Odessa National Medical University
Dept. of Internal Medicine # 2 with Postgraduate Education

LECTURE: SYSTEMIC CONNECTIVE TISSUE DISEASES

Lecturer: L.S.Kholopov, MD, PhD

2024

ICD-10: SYSTEMIC CONNECTIVE TISSUE DISORDERS

- M30. (0-8) Polyarteritis nodosa and related conditions
- M31. (0-9) Other necrotizing vasculopathies
- M32. (0-9) **Systemic lupus erythematosus**
- M33 Dermatopolymyositis
- M34 **Systemic sclerosis [scleroderma]**
- M35 Other systemic involvement of connective tissue

SYSTEMIC LUPUS ERYTHEMATOSUS

TO KNOW LUPUS IS TO KNOW MEDICINE

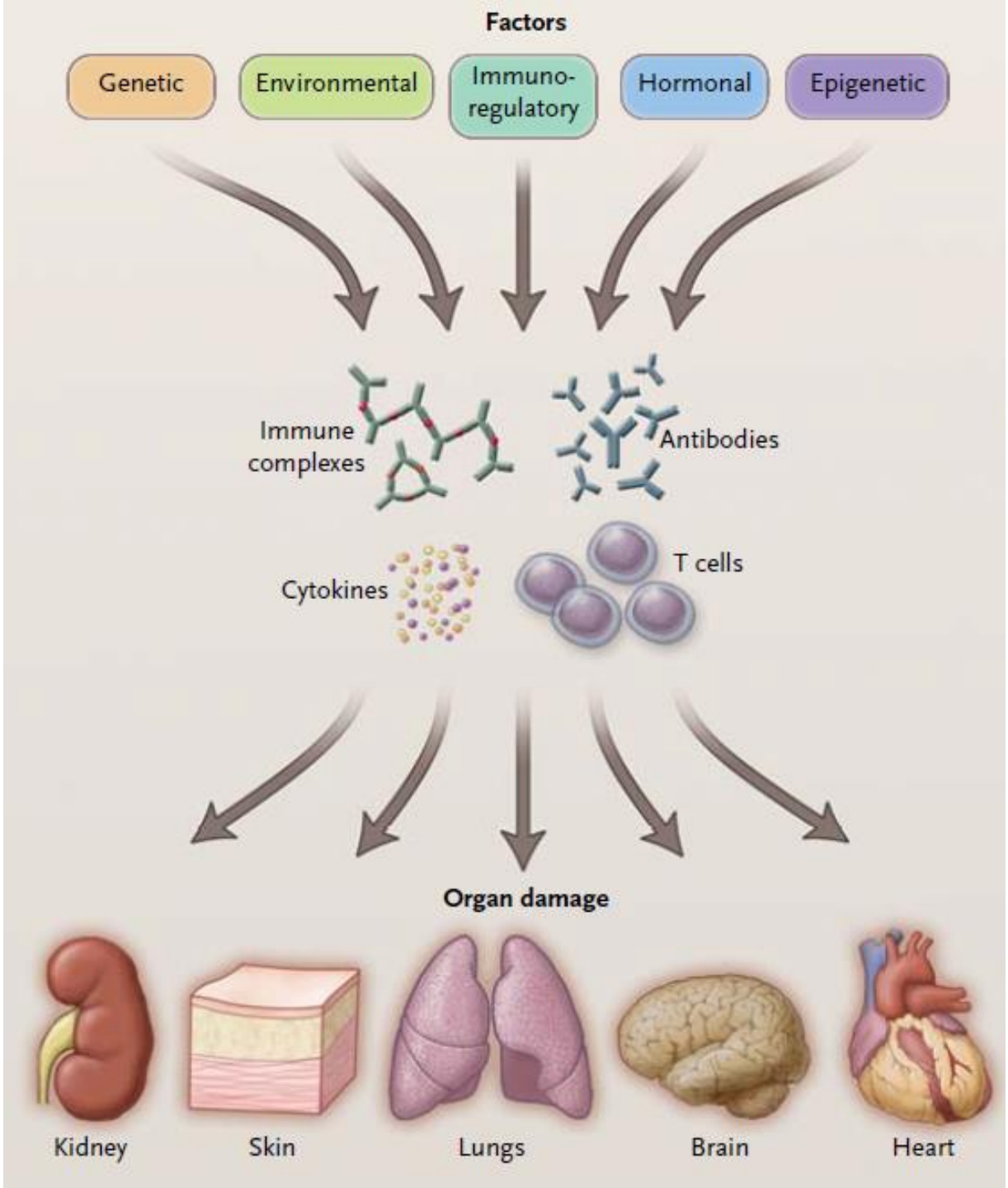
DEFINITION

- Systemic lupus erythematosus (SLE) is a multisystem disease that is caused by antibody production and complement-fixing immune complex deposition that result in tissue damage.

