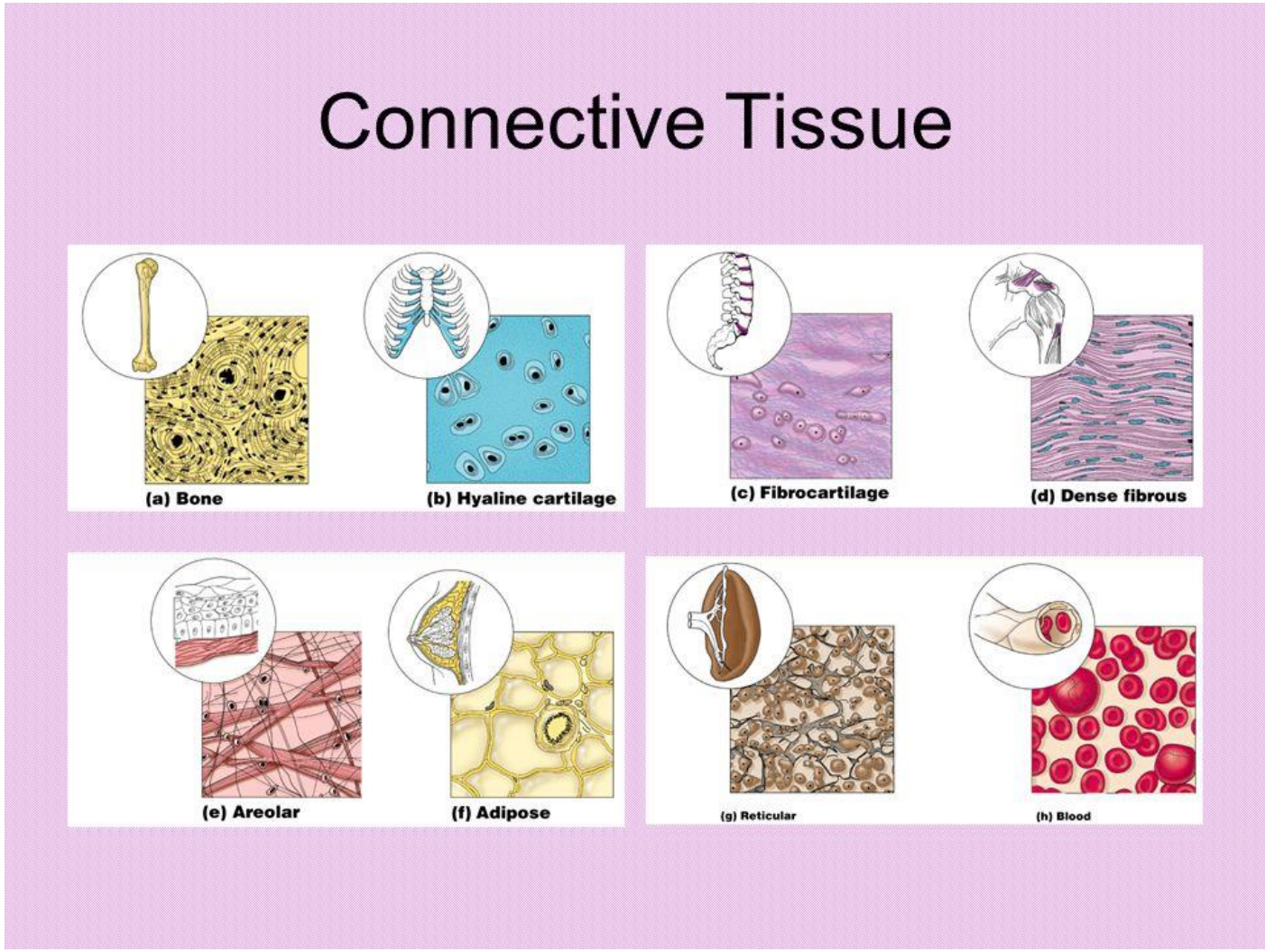
Lupus erythematosus

Agnieszka Kalińska-Bienias

Definition

Connective tissue diseases (collagenoses) - a group of inflammatory diseases with various symptomatology and autoimmune background in which the primary pathological changes include connective tissues



Classification

- Reumatoid arthritis
- **Lupus erythematosus (systemic, cutaneous)**
- **Scleroderma (systemic, limited - morphea)**
- **Dermatomyositis**
- Antiphospholipid Syndrome
- Sjögren Syndrome
- Mixed Connective Tissue Disease

Lupus erythematosus

Definition

Lupus erythematosus

autoimmune disease with a complex pathogenesis, in which the most important factor is the presence of antibodies against human own antigens located within the cell nucleus (antinuclear antibodies, ANA).

Main subsets of lupus erythematosus

→ *Cutaneous lupus erythematosus*

- *Discoid Lupus Erythematosus – DLE*

→ *Subacute Cutaneous Lupus Erythematosus - SCLE*

→ *Systemic Lupus Erythematosus, SLE*)

Fun fact: "Lupus" in Latin means wolf.
Relapses of the disease resemble wolf attacks

The joint features for all subsets of LE

- Typical skin changes
- Sensitivity to sunlight (UV radiation)
- Immunological features: (presence of antibodies)

→ Skin!!!: Ig deposits in granular and globular pattern along the dermal-epidermal junction (detected in lupus band test- LBT)

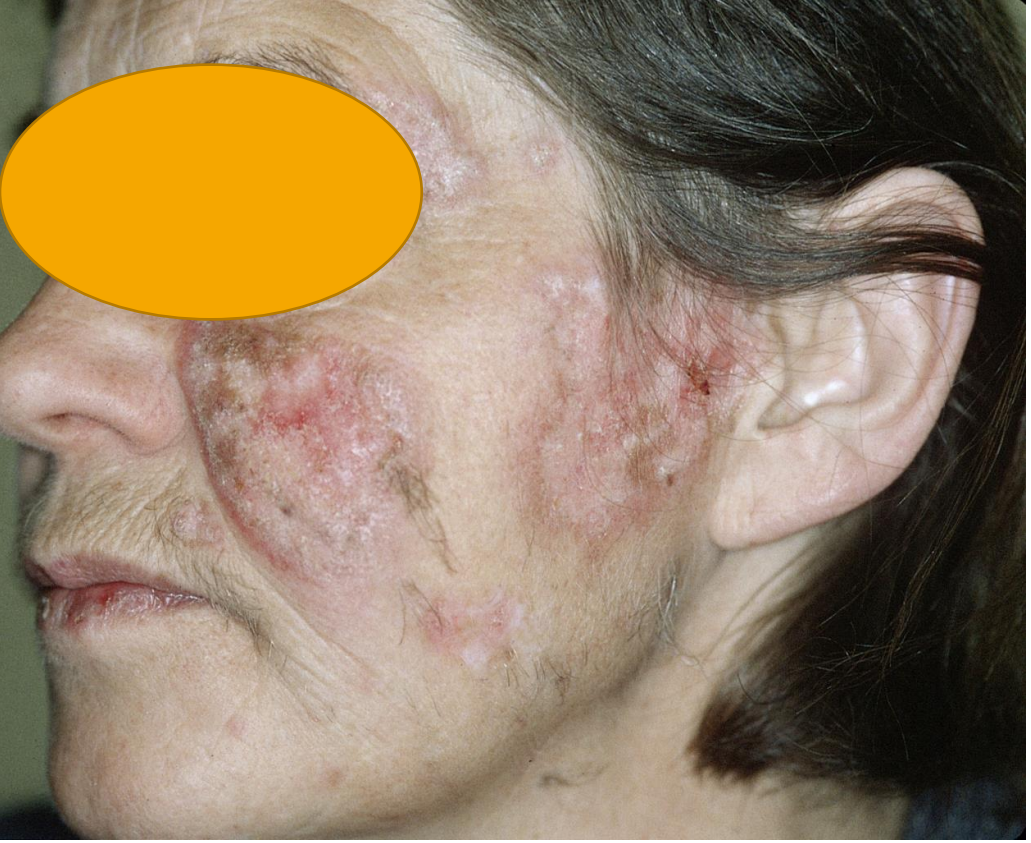
→ Serum!!! antinuclear antibodies (ANA)

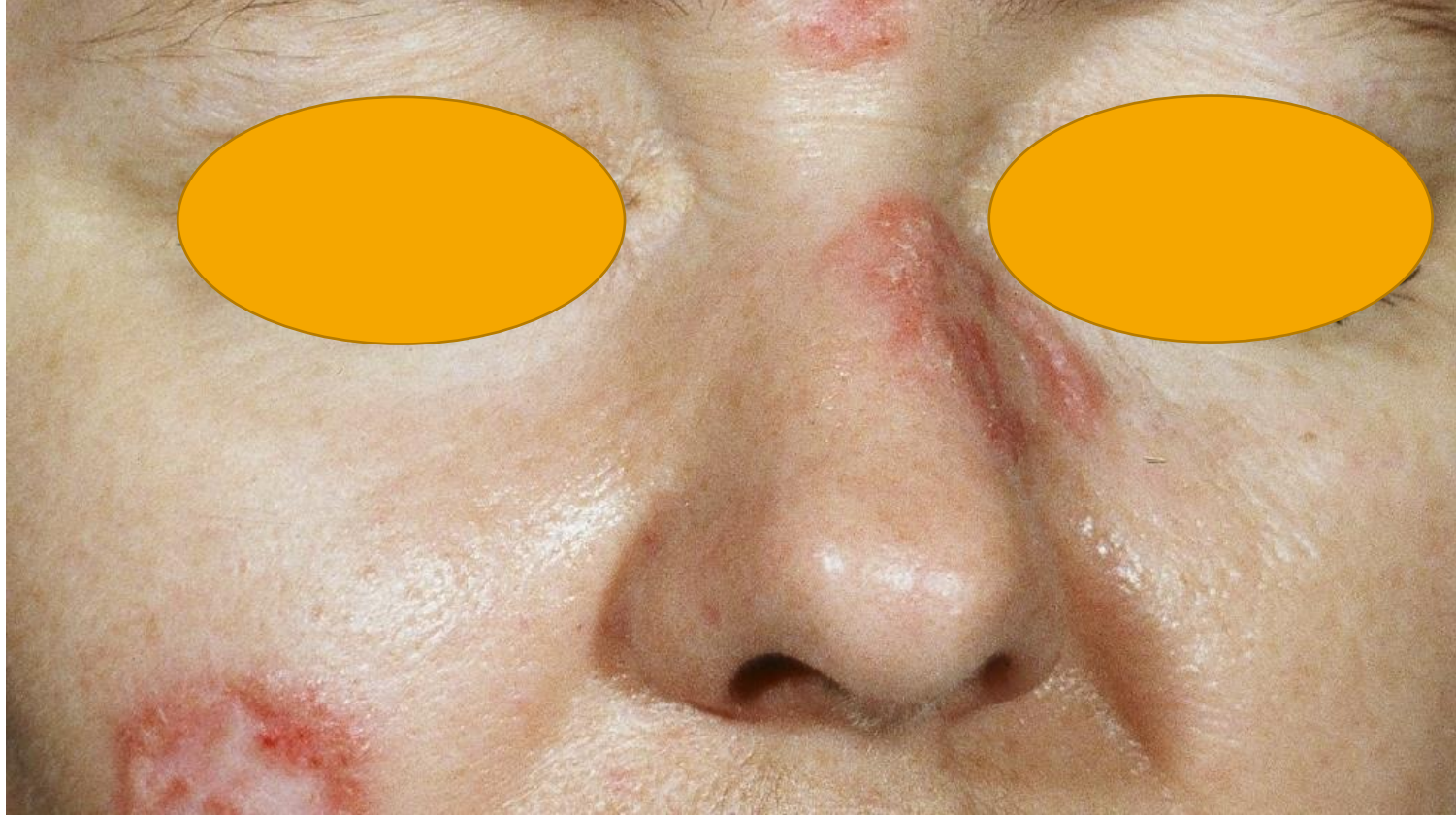
positive: 95% SLE, 90% SCLE, 20- 30% DLE

Discoid lupus erythematosus

Discoid lupus erythematosus (DLE)

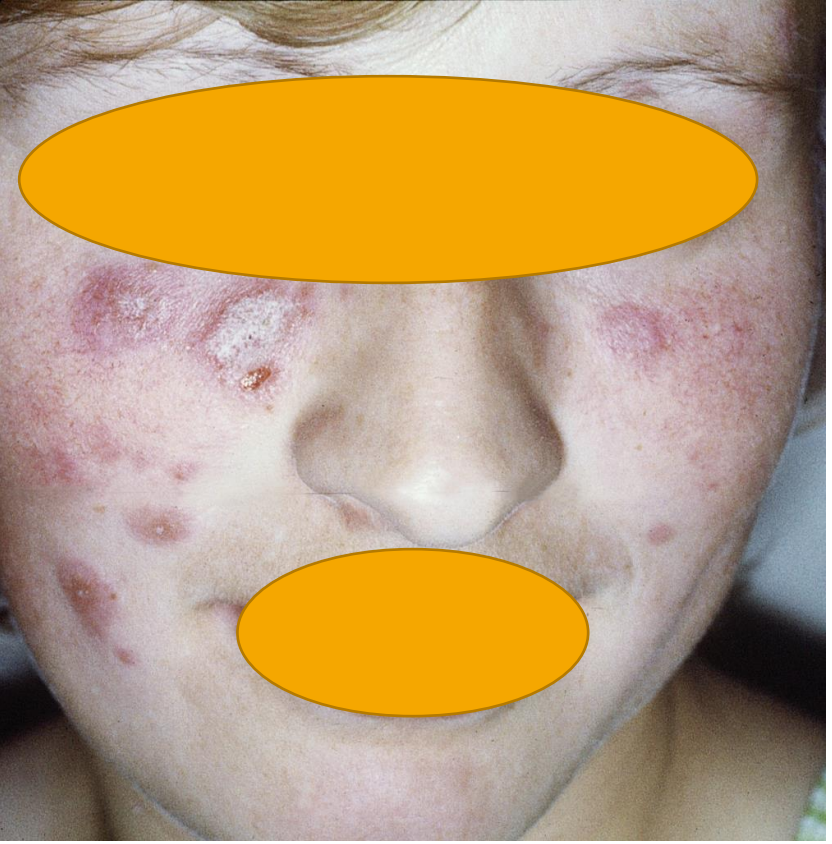
- Women & Men 2: 1- 4: 1
- The onset of the disease 20-40 years old
- May precede SLE !!!

