

**Immundermatology- skin and the
immune system. Allergic diseases-
dermatitis, urticaria**

Dr. Márta Marschalkó

- SIS-SALT
- Innate immune system in the skin
- TLR7, Imidazoquinolone treatment in dermatology, treatment of warts, molluscum contagiosum
- Cell mediated, antibody mediated skin diseases
- SALT-epidermotropismus-Cutaneous T cell lymphoma
- Allergic skin diseases-allergic contact dermatitis, urticaria, atopic dermatitis

FUNCTIONS OF SKIN

- protects against mechanical injury
- prevents entry of **microorganisms** and chemicals
- screens and reduces penetration of radiation
- **SIS- Skin Immune System or**
- **SALT-Skin Associated Lymphoid Tissue**
- thermoregulation
- sensory nervous function
- synthesis of D vitamin

Allergic-hypersensitivity reaction

HYPERSENSITIVITY

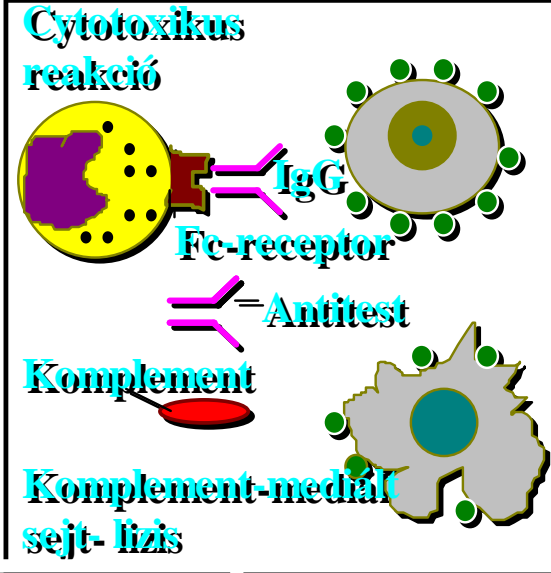
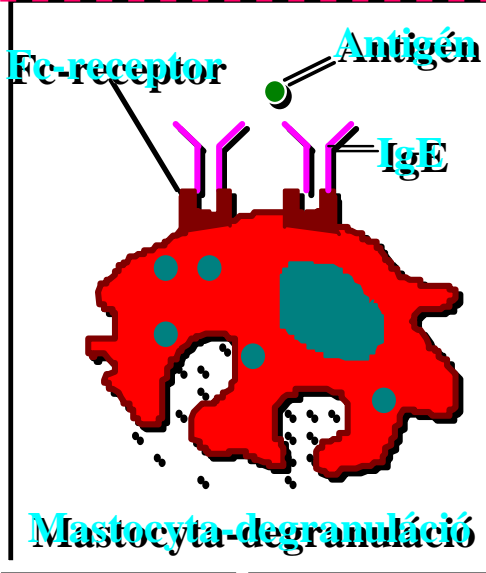
- **IN IMMUNOLOGICAL PRIMED INDIVIDUAL**
- **FURTHER CONTACT WITH ANTIGEN LEADS TO SECONDARY BOOSTING OF IMMUNE RESPONSE**
- **IF THE REACTION IS EXCESSIVE: GROSS TISSUE DAMAGE!**

COOMBS -GELL

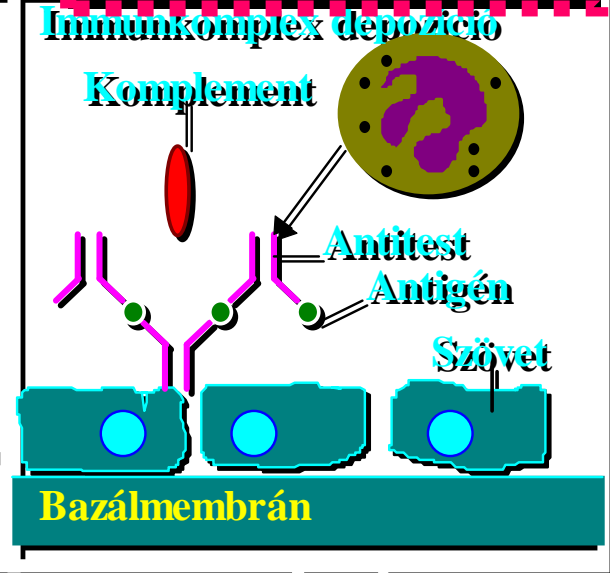
- **TYPE I,II,III :**
HUMORAL
- **TYPE IV:**
CELLULAR
IMMUNE
RESPONSE

Hypersensitivity reactions

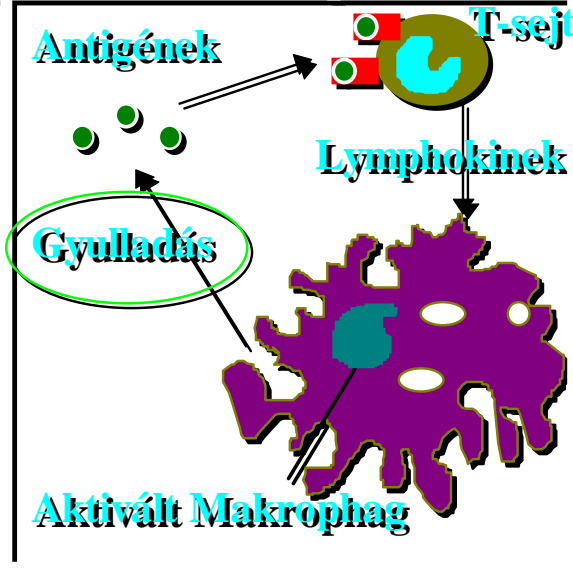
Typ I Mastocyte degranulation



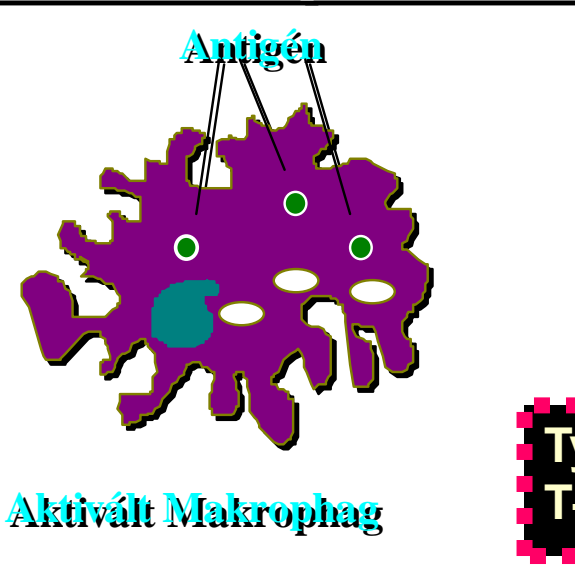
Typ III Immuncomplex med.



