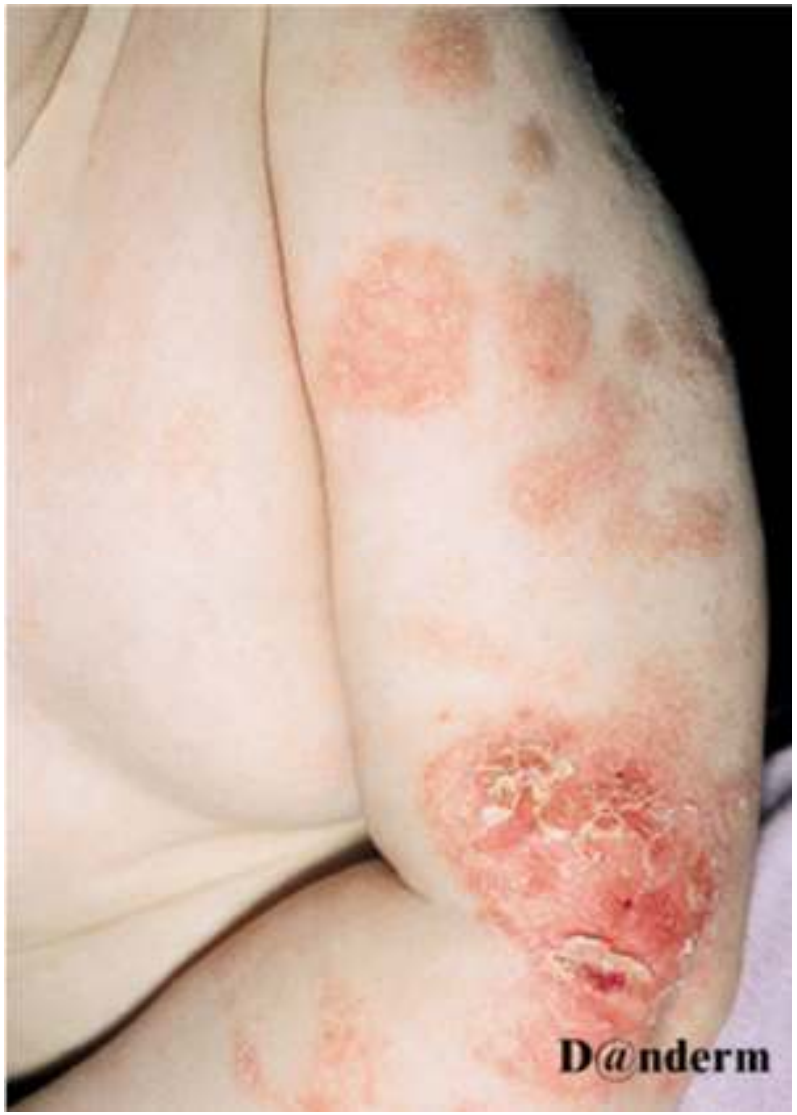
Dyshidrotic eczema

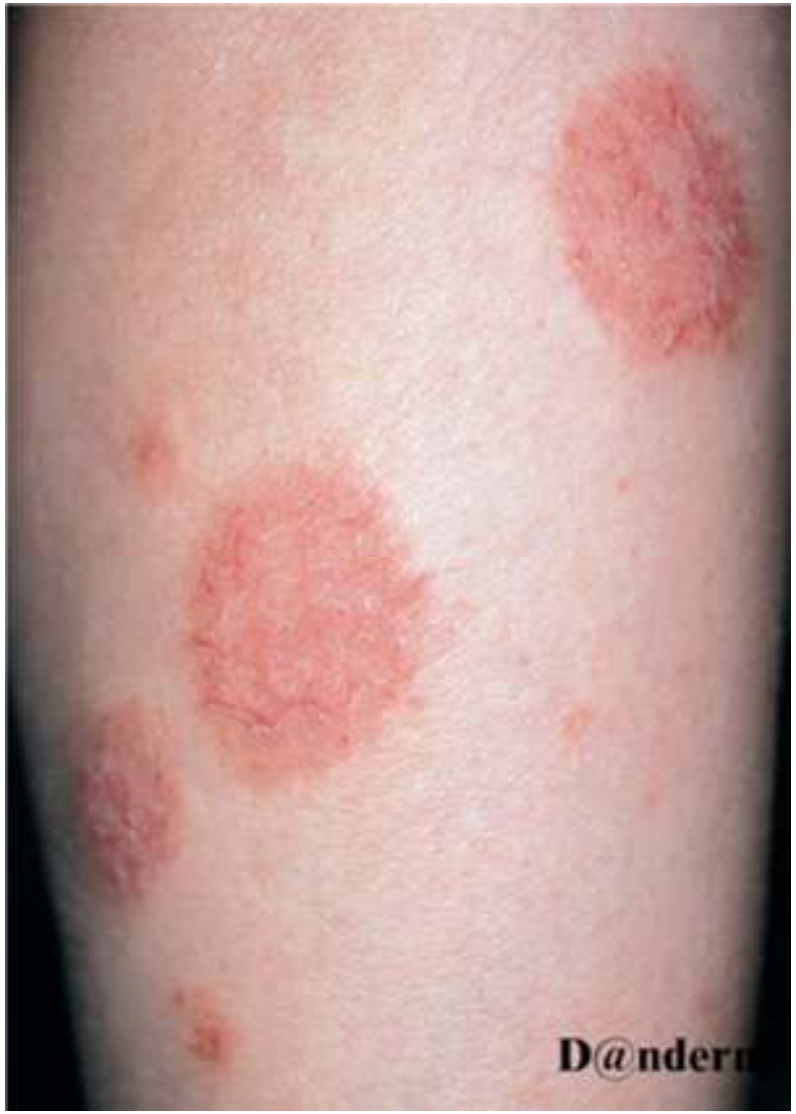


Nummular (discoid) eczema

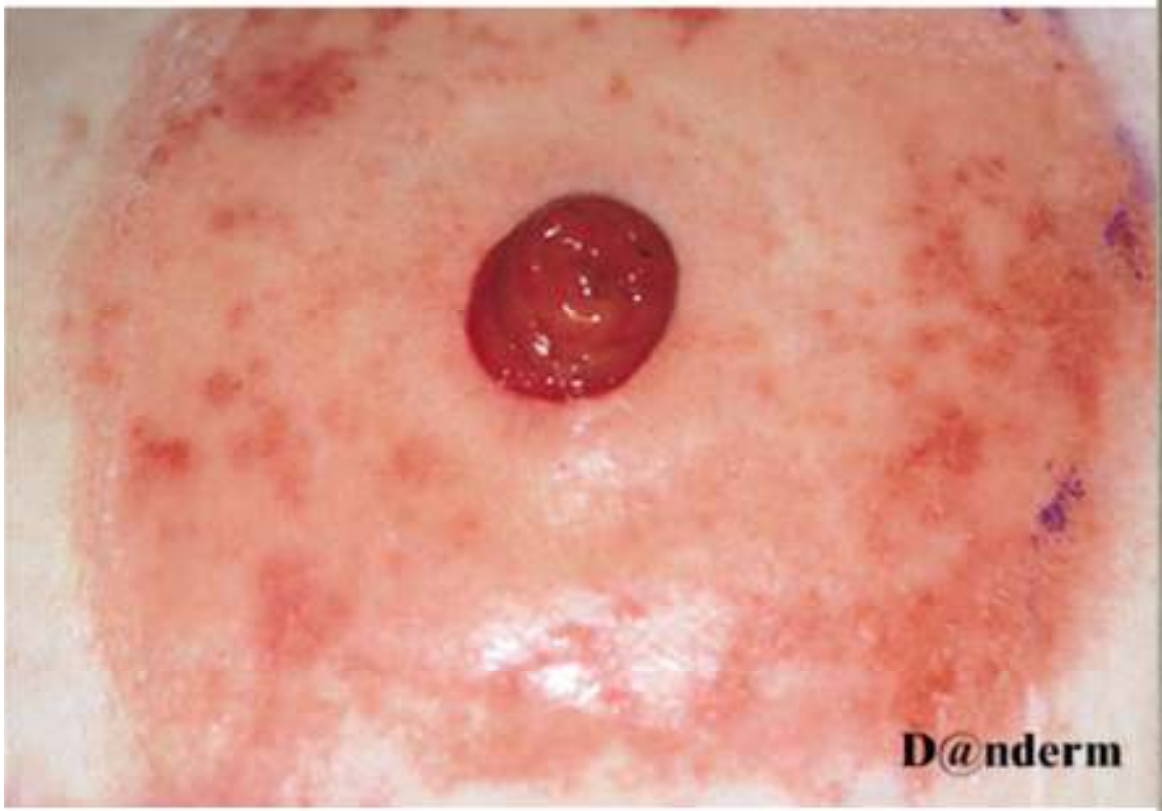
- Rapid onset of tiny papules and papulovesicles that form erythematous, coin-shaped plaques, ranged in size 1-10cm in diameter, resting on a background of dry skin
- Most commonly occur on the extensor surfaces of the lower extremities, and often a bilaterally symmetrical, may recur at the sites of previous involvement, and are typically pruritic
- It is related to dry skin, and aggravated by wool, soaps, frequent bathing, and *S. aureus* colonization – may be a clinical presentation of atopic eczema in adults.

