Immune disorders of the skin

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This Lecture was loaded in blackboard and you can find the material in: Jawetz, Meinik & Adelberg's MEDICAL MICROBIOLOGY, 27 th Edition & Essential of Clinical Immunology, 6th Edition

Learning objectives:

- ✓ To describe normal skin components
- ✓ Understand skin disorders mediated by T-cells
- ✓ Explain autoimmune skin diseases
- ✓ Describe immune skin disorders associated with systemic diseases

Skin components

LO.1

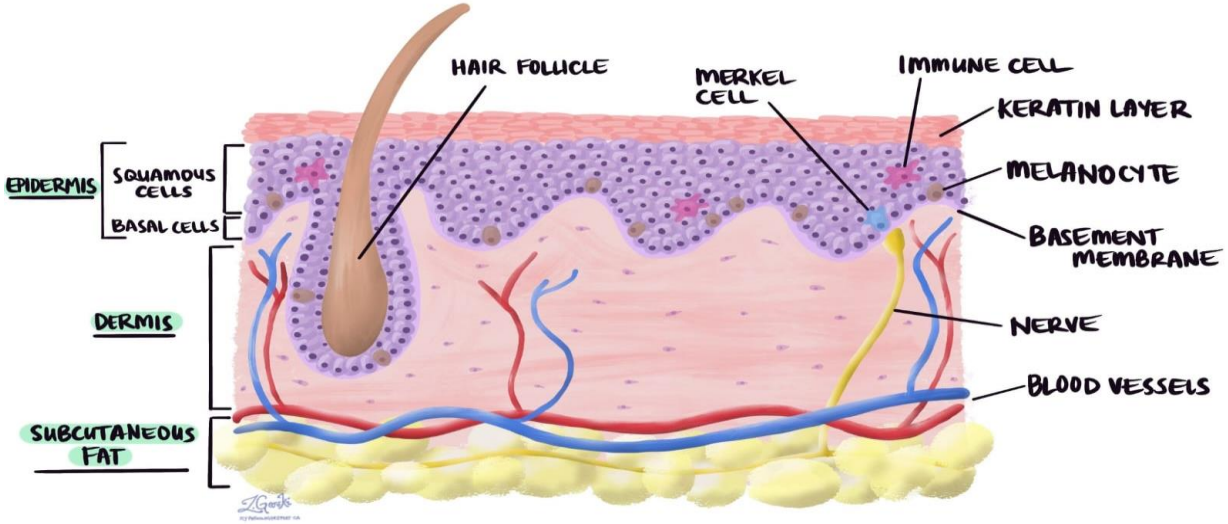
- Epidermis (keratinocytes)
- Dermis (vascular)

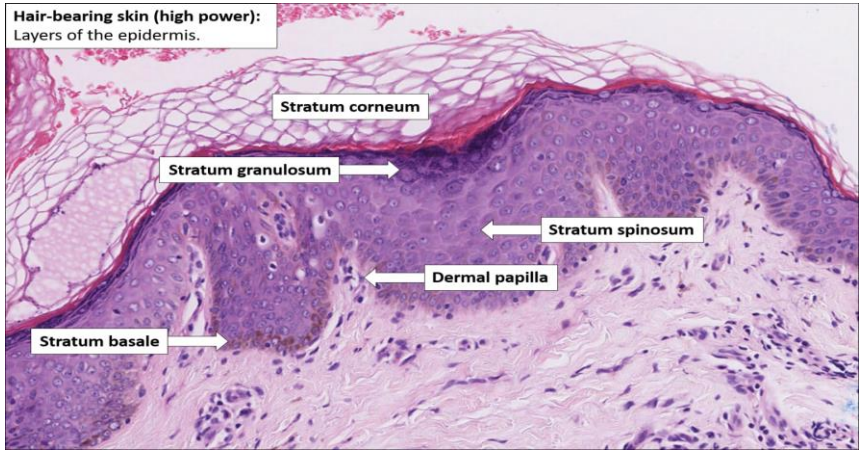
- Keratinocytes: in response to injury or ultraviolet radiation these cells produce cytokines and other inflammatory mediators that:

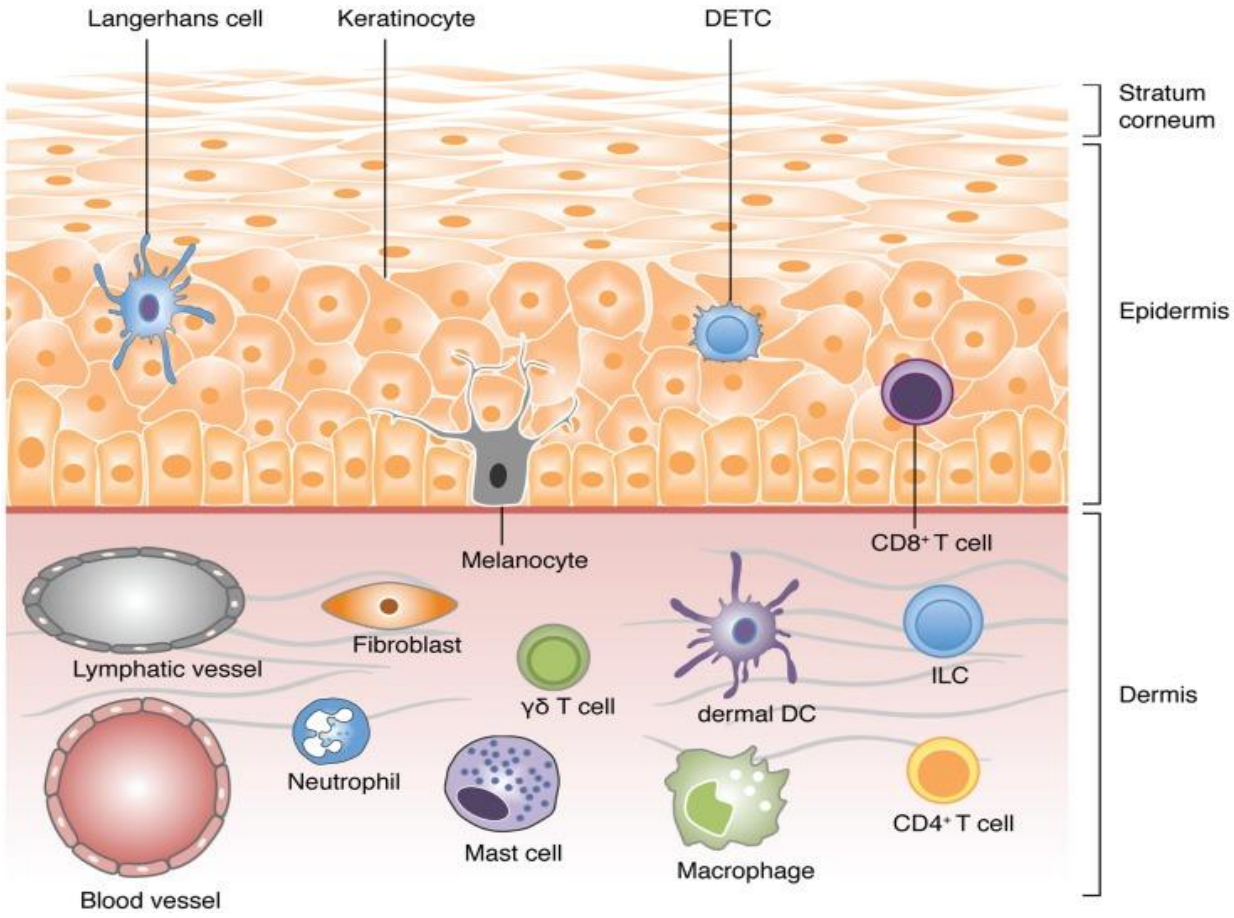
1. increase vascular permeability
2. attract and activate immune cells
3. induce the expression of adhesion molecules on nearby endothelial cells to allow immune cells access to the damaged tissue.