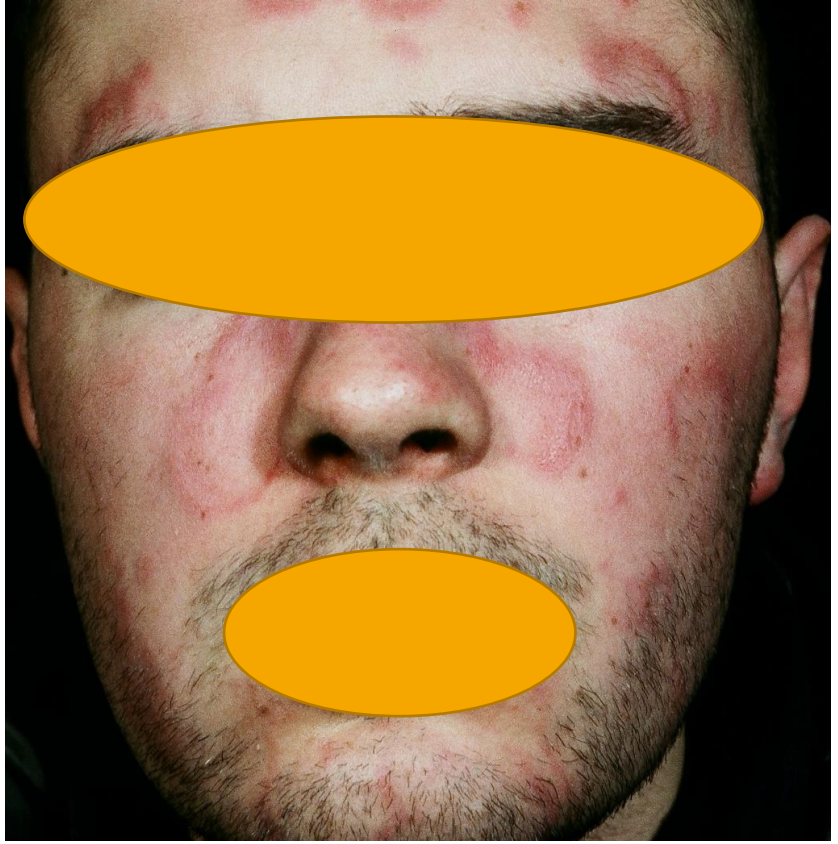


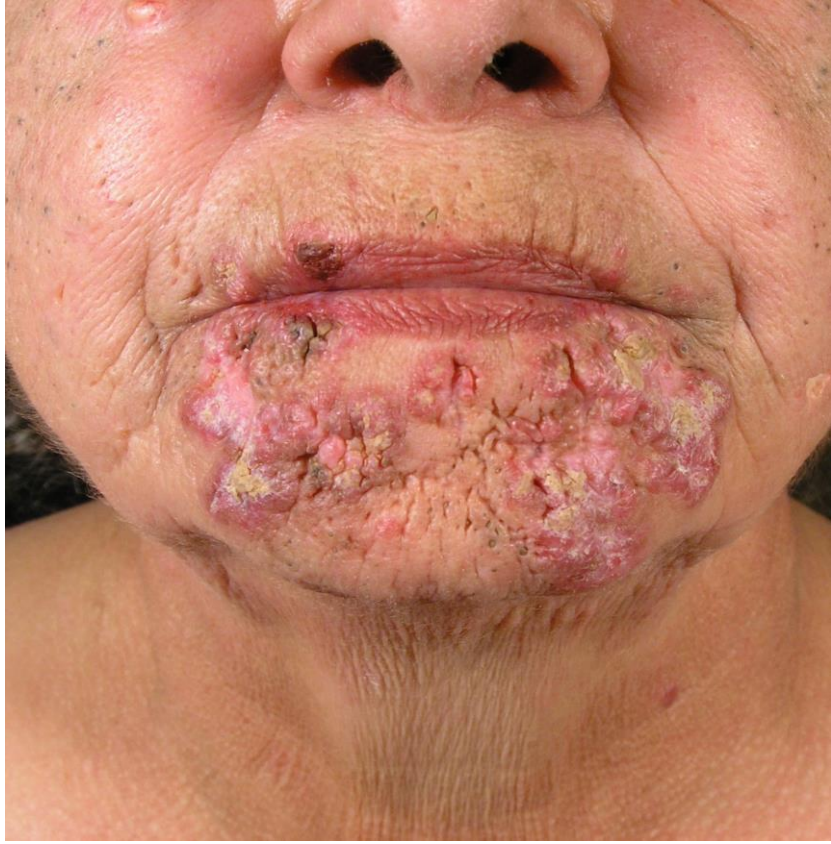


Clinical features

- Erythema, infiltrated papules and plaques on the erythematous basis, peripherally spreading, scaly in the center with hyperkeratosis followed by skin atrophy, scarring, discoloration
- Scales are difficult to remove
- Shape: round, oval, annular







Skin localisation

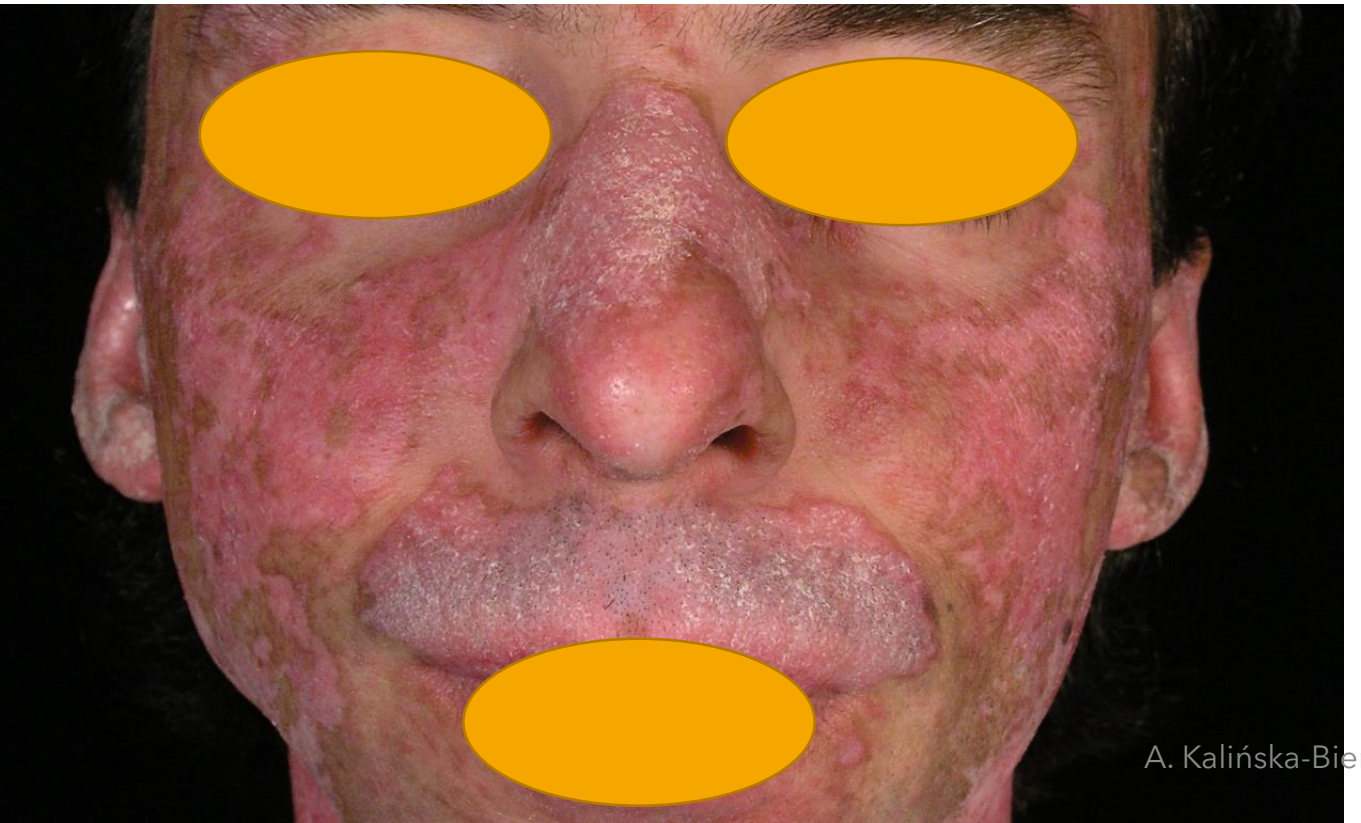
- UV-exposed areas: forehead, nose, cheeks, scalp, ears, rarely disseminated lesions on the trunk and limbs
- Lesions last for months to years
- No painful

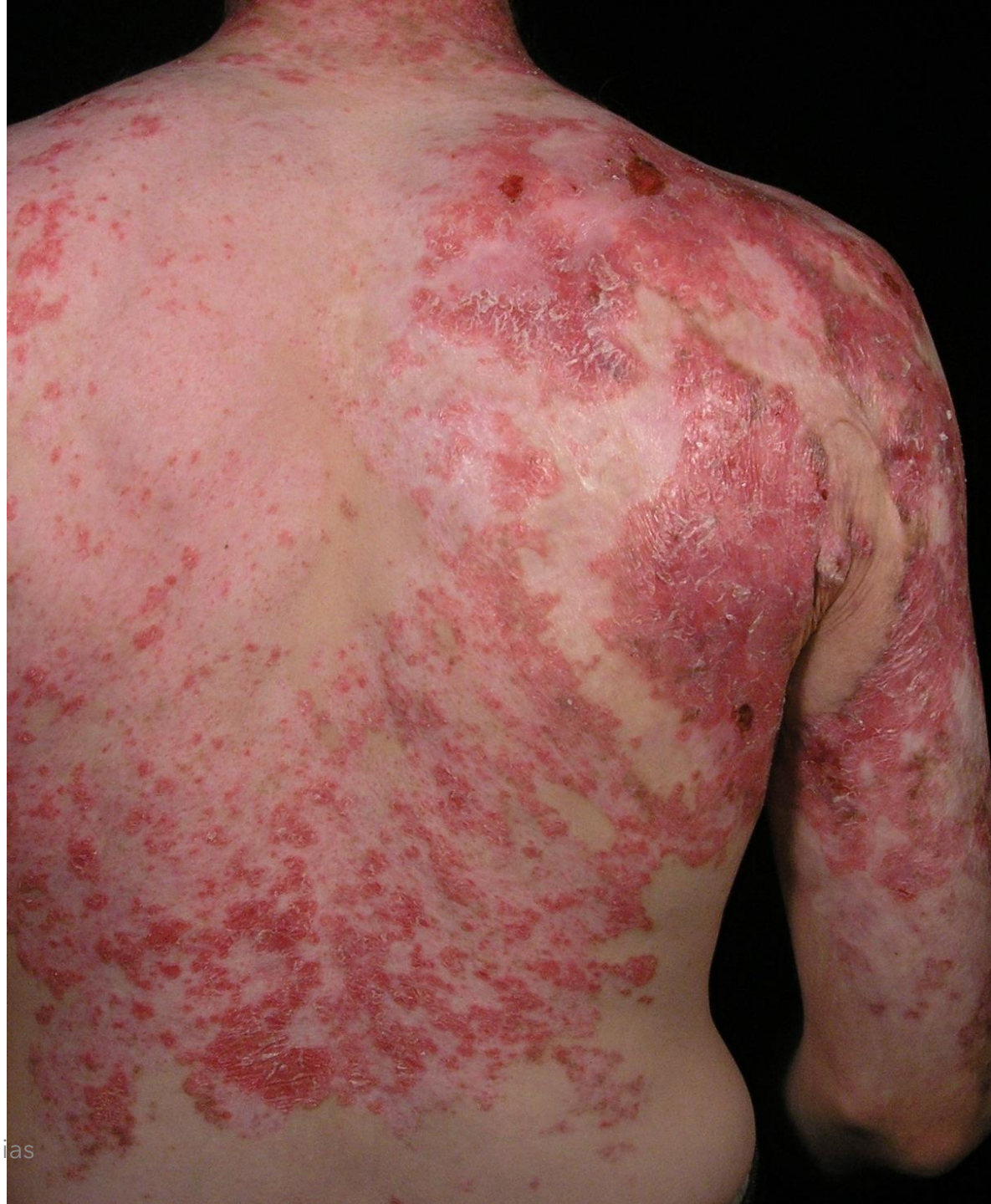
Clinical variants of DLE

- **Disseminated DLE**
- **Lupus tumidus**
- **Hypertrophic DLE**
- **Lupus eruthematosus panniculitis**
- **Mucous membrane lupus**
- **Chilblain lupus**
- **Lupus scarring alopecia**

Disseminated discoid lupus erythematosus, DDLE

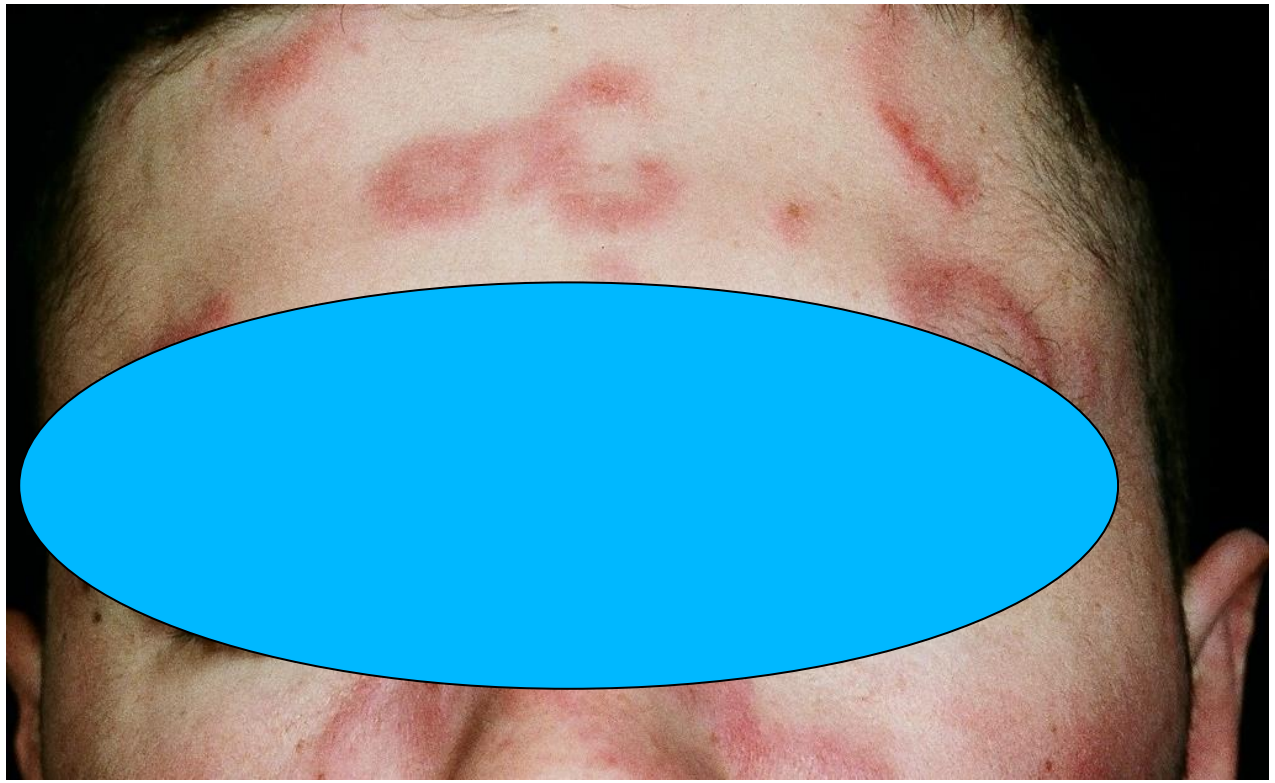
- Skin lesions go beyond the neckline and may affect the trunk, limbs (more often the upper ones)
- More common conversion to systemic lupus (SLE)





