

# 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  
histologically
- Spongiosis histologically revealed in all stages.

# 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.



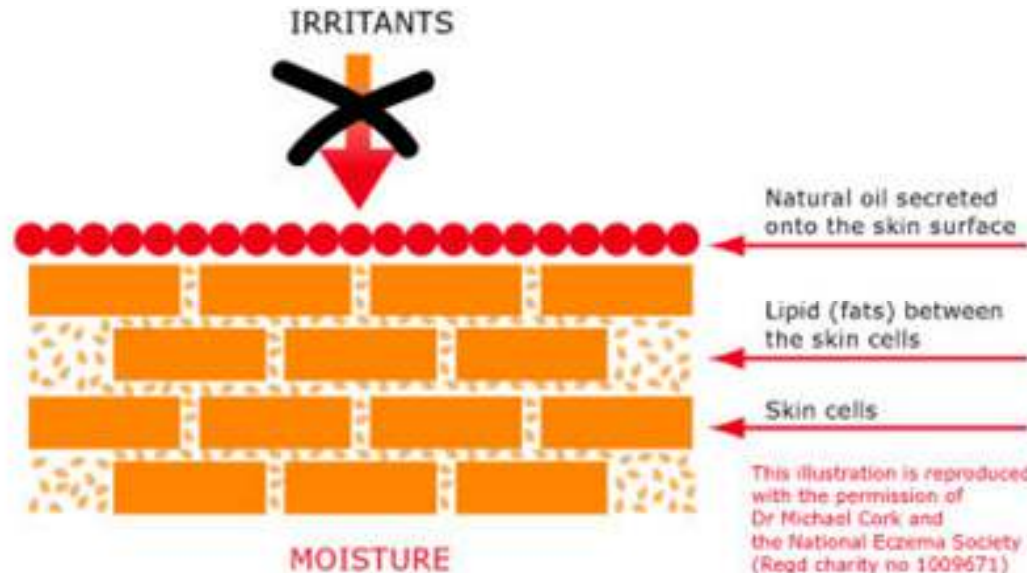
# PATHOGENESIS: compromised barrier function



## NORMAL SKIN BARRIER FUNCTION

### No eczema

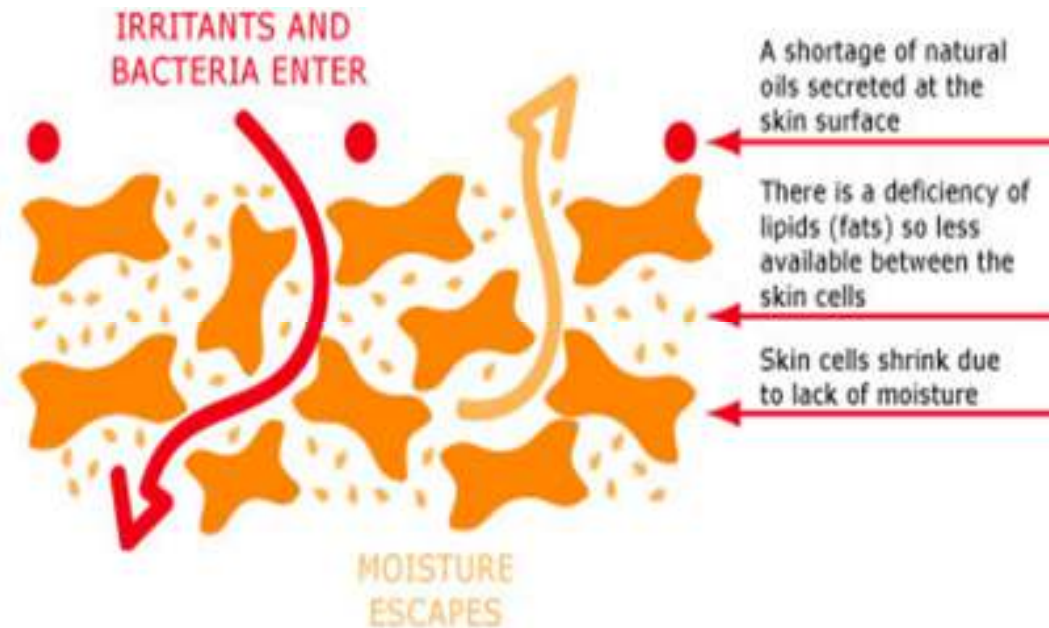
- Moisture is kept in
- Irritants from the atmosphere are kept out
- There is a high water content and a balance of lipids
- The skin is well hydrated (plenty of moisture) and supple



## BREAKDOWN OF THE SKIN BARRIER

### Eczema

- Moisture escapes
- The skin is dry and brittle, so cracks easily
- Irritants and bacteria can get into the skin causing redness, inflammation and itchy skin



# PATHOGENESIS:

## MHC classes and immunopathology

### ➤ **MHC class I**

- presents intracellular antigens (viral, bacterial, lipid, tumoral antigens) to lymphocytes T<sub>c</sub> CD8+ (cytotoxic)
- expressed on the surface of all nucleated cells

