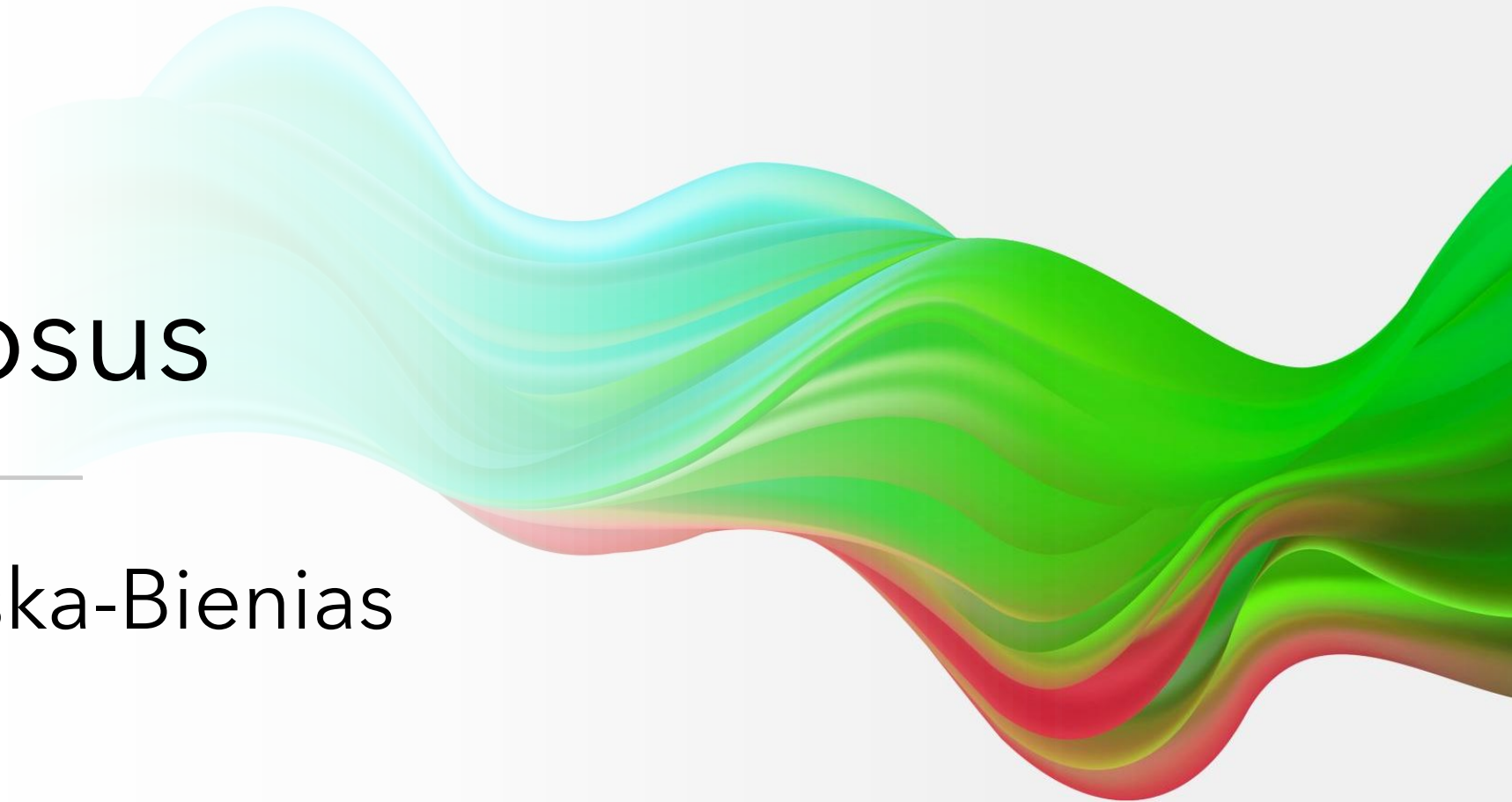




# Lupus erythematosus

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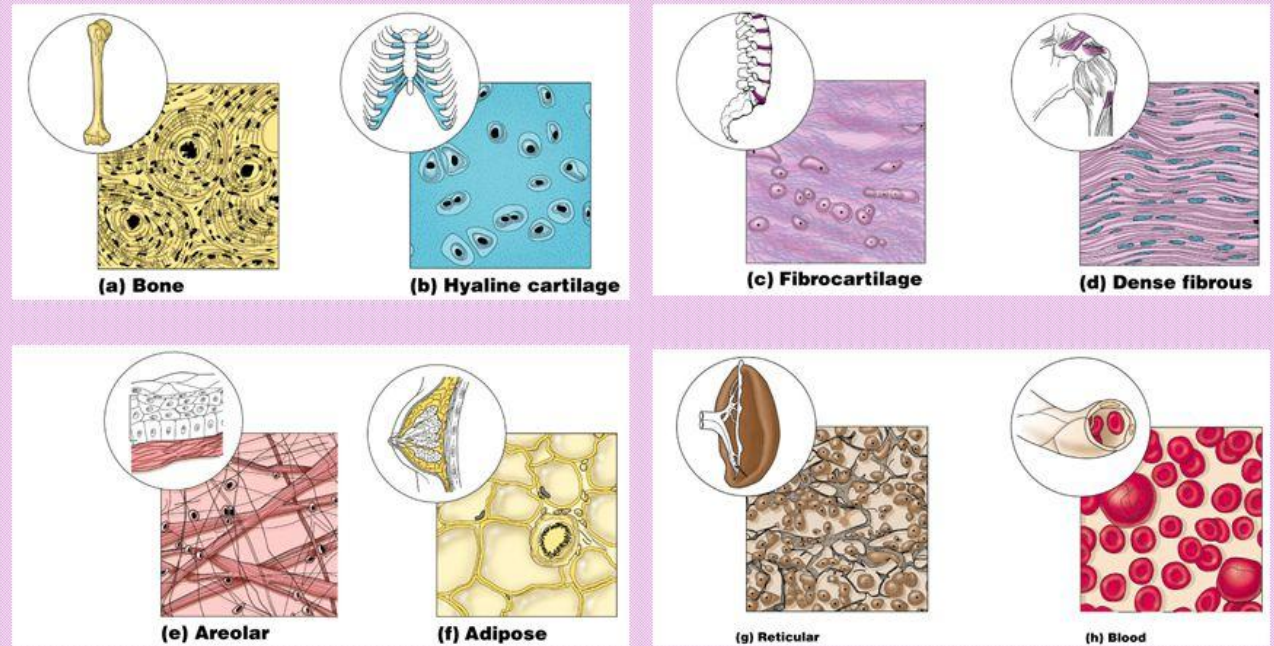
Agnieszka Kalińska-Bienias



## 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

## Connective Tissue



# 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 - CLE*
  - *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: 100% SLE, 90% SCLE, 20% DLE

# Cutaneous lupus erythematosus (CLE)



# Cutaneous lupus erythematosus (CLE)

Women & Men 2: 1- 4: 1

The onset of the disease 20-40  
years old

May be a symptom of SLE !!!

## Variants of CLE

- Discoid lupus erythematosus - DLE
- Lupus erythematosus tumidus - LET
- Hypertrophic LE
- Lupus erythematosus panniculitis
- Mucous membrane lupus
- Chilblain lupus



## 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

## Discoid lupus erythematosus, DLE

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



# Scarring scalp alopecia



features of scarring alopecia,  
which causes permanent hair  
loss

may be the only DLE location

# Lupus erythematosus tumidus



Outstanding hypersensitivity to UVR

Erythematosus infiltrations with smooth surface elevated above skin, without scarring