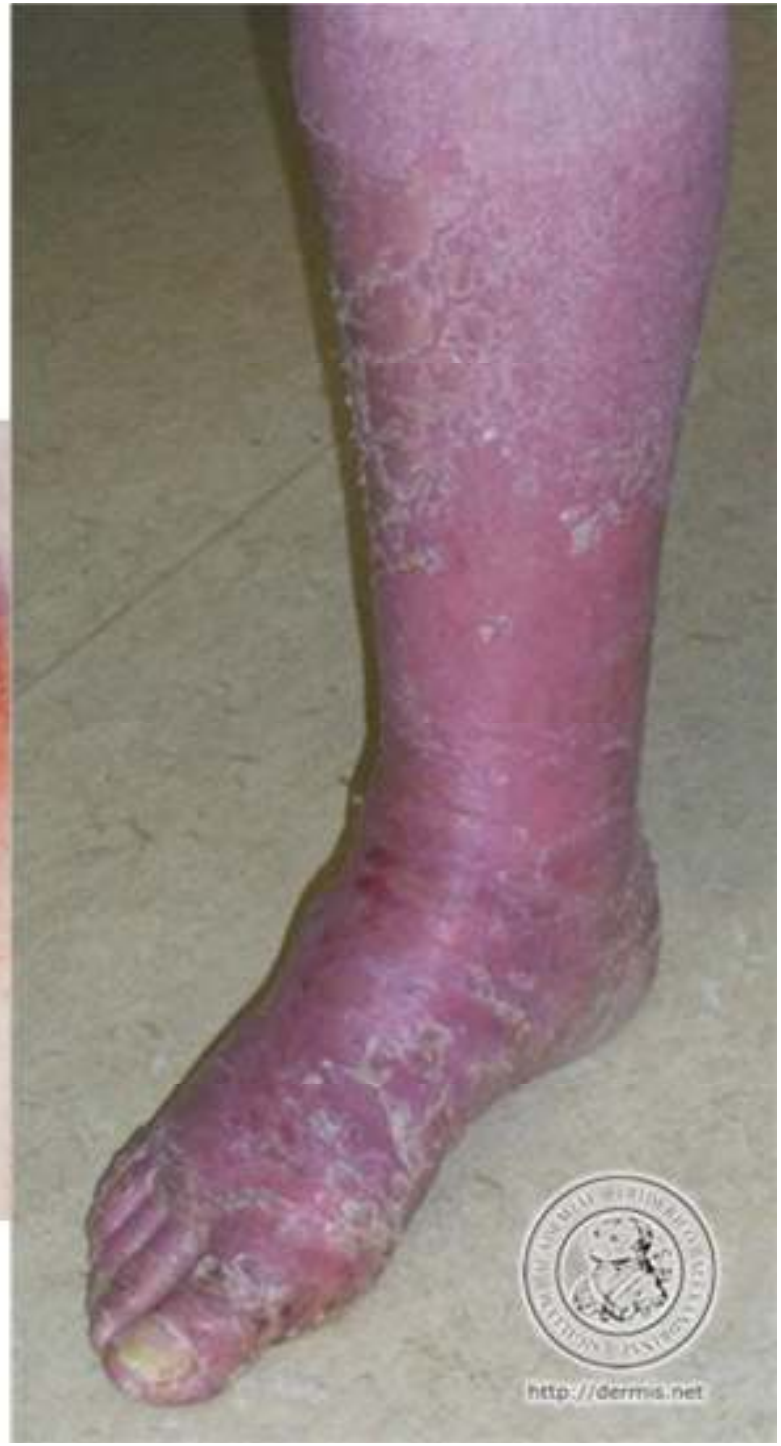
Nummular (discoid) eczema





Microbial eczema