### ➤ **MHC class II**

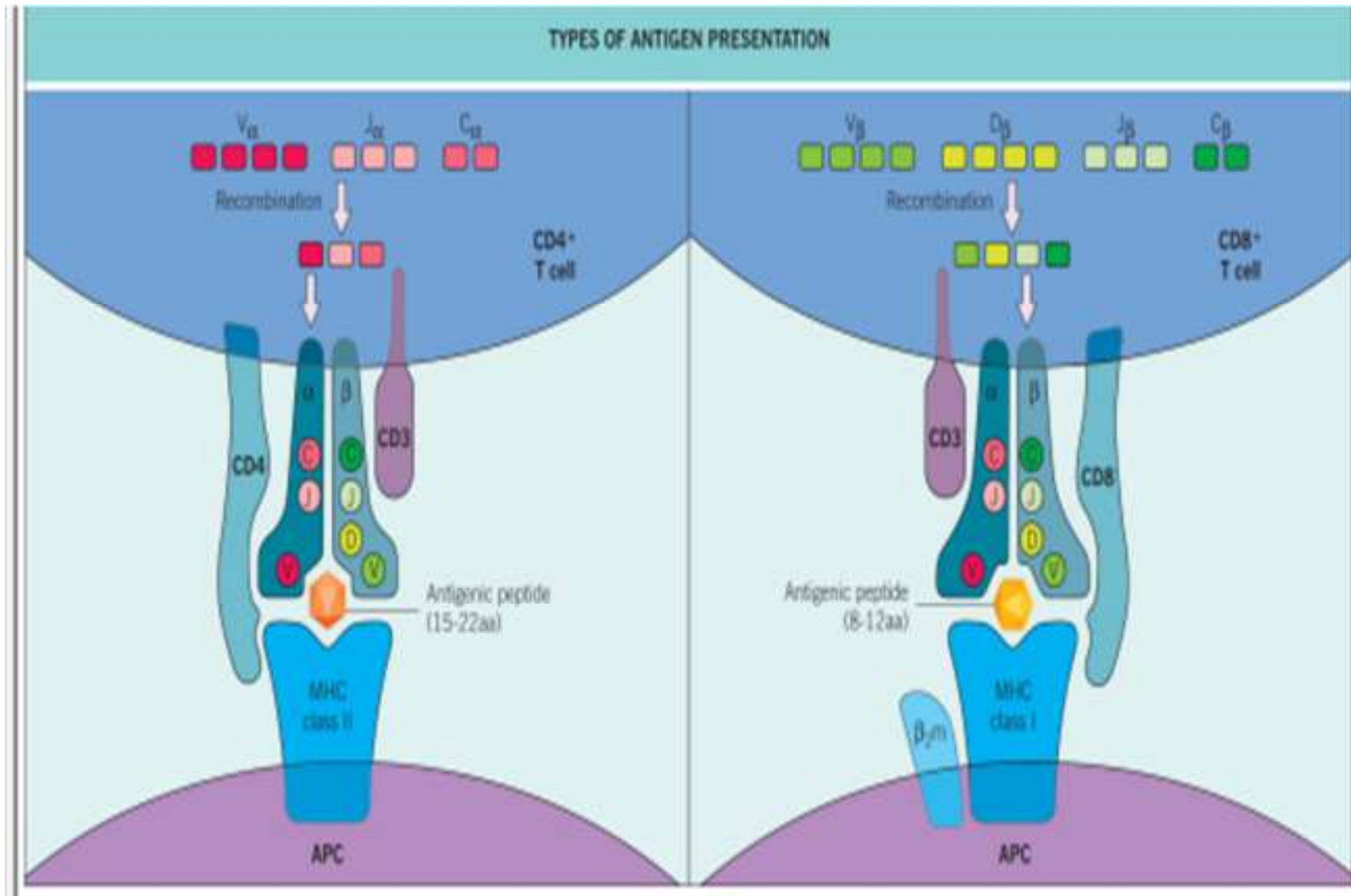
- presents extracellular antigens (contact allergens, bacteria, fungi, parasites) to lymphocytes T<sub>H</sub> CD4+ (helper)
- expressed on the surface of antigen presenting cells (APC).