Skin components

LO.1







Immune disorders of the skin

LO.2

Immune disorders of the skin can be classified into:

I. T-cell mediated skin diseases
II. Autoimmune skin disease
III. Skin manifestations of systemic diseases

I. T-cell mediated skin diseases

LO.2

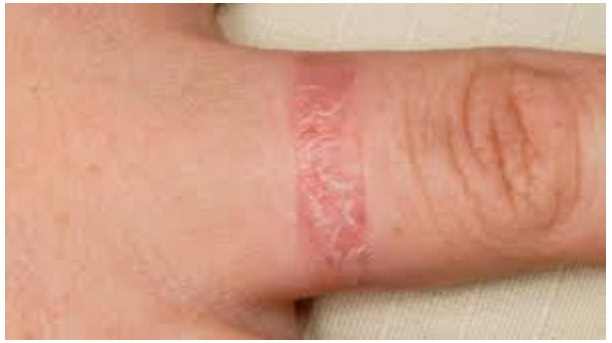
T cells play a central role in some of the most common skin diseases, the best understood are :

1. Contact dermatitis mediated by Th1 cells
2. Atopic eczema mediated largely by Th2 cells
3. Psoriasis also appears to be mediated largely by T cells

1. Contact dermatitis

LO.2

- Contact dermatitis is an inflammatory skin disease caused by Th1-cell-mediated (type IV) hypersensitivity to external agents that come into contact with the normal intact skin.



Some agents responsible for allergic contact dermatitis LO.2

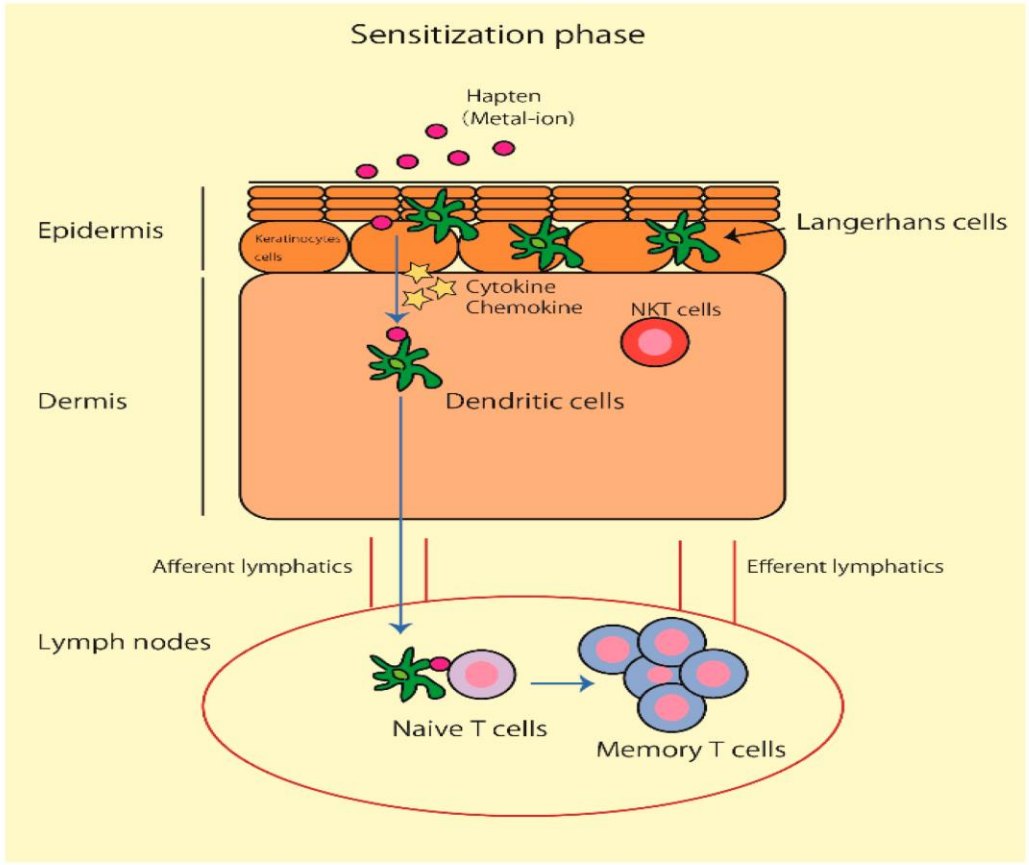
Material	Agent	Examples of exposure
Metals	Nickel	Clasps, necklaces, watch-straps
	Chromate	Cement (building site workers)
	Cobalt*	
Medications	'Para'-group chemicals	Benzocaine-type anaesthetics, sulphonamide antibiotics, PABA-containing substances (e.g. sunscreens) and oral hypoglycaemic agents(sulphonylureas)
	Phenothiazines	Phenothiazine-based antihistamines
	Neomycin	Topical antibiotics
Plastics	Epoxyresins, acrylates	Construction industry, glues
Rubber	Accelerators	Tyre industry, rubber gloves, shoes, clothing, household 'grips', etc.
Plants	Poison ivy (USA only)	
	Primula	
	Chrysanthemum	
	Geranium	
Cosmetics	Perfumes	
	Preservatives	
	Lanolin	

Agents causing contact dermatitis:

LO.2

Pathogenesis of .D

LO.2



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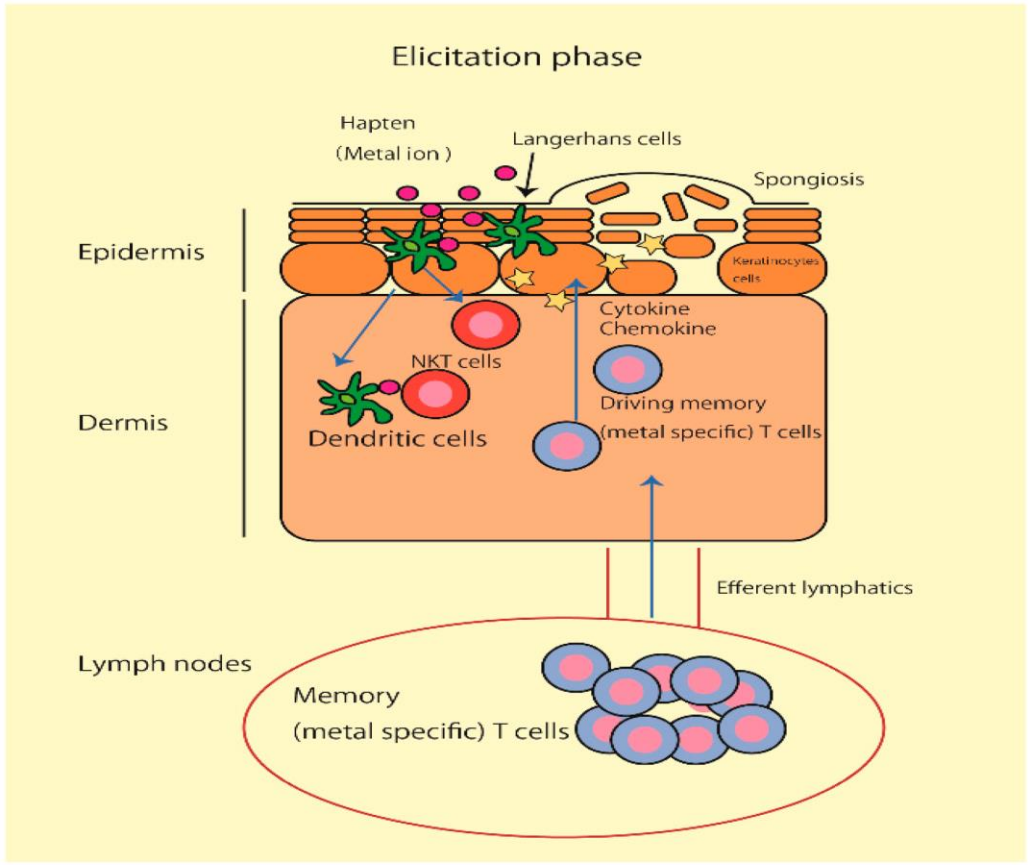