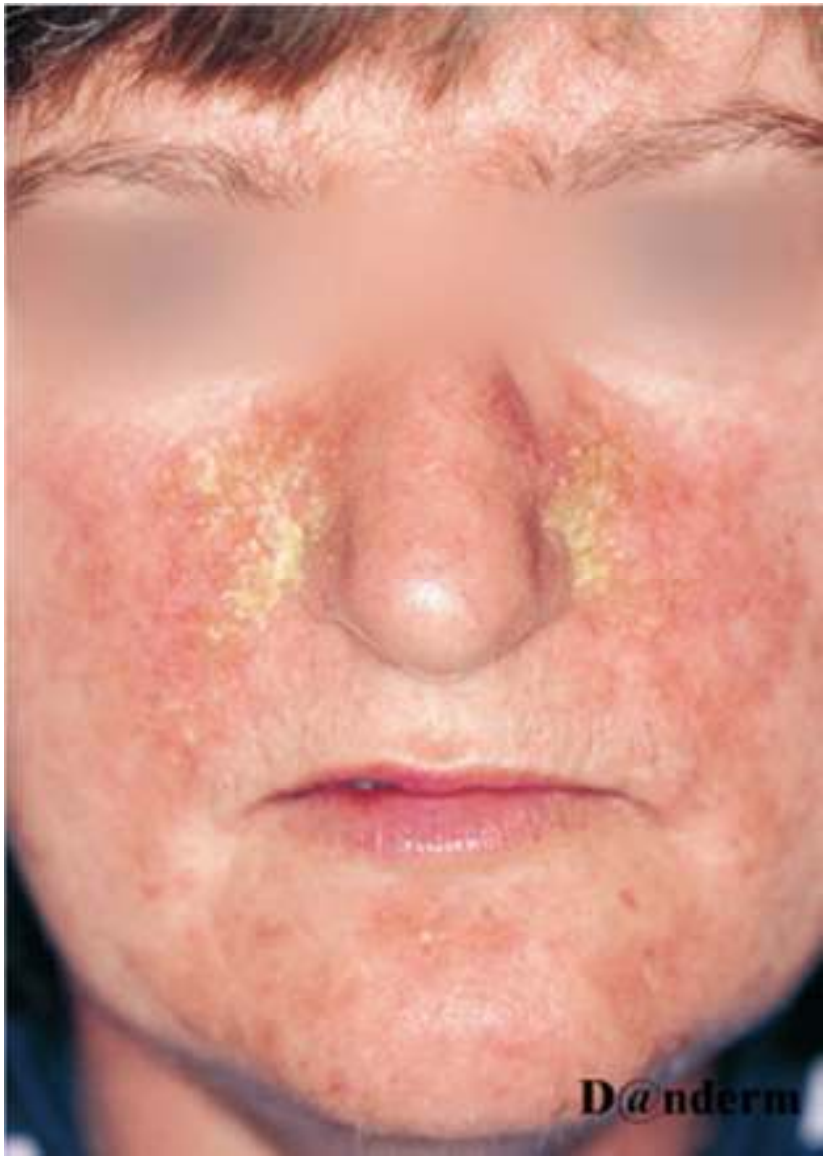


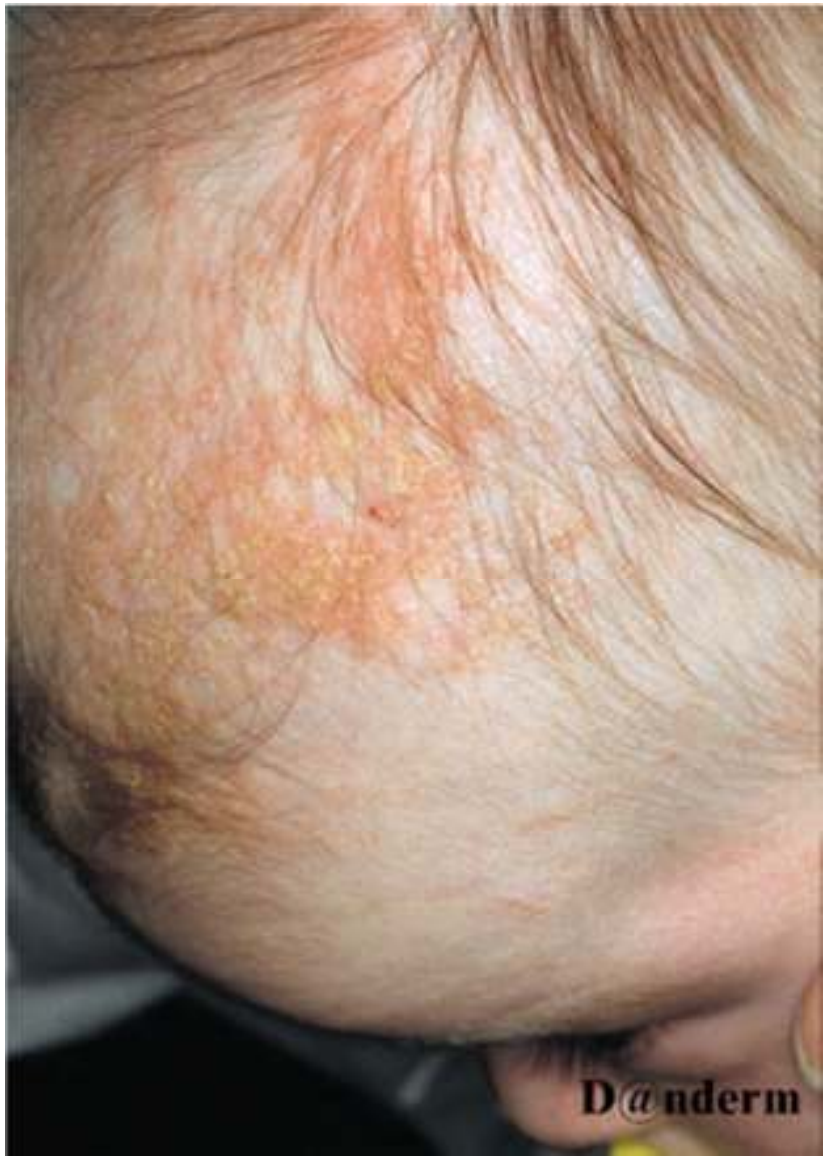


Seborrheic eczema (dermatitis)