EPIDEMIOLOGY

- The prevalence of lupus ranges from approximately 40 cases per 100,000 persons among Northern Europeans to more than 200 per 100,000 persons among Africans.
- Female : Male = 9 : 1
- The life expectancy of such patients has improved from an 4-year survival rate of 50% in the 1950s to a 15-year survival rate of 80% today.
- Even so, a patient in whom lupus is diagnosed at 20 years of age still has a 1 in 6 chance of dying by 35 years of age.
- Peak age of onset: 20-30 yrs

N Engl J Med 2008;358:929-39.



PATHOGENESIS OF SLE

- Genetic, environmental, hormonal, epigenetic, and immunoregulatory factors act either sequentially or simultaneously on the immune system.
- The action of pathogenic factors results in the generation of autoantibodies, immune complexes, autoreactive or inflammatory T cells, and inflammatory cytokines that may initiate and amplify inflammation and damage to various organs.
- The target organ affected may be further damaged by local factors.

AMERICAN COLLEGE of RHEUMATOLOGY
Empowering Rheumatology Professionals

Arthritis & Rheumatology
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SPECIAL ARTICLE

2019 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Systemic Lupus Erythematosus

Martin Aringer,[1] Karen Costenbader,[2] David Daikh,[3] Ralph Brinks,[4] Marta Mosca,[5] Rosalind Ramsey-Goldman,[6] Josef S. Smolen,[7] David Wofsy,[8] Dimitrios T. Boumpas,[9] Diane L. Kamen,[10] David Jayne,[11] Ricard Cervera[12]

Recommendation

2019 update of the EULAR recommendations for the management of systemic lupus erythematosus