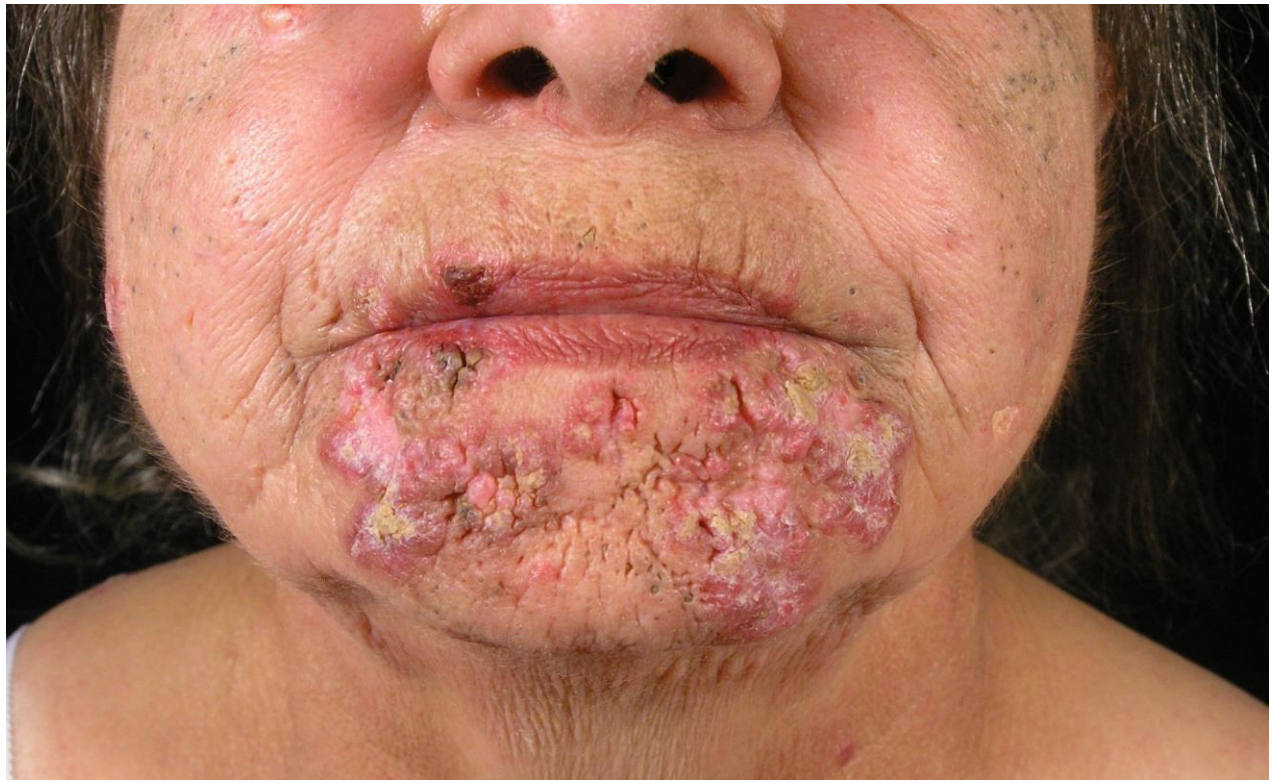
A. Kalińska-Bienias

Lupus tumidus



- **Outstanding hipersensitivity to UVR**
- **Erythematosus and infiltrations with smooth surface elevated above skin, without scarring**
- **Skin lesions located on the sun-exposed areas**
- **Possitive LBT 50%**

Hyperkeratotic DLE



thickened and warty plaques with severe hyperkeratosis

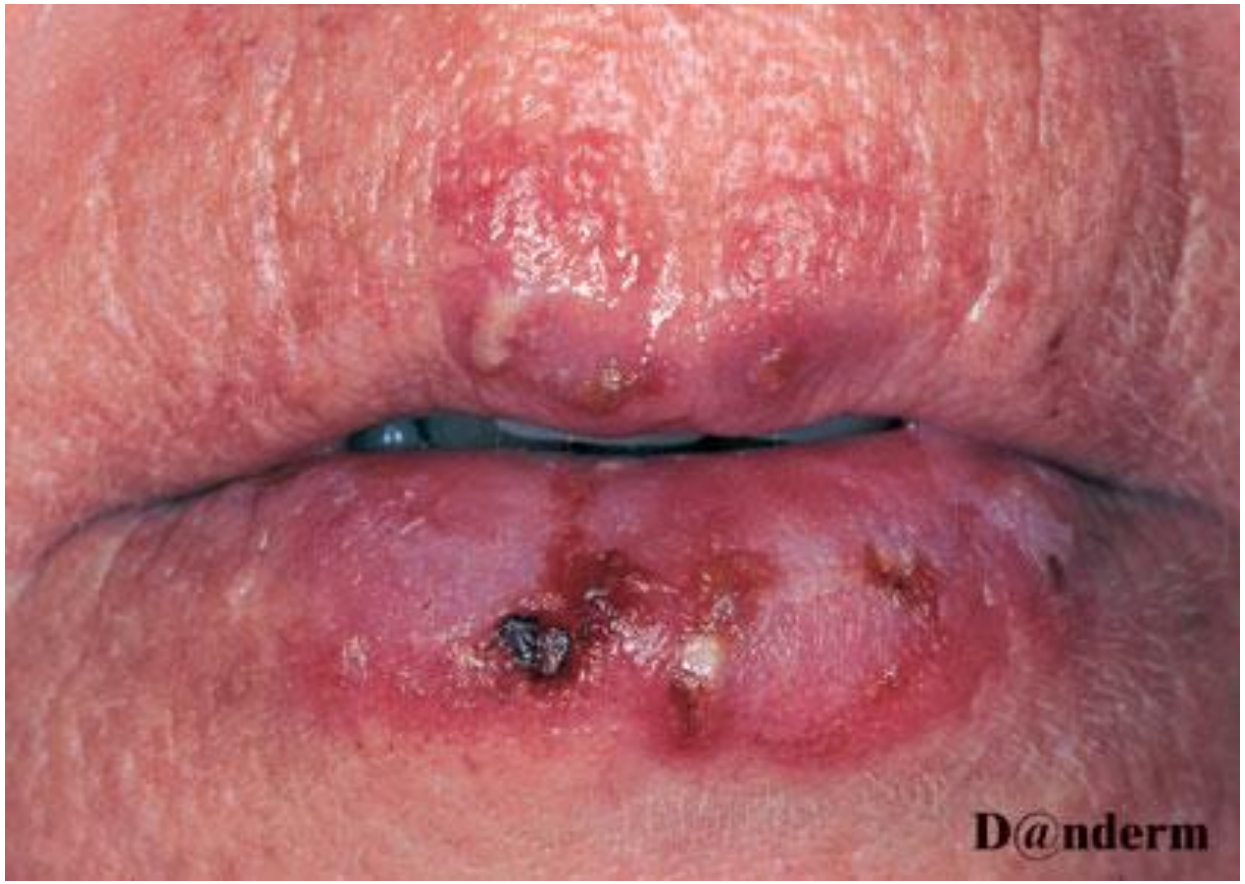
may stimulate the development of cancerous changes

Treatment: low dosage of acitretin

Mucosal lupus erythematosus

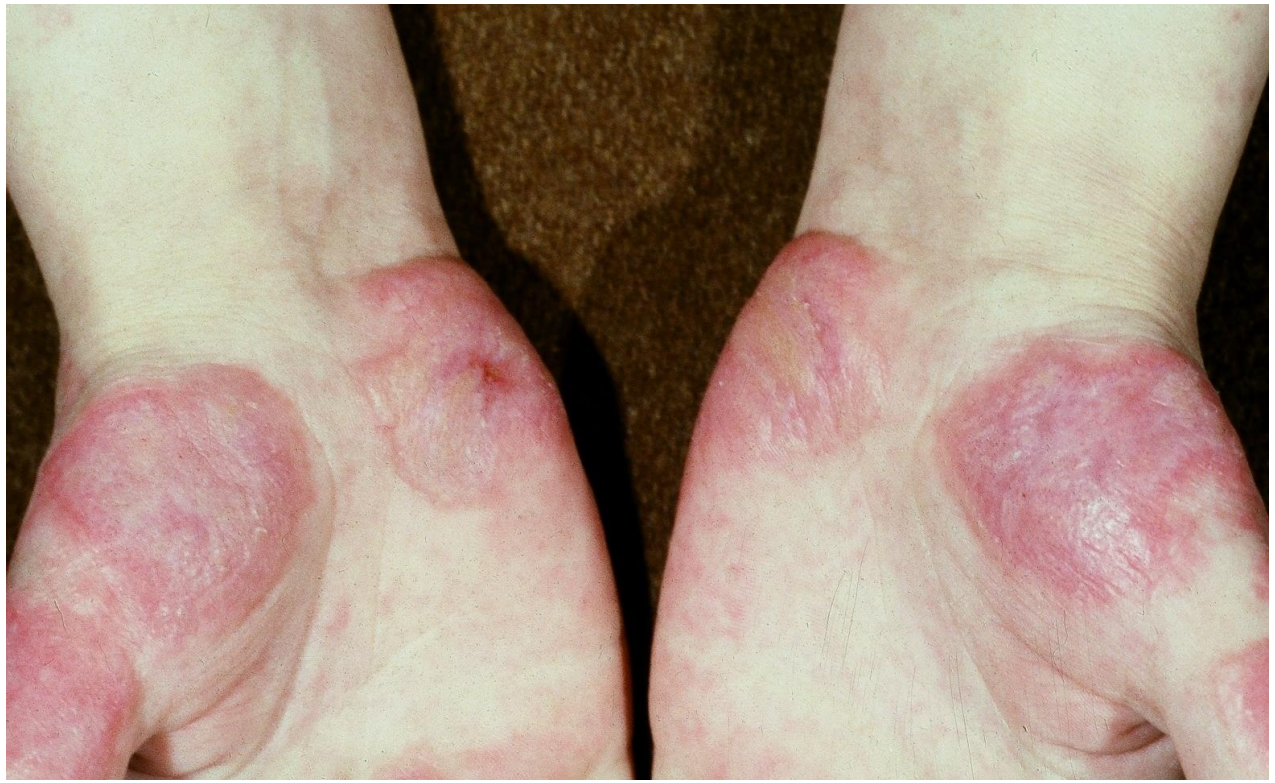
Changes on the mucous membranes may concern: the lips, the palate, cheeks, genitals

On the mucous membranes there are whitish deposits - like leukoplakia, they may have a tree-like pattern.



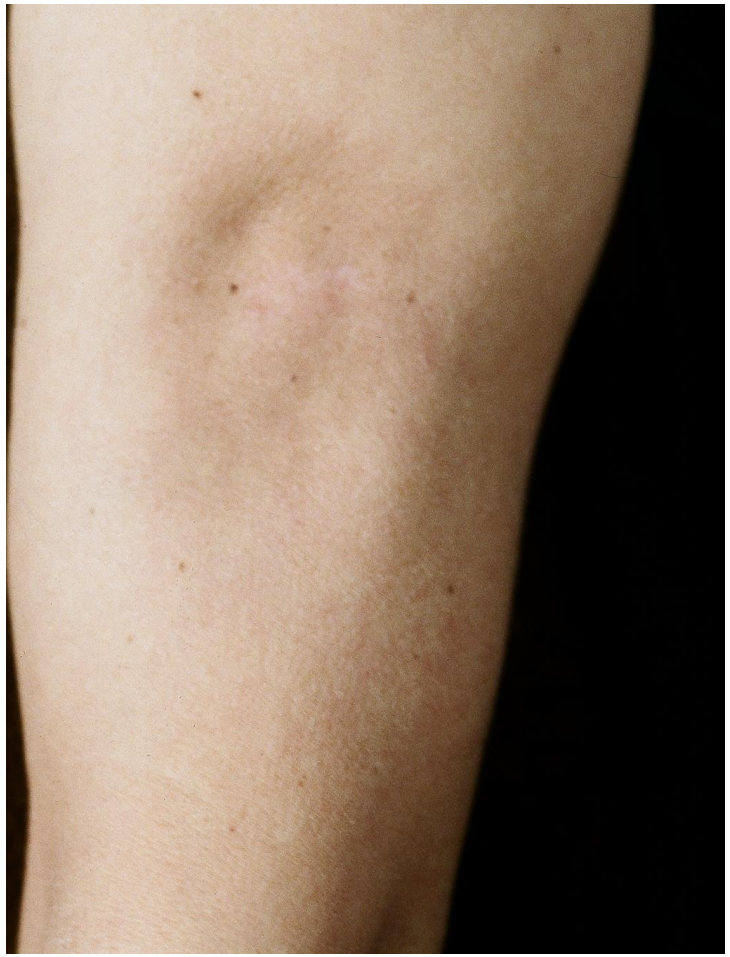
On the lips: erythematous plaques with whitish hyperkeratosis, rarely: erosions