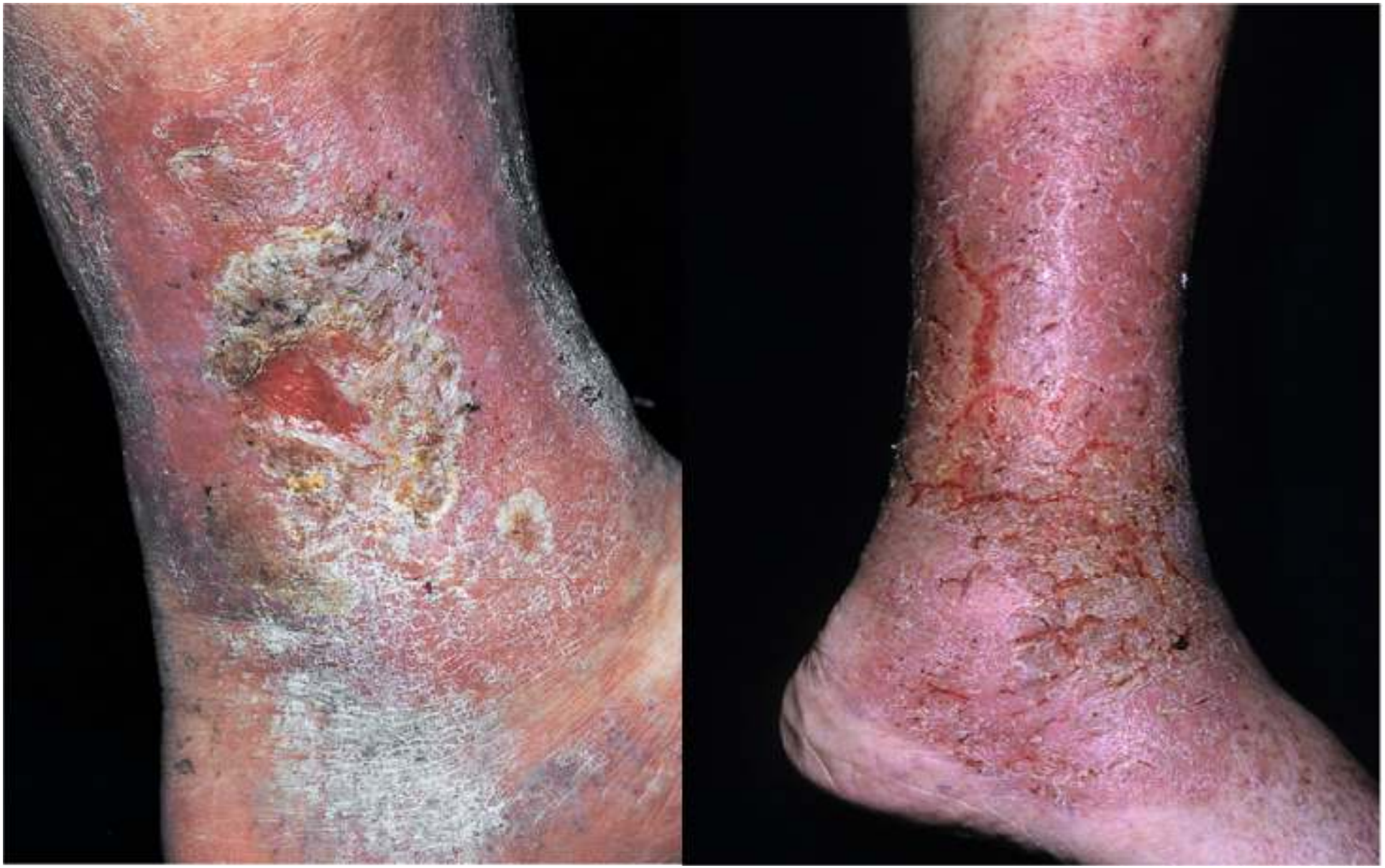
- Presents in infants from 2-10 weeks until 8-12 months, and then reappears at puberty
- In adults, from the beginning – dandruff; then dull or yellowish-red, sharply marginated, non-pruritic lesions covered with greasy scales on medial eyebrows, glabella, naso-labial crease, eyelid margins, post-auricular and ear canal, presternal or interscapular areas; intertriginous areas, such the inframammary crease, umbilicus, anogenital and genitocrural folds are occasionally involved
- Sensitizing to Pityrosporum or Malassezia yeasts