Skin lesions located on the sun-exposed areas

Positive LBT 50%

# Hyperkeratotic LE



thickened and warty plaques with severe hyperkeratosis

Treatment: low dosage of acitretin

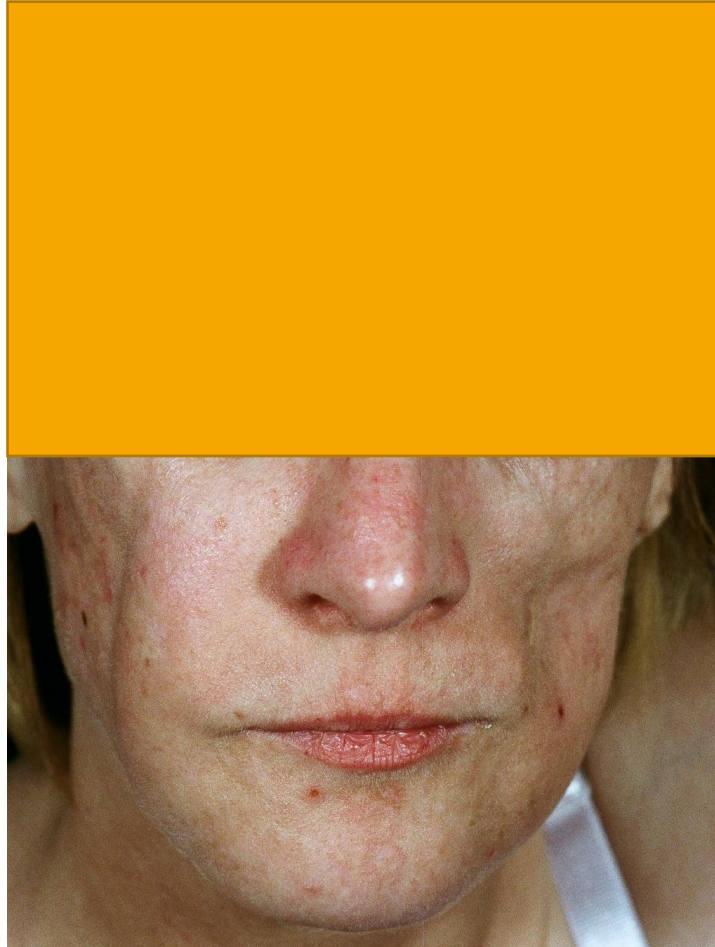
# Childblain lupus



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 panniculitis



affects subcutaneous  
tissue

may involve face, buttocks,  
arms, thighs

## Mucosal lupus erythematosus

Changes on the mucous membranes - ulcers  
- may concern: the palate and cheeks

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

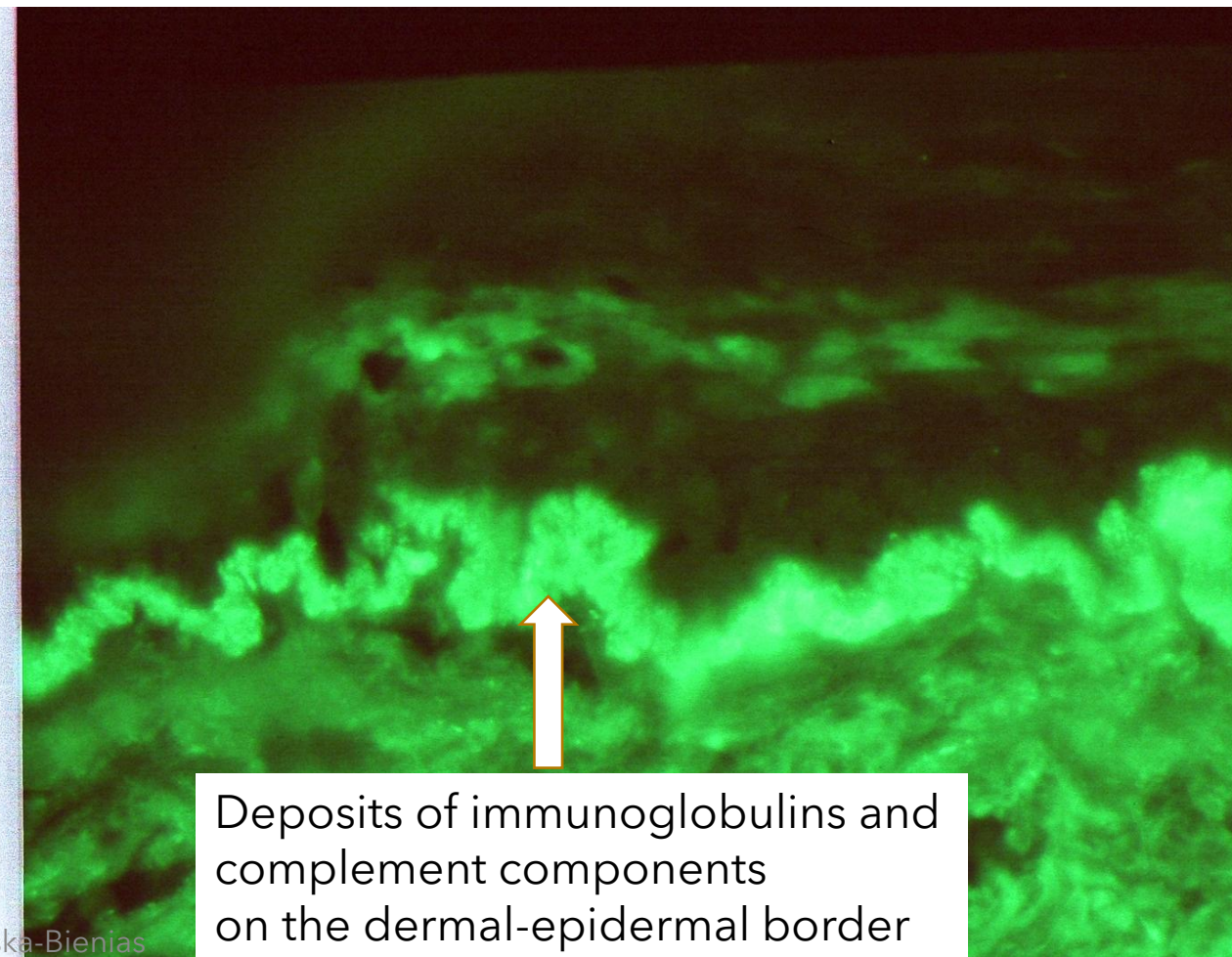
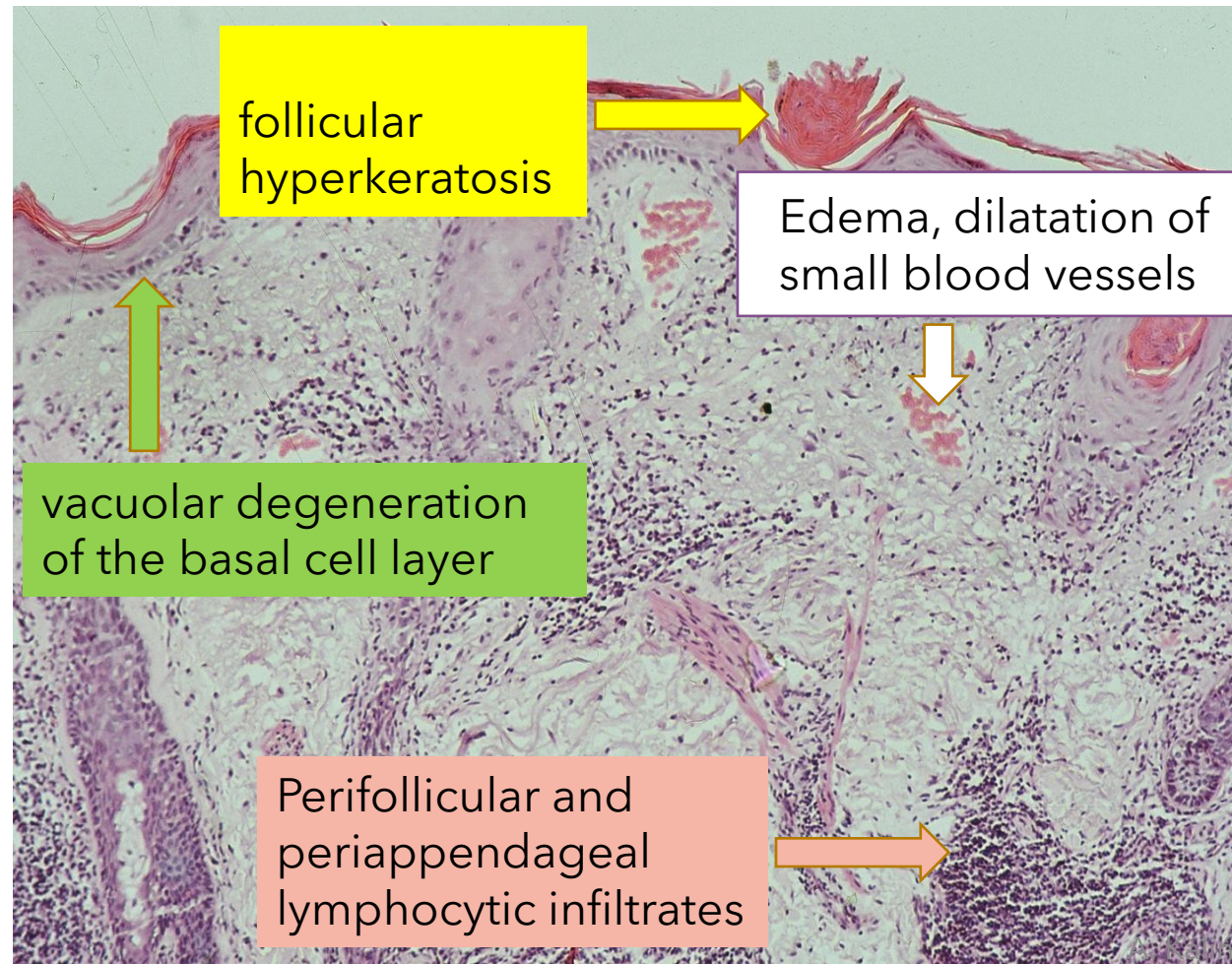


On the lips: erythematous plaques with whitish hyperkeratosis

# Diagnostics of LE- skin biopsy

Histopathological examination

Direct immunofluorescence test



# Treatment



## **Systemic treatment**

antimalarial drugs (hydroxychloroquine, chloroquine)  
glucocorticosteroids: medium and small, gradually  
reduce after clinical improvement 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  
SCLE

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# Subacute cutaneous lupus erythematosus (SCLE)



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, 30-50% - SLE



The presence of ANA in 90% with  
characteristic: Ro(SS-A) and La(SS-B)

# SCLE- types

- SCLE annularis
- SCLE psoriasiformis

In SCLE - healing with  
hypopigmentations/hyperpigmentations  
teleangiectasions