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

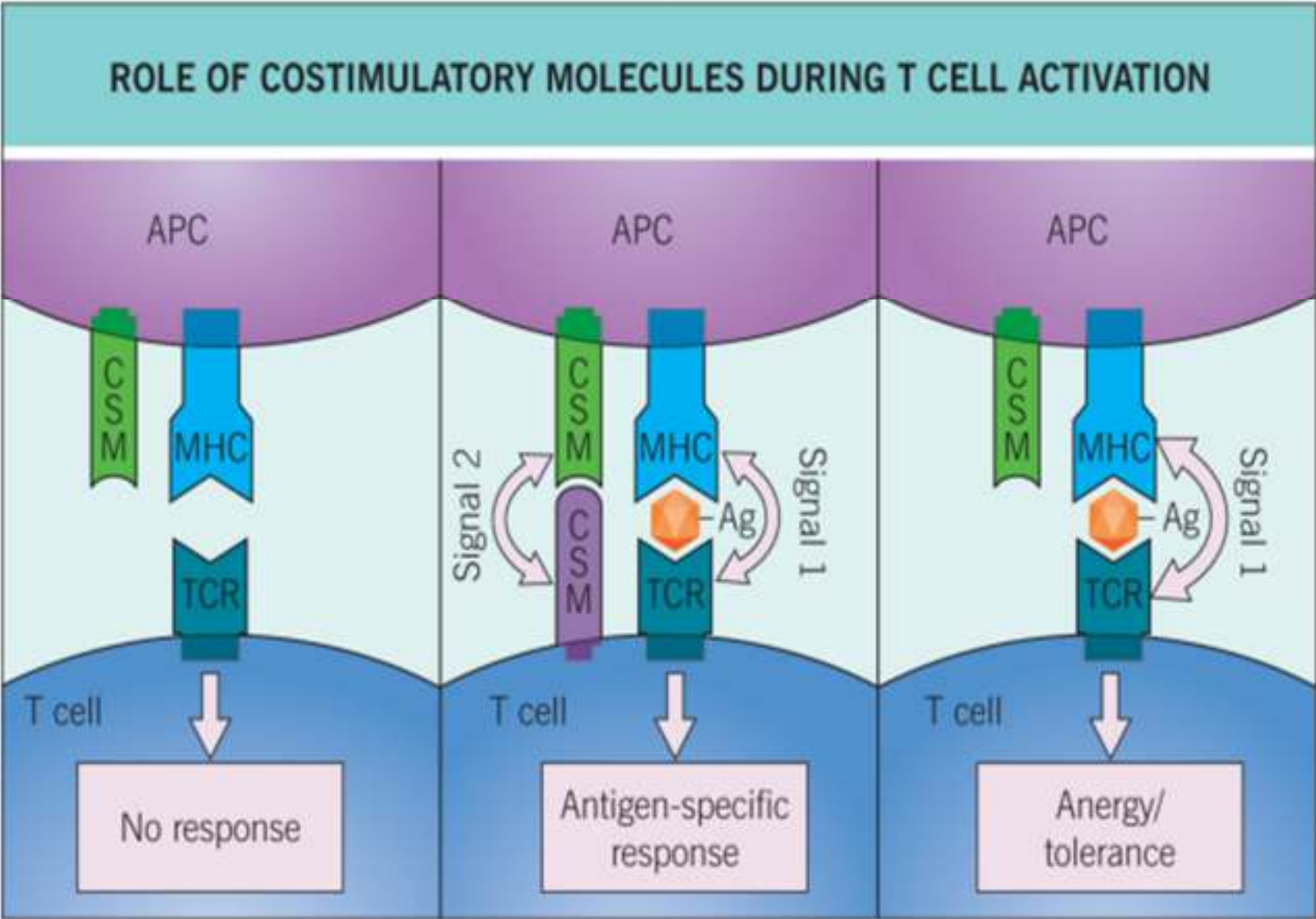
*Clasa I = genes A, B și C ⇒ HLA-A, HLA-B and HLA-C*