Seborrheic eczema

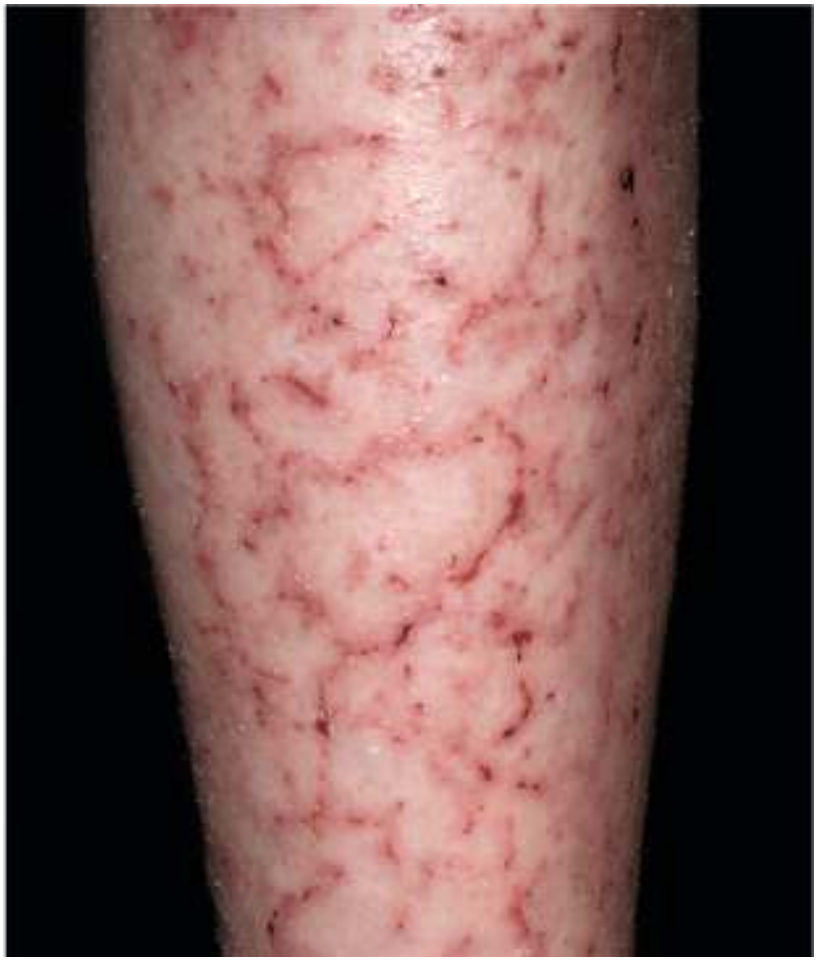




Stasis (varicose) eczema



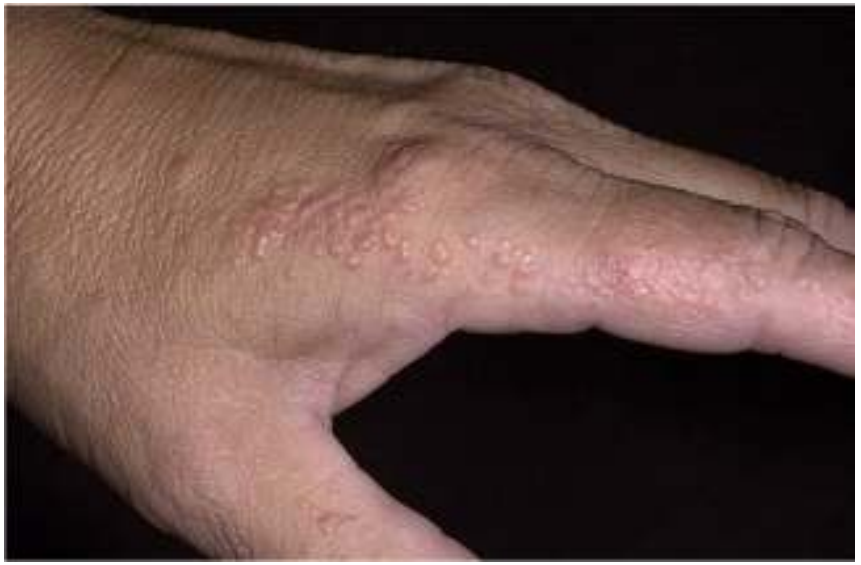
Asteatotic (xerotic) eczema

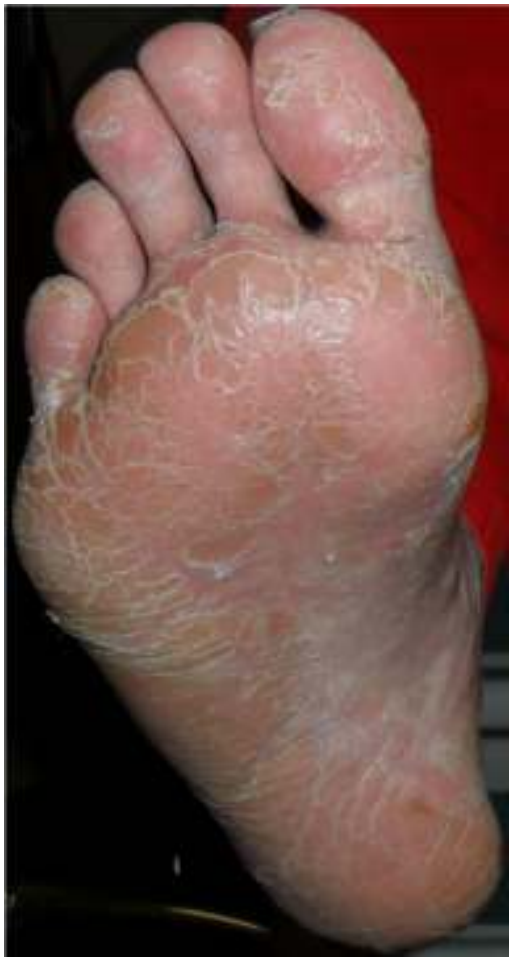


Id reaction, or autoeczematization

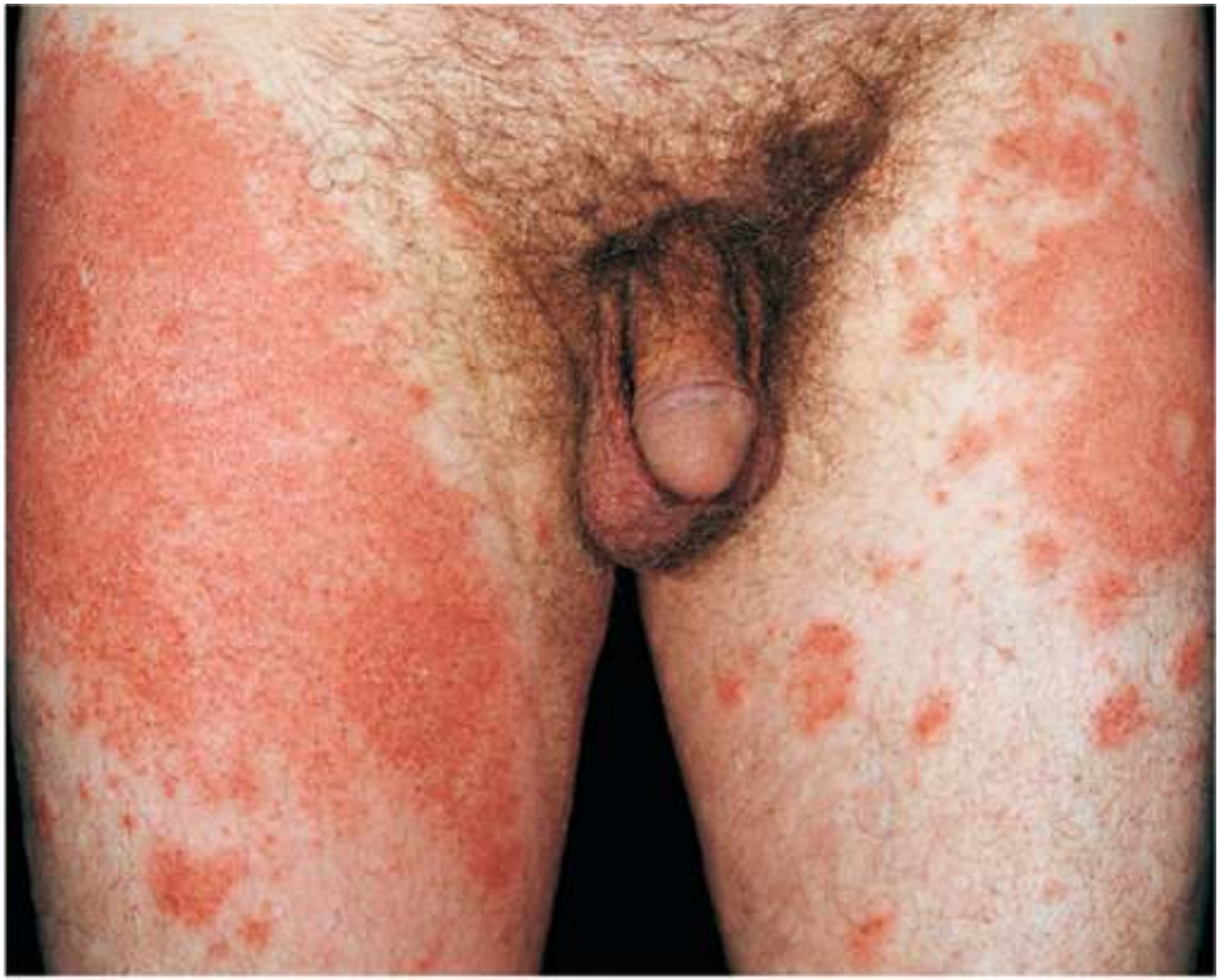
- A generalized acute cutaneous reaction to a variety of stimuli, including infectious and inflammatory skin conditions.
- The pruritic rash that characterizes the id reaction, which is considered immunologic in origin, has been referred to as candidid, dermatophytid, pediculid, or bacterid when associated with a corresponding infectious process.

Id reaction, or autoeczematization