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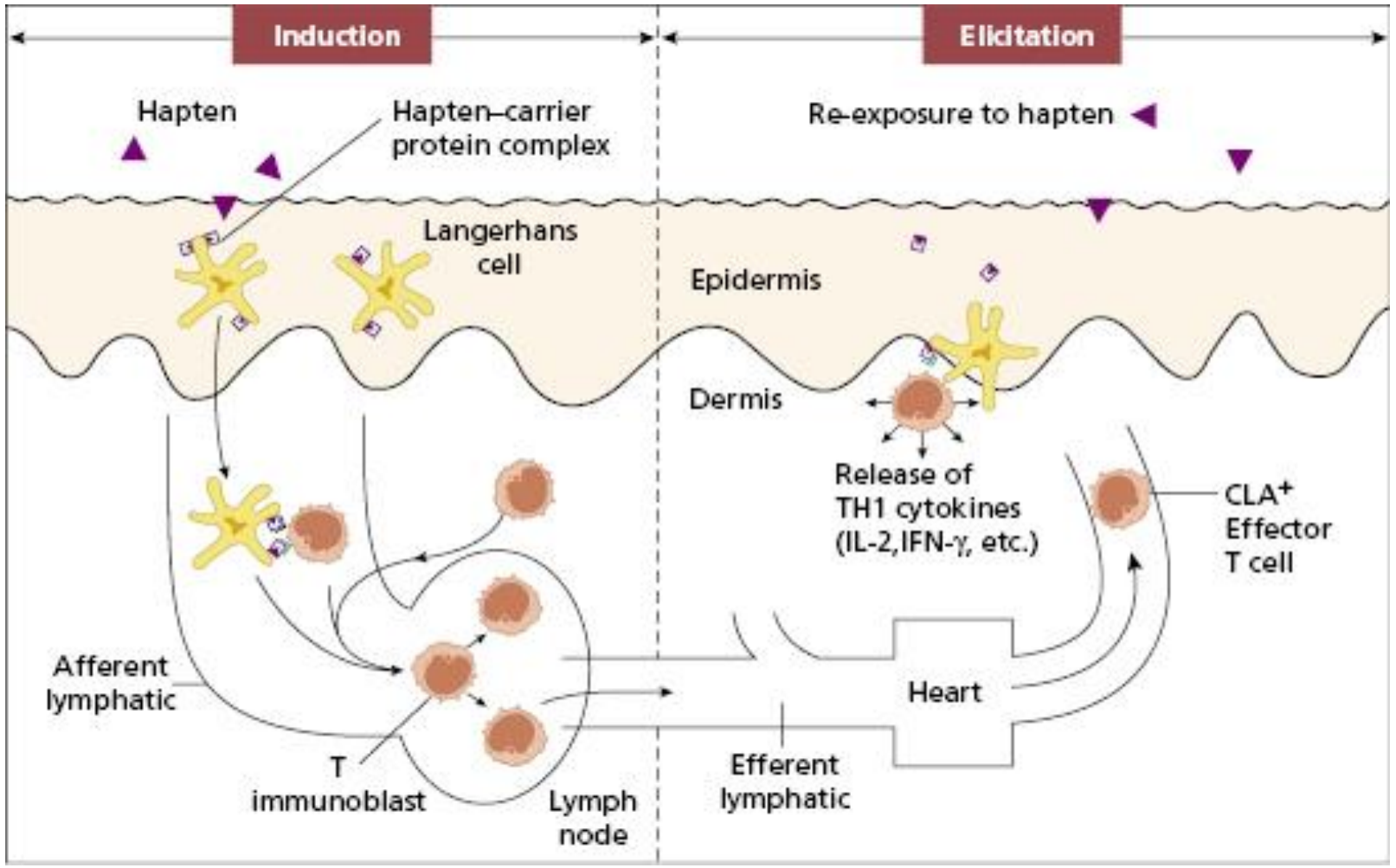
LO.2


Induction
Elicitation
Hapten
Hapten–carrier
protein complex
Re-exposure to hapten
Langerhans
cell
Epidermis
Dermis
Release of
TH1 cytokines
(IL-2,IFN-γ, etc.)
CLA+
Effector
T cell
Afferent
lymphatic
Heart
T
immunoblast
Lymph
node
Efferent
lymphatic

Diagnosis

LO.2

- Careful medical history
- The distribution of the lesions
- Patch testing

Management:

- Identification and elimination of the agents
- Antihistamine
- Corticosteroid
- Antibiotics