Typ I.



Typ IV.



Typ III.

Typ IV T-cell mediated

- **I. reagin type mastocyte degranulation**
ANTIBODY: IgE
- **II. complement mediated lysis**
ANTIBODY: IgG
- **III. Arthus- immuncomplex mediated**
IgG, IgA, IgM, in immuncomplexes
- **IV. cellular: eczema type, or tuberculin**
type LYMPHOCYTE

Allergic skin diseases

- Allergic dermatitis (contact-hypersensitivity reactions to haptens)
- Allergic dermatitis (hypersensitivity reactions to microbial antigens)
- Atopic dermatitis
- Urticaria
- Allergic-hypersensitivity vasculitis
- Allergic drug reactions

Allergic skin diseases

- Allergic dermatitis (contact-hypersensitivity reactions to haptens) **Type IV**
- Allergic dermatitis (hypersensitivity reactions to microbial antigens) **Type IV**
- Atopic dermatitis **Type I, type IV**
- Urticaria **Type I**
- Allergic-hypersensitivity vasculitis **Type III**
- Allergic drug reactions **Type I, II, III, IV**

SIS, SALT

IS : REGIONAL SPECIALISATION

- **BALT-Bronchus Associated Lymphoid Tissue**
- **GALT-Gut Associated Lymphoid Tissue**
- **SALT- Skin Associated Lymphoid Tissue**
- **CALT-Conjunctiva Associated Lymphoid Tissue**

Immune system

- **Innate:**

- more evolutionarily primitive
- Rapid response to foreign agents by cell receptors and molecules

- **Adaptive:**

- T and B cells with antigen-specific receptors produce a slower, but more specific and coordinated IR
- Leading to expansion of a memory phenotype

SIS

Innate immune system in the skin

-TLR-s, chemokines

Adaptive immune system in the skin

- T-cell mediated diseases- psoriasis, cutaneous T-cell lymphoma
- Antibody mediated diseases- autoimmune bullous diseases, immunocomplex diseases

Allergic diseases-urticaria, dermatitis-eczema, atopy, drug allergy, vasculitis

SIS

Innate immune system in the skin

-TLR-s, chemokines

Adaptive immune system in the skin

- T-cell mediated diseases- psoriasis, cutaneous T-cell lymphoma
- Antibody mediated diseases- autoimmune bullous diseases, immunocomplex diseases

**Allergic diseases:urticaria,
dermatitis-eczema, atopy, drug
allergy, vasculitis**

Immune mediated skin diseases

- Autoimmune diseases- LE, autoimmune bullous diseases, psoriasis-**Treg (regulatory T cells)**
- Allergic skin diseases- atopy, contact dermatitis, urticaria, vasculitis, drug hypersensitivity
- Infectious diseases- **innate immunity, chemokines, $\gamma\delta$ epidermal T cells**
- Tumors- **$\gamma\delta$ T cells- CTCL**

- Lupus erythematosus, dermatomyositis, scleroderma
- Pemphigus, pemphigoid, dermatitis herpetiformis Duhring
- Psoriasis

- Atopic dermatitis
- **Contact dermatitis, Eczema**
- **Urticaria**
- Vasculitis
- Drug hypersensitivity reactions

Immune mediated skin diseases

- Autoimmune diseases- LE, autoimmune bullous diseases, psoriasis-**Treg (regulatory T cells)**
- Allergic skin diseases- atopy, **contact dermatitis, urticaria**, vasculitis, drug hypersensitivity
- Infectious diseases- **innate immunity, chemokines, $\gamma\delta$ epidermal T cells**
- Tumors- **$\gamma\delta$ T cells**

1. Cell mediated immune reactions

- Contact dermatitis, eczema
- Psoriasis
- Drug reactions
- Cutaneous T-cell lymphoma

T cell activation in the skin

- **Initiator: 1. Antigen driven activation of epidermal Langerhans cells**
- **2. Antigen presenting Langerhans cells access the draining lymph node**
- **3. In the lymph node: T cell clone activation, proliferation**

Immune response

- Induction of immune response:
- requires a specific antigen-presenting cell (APC) to process the antigen into peptides
- Subsequently activate antigen-specific T-cells via T-cell receptor and costimulatory molecule interactions

Psoriasis vulgaris

Langerhans cell

- **Antigen presenting cell, dendritic cell**
- **Progenitor: CD34 +haematopoietic progenitor cell, CD 14+ peripheral blood monocytes**
- **Receptors: Fc γ , Fc ϵ**
- **Morphology: monocyte-like cells with short processes**

Langerhans cell

- **Ultrastructure: Birbeck granule (disk with tennis-racket appearance)**
- **LC phenotype: E-cadherin, Lag, Langerin**
- **CD1a+, CD11c+**

Langerhans cell immigration/emmigration

- **TNF α** produced by activated keratinocytes
- **Chemokines: MIP-3 α** (macrophage inflammatory protein)

SALT-EPIDERMOTROPISM

- **A SUBSET OF RECIRCULATING LYCY-S DISPLAY A SPECIAL AFFINITY FOR SKIN**
- **SKIN-SEEKING LYCY-S ROUTINELY ENTER THE SKIN /AG RECOGNITION/S**
- **AG ACTIVATED LYCY-S, AG BEARING LANGERHANS CELLS TRAVEL THROUGH DRAINING LYMPH TO REGIONAL LYMPH NODE**