Annular SCLE



Psoriasiform SCLE

# Systemic lupus erythematosus SLE

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# 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 - 50 cases per 100,000 people
- the incidence of SLE ranges from 2-8 cases per 100,000 people/yearly
- 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 other 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)

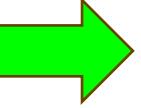
## Environmental factors

- 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

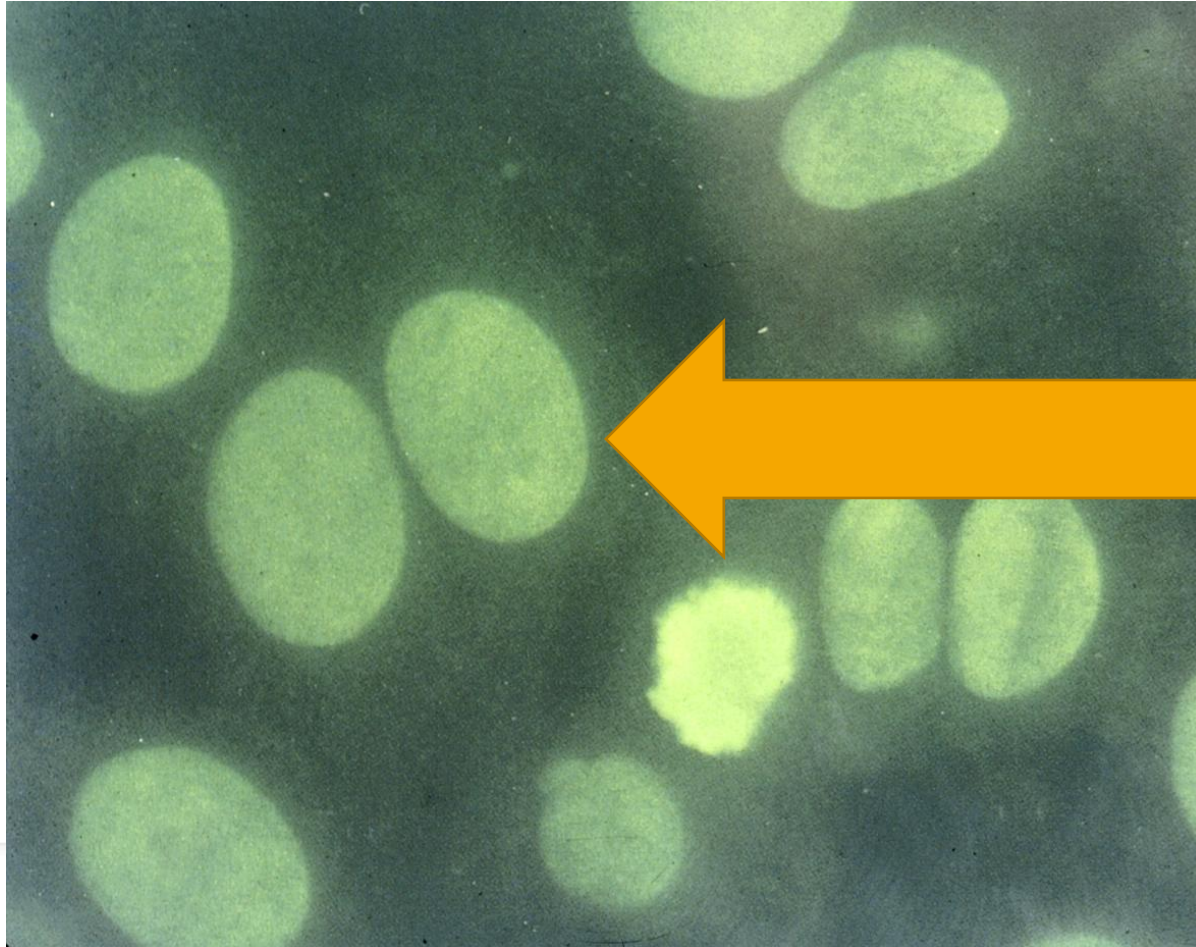


## ANA at a titer of $\geq 1:80$ on HEp-2 cells

Clinical domains	Points	Immunological domains	Points
Fever	2	Antiphospholipid antibodies	
Hematologic		Anticardiolipin antibodies or anti- $\beta$ 2GPI 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	Anti-Sm or Anti-dsDNA	6
Oral ulcers	2		
Subacute cutaneous OR discoid lupus	4		
Acute cutaneous lupus	6		
Serosal			
Pleural or pericardial effusion	5		
Acute pericarditis	6		
Joint involvement			
synovitis $\geq 2$ joints or tenderness $\geq 2$ and morning stiffness $\geq 30$ 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