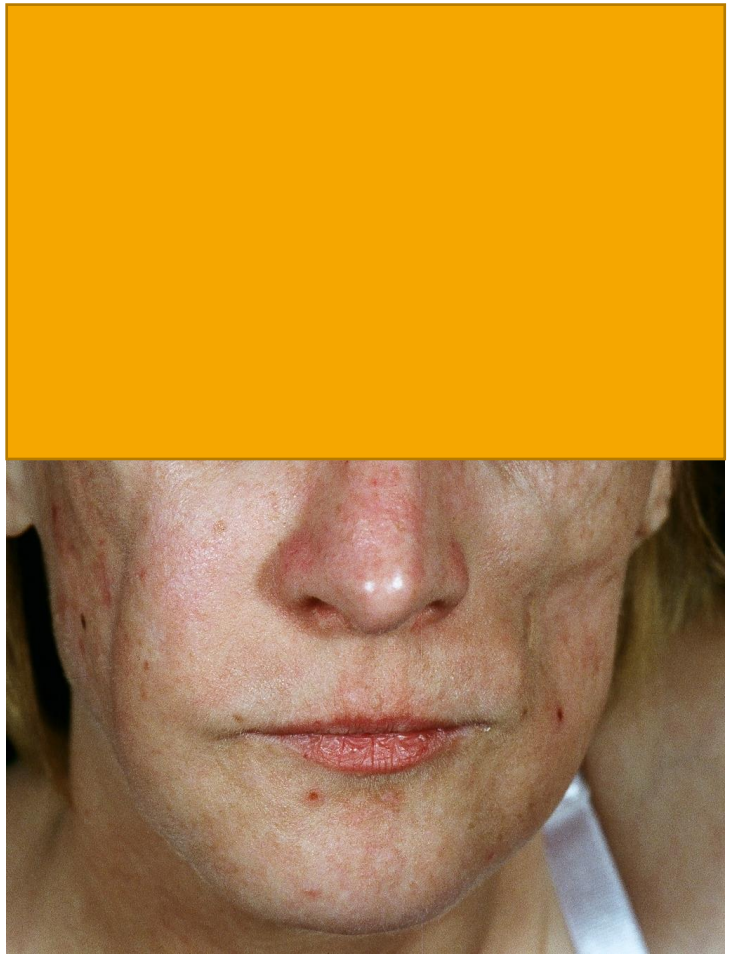
Childblain lupus



- Skin lesions mainly erythematous with visible vasculitis, violet coloured
- Located on the distal part of the body: nose, ears, digital pulps of fingers, exposed to cold

Lupus erythematosus panniculitis



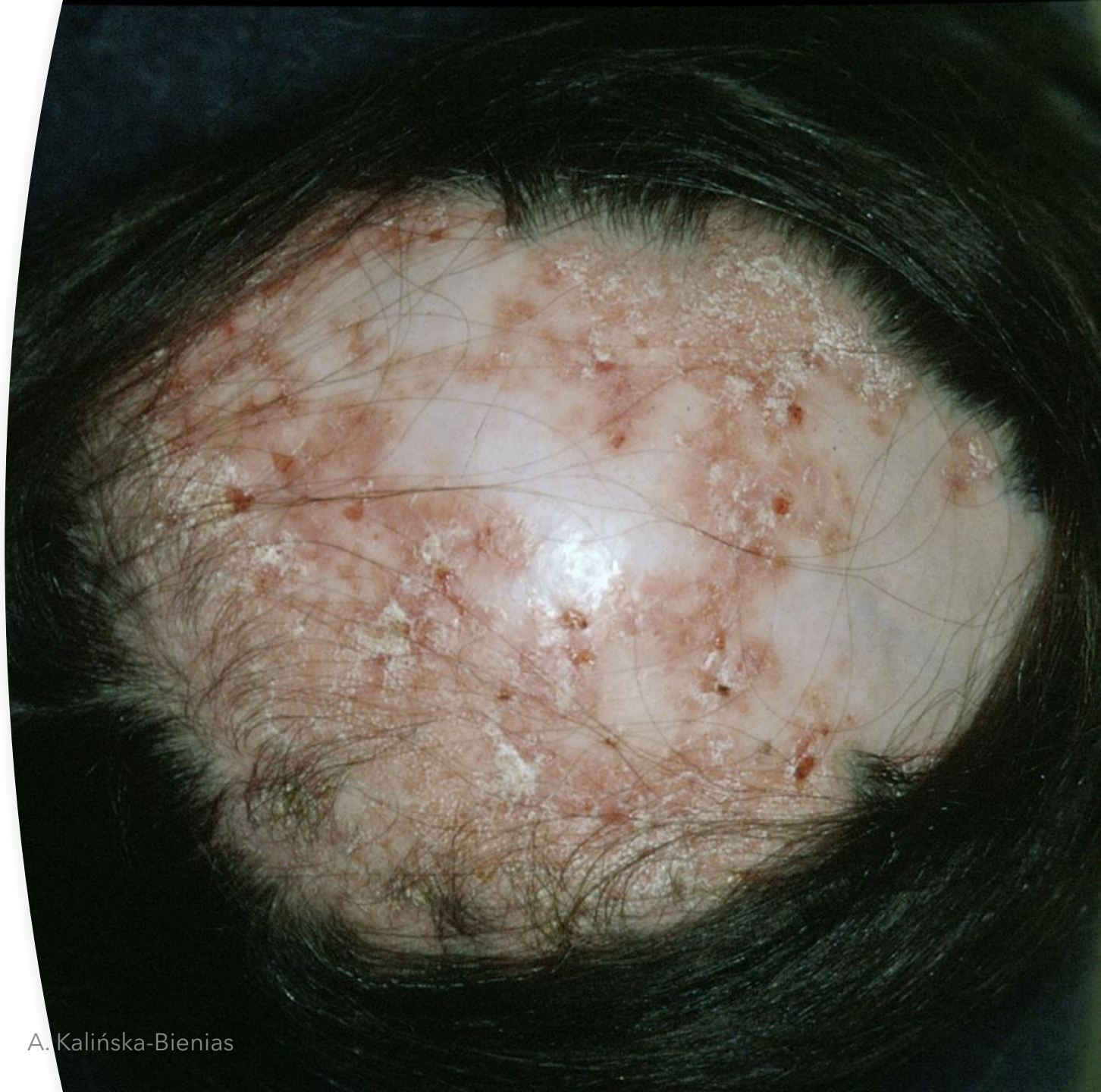


- affects subcutaneous tissue
- may involve face, buttocks, arms, thighs

Scarring scalp alopecia

- features of scarring alopecia, which causes permanent hair loss.

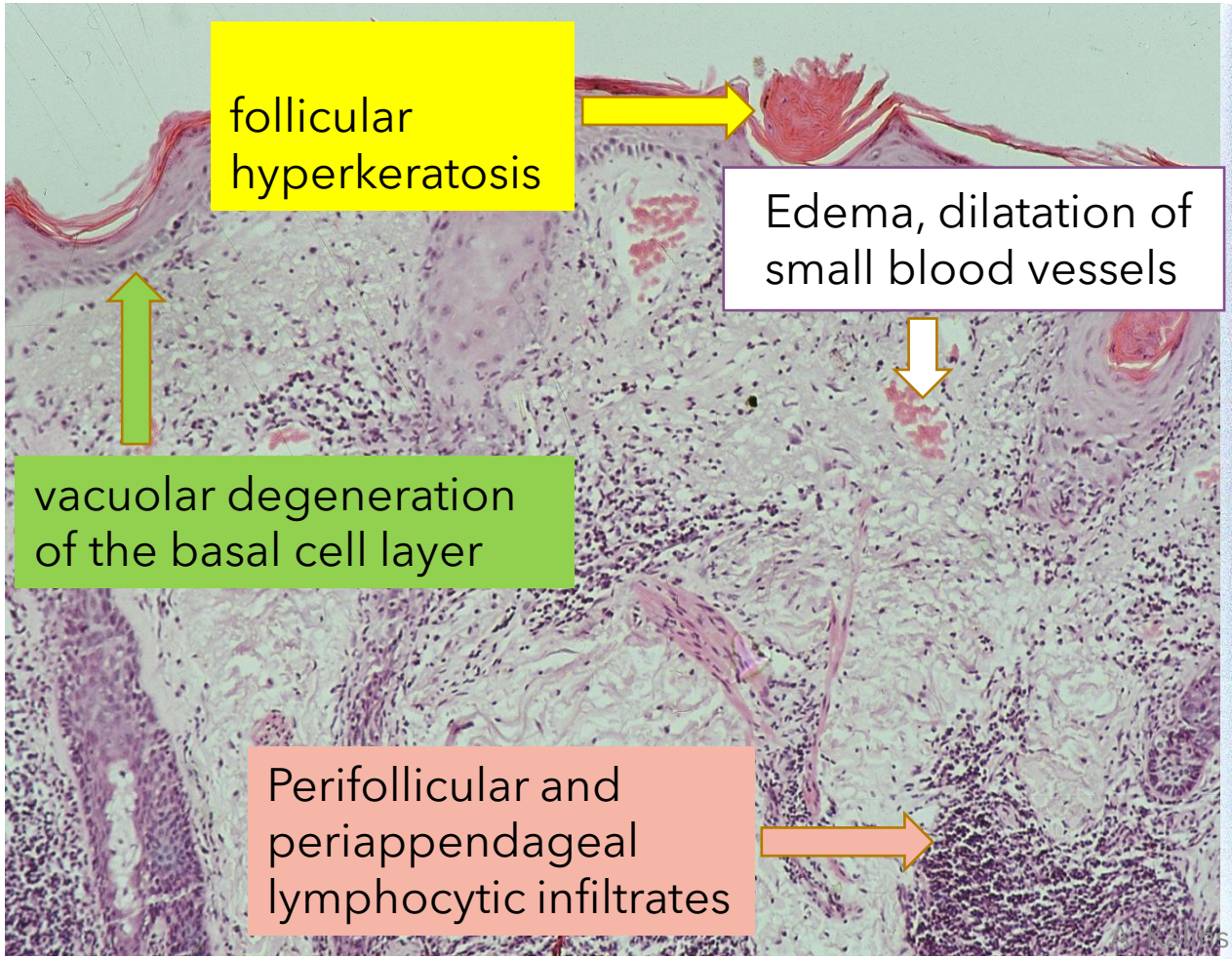
- may be the only DLE location.

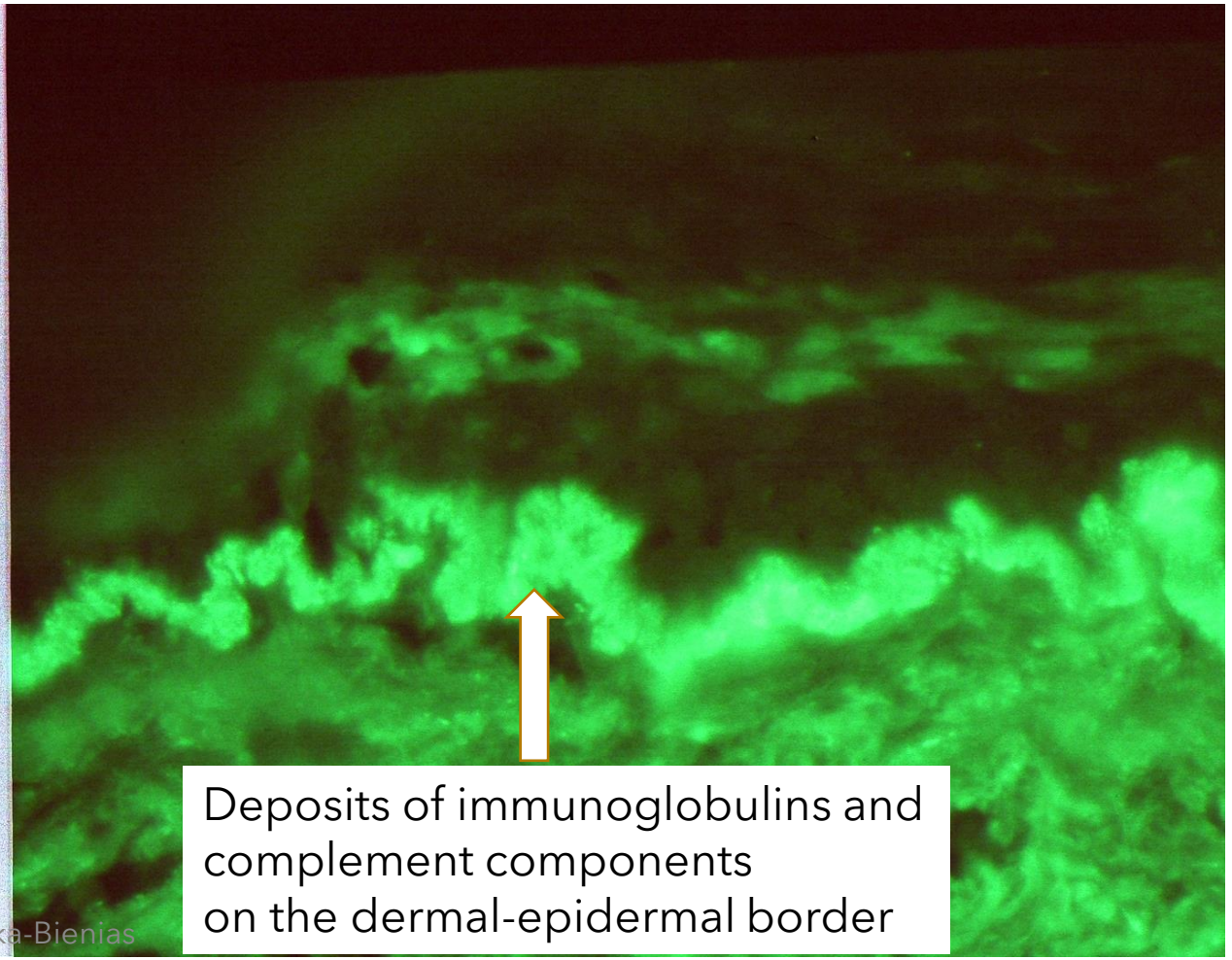


A. Kalińska-Bienias

Diagnostics of DLE- skin biopsy

Histopathological examination Direct immunofluorescence test





Treatment

Systemic treatment

antimalarial drugs (chloroquine, hydroxychloroquine)

glucocorticosteroids: medium and small, gradually reduce after clinical amendment to withdrawal

retinoids: acitretin, isotretinoin

Topical treatment

glucocorticosteroids

inhibitory calcineurins (tacrolimus, pimecrolimus)