EPIDERMIS

Horny layer

Granular layer

Prickle cell layer

Melanocyt

KC

Langerhans cell

Lymphocyte

Basal layer

DERMIS

Lymphocyte

Basal membrane

Lymphocyte

Fibroblast

Langerhans cell

Langerhans

mastocyt

Langerhans cell

Langerhans ce

T cell activation

- Initiator: 1. Antigen driven activation of epidermal **Langerhans cells**
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T-cell mediated skin diseases

- Eczema
- (Dermatitis)
- Psoriasis

Dermatitis-allergic dermatitis- eczema

- Type IV hypersensitivity reaction
- T-cell mediated
- Allergen: small molecules-hapten, microbial allergens (associated with different clinical features)
- Clinical manifestation: inflammation, hyperaemia, vesicle formation

Acut eczema/dermatitis

Dermatitis-allergic dermatitis- eczema

- Common disease
- Generally mild, rarely severe
- Acute or chronic (depending on the allergen's presence)
- No serious complications
- Associated with disturbing symptoms: itching, wheeping, sometimes hindering the original occupation, normal everyday life

Allergic contact dermatitis

- ACD: inflammation of the skin manifested by varying degrees of:
- erythema, edema and vesiculation
- Delayed type allergy resulting with cutaneous contact with a specific allergen to which the patient has developed a specific sensitivity
- (Eczema)

Immunological events in allergic dermatitis

TYPE IV. allergic reaction

- **CONTACT DERMATITIS /sensitisation to certain simple chemicals/**
- **ALLERGIC REACTION TO CERTAIN BACTERIA, VIRUSES AND FUNGI**
- **REJECTION OF TRANSPLANTATED TISSUE**

CONTACT DERMATITIS

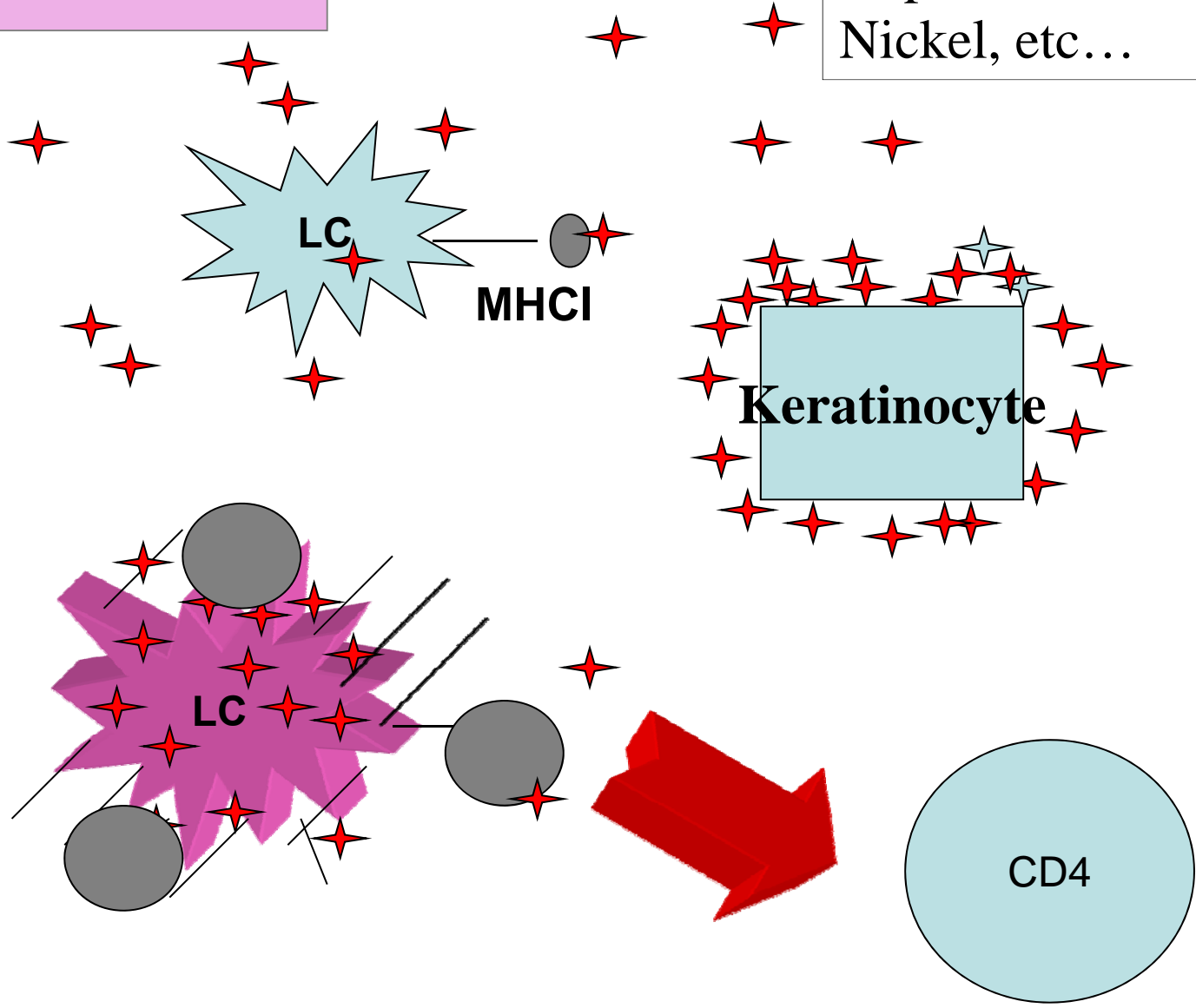
- HAPTENS:
STIMULATE THE
LANGERHANS
CELLS--increased
cytokin synthesis
- ACTIVATED
LANGERHANS
CELLS LEAVE THE
EPIDERMIS AND
MIGRATE TO THE
REGIONAL LYMPH
NODE: they present
the MHC-coupled
antigen to T cells