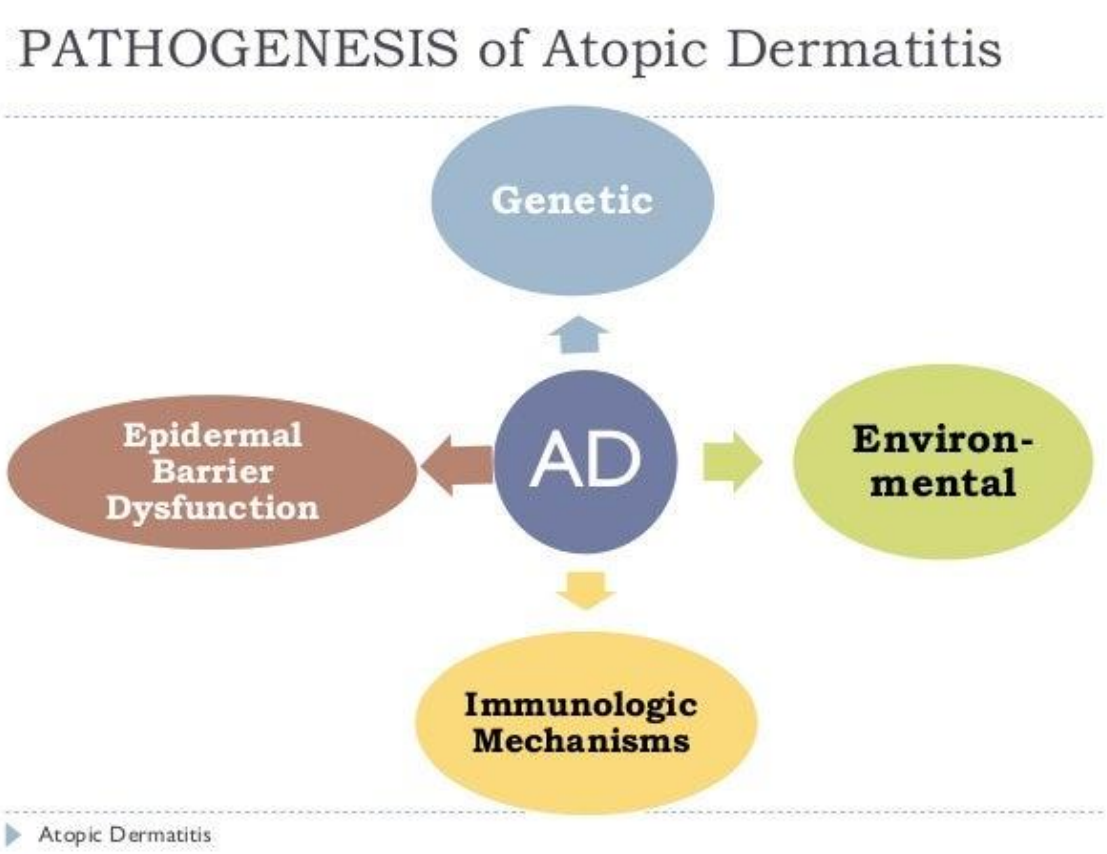
2.Atopic eczema

LO.2

- Is a common disorder, occurring predominantly in childhood, which appears to be caused by barrier dysfunction with subsequent altered exposure to common allergens that results in a Th2 hypersensitivity reaction.
- It is often associated with an elevated serum level of immunoglobulin E (IgE) and a personal or family history of atopy(eczema, asthma, and allergic rhinitis).

Predisposing factors

LO.2



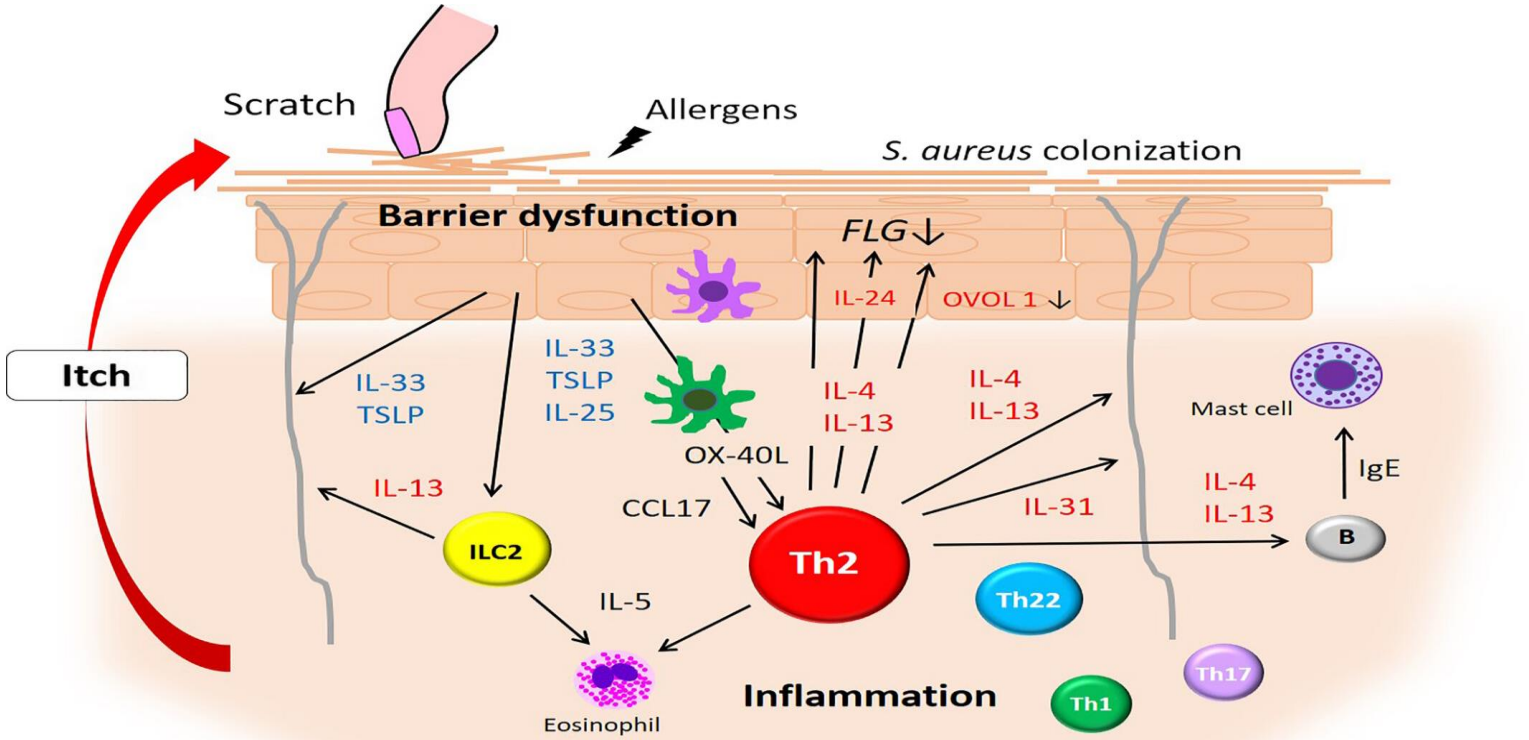
Pathogenesis of A.D

LO.2

- Abnormal skin barrier------→ penetration of allergens and microbes -----→ trigger an inflammatory cascade by stimulating Th2 cells excessively.
- Affected skin has increased concentrations of inflammatory cytokines and greater eosinophil infiltration.
- Allergens -----→ increase peripheral eosinophilia and serum IgE levels, ----→ increased release of histamine and vascular mediators -----→ edema and urticaria and thus cause persistence of the cycle of itch, scratch, and rash.
- Contact irritants such as sweating, wool, and detergents cause itching. Skin damage caused by scratching releases inflammatory cytokines and further stimulates itch.

Pathogenesis of A.D

LO.2



3. Psoriasis

LO.2

- It is a chronic, non-infectious skin inflammation involving keratin synthesis that results in psoriatic patches. The skin cells replicate at an extremely rapid rate resulting in formation of new cells that are produced 8 times faster than normal but the rate at which old cells sloughed off is unchanged, this cause the cell build up on skin surface, forming thick patches or plaque of red sores, covered with flaky, silvery white dead skin cells (scale). They usually appear on the elbows, knees, lower back and scalp.

- Age of incidence is between 15 and 30 years or 50 and 60 years and there is genetic predisposition.

Risk factors:

LO.2

- Stress
- Smoking, alcohol
- Trauma
- Obesity
- Hormonal changes
- Climate
- Autoimmune disease
- Medication – lithium salt, beta blockers

Clinical manifestation

LO.2

- The first sign is ‘red spot’ on the body.
- Patches of the skin is dry, swollen and inflamed covered with silvery flakes.
- Raised and thick skin.
- Pain, itching and burning.
- Yellow discoloration, pitting and thickening of the nails are noted if they are affected.
- Cracked and bleeding points, if the scale are scraped away.
- Koebner phenomenon – it develops at the site of injury such as scratch or sunburn.