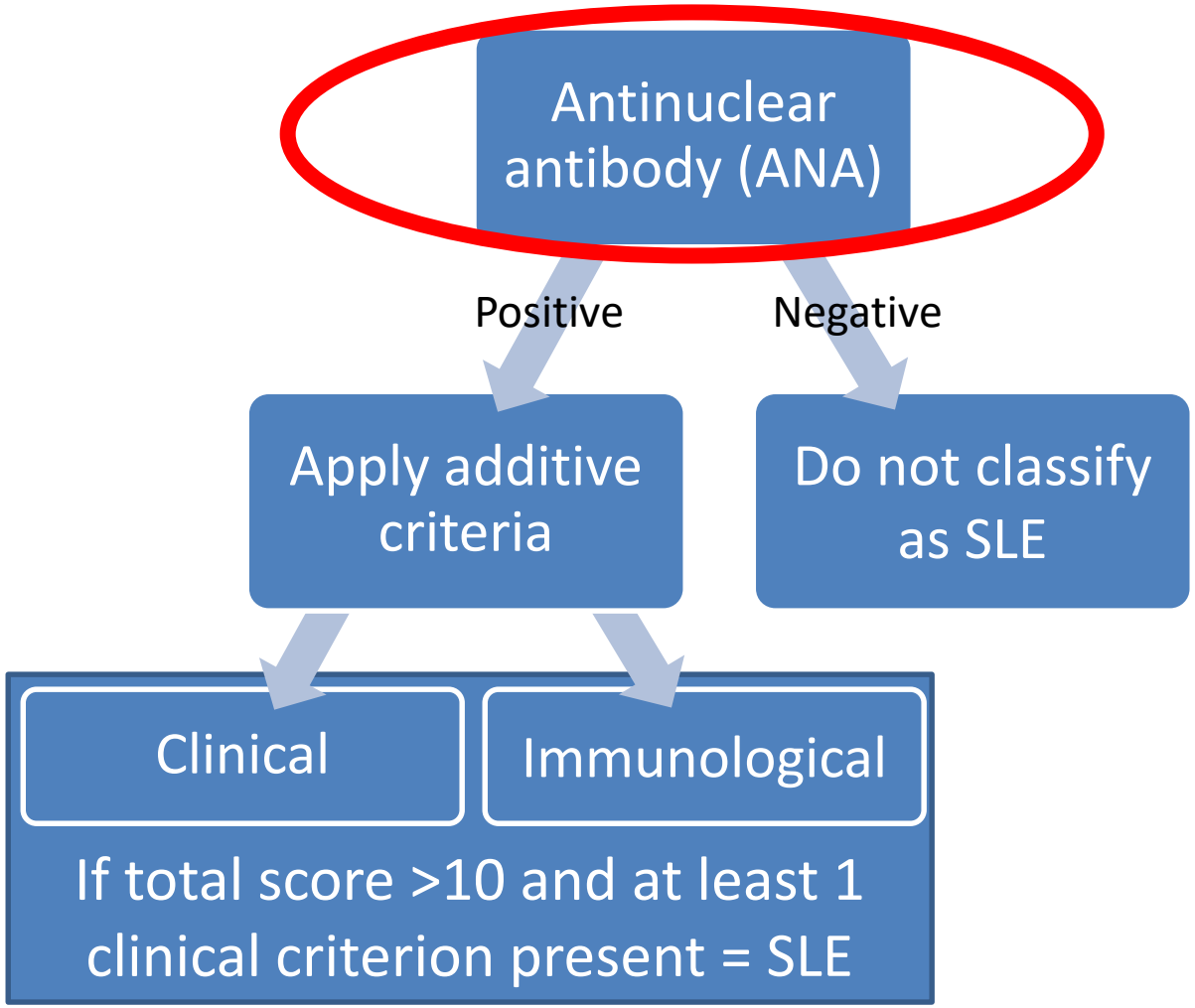
Antonis Fanouriakis,[1] Myrto Kostopoulou,[2] Alessia Alunno,[3] Martin Aringer,[4] Ingeborg Bajema,[5] John N Boletis,[6] Ricard Cervera,[7] Andrea Doria,[8] Caroline Gordon,[9] Marcello Govoni,[10] Frédéric Houssiau,[11] David Jayne,[12] Marios Kouloumas,[13] Annegret Kuhn,[14] Janni L Larsen,[15] Kirsten Lerstrøm,[16] Gabriella Moroni,[17] Marta Mosca,[18] Matthias Schneider,[19] Josef S Smolen,[20] Elisabet Svenungsson,[21] Vladimir Tesar,[22] Angela Tincani,[23] Anne Troldborg,[24] Ronald van Vollenhoven,[25] Jörg Wenzel,[26] George Bertsias,[27] Dimitrios T Boumpas[1,28,29]