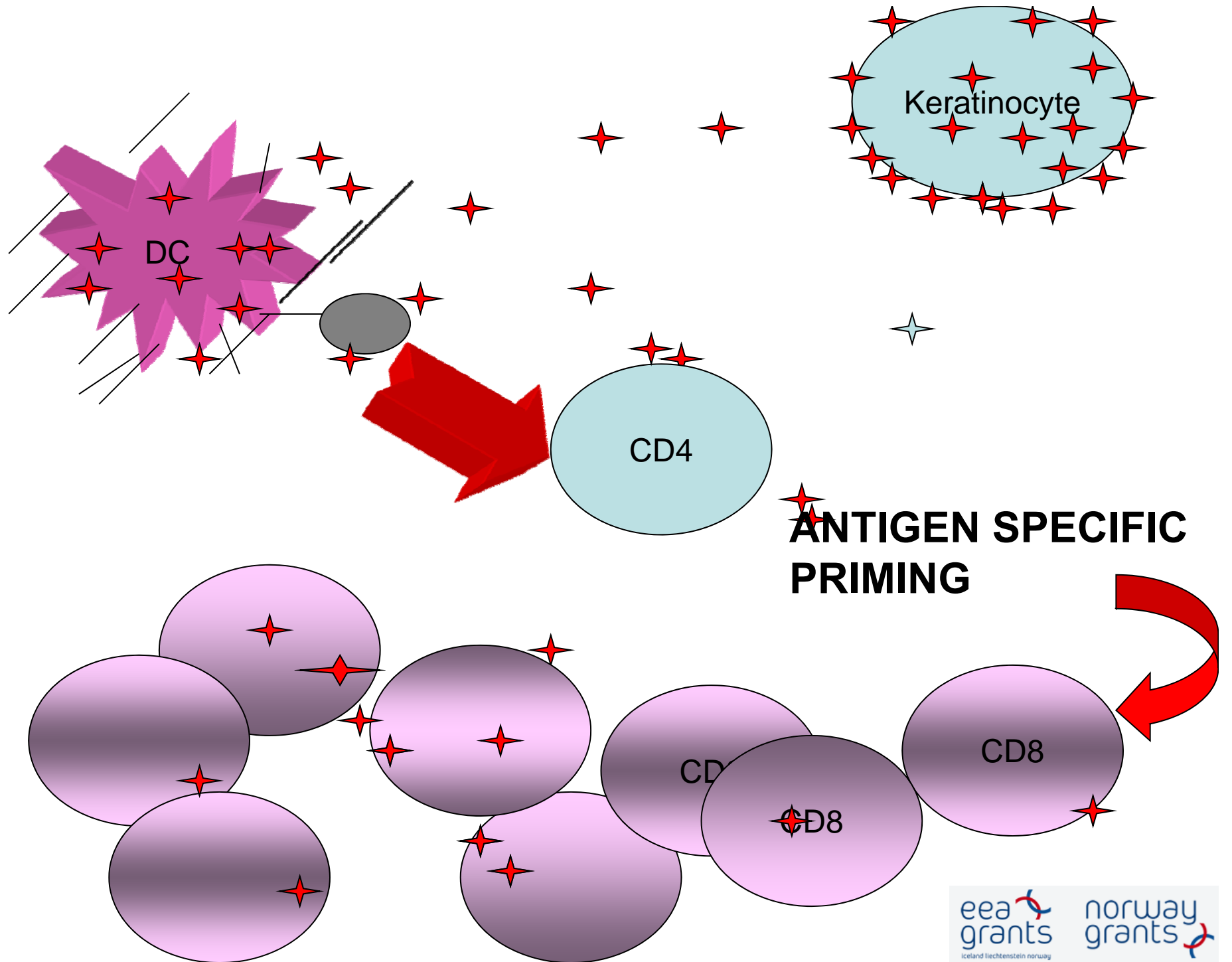
Contact dermatitis

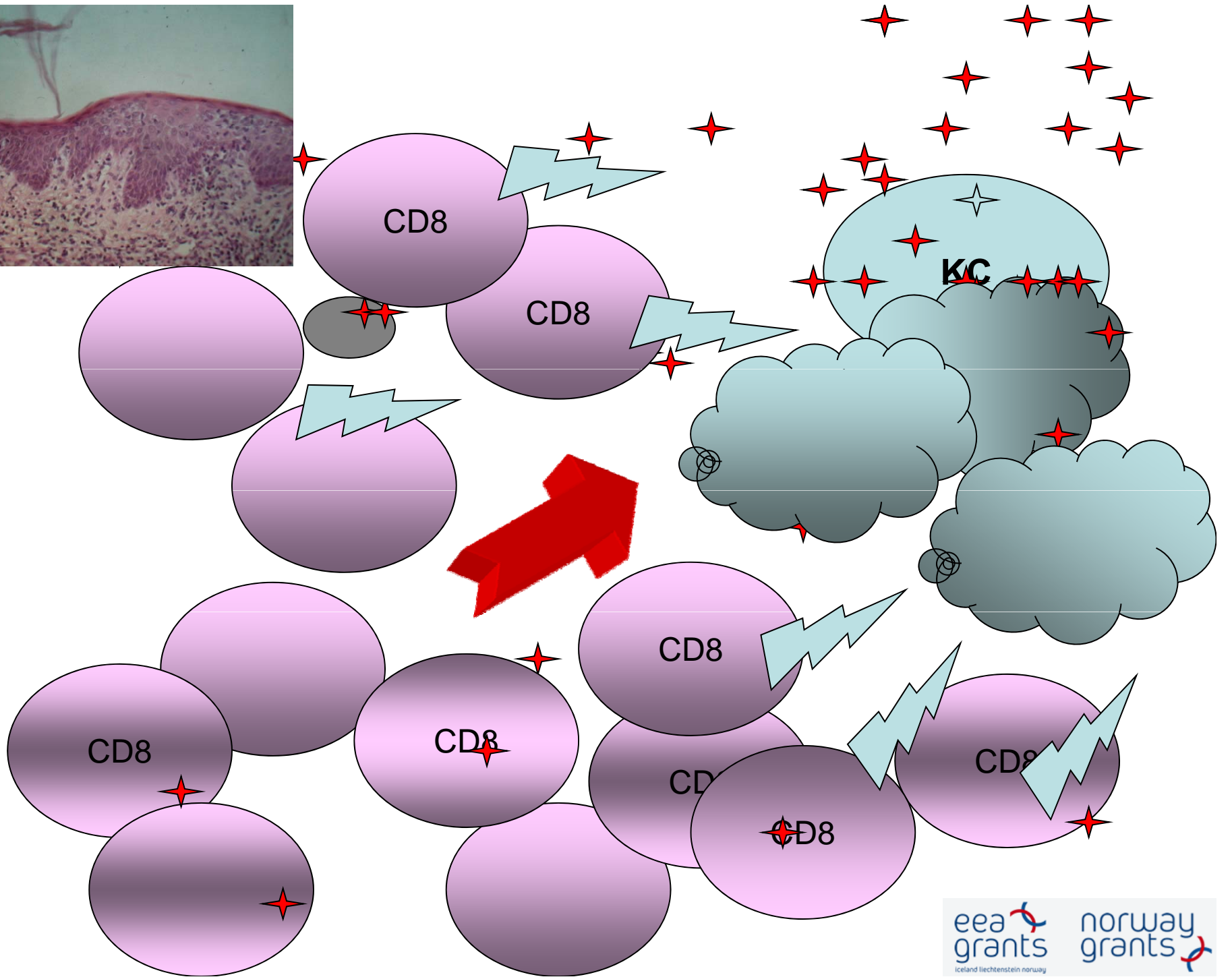
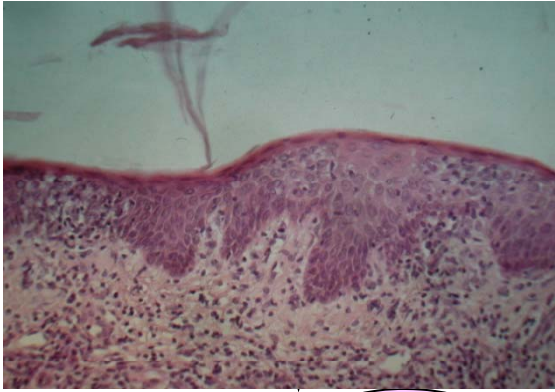
- **Effector phase:**
- Activated, proliferated antigen-specific T-cells: migrate back to the skin (epidermis)