Pathophysiology

LO.2

E/F

↓

Hyperactivity of T-cells

↓

Epidermis infiltration & keratinocyte proliferation

↓

Deregulated inflammatory response

↓

Large production of various cytokines

↓

Superficial blood vessels dilated and vascular engorgement

↓

Epidermal hyperplasia & improper cell maturation

↓

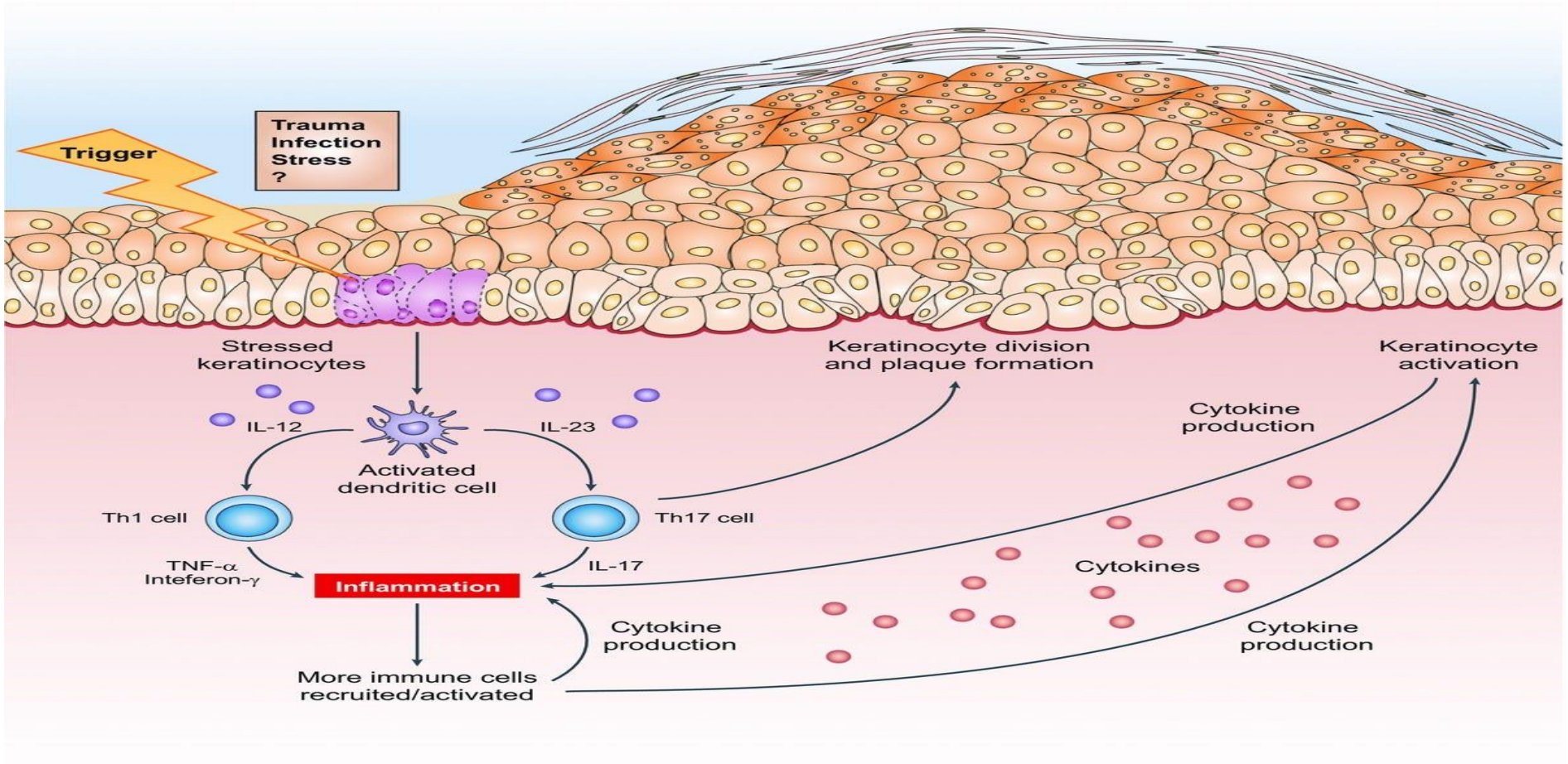
Fails to release adequate lipid which lead to flaking, scaling presentation of psoriasis lesion

↓

Silvery scale of the skin

Pathophysiology

LO.2



Diagnosis

LO.2

- Clinical examination
- Skin biopsy
- X-ray if joints are affected
- Complete blood count
- Comprehensive metabolic panel (kidney and hepatic function), pregnancy, tuberculosis, HIV and hepatitis tests may be considered if systemic treatment is planned

LO.2

Why it is important to consider pregnancy, tuberculosis, HIV and hepatitis tests if systemic treatment is planned for psoriasis?

II. Autoimmune skin disease

LO.3

- Many different antigens within the skin can be targeted, including several adhesion molecules, melanocytes and hair follicles.
- The disease phenotype varies accordingly, from life-threatening disruption of the integrity of the skin to patchy loss of pigmentation.
- Autoimmune skin disease include:

1. Bullous skin diseases
2. Vitiligo
3. Alopecia

LO.3

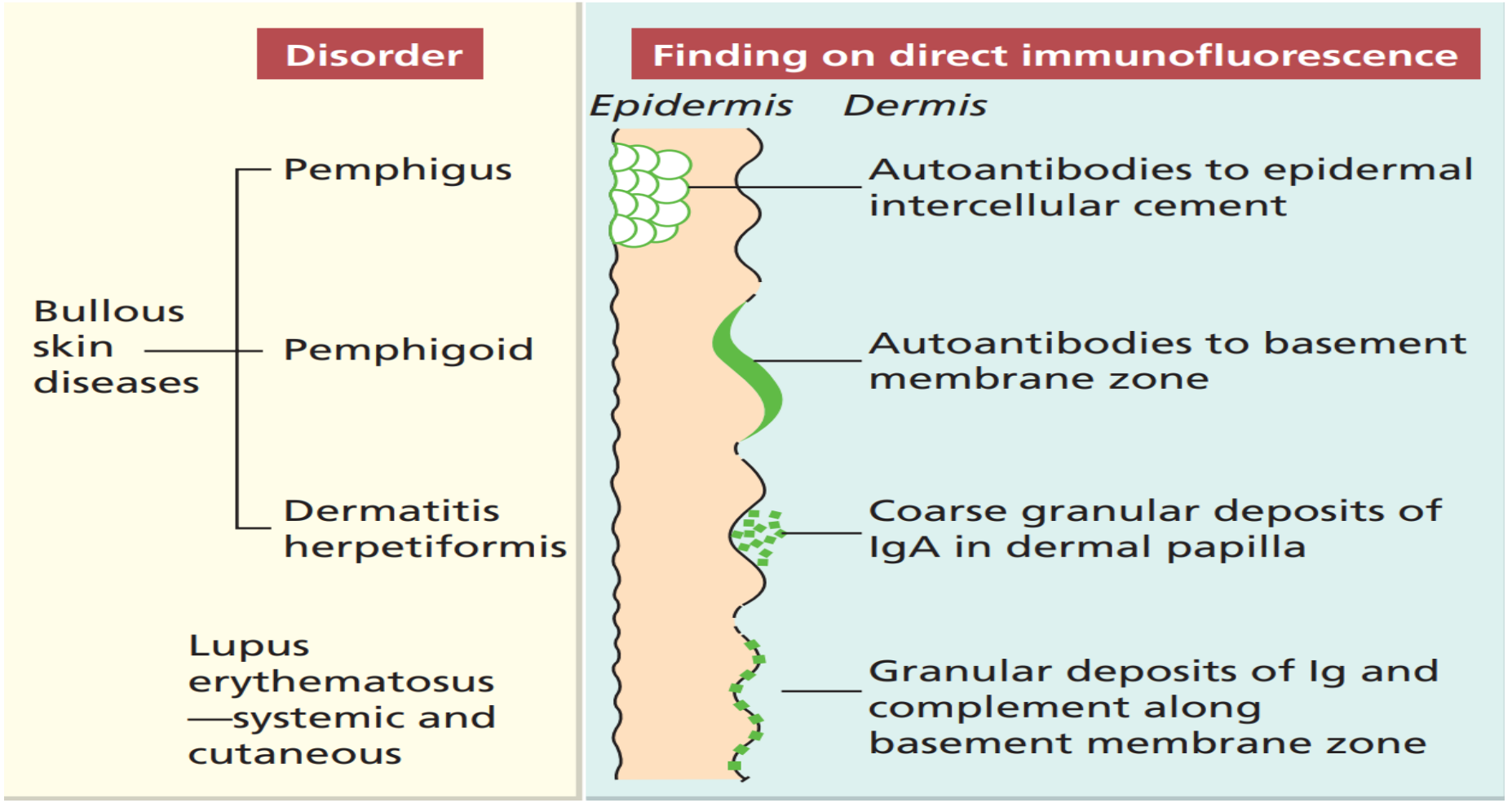
• 1. Bullous skin diseases :