Handling editor David S

ABSTRACT

the EULAR recommendations for lupus, capital-

Classification criteria for SLE



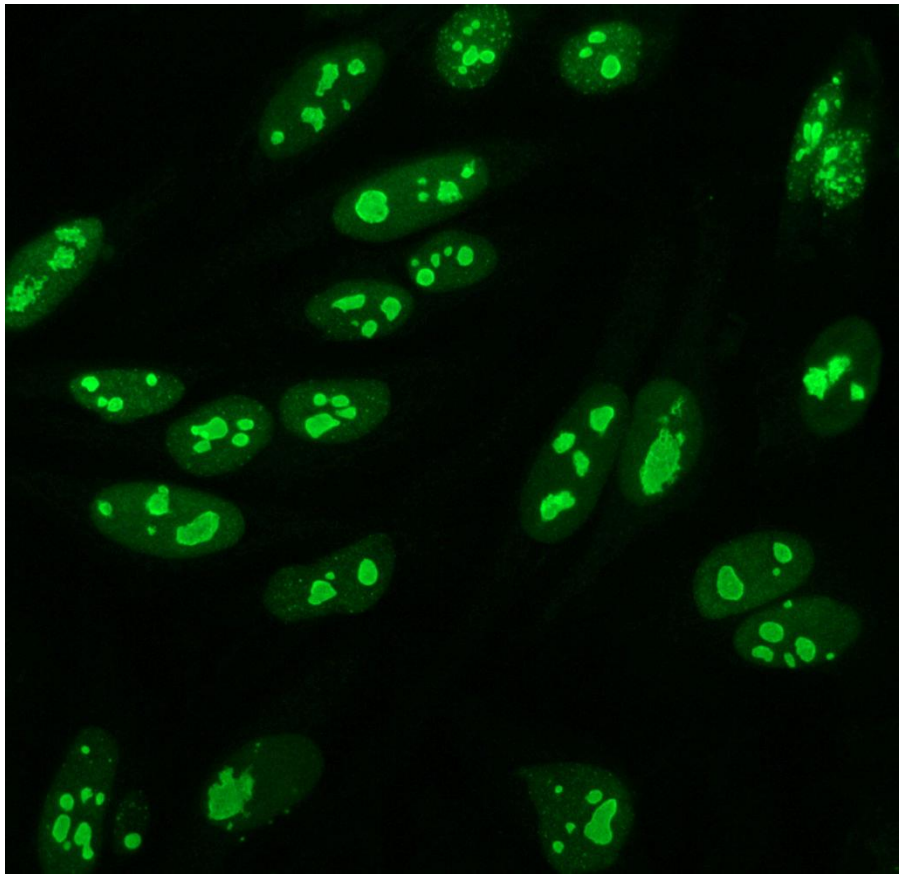
2019 EULAR / ACR Classification Criteria for SLE. Arthr. & Rheum. 2019, 71, 9, 1400–12

Classification criteria for SLE

Entry criterion

- **Antinuclear antibodies** (ANA) - at a titer of ≥1:80 on HEp-2 cells or an equivalent positive test at least once.

- **ANAs**, also known as **antinuclear factor** or **ANF** are autoantibodies that bind to contents of the cell nucleus.



Nucleolar staining pattern of ANAs.