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

# Antigen presentation

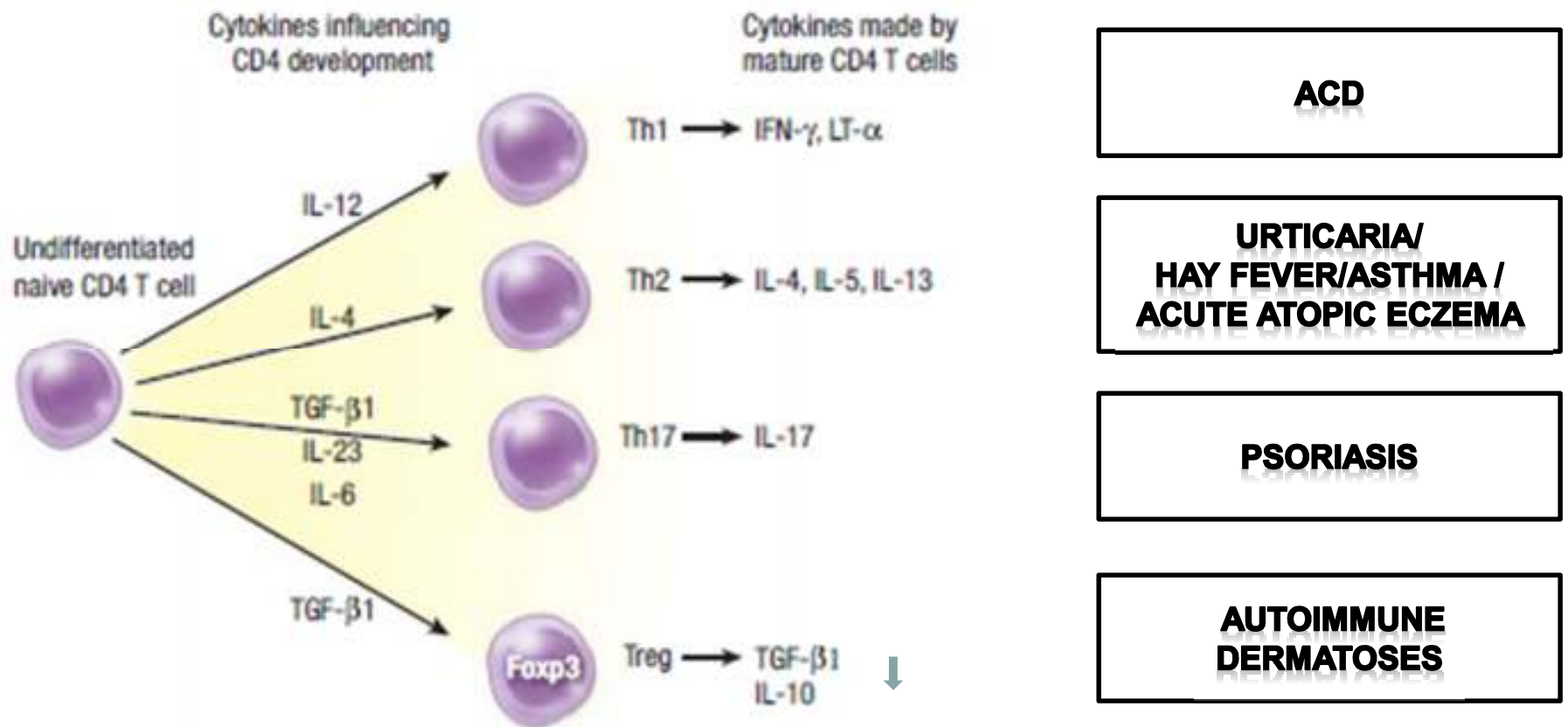


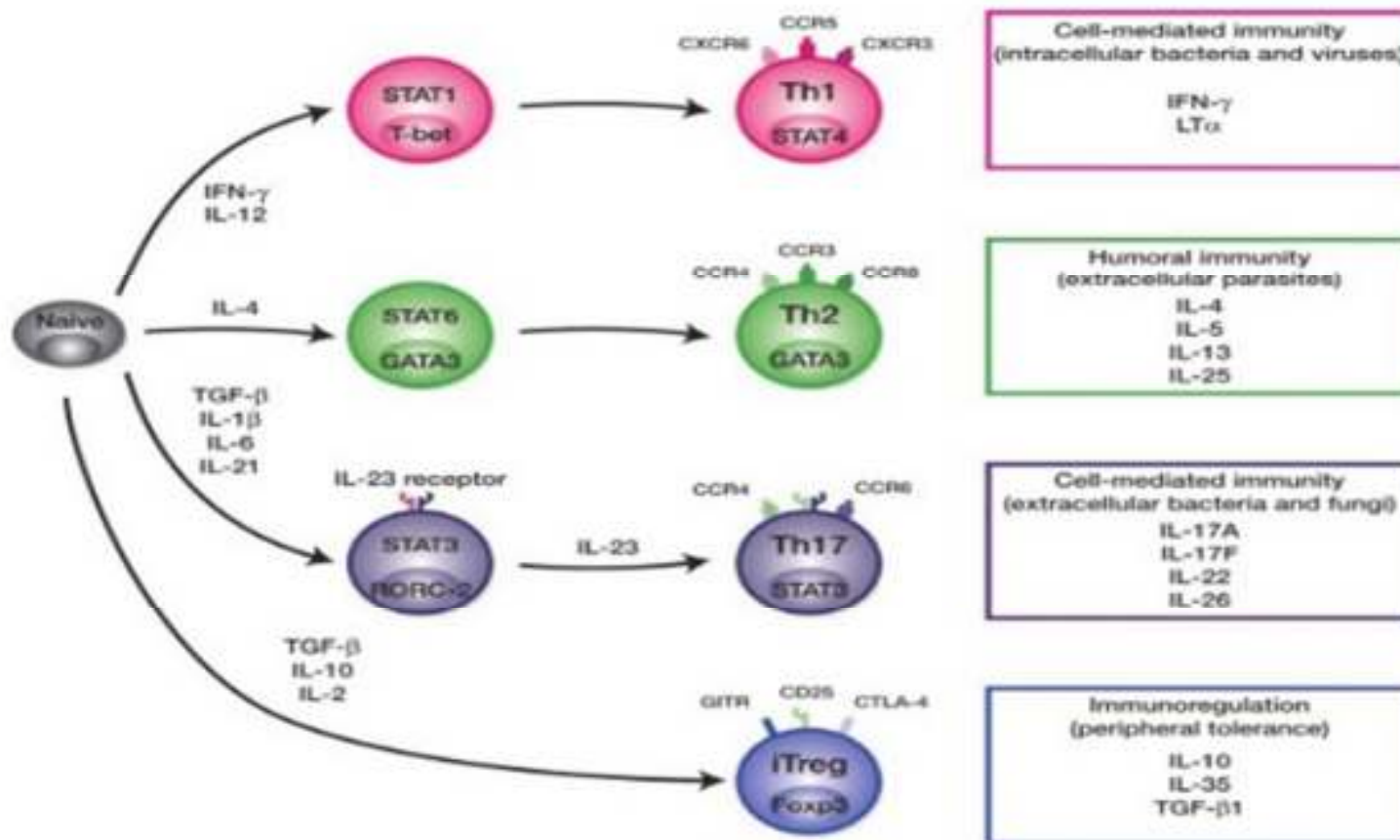
# Co-stimulation and T-cell response





# Cytokine profile of CD4 