Is a group of acantholytic conditions caused by autoantibodies against various epidermal cell junction proteins, commonly presenting with flaccid blisters, erosions or scaling, Caused by IgG or IgA autoantibody against epidermal antigens (commonly desmoglein 1 and desmoglein 3)

- Include:
- Pemphigus vulgaris,
- Bullous pemphigoid
- Pemphigoid gestationis
- Dermatitis herpetiformis

Bullous skin disease

LO.3



Pemphigus vulgaris:

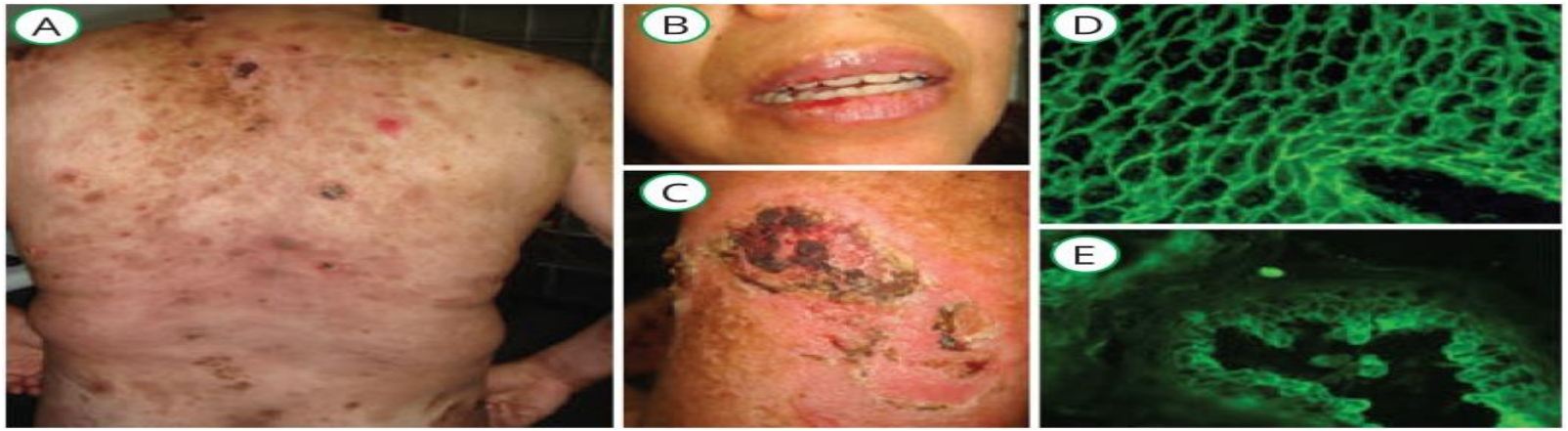
LO.3

Antibodies (IgG c lass) and complement (C3) react with the cell surfaces of keratinocytes in the epidermis

The main antigenic target is the adhesion molecule, desmoglein

The lesion:

Blisters, erosions and crusts (A, B, C), positive anti-epithelial antibodies detected and direct immunofluorescence shows intraepidermal blister with acantholytic cells (E).



LO.3

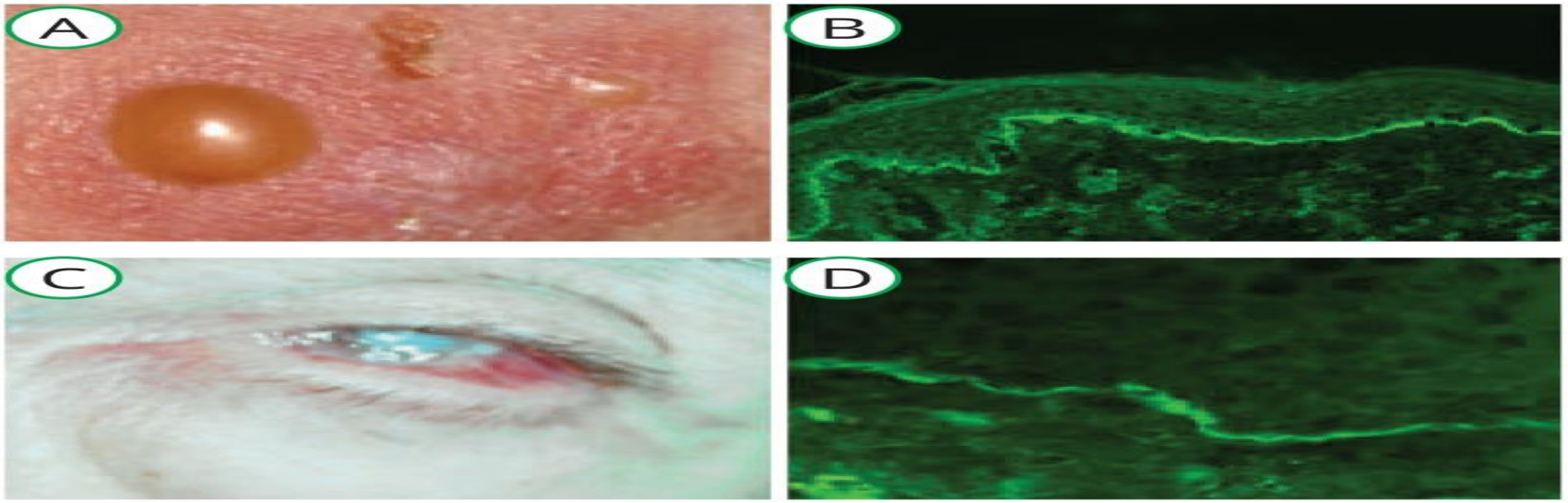
Bullous pemphigoid:

Patients have circulating antibodies to basement membrane zone (BMZ).

The lesion:

Blisters are large and tight and are surrounded by erythema and urticarial area fig:A &C.