Eczema-dermatitis

Hapten: Chromate,
Nickel, etc...

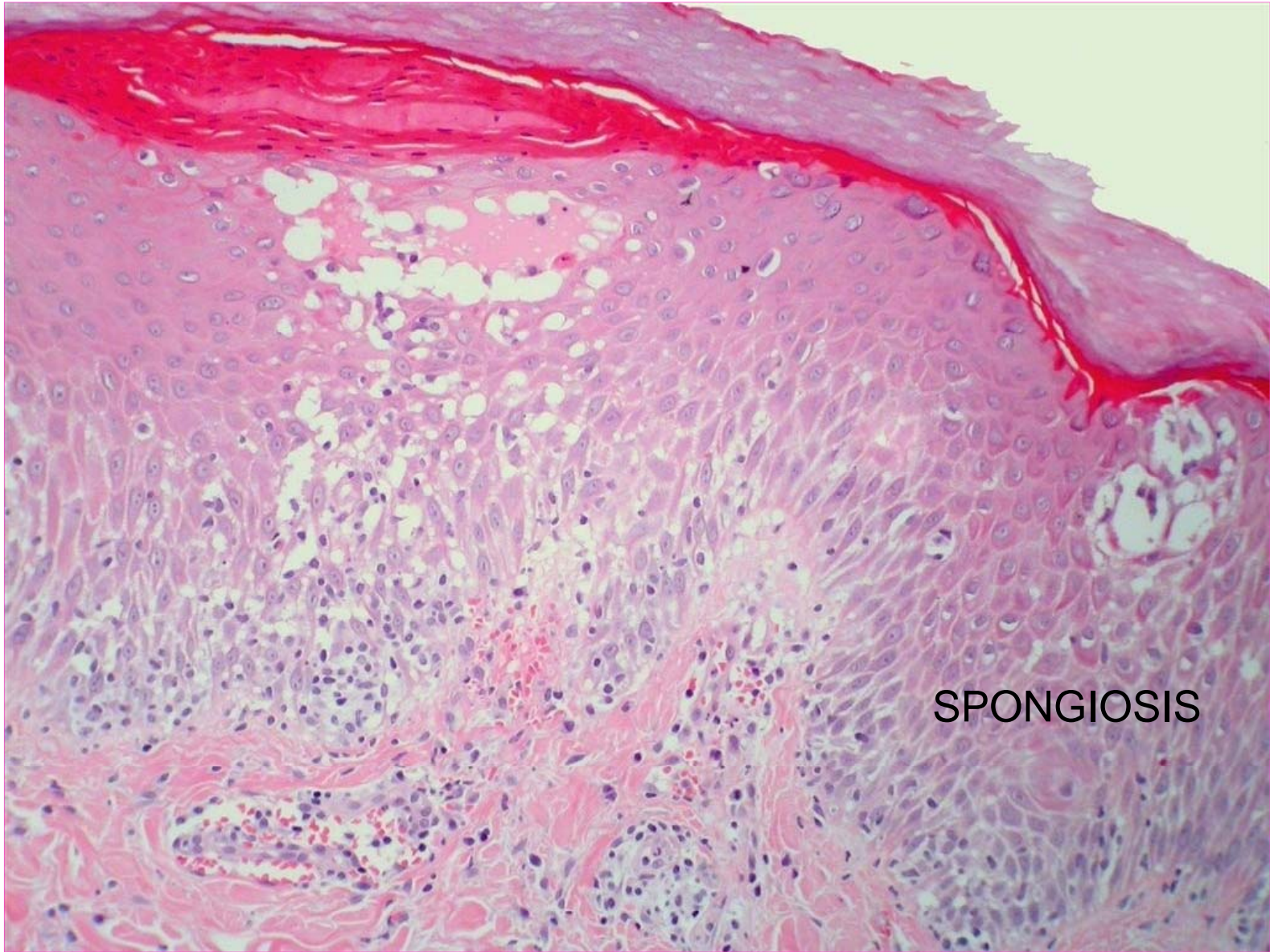






Contact eczema/dermatitis

*Spongiotic vesicle due to
immune reaction*



SPONGIOSIS

TYPE IV.