Classification criteria for SLE

Constitutional	
Fever	2
Hematologic	
Leukopenia	3
Thrombocytopenia	4
Autoimmune hemolysis	4
Neuropsychiatric	
Delirium	2
Psychosis	3
Seizure	5
Mucocutaneous	
Non-scarring alopecia	2
Oral ulcers	2
Subacute cutaneous OR discoid lupus	4
Acute cutaneous lupus	6
Serosal	
Pleural or pericardial effusion	5
Acute pericarditis	6
Musculoskeletal	
Joint involvement	6
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Antiphospholipid antibodies	
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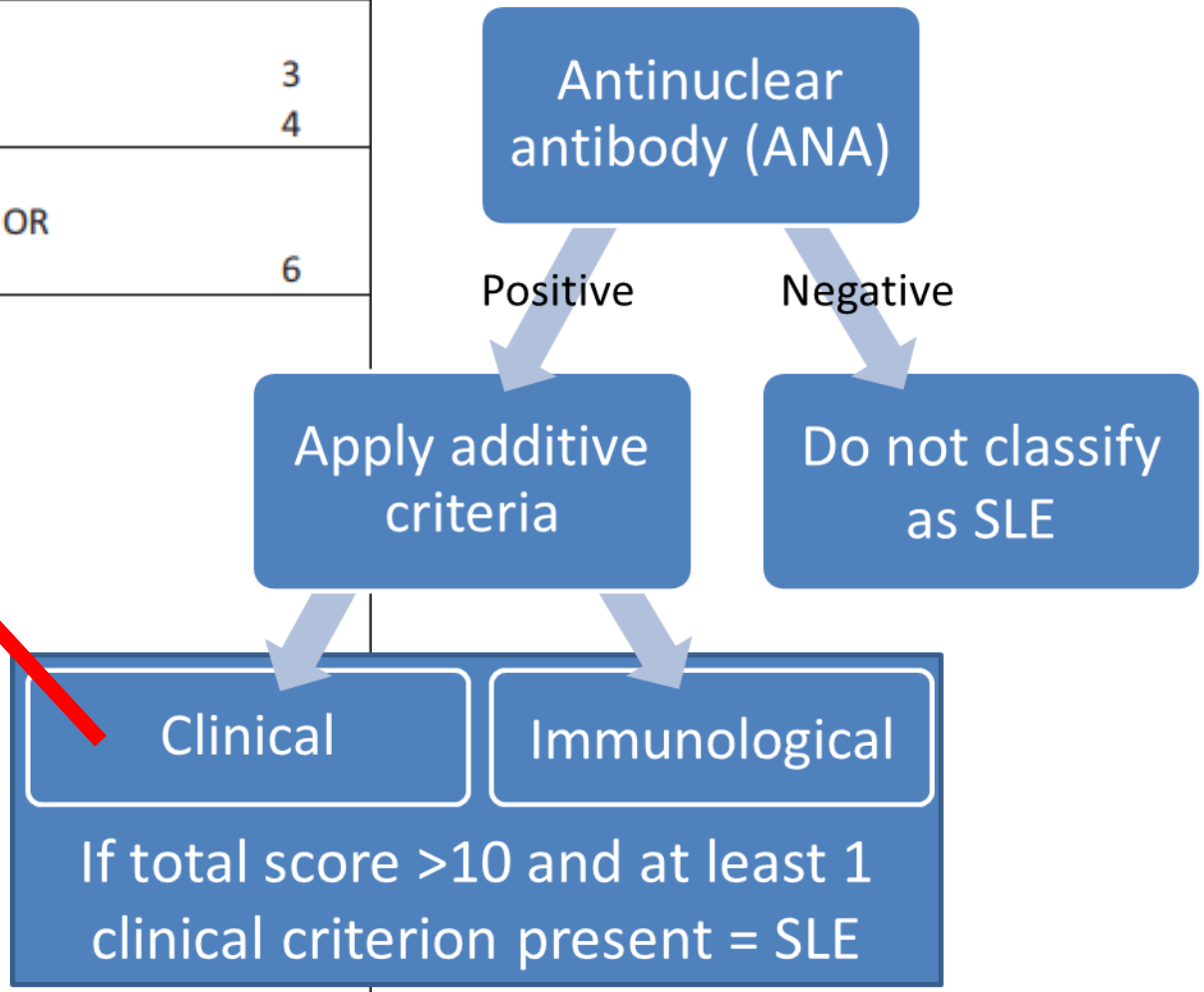