lymphocytes

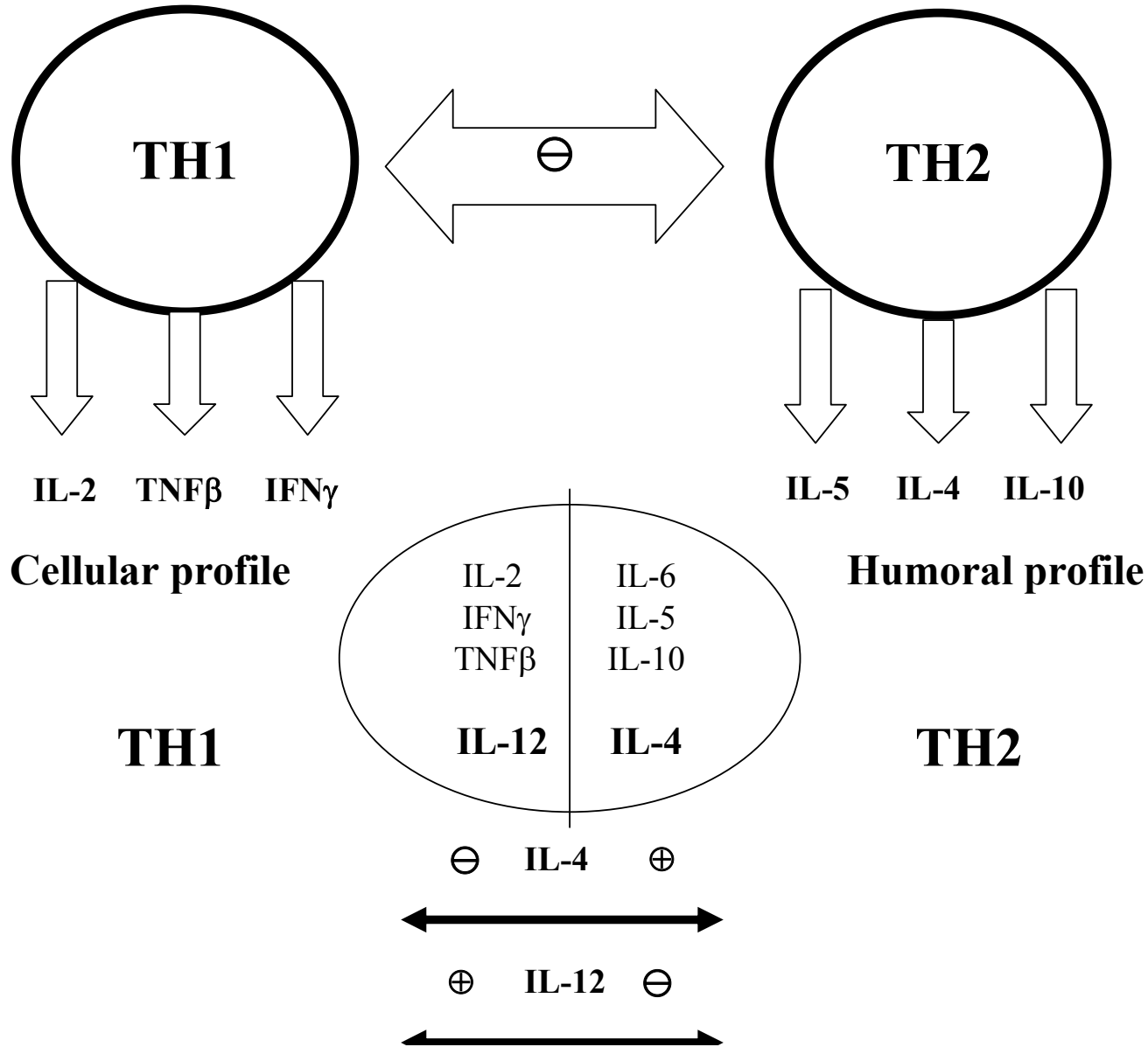




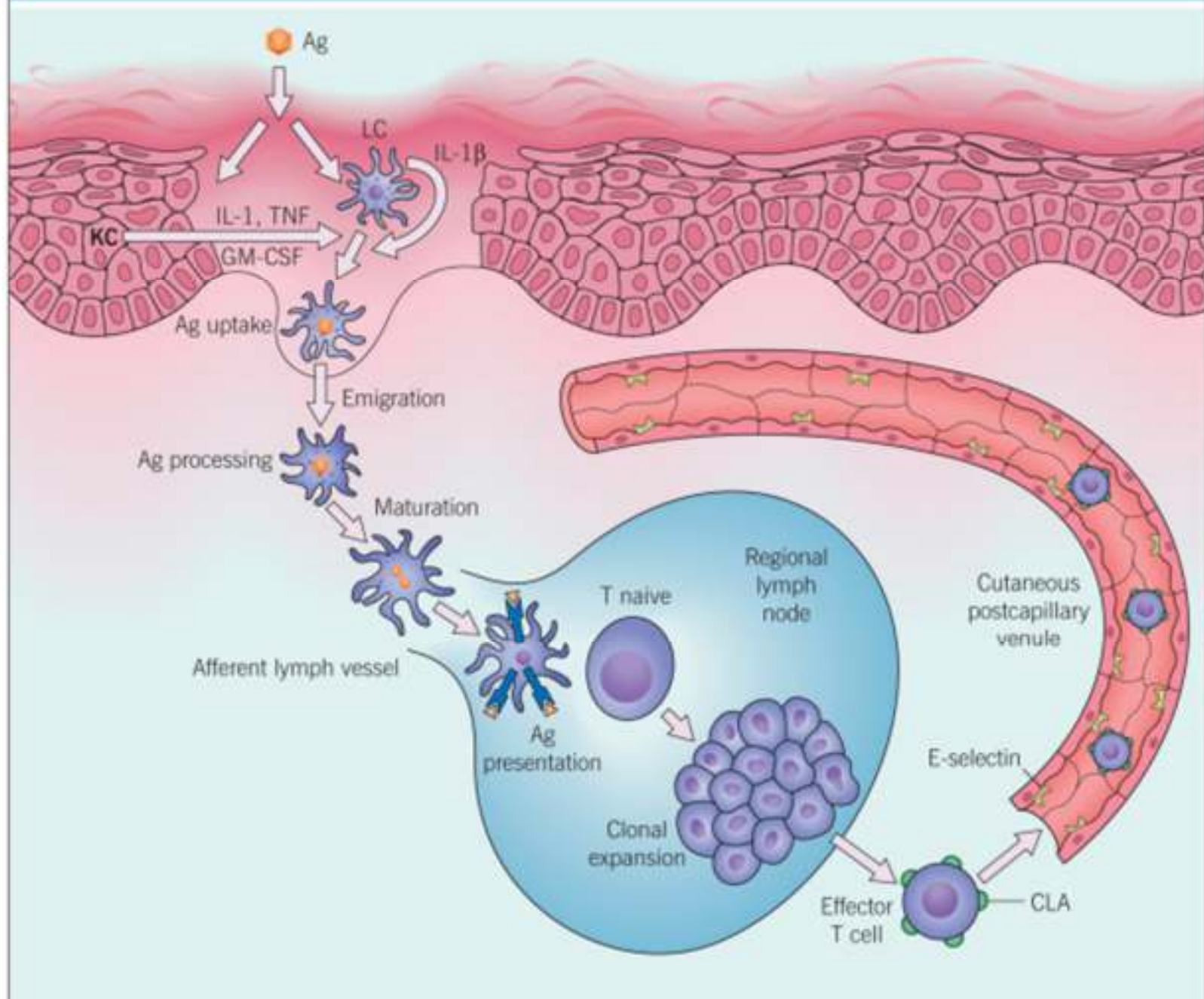
- Interleukin-23 (IL-23) helps to maintain the lesion by leading to the development of Th17 cells.
- These in turn produce necrosis factor-alpha (TNF-a), IL-17 and IL-22.
- IL-22 is believed to drive many of the epidermal changes in psoriasis.
- Many autoimmune diseases, including psoriasis, are characterized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