- **CONTACT DERMATITIS /sensitisation to certain simple chemicals/**
- **REJECTION OF TRANSPLANTATED TISSUE**
- **ALLERGIC REACTION TO CERTAIN BACTERIA, VIRUSES AND FUNGI**

CONTACT DERMATITIS

- HAPTENS:
STIMULATE THE
LANGERHANS
CELLS--increased
cytokin synthesis
- ACTIVATED
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CELLS LEAVE THE
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NODE: they present
the MHC-coupled
antigen to T cells

Contact dermatitis

- **Effector phase:**
- Activated, proliferated antigen-specific T-cells: migrate back to the skin (epidermis)

Haptens

- Small molecules (<500 d)
- Must bind to carrier proteins on the Langerhans cell
- 3000 chemicals are well documented as specific causes of allergic contact dermatitis

Eczema/dermatitis

- Common, non-infective inflammatory disorder
- May be provoked: by external or internal factors
- **Eczema-dermatitis-eczematous dermatitis are synonymous terms**

Clinical features

- Itching
- Exuding (weeping)
- Later: crusting, scaling area of inflammation

acute/subacute dermatitis

Hand eczema/dermatitis

Secondary lesions

- Erosion
- Superinfection
 - Impetiginisation
 - Erysipelas
 - Fissure
 - Secondary sensibilisation: contact, bacterial

Allergic contact dermatitis (ACD)

- Delayed type of induced sensitivity resulting from cutaneous contact with a specific allergen to which the patient developed a specific sensitivity
- Causes: small molecules- haptens- (500 d)
- More than 3000 chemicals are documented as specific causes of ACD

Causes of allergic contact dermatitis

- Approximately 25 chemicals appear to be responsible for as many as one half of all cases of ACD
- Poison ivy- in USA
- Nickel is the leading cause of ACD in the world –
- Clinically: manifested as dermatitis at the sites where nickel containing materials are worn (earrings, necklaces)

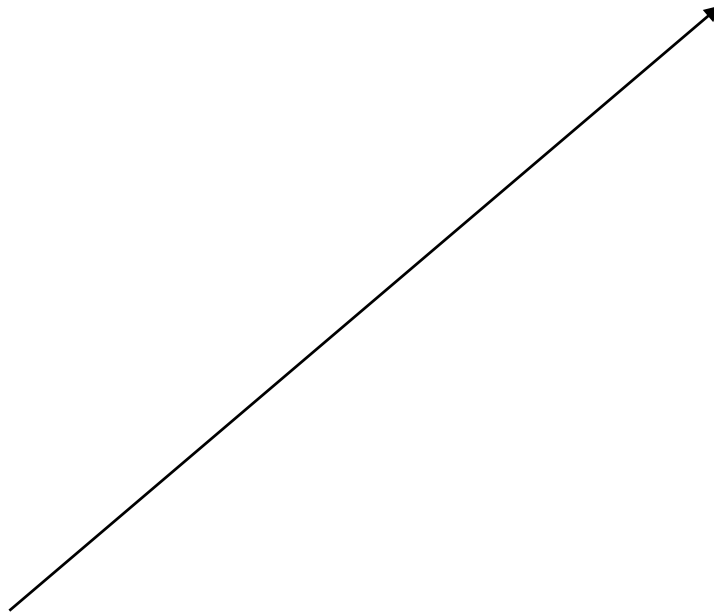
Occupational allergy

- typically is manifested as hand dermatitis
- Nickel as occupational allergen:
hairdressers, retail clerks, domestic cleaners, metalworkers
- Rubber gloves: chemicals in rubber gloves: clinical symptoms typically occurs on the dorsal aspects of the hand

- Dyes, permanent press and wash and wear chemicals added to textiles typically develop dermatitis on the trunk, maximally on the lateral sides
- Preservative chemicals added to cosmetics, moisturizers, topical medication –
- Fragrances in cosmetics
- Mercury based dental amalgam filling (due to elemental mercury vapour)

inflammation

Scaling, hyperkeratosis



- Nickel- jewelry
- Chromate-(in cement)- in bricklayers
- Formaldehyde-as preservative chemical, widely used in shampoos, lotions, moisturizers, cosmetics
- Fragrances: in cosmetics, perfumes, colognes, aftershaves, deodorants, soaps
- Mercury.: in amalgam fillings, teething-powder, antiparasitic drugs

Allergic contact dermatitis-fragrance in deodorant

vesicle



bulla



Contact dermatitis

inflammation

Contact dermatitis due to topical remedies

- chlorocid
- phenylbutazon
- neomycin
- iodine
- Preservatives:
paraben
- Kathon CG
- propylenglycol
- lanolin
- salicylat
- propolis
- resorcin
- hexachlorophen
- topical corticosteroids

angioedema

Phenylbutazon

Fastum gél

Eczema/dermatitis

- **Contact**
- Microbial
- Seborrhoic
- Atopic

Nummular dermatitis

NUMMULAR PLAQUES



Nummular dermatitis (eczema microbiale)

- ALLERGEN:
- BACTERIUM PROTEIN,
POLYSACCHARID
- LIPID
- NUCLEOPROTEIN
- MUCOPEPTID

NUMMULAR DERMATITIS

Contact-photocontact dermatitis

Dyshidrotic eczema, pompholyx

- Morphologic term
- Deep-seated vesicles on the sides of the fingers, on the palms
- Cause: ICD, allergic contact dermatitis