PHOTOPROTECTION, SPF 50+

Management

Avoiding infections

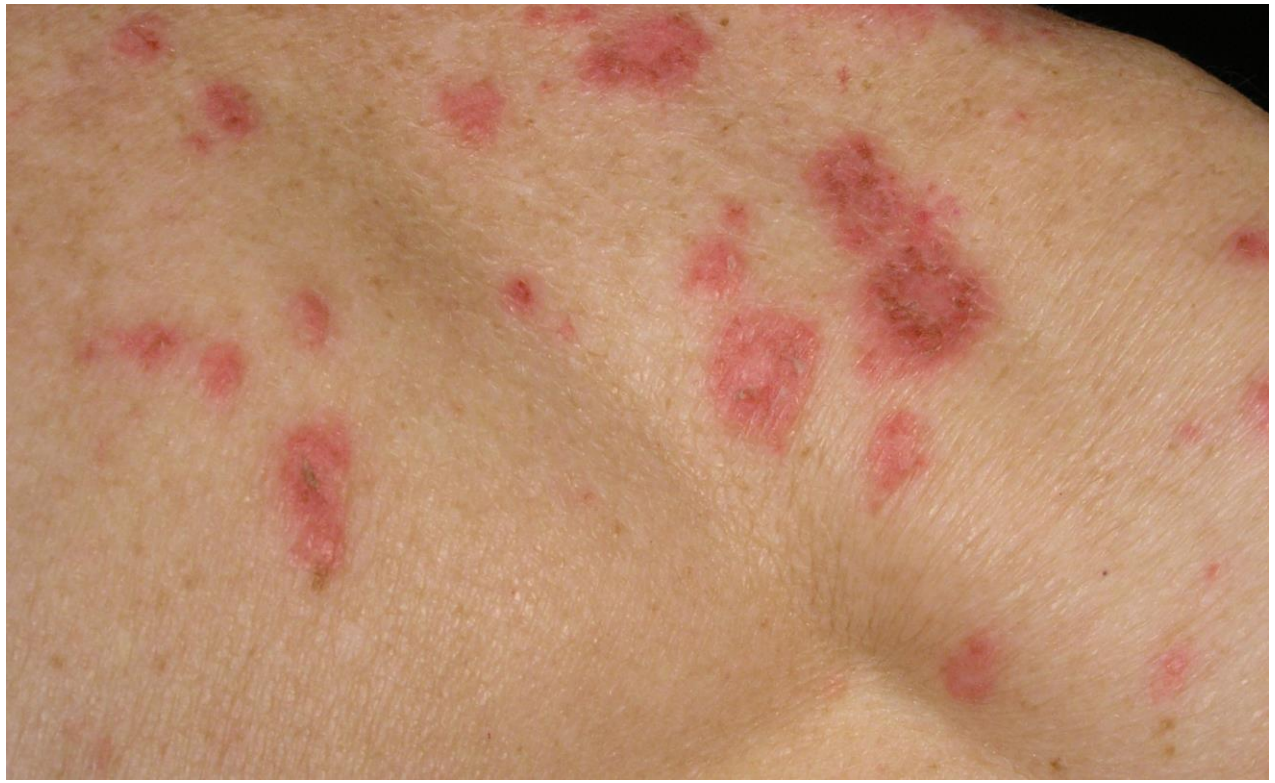
Avoiding stress

Not using estrogens (contraception)

Avoidance of phototoxic and photoallergic drugs

Subacute cutaneous lupus erythematosus

Subacute cutaneous lupus erythematosus (SCLE)



- **described in 1979, particular form of LE with benign course**
- **more frequent in women aged 30 – 40**
- **may be associated with drug-induced lupus**

SCLE – characteristic features

- Particular skin changes
- Outstanding photosensitivity
- Slight arthritis, leucopenia, without nephritis
- The presence of ANA in 90% with characteristic: Ro(SS-A) and La(SS-B)

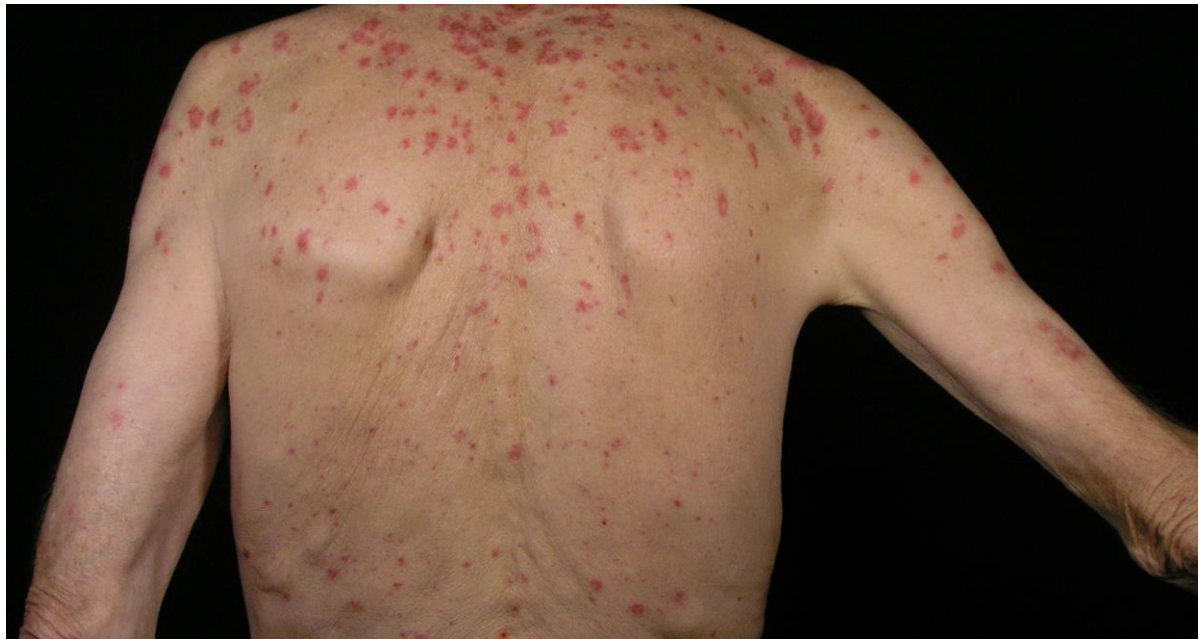
SCLE- types

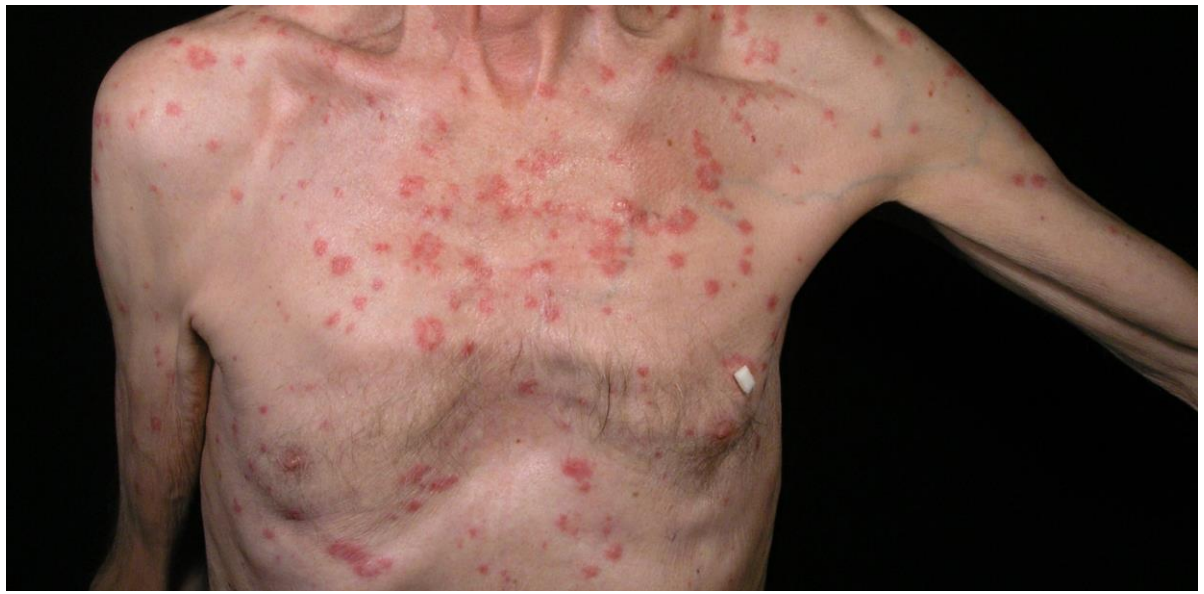
- SCLE annularis

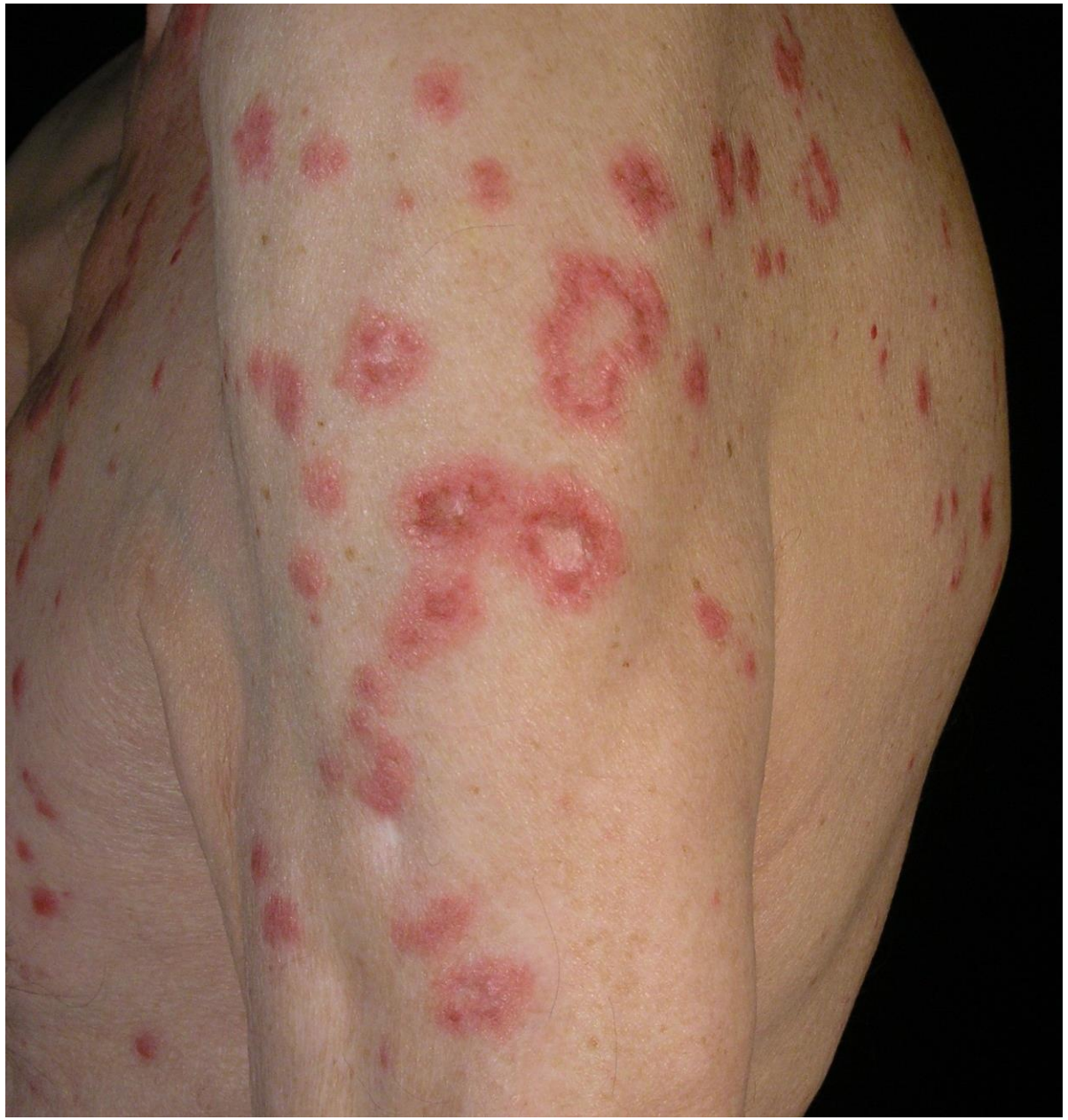
- SCLE psoriasiformis

(without follicular hyperkeratosis and scarring)

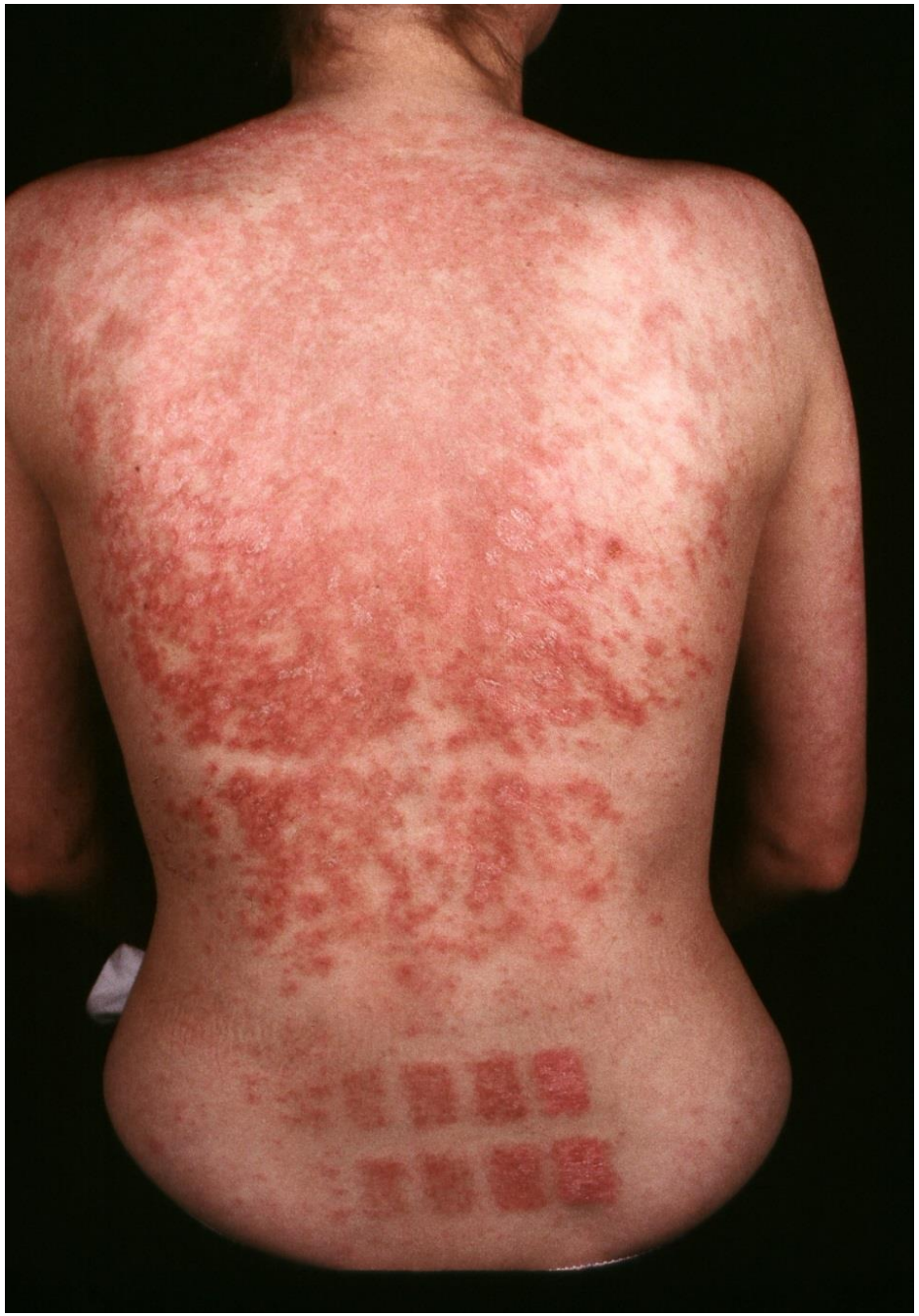
In SCLE - healing with hypopigmentations and teleangiectasions