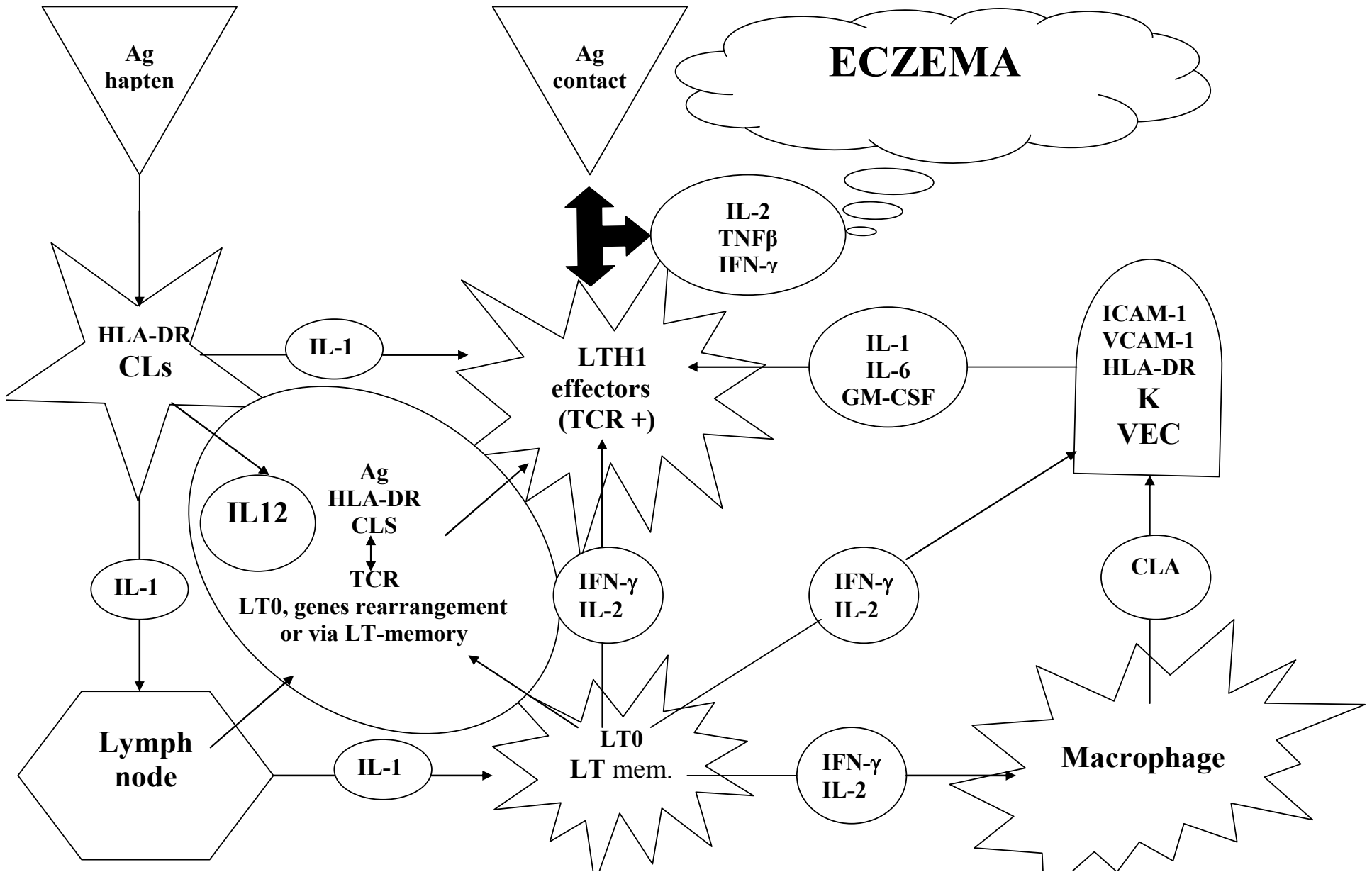
Journal of Investigative Dermatology 2009;129:1339-1350.