DYSIDROTIC ECZEMA

TYPE I: ANAPHYLACTIC HYPERSENSITIVITY

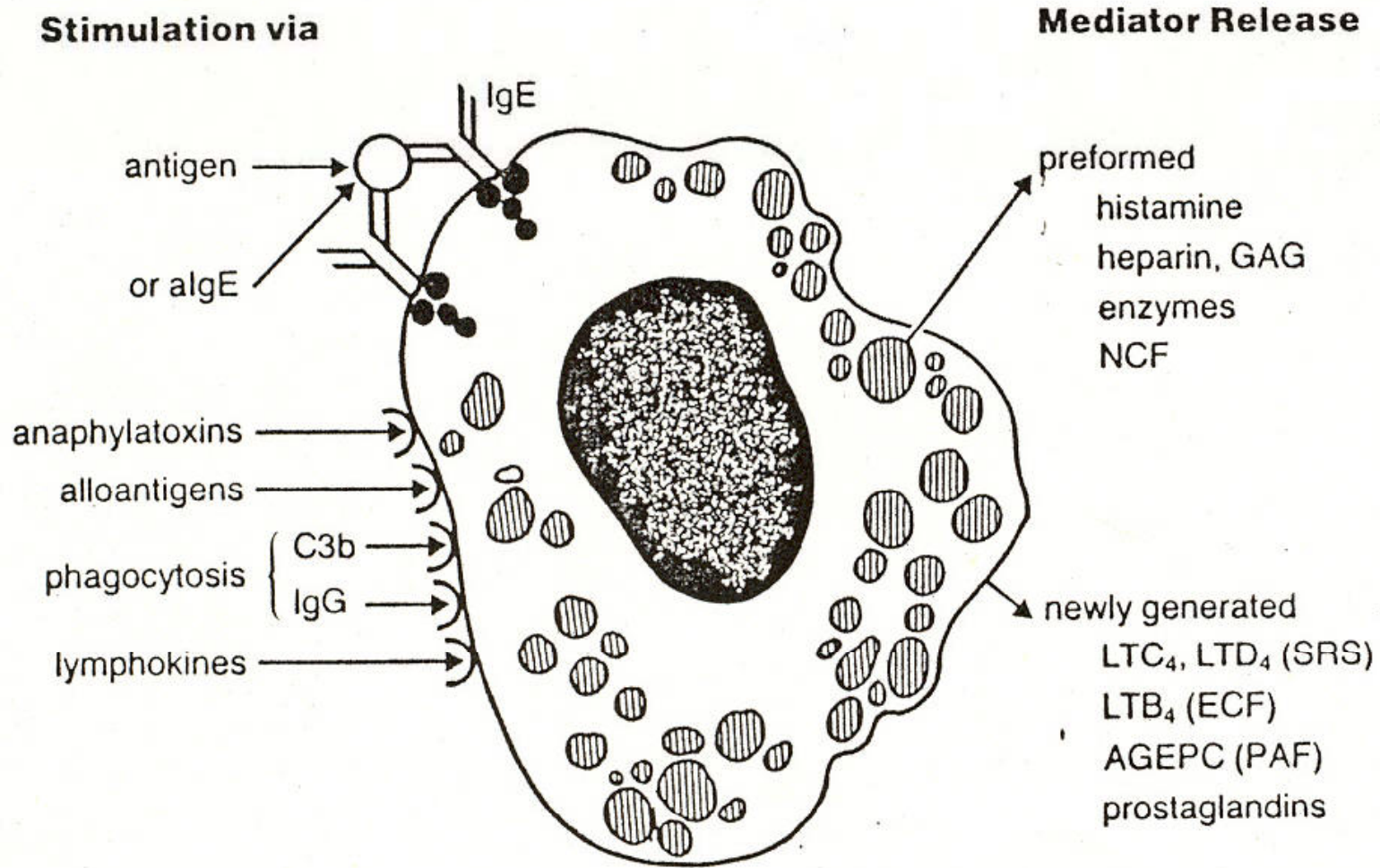
- GENERALISED ANAPHYLAXIS:
- CONSTRICTION OF BRONCHIOLUS,
BRONCHUS
- SMOOTH MUSCLE CONTRACTION
- CAPILLARY DILATATION
- HISTAMIN

Urtica- wheal

HISTAMIN RELEASE

- **IMMUNOLOGICAL**
- **IGE CROSSBINDING**
- C3A, C5A
/immunoglobulin
aggregates, IC,
endotoxin,
polysaccharid,

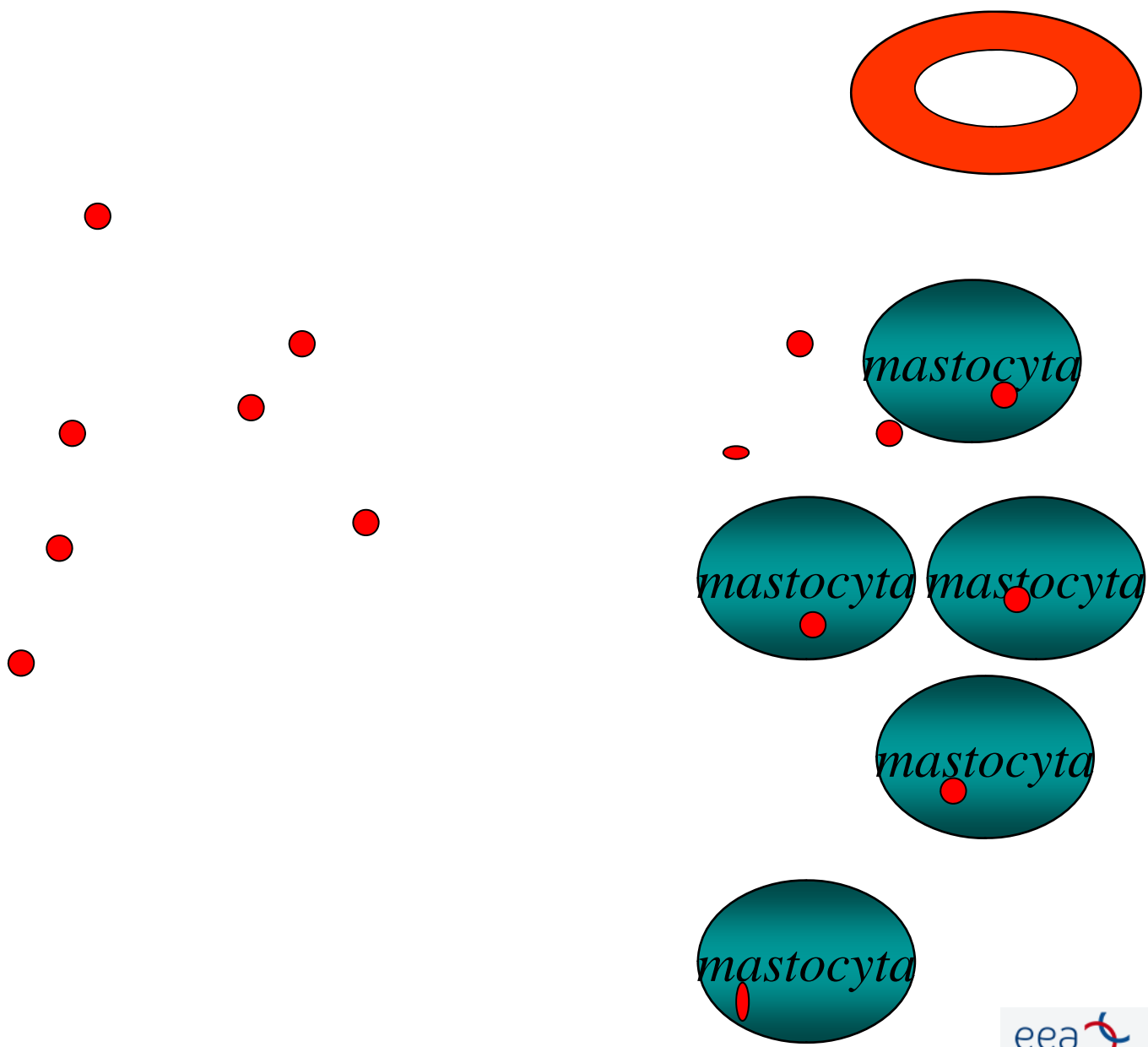
- **NON
IMMUNOLOGICAL:**
- Drugs, foods,
chemicals
- arachidonsav
acs:cyclooxygenase
inhibitors /aspirin/
- cyclic nucleotids
/cAMP,
phosphodiesterase/