# Diagnostics of circulating antibodies (ANA)



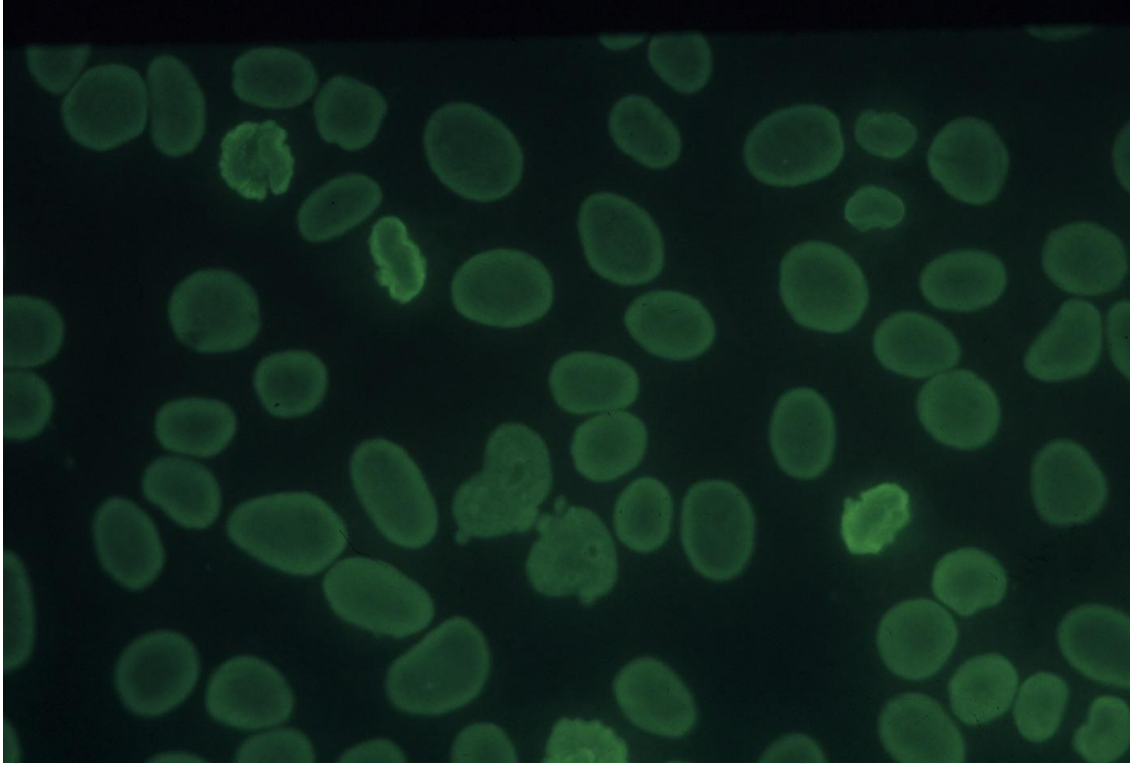
## ***ANA are detected by***

***- Indirect immunofluorescent study on the substrate - Hep-2 cells***

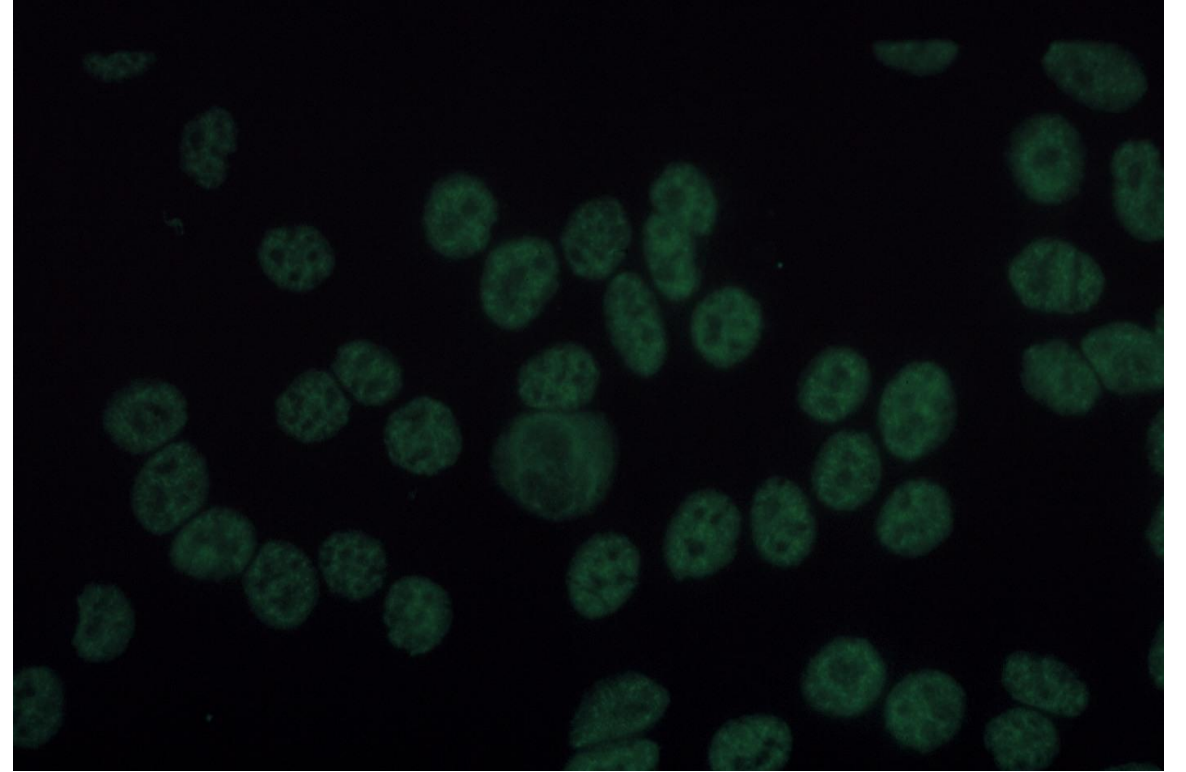
***(these are human epithelial cells derived from laryngeal cancer because of large cell nucleus)***