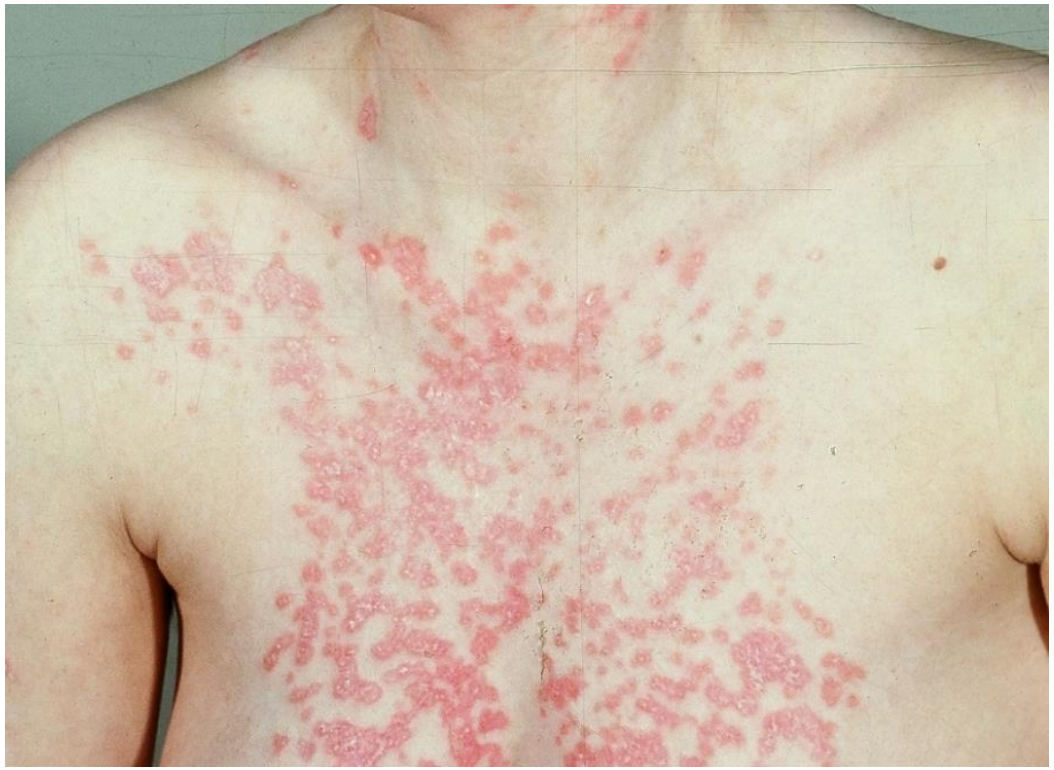






Annular SCLE





Psoriasiform SCLE

Systemic lupus erythematosus

Systemic lupus erythematosus (SLE)

Chronic disease of multifactorial and autoimmune etiology, in which the functioning of many systems and organs is disturbed.

- onset of the disease 16 - 55 years of age
- women and men 8 : 1
- the frequency 25 - 51 cases per 100,000 people
- the incidence of SLE ranges from 2-8 cases per 100,000 people
- Recurrence – often after exposure to UV radiation, infection, stress, hormonal factors (estrogens), medications (usually procainamide and hydralazine)

Etiopathogenesis

Genetic predisposition

- Many studies have revealed a number of gene polymorphisms influencing the development of SLE. They include, among others genes involved in the presentation of HLA class II antigens DR3 and DR2 and HLA class III.
- Mutations of the genes of the complement have also been demonstrated (C1q / r / s, C2, C4)

Environmental factors

- Ultraviolet (UV) radiation, especially UVB radiation with a wavelength of 290-320 nm, exacerbates skin and organ changes.
- Some medications can induce SLE symptoms (e.g. hydralazine, isoniazid).

Abnormal cellular and humoral responses

- The disorders concern both the number and function of immunocompetent cells, their hyper-reactivity, impaired autotolerance and removal of immune complexes.

!!! The exact etiopathogenesis of SLE is not fully understood

Diagnostic criteria for systemic lupus according to SLICC *(Systemic Lupus International Collaborative Clinics) - 2012*

1. Acute cutaneous lupus erythematosus

Lupus malar rash

Bullous lupus

Toxic epidermal necrolysis variant of SLE

Maculopapular lupus rash

Photosensitive lupus rash or subacute cutaneous lupus erythematosus

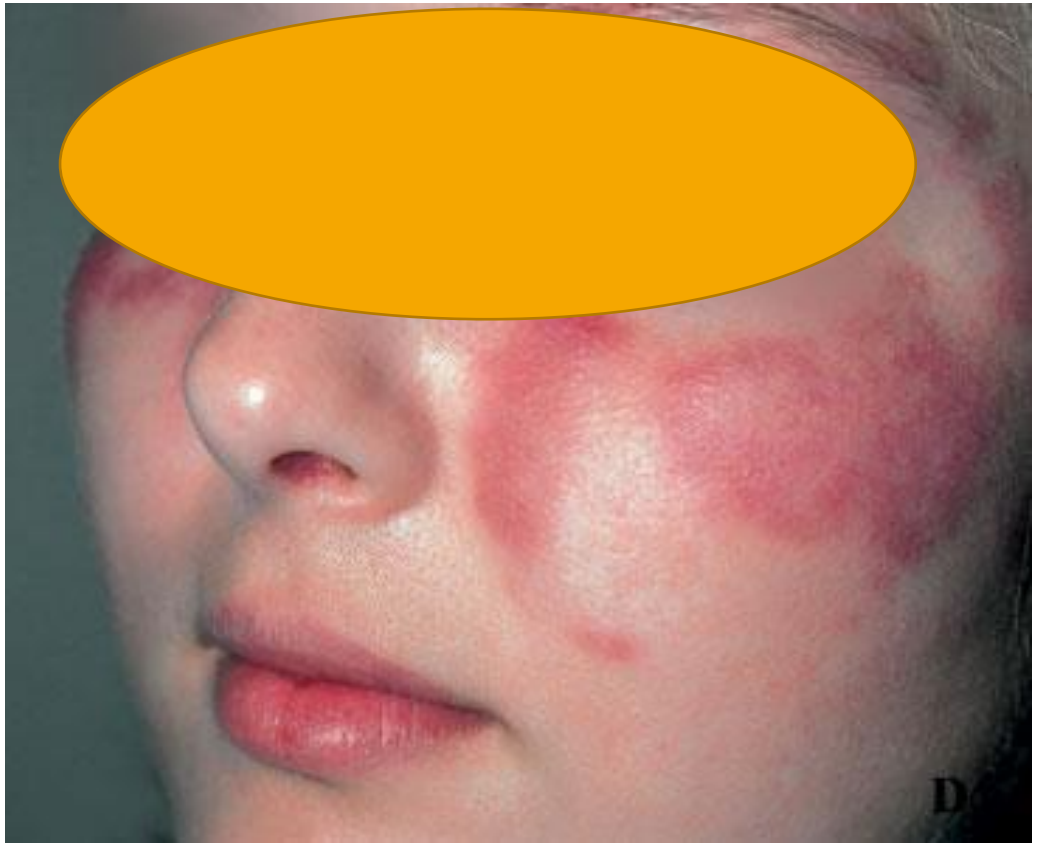
2. Chronic lupus erythematosus

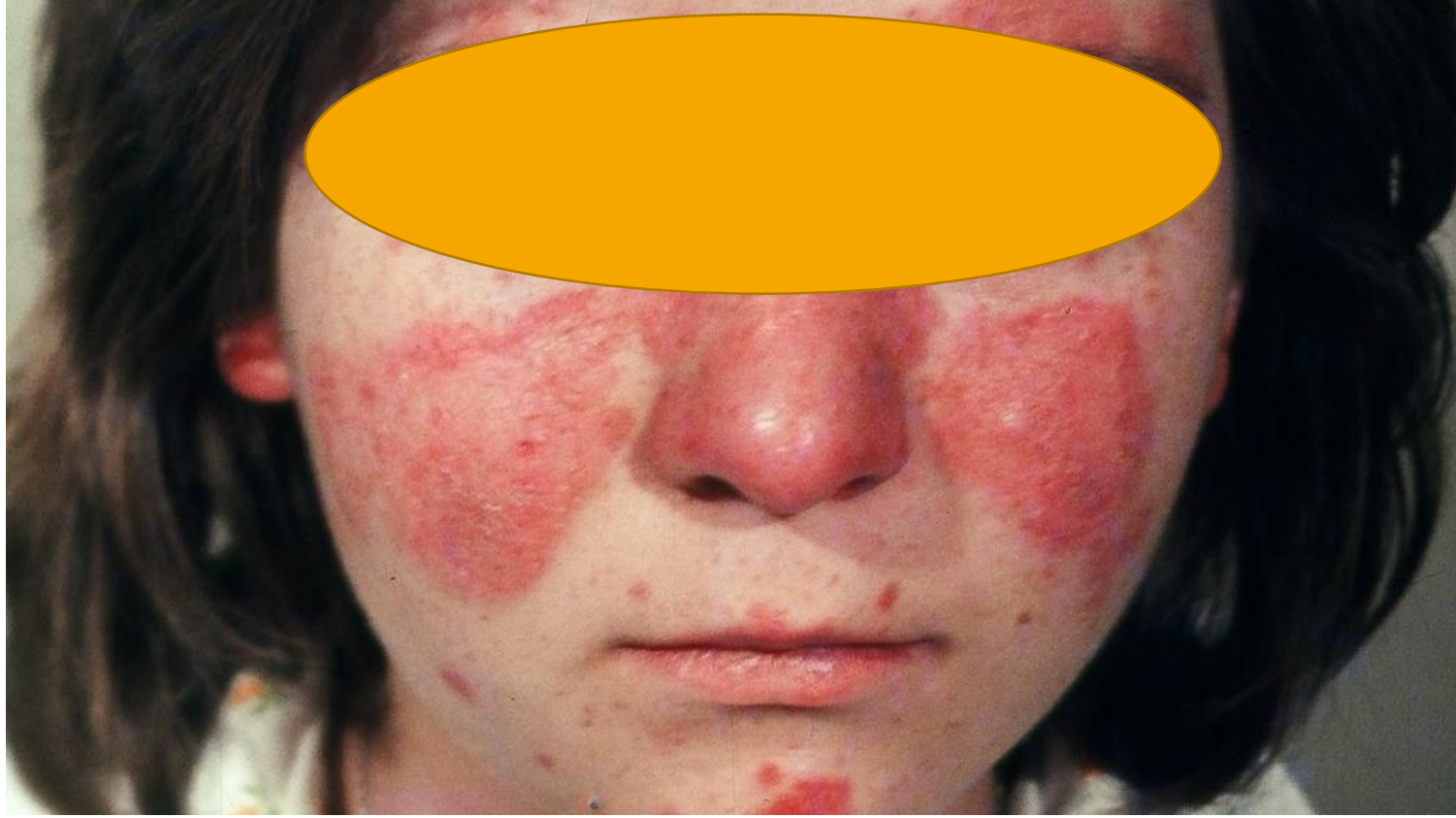
Discoid erythematosus (DLE, DDLE)
Hypertrophic (verrucous) lupus
Lupus panniculitis (profundus)
Mucosal lupus
Lupus tumidus
Chilblain lupus
Discoid lupus/lichen planus overlap