# INTERACTION TH1/TH2

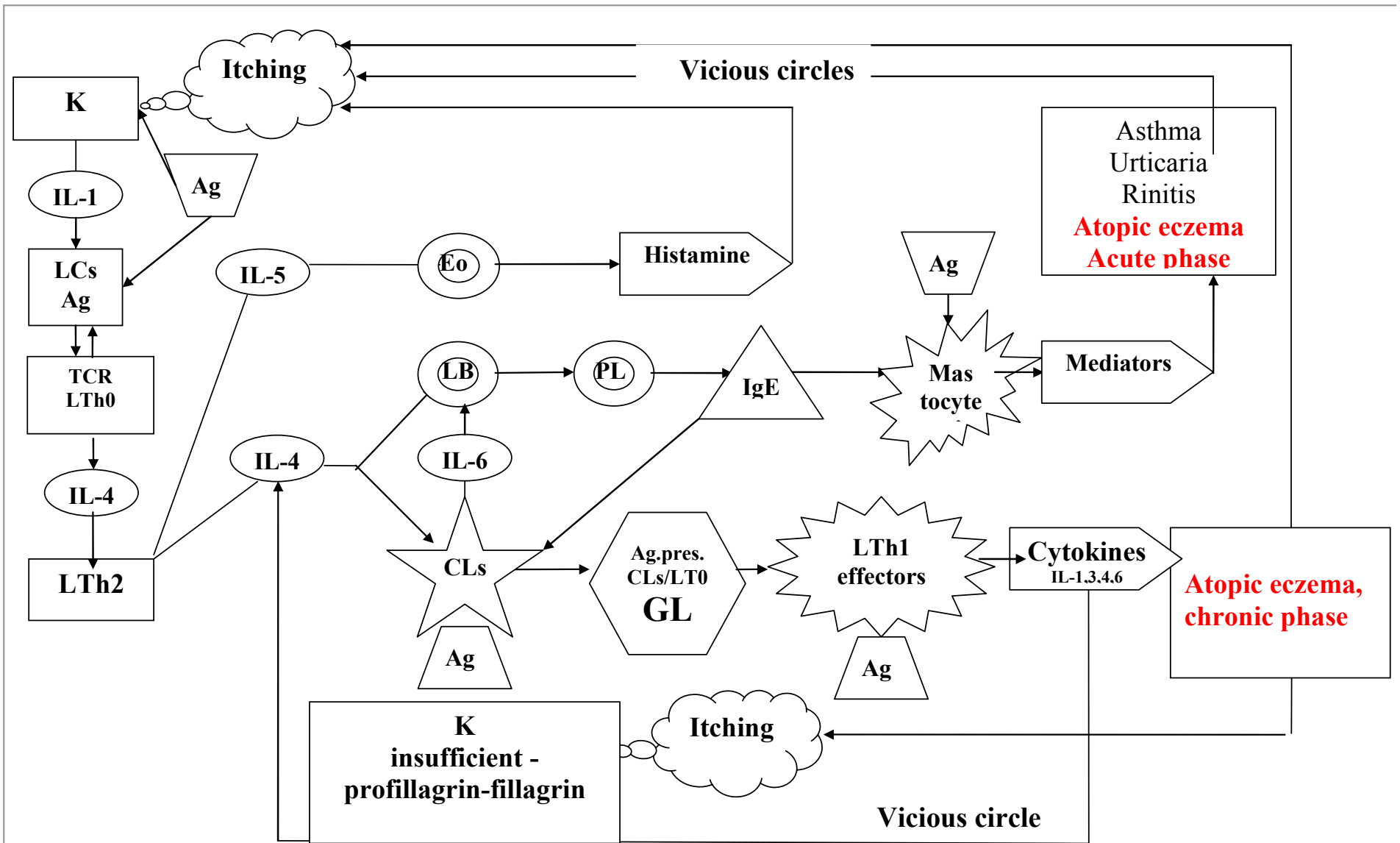


## INDUCTION OF CONTACT HYPERSENSITIVITY



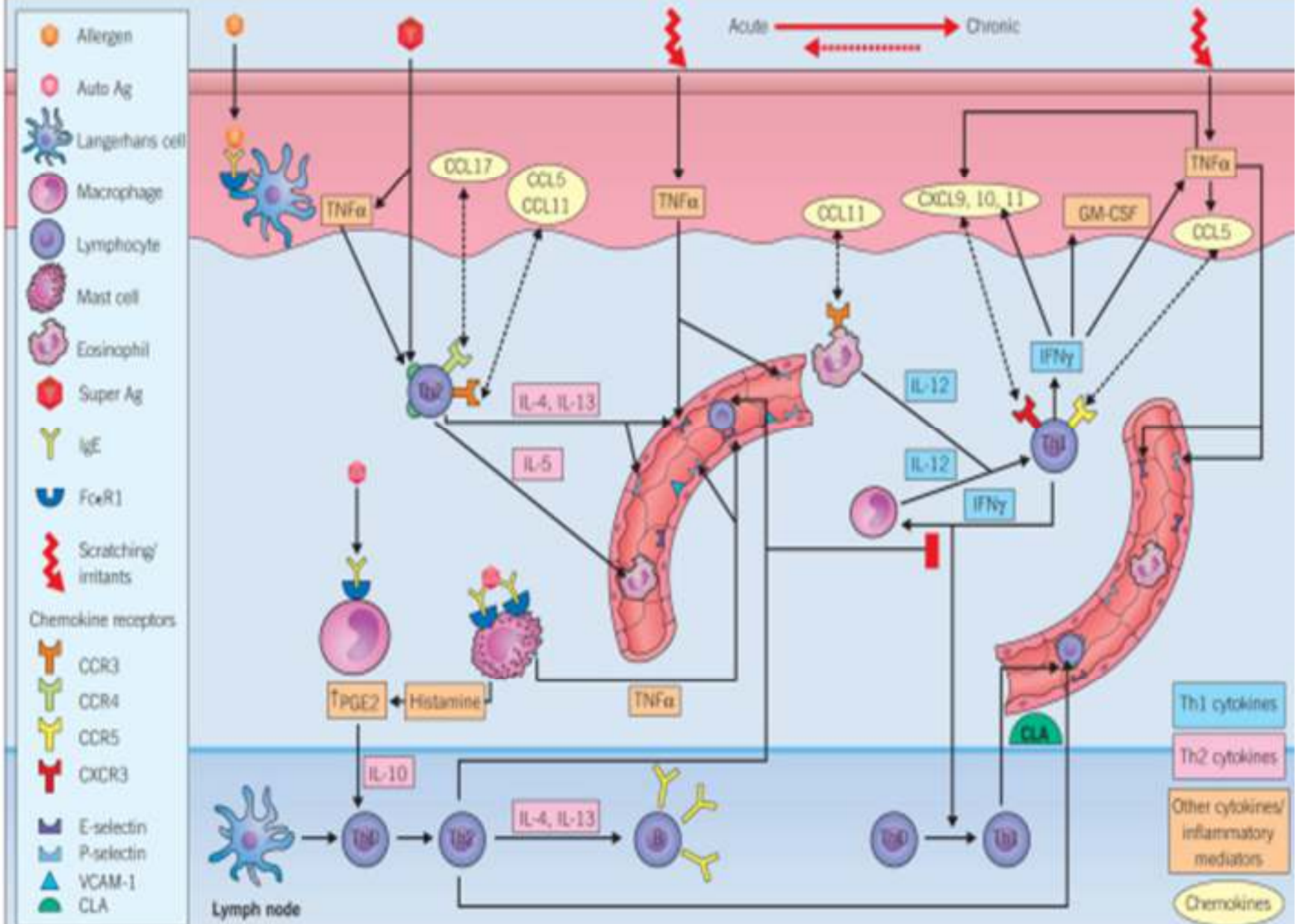


**TH1 RESPONSE / TYPE 4 GELL-COOMBS**



**ATOPIC IMMUNOPATHOLOGY: CONCURRENT TYPE1/TYPER4 GELL-COOMBS,  
CONCURRENT RESPONSE PROFILE TH1/TH2**

# IMMUNOPATHOGENESIS IN ACUTE AND CHRONIC ATOPIC DERMATITIS



# 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 malabsorption; 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
<u>Jewelry</u> , zippers or buckles containing <u>nickel</u>	Food containing nickel such as cocoa, beans, tinned foods. Nickel alloy on an intratubal birth control device.
<u>Balsam of Peru</u> in <u>cosmetics</u> and <u>perfumes</u>	Spices such as <u>cinnamon</u> , vanilla, cloves that are used to flavor foods, drinks and medicines
<u>Formaldehyde</u> 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
<u>Parabens</u> in cosmetics and pharmaceutical/self-hygiene products	Paraben-containing foods such as marinated fish products, jams and jellies, pickles and preserves
Propylene glycol in <u>topical corticosteroid cream</u>	Propylene glycol in oral <u>antihistamine</u> tablets
Direct contact with plants or pollens from the <u>Compositae</u> group of plants	Vegetable and herbs such as <u>lettuce</u> , endive, <u>chamomile</u> and echinacea
<u>Ethylenediamine</u> in topical <u>antibiotic/steroid</u> creams	Intravenous or oral administration of aminophylline
<u>Neomycin</u> in over-the-counter <u>antiseptic</u> 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.corneum 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 off 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 (discoïd) 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



<http://dermis.net>

# 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.

### *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.

#### **Testing cellular immunity:**

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

#### **Presumptive tests**

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

# 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

<b>Test substance</b>	<b>Allergic reactions (%)</b>	<b>Relevant reactions (%)</b>
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 corticosteroids are: clobetasol dipropionate 0,05% (Dermovate), bethamethasone dipropionate 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.
  - **immunosuppressive 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
  - Extracorporeal photopheresis
  - High-dose UVA therapy (340-400 nm)
  - Combination of UVB irradiation with UVA irradiation
  - Narrow-band UVB.