Id reaction, or autoeczematization, or generalized eczema



LAB

In vitro:

Testing humoral immunity:

- passive hemagglutination test;
- precipitation test radial immunodiffusion (Mancini);
- IgE test (RAST, ELISA);
- complement fixation tests;
- human basophil degranulation test;
- immune complex test.
- immunoelectrophoretic analysis , etc.

Testing cellular immunity:

- lymphocyte blast trasformation test;
- macrophage migration inhibition test;
- immuno-cyto-adherence tests (rosetting tests).

Presumptive tests

- eosinophil blood count;
- histaminemia;
- histaminuria;
- blood histaminopexia.

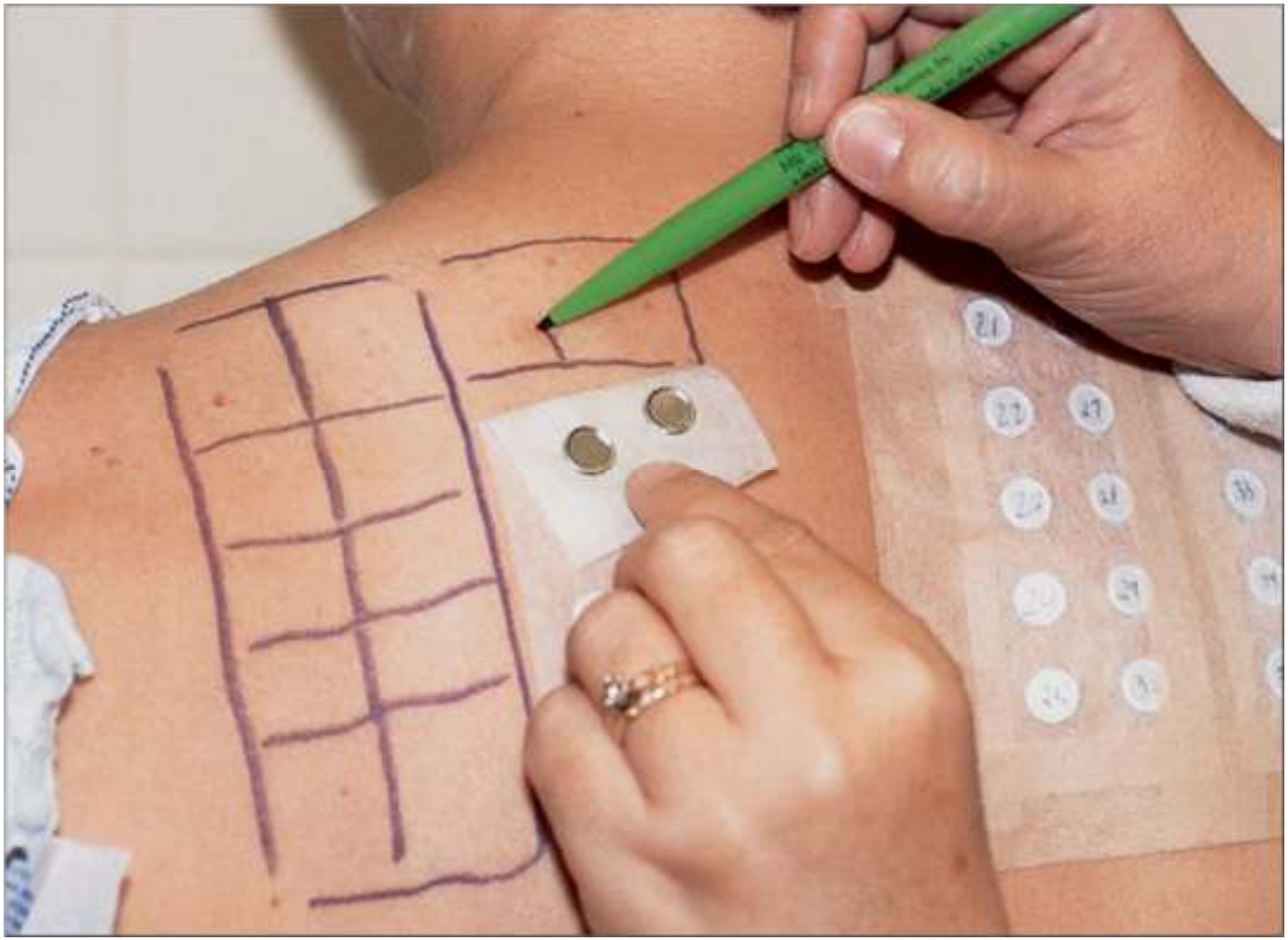
In vivo:

- patch test – type IV hypersensitivity;
- prick/scratch test – type I hypersensitivity;
- intradermal reaction (idr) – type IV for specific infections.

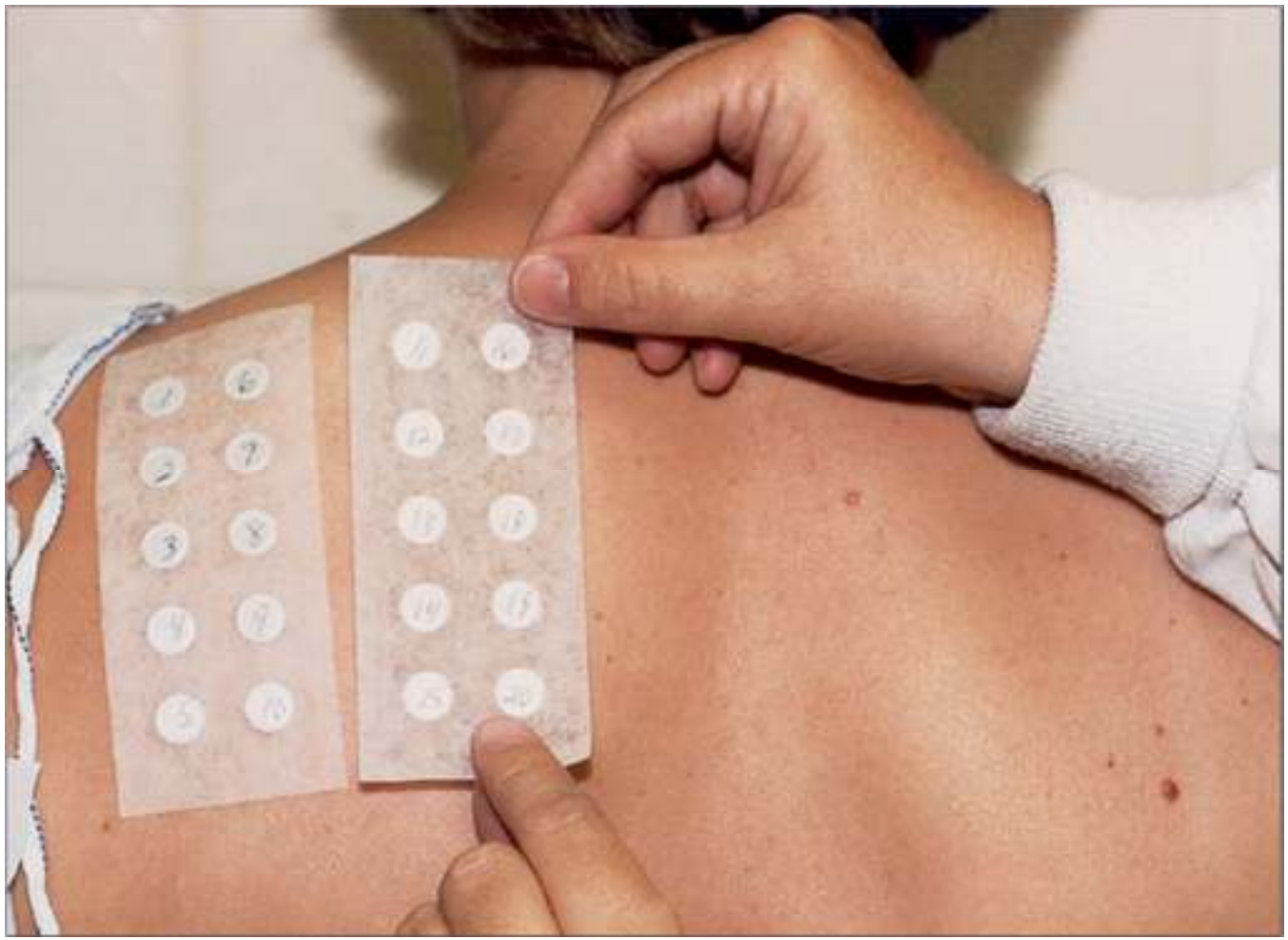
Other: direct microscopy and culture; parasitological diagnosis; photobiological testing; coprological examination; Tzanc cytology; fibroscopy, X-ray and ultrasound exams, etc.