3. Oral ulcers

4. Nonscarring alopecia (diffuse thinning or hair fragility with visible broken hairs)

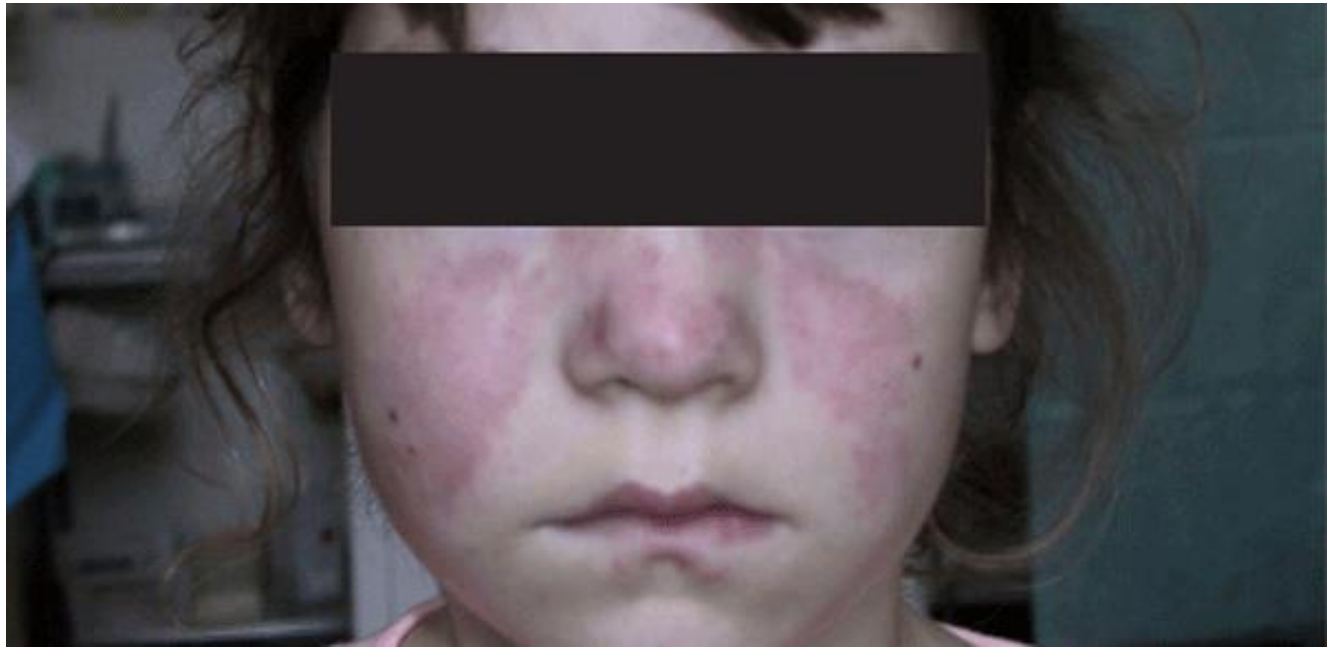
Arthritis Rheum., 2012; 64: 2677-2686

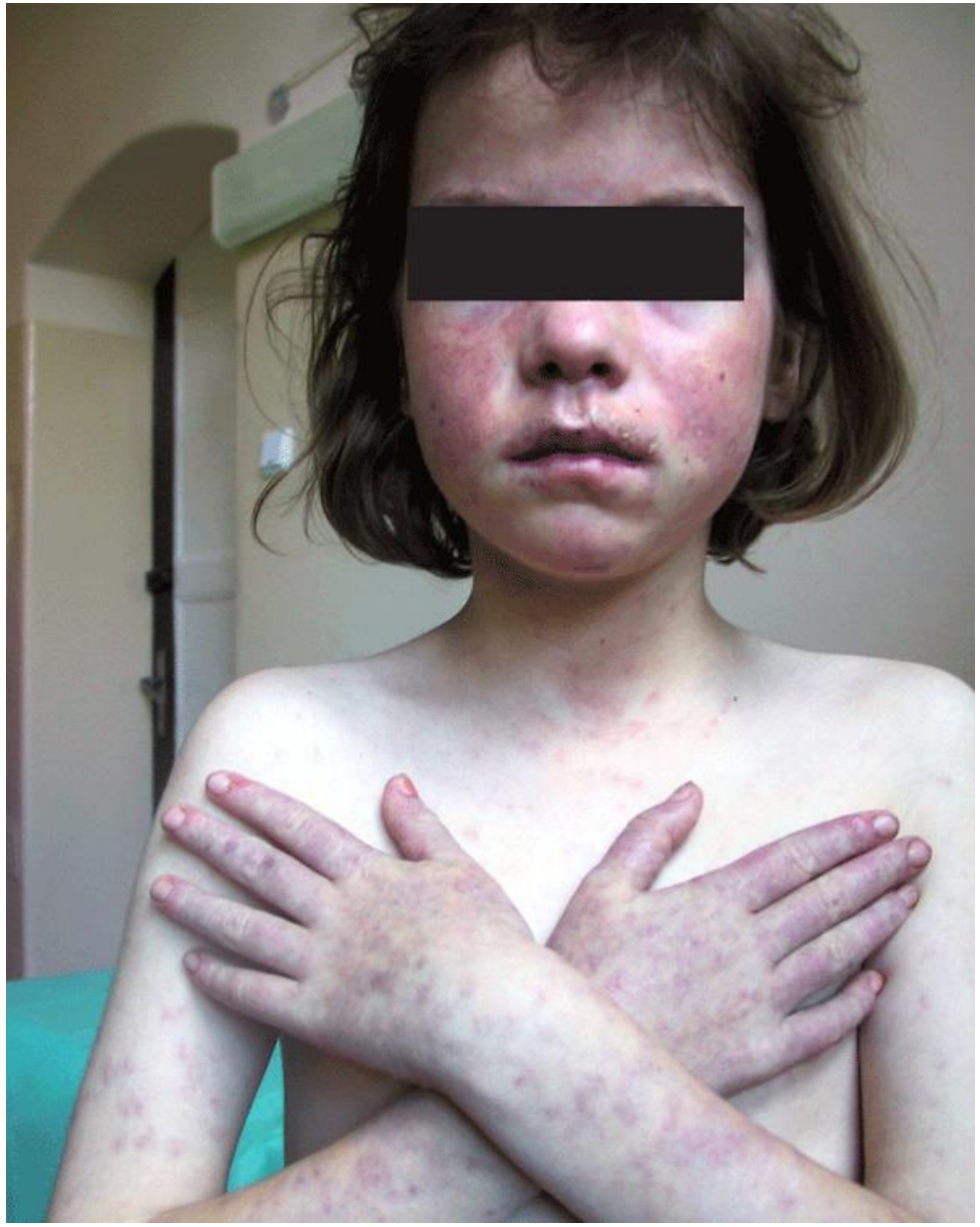




Lupus malar rash

- A well-defined, butterfly-shaped erythema on the cheeks and bridge of the nose
- **!!! No involvement of the nasolabial folds**



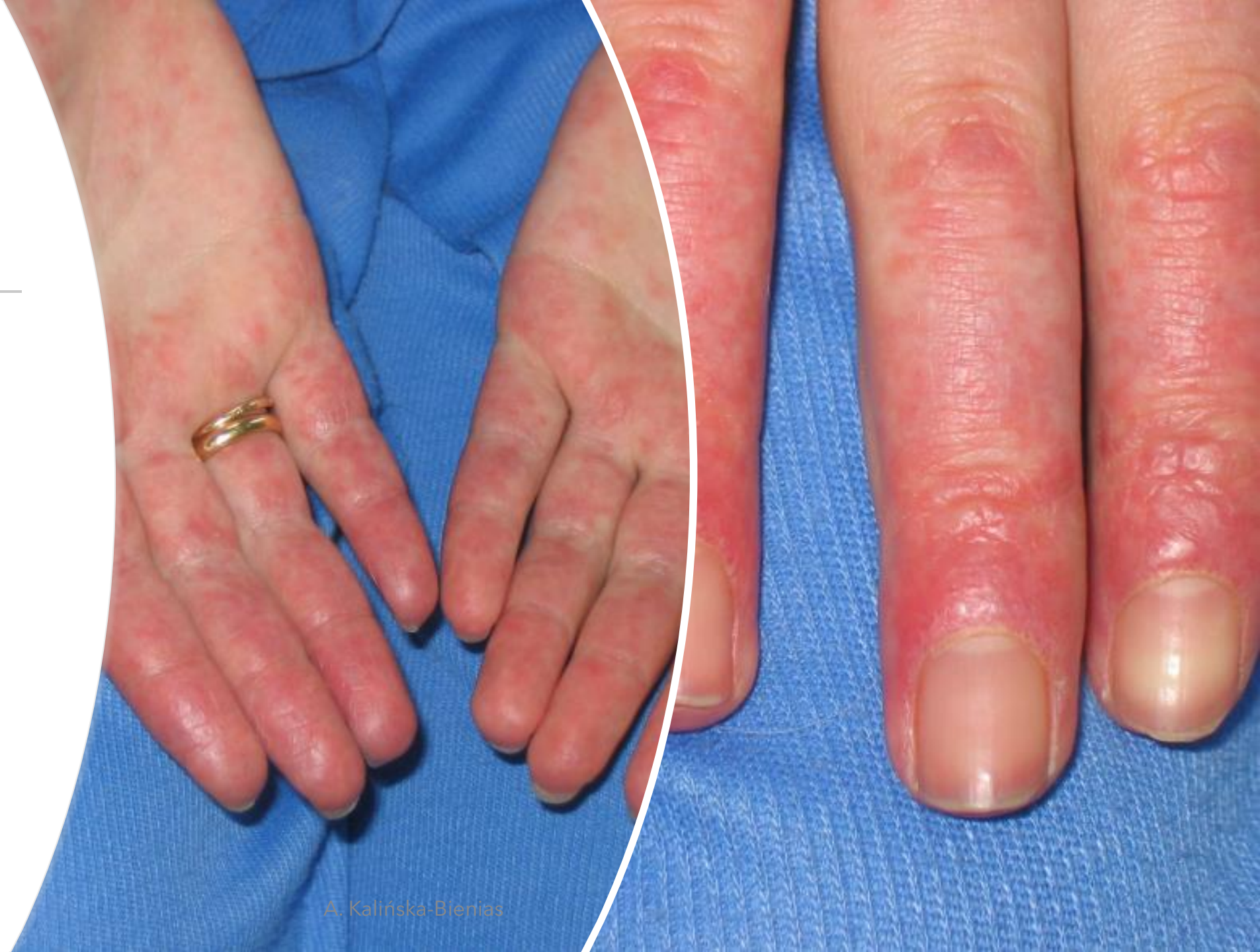


Maculopapular lupus rash

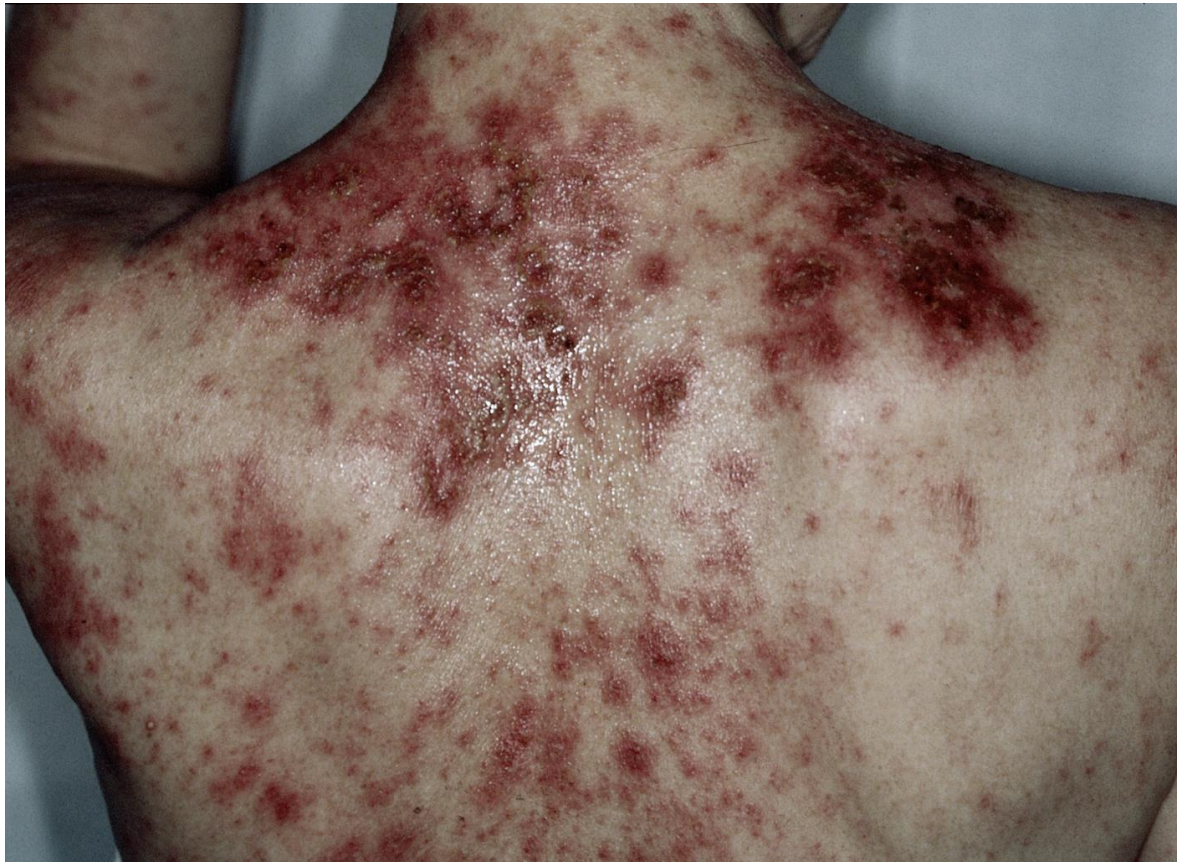
- Usually symmetrical lesions affecting the trunk and limbs

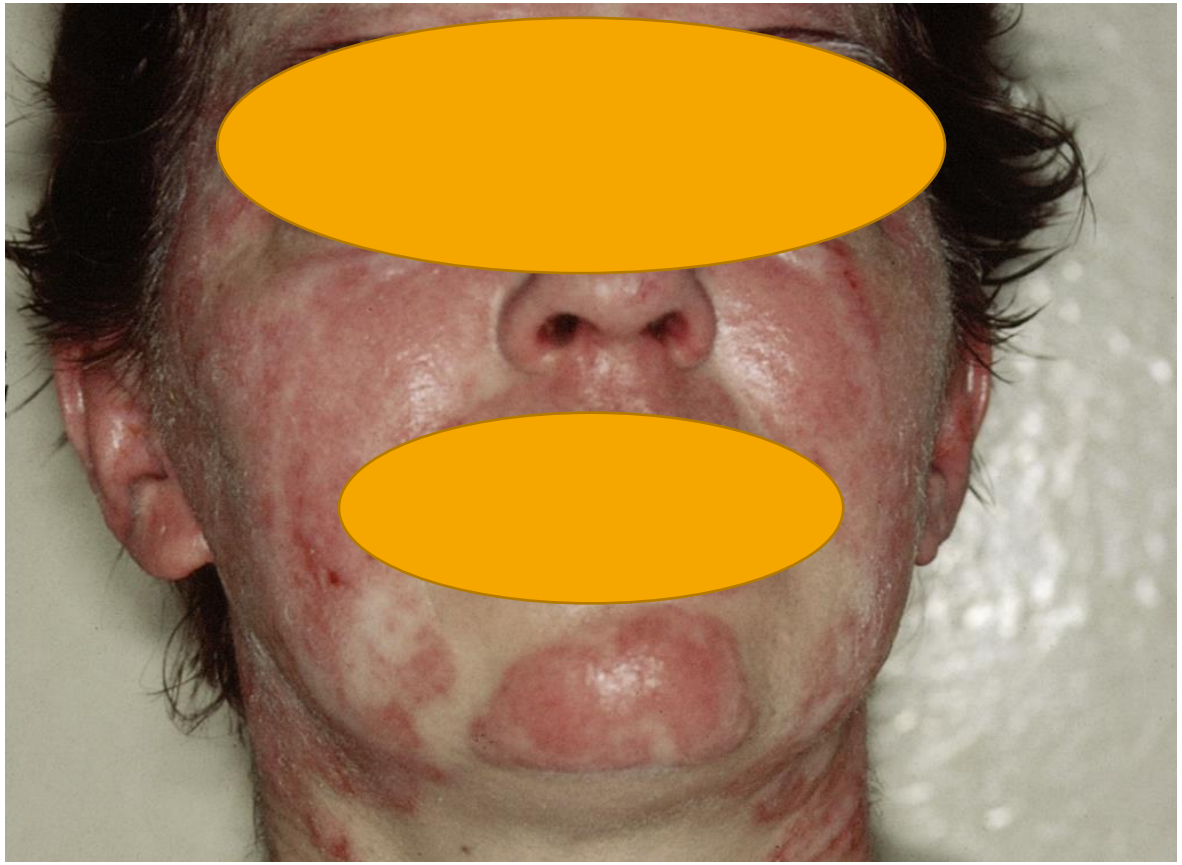
Maculopapular lupus rash

- Symmetrical, often within the fingertips and nail folds



Toxic epidermal necrolysis variant of SLE





Non-scaring alopecia

A. Kalińska-Bienias

5. Arthritis

6. Serositis

7. Renal involvement - 24-hour urine test - 500 mg protein/24 hours or red blood cell casts

8. Neurologic abnormalities (seizures, psychosis)

9. Hemolytic anemia

10. Leukopenia (< 4000/mm³) lub lymphopenia (< 1000/mm³)

11. Thrombocytopenia (< 100 000 mm³)

Immunologic criteria

1. ANA level above laboratory reference range

2. presence of anti-dsDNA antibody

3. presence of antibody to Sm antygen (anti-Sm)