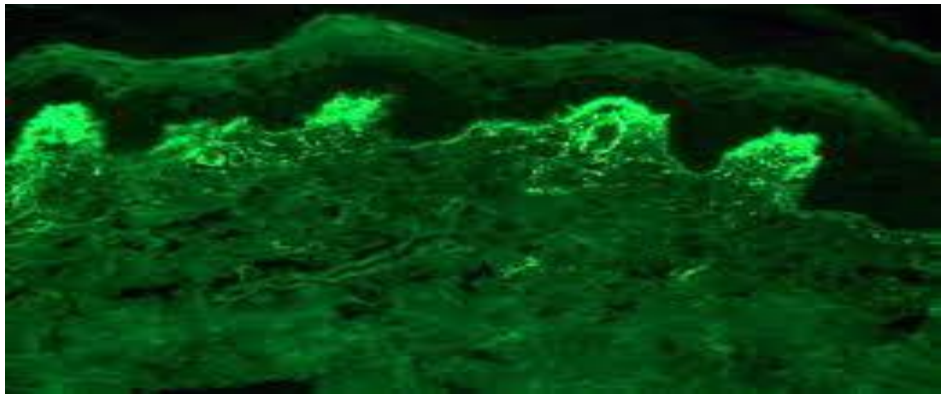
Immunofluorescence shows deposition of IgG and C3 as a continuous (‘linear’) band along the basement membrane zone fig: B&D.

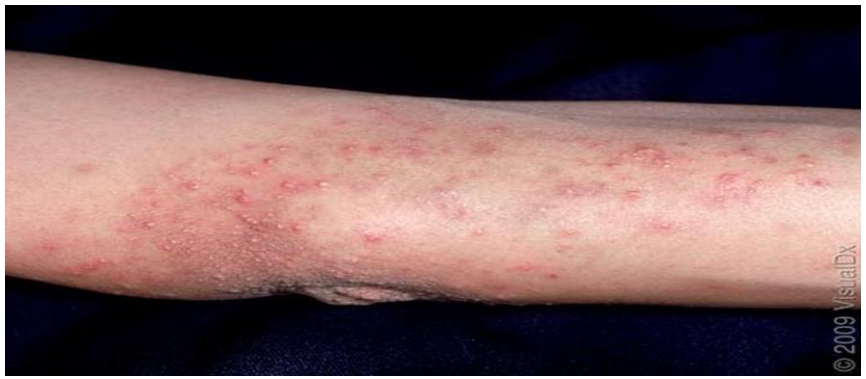


Dermatitis herpetiformis :

LO.3

- Dermatitis herpetiformis (DH) is characterized by groups of extremely itchy, small vesicles on extensor surfaces such as the elbows, knees, buttocks, neck and shoulders.
- Although most patients are aged 20–40 years at diagnosis, any age group can be affected.
- Direct immunofluorescence of skin in DH shows deposition of IgA in a granular fashion in the tips of dermal papillae.





Diagnosis

LO.3

Made on clinical, histopathologic, immunopathologic and serologic findings

1. Biopsy for H&E taken from the edge of the blister
2. Direct immunofluorescence (most sensitive)
3. Biopsy taken from the perilesional skin
4. Enzyme linked immunosorbent assay
5. Indirect immunofluorescence
6. Immunoblotting and immunoprecipitation (less used)

2. Vitiligo

LO.3

- Vitiligo consists of patches of skin depigmentation anywhere on the body. These changes result from loss of melanocytes from the epidermis via a process that is thought to be autoimmune.

- **Pathogenesis:** IgG antibodies to melanocytes and, in particular, to tyrosinase, a key enzyme in melanin synthesis, have been found in about 80% of patients with vitiligo and there are strong clinical associations with organ-specific autoimmune diseases, such as thyroid disease, diabetes mellitus, pernicious anemia and idiopathic Addison's disease

Vitiligo

LO.3

3. Alopecia areata

LO.3

- Alopecia is characterized by limited patchy loss of hair (alopecia areata) or loss of all scalp hair (alopecia totalis) or all body hair (alopecia universalis).
- Alopecia affects children and adults of all ages and races. Association with other organ-specific autoimmune diseases suggest that an autoimmune process may be responsible .
- Recent evidence suggests that alopecia areata can be considered a T-cell–mediated autoimmune disease in which the gradual loss of protection provided by immune privilege of the normal hair follicle plays an important role. Recently, genome-wide association studies have identified susceptibility loci common to alopecia areata in some immune genes, namely in the MHC and IL-2R.

III.Skin manifestations of systemic diseases :

LO.4

1. C1 inhibitor deficiency
2 .Vasculitis
3 .Cryoglobulinaemia
4 .Lupus erythematosus
5 .Systemic sclerosis

1. C1 inhibitor deficiency (Angioedema)

LO.4

2 .Vasculitis

LO.4

- inflammation of blood vessels that may associated with different underlying conditions include:

1.Drugs

2.Infections

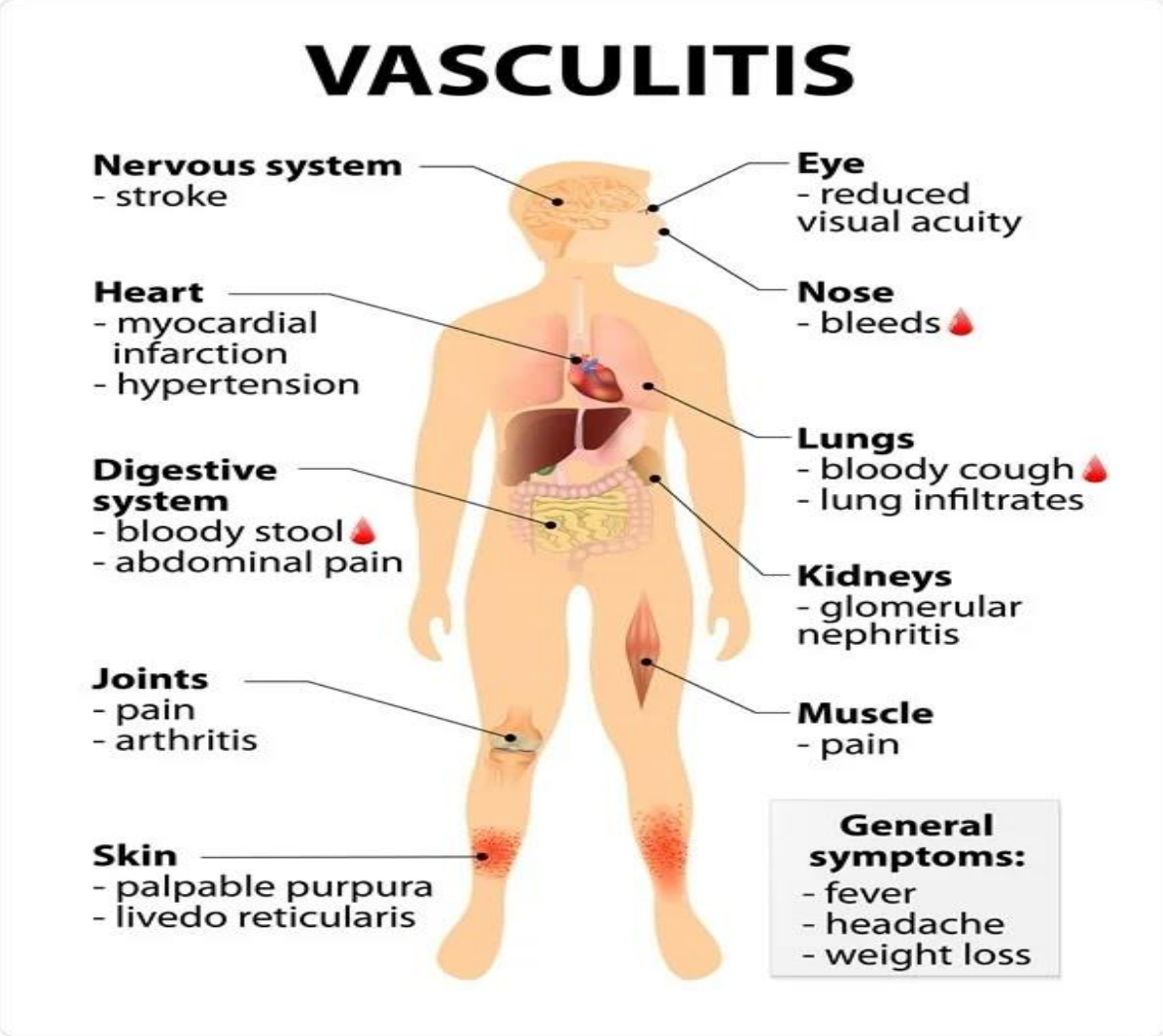
3. Injection of foreign proteins

4.Autoimmune disease

5. Cryoglobulinemia

The condition may results from circulating antigens that are produced on an intermittent or continuous basis; which lead to chronic immune complex-induced injury.