***- Immunoblot***

***- ELISA***



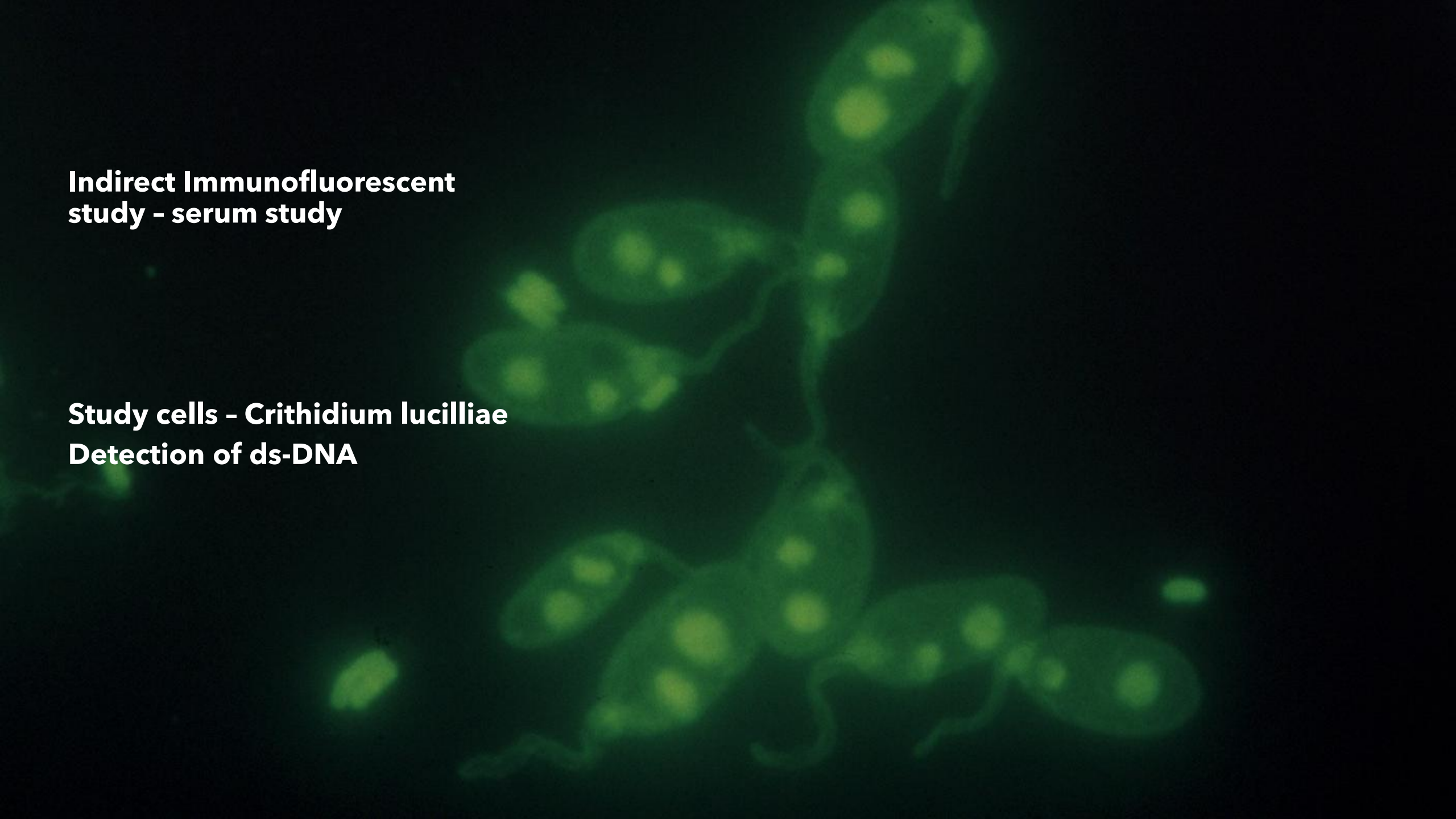
Shining typical for  
anti-ds.-DNA antibodies