Patch-test: allergens distribution on Finn chambers

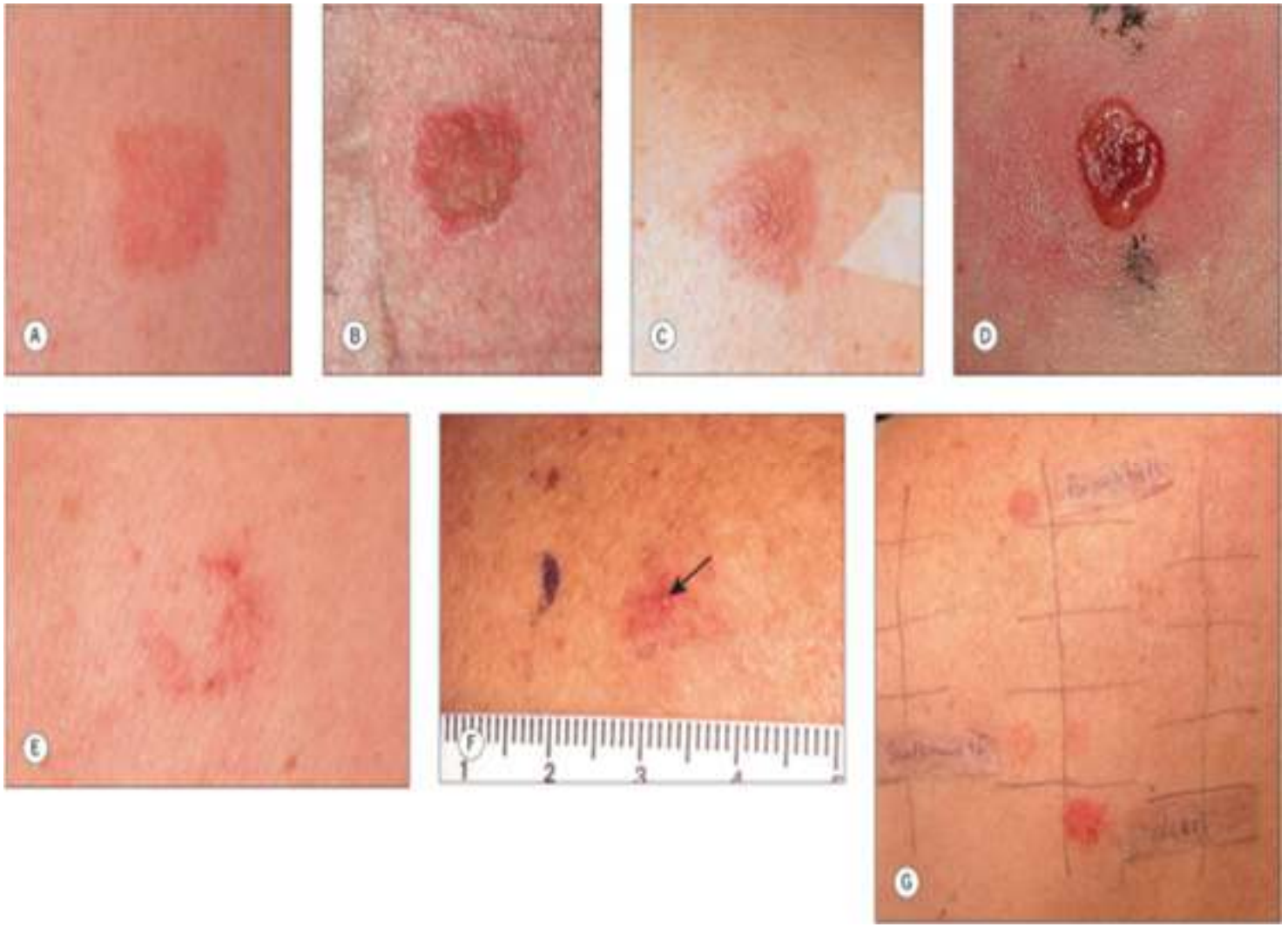
Patch-test: allergens marking



Patch-test: placing adhesive tapes



Patch test results: A. + ; B. ++ . C ++–+++ . D +++ . E Erythematous papules at the edge of the Finn chamber application site (rim effect).
F Pustular reaction at the site of a nickel patch test (arrow points to pustule).
G Three different patch test reactions: +/− to quaternium-15, + to formaldehyde, and ++ to nickel.



TOP TEN ALLERGENS AS IDENTIFIED BY THE NORTH AMERICAN CONTACT DERMATITIS GROUP

Test substance	Allergic reactions (%)	Relevant reactions (%)
Nickel sulfate	16.7	49.4
Neomycin sulfate	11.6	32.3
Balsam of Peru	11.6	80.7
Fragrance mix	10.4	83.5
Thimerosal	10.2	7.2
Sodium gold thiosulfate	10.2	37.3
Quaternium-15	9.3	84.3
Formaldehyde	8.4	69.6
Bacitracin	7.9	42.6
Cobalt chloride	7.4	43.8

Top ten allergens as identified by the North American Contact Dermatitis Group.
Adapted from North American Contact Dermatitis Group patch-test results, 2001–2002 study period. Dermatitis. 2004;15:176–83.

Eczema: treatment and prevention

- 1. Avoidance of as many irritants as possible;
- 2. Allergen avoidance;
- 3. Systemic therapy: antihistamines, glucocorticoids in severe cases;
- 4. Topical treatment:

✓ Drying agents (aluminum sulfate, calcium acetate), in acute, vesicular, weeping eruptions;

✓ Corticosteroids: can be super, high, mid or low potent.

a. from superpotent corticosterids are: clobetasol dipropionate 0,05% (Dermovate), bethamethasone dipripionate 0,5% (Locacorten) et al.

b. high potency corticosteroids are: fluocinonide 0,05% (Cyclocort), methylprednisolone aceponate 0,1% (Advantan), mometasone furoate 0,1% (Elocom), hydrocortisone butirate 0,1% (Locoid) et al.

c. mid potency corticosteroids are: fluticasone propionate 0,05% (Cutivate) et al.

d. low potency are: hydrocortisone acetate 0,25-2,5% et al.

✓ Solutions, lotions, gels or sprays are recommended for inflammatory, exudative lesions and for hairy areas.

✓ Creams and lotions are best intertriginous locations.

✓ Ointments have good action on chronic thickened lesions.

Atopic eczema: treatment / prevention

- Avoidance of irritants and allergens.
- **Systemic therapy:**
- **antihistamines:** H1/H2 antihistamines; ketotifen; sodium cromolin, etc.
- **immunosupressive drugs: corticosteroids** (0,5 – 1 mg/kg/day, 7-21 days); **cyclosporine A** (2-5 mg/kg/day in short-term therapy); **azathioprine** (50 mg twice daily); **mycophenolate mofetil** (2 g/day, orally**); interferon gamma; omalizumab**
- **Topical treatment:**
  - Wet-to-dry compresses for acute, inflammatory and weeping phase
  - Topical corticosteroids
  - Topical antibiotics
  - Topical immunomodulators – Tacrolimus or Pimecrolimus
  - **Lubricants (emolients)**
- **Physical therapy:**
- PUVA
- Extracorporal photopheresis
- High-dose UVA therapy (340-400 nm)
- Combination of UVB irradiation with UVA irradiation
- Narrow-band UVB.