LO.4


VASCULITIS
Nervous system
- stroke
Heart
- myocardial infarction
- hypertension
Digestive system
- bloody stool
- abdominal pain
Joints
- pain
- arthritis
Skin
- palpable purpura
- livedo reticularis
Eye
- reduced visual acuity
Nose
- bleeds
Lungs
- bloody cough
- lung infiltrates
Kidneys
- glomerular nephritis
Muscle
- pain
General symptoms:
- fever
- headache
- weight loss

3.Cryoglobulinemia

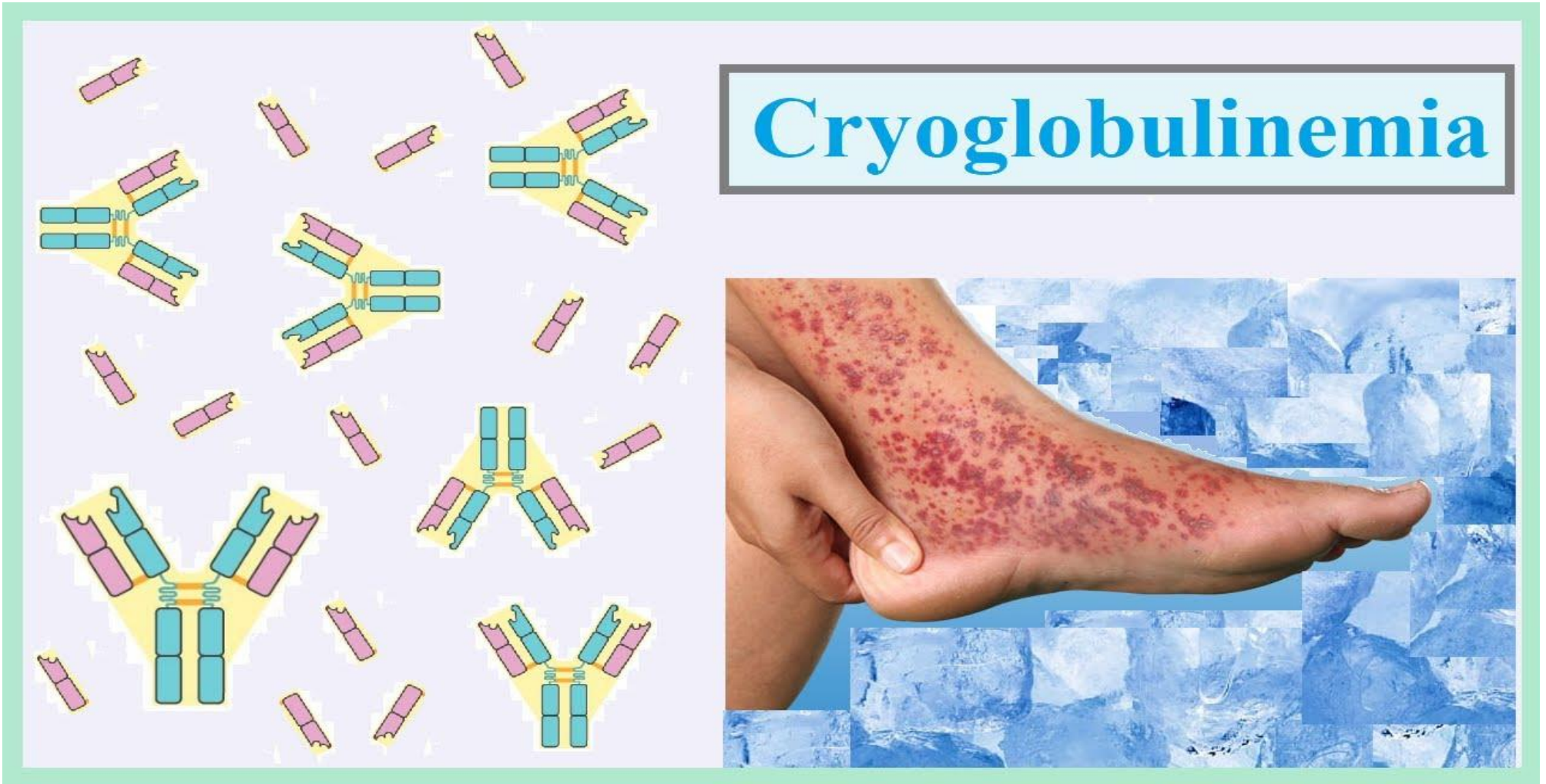
LO.4

- Cryoglobulin is a circulating protein, specifically immunoglobulin (i.e. IgG, IgM, IgA, or light chain), that clumps together or precipitates when exposed to cold and dissolves when warmed.

Symptoms

- bruising
- rashes, purpura
- skin ulcers
- gangrene
- joint pain, muscle pain
- weakness, fatigue
- Raynaud phenomenon

LO.4



4. Lupus erythematosus

LO.4

- The clinical features of lupus erythematosus (LE) range from a severe disease involving many organs, including the kidney, joints, brain and skin (SLE) to a benign, chronic, purely cutaneous form, called discoid lupus erythematosus (DLE).

Lupus erythematosus

LO.4

Characteristic features of the different forms of cutaneous lupus erythematosus (LE)

LO.4

	Discoid LE	Subacute cutaneous LE	Systemic LE
Usual age of onset, years	30–40	<40	<40
Skin features	Oedematous plaques with scaling	Widespread	Almost anything
	and follicular plugs	Symmetrical	
	Scarring	Non-scarring erythematous plaques	
	Face, ears, scalp	Upper chest, back, shoulders	
Systemic features	None	Joint pains, fever, malaise	Almost any organ affected
Antinuclear antibodies present in	25%	80%	95%
dsDNA antibodies present in	0%	30%	70–85%
Anti-Ro antibodies present in	<5%	70%	30%
Predominant HLA type	B7	B8, DR3	B8, DR3
Positive direct immunofluorescence of:			
Lesional skin	90%	40%	90%
Normal, sun-exposed skin	0%	20%	75%

5.Systemic sclerosis

LO.4

- Systemic sclerosis is a chronic fibrosing disease of unknown aetiology. It can affect the skin, blood vessels, musculoskeletal system and many internal organs. Since indurated and thickened skin is the most striking feature of the disease, the term scleroderma is often used as a synonym for systemic sclerosis.
- Autoantibodies to an enzyme important in controlling coiling of DNA superhelices are found almost exclusively in patients with systemic sclerosis.

LO.4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Scleroderma
Thick, waxy skin
Cleveland Clinic


THANK
YOU