MASTOCYTE

I.TYP. ANAPHYLACTOID, REAGIN reaction

- **ANTIBODY:** IGE
- **ANTIGEN:** AEROALLERGEN, POLLEN, FOOD, DRUG
- **CLINICAL MANIFESTATION:** URTICA, ASTHMA, RHINITIS, CONJUNCTIVITIS, DIARRHOEA, ANAPHYLACTIC SHOCK
- **ATOPY**
- **ATOPIC DERMATITIS**



Urtica- wheal

HISTAMIN

- INCREASE IN VASCULAR PERMEABILITY
- END ARTERIOLA DILATATION
- NERVE ENDINGS STIMUALATION
- BRONCHUS SPASMUS
- HEADACHE, GASTRIC SECRETION INCREASE

MAST CELL MEDIATORS

- **PREFORMED:**

- HISTAMIN
- HEPARIN
- PAF
- EOSINOPHIL,
NEUTROPHIL
CHEMOTACTIC
FACTORS

- **NEWLY
SYNTHETISED:**

- LEUKOTRIEN
B4,C4,D4
- PROSTAGLANDIN
- THROMBOXAN

URTICARIA

- **PRURITIC WHEELS**
- **ACUTE DERMAL OEDEMA**
- **ANGIOEDEMA:
larger area of
oedema involving
the dermis and
subcutis**

URTICARIA

- **IMMUNE
/ALLERGIC/**

- **NON-IMMUNE**

Classification of urticaria on the basis of its duration, frequency and causes

- A. Spontaneous urticaria
 - 1. acute urticaria
 - 2. chronic urticaria
 - -chronic continuous urticaria
 - -chronic recurrent urticaria

- B. Physical urticaria
 - 1.dermographic urticaria
 - 2.delayed pressure urticaria
 - 3.cold contact urticaria
 - 4.heat contact urticaria
 - 5.solar urticaria
 - 6.vibratory urticaria/angioedema

- C. Special types of urticaria
- 1.cholinerg urticaria
- 2.adrenerg urticaria
- 3.contact urticaria (allergic or pseudoallergic)
- 4.aquagenic urticaria

- D. Different diseases related to urticaria
- 1. urticaria pigmentosa
- 2. urticarial vasculitis
- Familial cold urticaria (a vasculitis)

ACUTE URTICARIA

- **SUDDEN ONSET**
- **IGE MEDIATED TYPE I. REACTION**
- **ALLERGEN:FOOD /egg, fish /**
- **DRUG**
- **?**

Chronic urticaria

- The cause often remains elusive even after thorough and persistent investigation

Urtica

CHRONIC IDIOPATHIC URTICARIA

- **AUTOANTIBODIES TO IGE**
- **AUTOANTIBODIES TO IGE
RECEPTOR**

Urtica- wheal

Urtica

URTICARIA-MANAGEMENT

- **any underlying cause should be eliminated**
- **provoking factors /aspirin, food, drug, swimming/ are to be avoided**
- **underlying diseases /malignant tumors, autoimmune diseases/ are to be treated**

Urtica

ANAPHYLACTIC SHOCK

- **ADRENALINE /IM/**
- **0,5-1,0 MG: 0,5-1,0ML OF 1/1000**

Angioneurotic oedema

Food allergy, intolerance

- Allergy:
- IgE mediated
- Oral pruritus, oedema, nausea, vomitus, abdominal pain, diarrhoea, asthma, rhinitis, urticaria, angineurotic oedema, anaphylaxis

- Intolerancia:
- Pharmecogenetic, toxic, anyagcsere, v.
- Histamin containing foods
- tyramin- migraine
- Na-glutamat:flush, headache, abdominal pain
- Laktase deficiency: diarrhoea

I.TYP. ALLERGIC DISEASES: TREATMENT

- **ALLERGEN**
- **IGE SYNTHESIS**
- **MAST CELL
DEGRANULATION**
- **MEDIATOR
INHIBITION**
- **avoidance**
- **hyposensibilisation**
- **Mast cell membrane
stabilization /Na-
chromoglykát/**
- **antihistamines**