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)

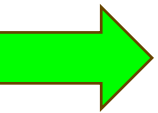
# Antinuclear antibodies- ANA

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

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Clinical domains	Points	Immunological domains	Points
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Hematologic		Anticardiolipin antibodies or anti- $\beta 2$ GPI antibodies or lupus anticoagulant	2
Leukopenia	3		
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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**





## 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 erythemas affecting the trunk and limbs

# Maculopapular lupus rash

- Symmetrical, often within the fingertips and nail folds



# Toxic epidermal necrolysis variant of SLE





## Non-scarring alopecia

# SLE

Chronic inflammation in many tissues and organs

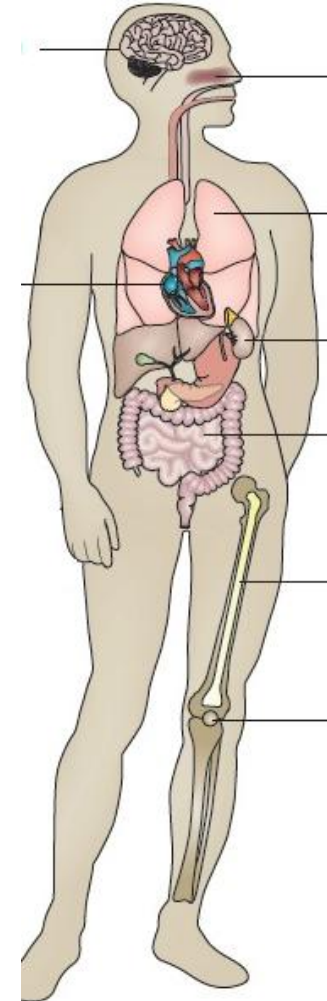
It may start with few symptoms

Symptoms often dominate  
in one organ

A course with periods of exacerbations and remissions

10-40% of remissions are long lasting over 1 year

In older people the course is slightly milder



# General symptoms in SLE

- Chronic fatigue
- Loss of appetite, weight loss
- Enlarged lymph nodes
- Low-grade fever, fever
- Headaches
- Night sweats

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**SLE at least 10 points**

# Hematological symptoms

Leukopenia	< 4000/mm <sup>3</sup>
Thrombocytopenia	< 100000/mm <sup>3</sup>
Hemolytic anemia	Confirmed hemolysis: reticulocytosis, low haptoglobin, increased indirect bilirubin, increased lactate dehydrogenase (LDH), positive direct Coombs test

# Symptoms and changes in the musculoskeletal system

Joints	<ol style="list-style-type: none"><li>1) inflammation of the synovium affecting 2 or more joints characterized by swelling or effusion</li><li>2) pain in 2 or more joints and morning stiffness lasting at least 30 minutes</li></ol>
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# lupus nephritis

lupus nephritis	Class II: Mesangioproliferative lupus nephritis Class V: Membranous lupus nephritis
lupus nephritis	Class III: Focal lupus nephritis Class IV: Diffuse lupus nephritis

Proteinuria	Proteinuria > 0.5 g/in 24-hour daily urine collection or abnormal protein/creatinine ratio in urine
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# Neurological and psychiatric symptoms

Delirium	change in consciousness, development of symptoms over a period of several hours to <2 days, fluctuation of symptoms throughout the day, acute/subacute change in cognitive function, change in behavior, mood or affect
Psychosis	delusions, hallucinations
Convulsions	generalized or partial seizure

# Serositis

Pleural or pericardial effusion	Pleural and/or pericardial effusion confirmed by imaging methods (USG/ECHO, X-ray, CT, MRI)
Acute pericarditis	pericardial chest pain (usually sharp, worsening on inspiration, improving in the sitting position when bending forward), pericardial rub, ECG with new ST elevations or PR(PQ) depressions, new or increasing pericardial effusion on imaging studies (USG) /ECHO, X-ray, CT, MRI)

# 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

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