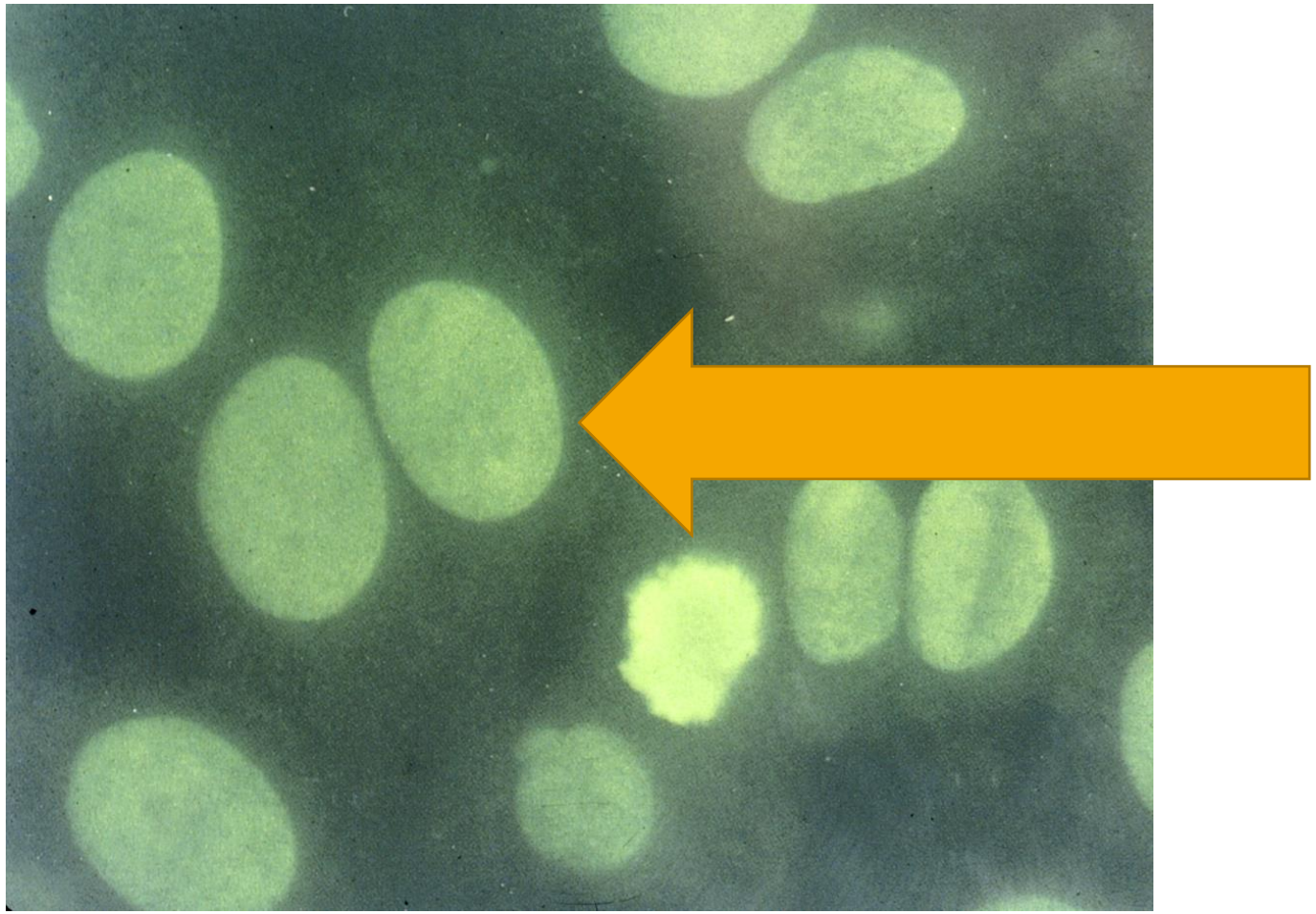
4. Antiphospholipid antibody positivity: positive test for lupus anticoagulant and/or false-positive test for rapid plasma reagin, positive for anticardiolipin antibody level (IgA, IgG, or IgM) and/or anti–2-glycoprotein I (IgA, IgG, or IgM)

5. Low complement : C3 , C4, CH50

6. Positive direct Coombs' test in the absence of hemolytic anemia

The patient must satisfy at least 4 criteria, including at least one clinical criterion and one immunologic criterion.

Diagnostics of circulating antibodies (ANA)

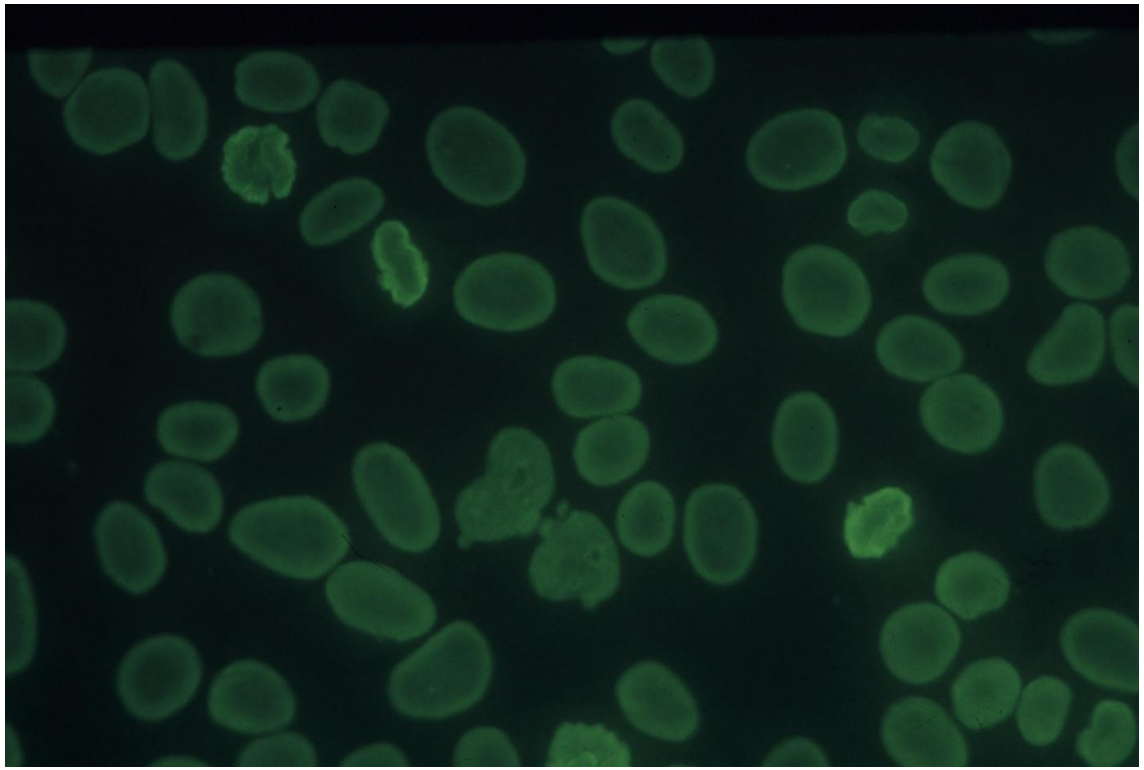


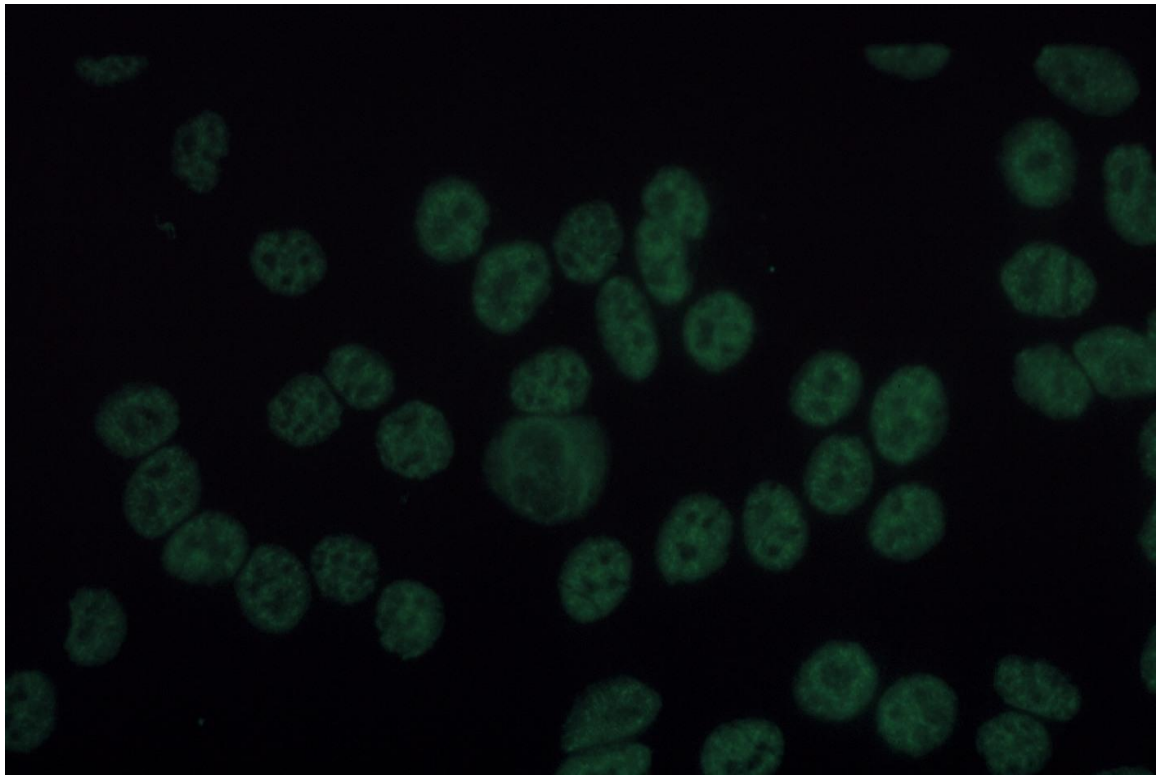
ANA are detected by

- Indirect immunofluotescent study on the substrate - Hep-2 cells

(these are human epithelial cells derived from laryngeal cancer because of large cell nucleus)

- ***Immunoblot***
- ***ELISA***
- ***Immunodifussion***





Shining typical for
anti-ds.-DNA antibodies

Shining typical for

anti-Sm antibodies

Indirect Immunofluorescent study – serum study

Study cells – Crithidium lucilliae

Detection of ds-DNA

Antinuclear antibodies- ANA

- Anti-double-strand DNA antibodies (ds.-DNA)
- Anti-Sm antibodies
- rRNP antibodies
- SS-A (Ro), SS-B (La)
- Anticardiolipin antibodies (lupus anticoagulant)

Antinuclear antibodies- ANA

- Anti-double-strand DNA antibodies (ds.-DNA) - kidney involvement, severe course
- Anti-Sm antibodies – neurological symtoms
- rRNP antibodies – neurological symptoms
- SS-A (Ro), SS-B (La) – skin lesions, neonatal lupus
- Anticardiolipin antibodies (lupus anticoagulant) – thrombosis, pregnancy loss

ANA at a titer of ≥1:80 on HEp-2 cells

Clinical domains	Points	Immunologigcal domains	Points
Fever	2	Antiphospholipid antibodies	
Hematologic		Anticardiolipin antibodies or anti-β2GPI antibodies or lupus anticoagulant	2
Leukopenia	3		
Thrombocytopenia	4		
Autoimmune hemolysis	4		
Neuropsychiatric		Complements	
Delirium	2	C3 or C4 low	3
Psychosis	3	C3 and C4 low	4
Seizure	5		
Mucocutaneous		SLE-specific antibodies	
Non-scarring alopecia	2		
Oral ulcers	2	Anti-Sm or	6
Subacute cutaneous OR discoid lupus	4	Anti-dsDNA	
Acute cutaneous lupus	6		
Serosal			
Pleural or pericardial effusion	5		
Acute pericarditis	6		
Joint involvement			
synovitis≥ 2 joints or tenderness ≥ 2 and morning stiffness ≥ 30 minutes	6		
Renal			
Proteinuria >0.5 g/24 hours	4		
Class II or V lupus nephritis	8		
Class III or IV lupus nephritis	10		

SLE at least 10 points

Treatment

Systemic treatment:

- Glucocorticosteroids (prednisone 1-2 mg / kg)

- possibly pulses with methylprednisolone iv

- Antimalarial drugs – hydroxychloroquine, chloroquine
- immunosuppressants: azathioprine, cyclophosphamide, cyclosporine, mycophenolate mofetil
- Intravenous immunoglobulin infusions (IVIG), biological agents such as belimumab, rituximab

Topical treatment:

- Glucocorticosteroids, calcineurin inhibitors
- protection against UV !!!!, SPF 50+

Thank You