2019 EULAR / ACR Classification Criteria for SLE. Arthr. & Rheum. 2019, 71, 9, 1400–12

Classification criteria for SLE

Clinical criteria

Constitutional

- **Fever –** Temperature >38.3°C – **2 points**

Do not count a criterion if there is a more likely explanation than SLE.
Occurrence of a criterion on at least one occasion is sufficient.
Criteria need not occur simultaneously.

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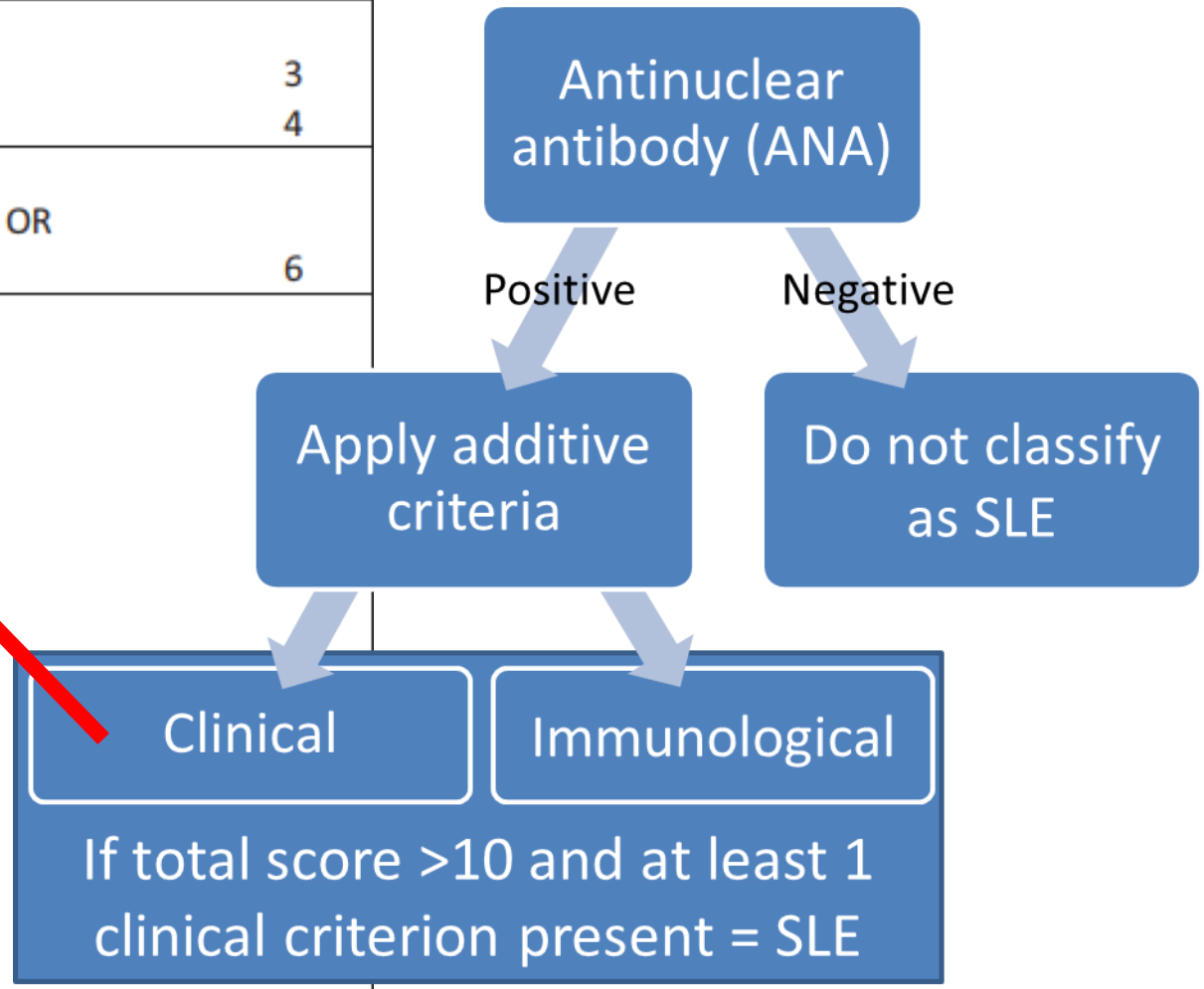


2019 EULAR / ACR Classification Criteria for SLE. Arthr. & Rheum. 2019, 71, 9, 1400–12

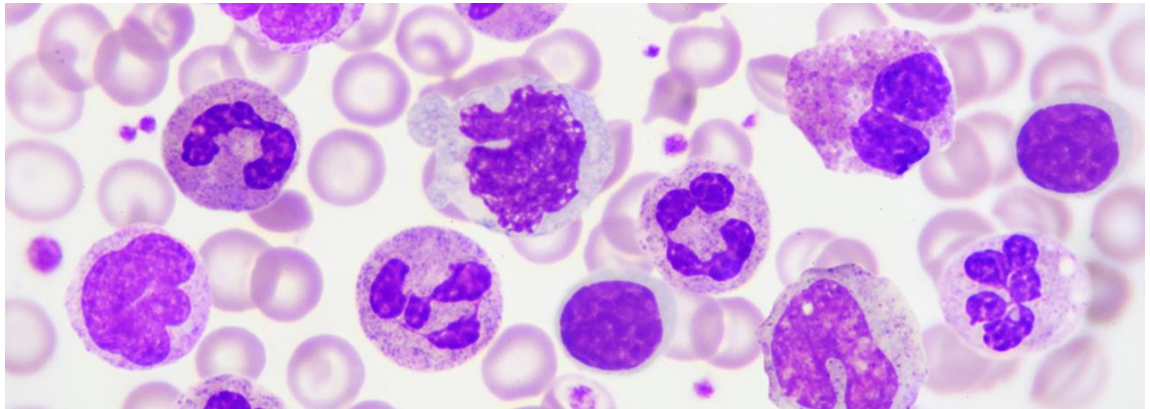
Classification criteria for SLE

Clinical criteria

Hematological

- **Leukopenia –** WBC count <4,000 / mm3 – **3 points**
- **Thrombocytopenia –** Platelet count <100,000 / mm3 – **4 points**
- **Autoimmune hemolysis –** Evidence of hemolysis, such as reticulocytosis, low haptoglobin, elevated indirect bilirubin, elevated LDH, AND positive Coombs' (direct antiglobulin) test – **4 points**

Within each domain, only the highest weighted criterion is counted toward the total score



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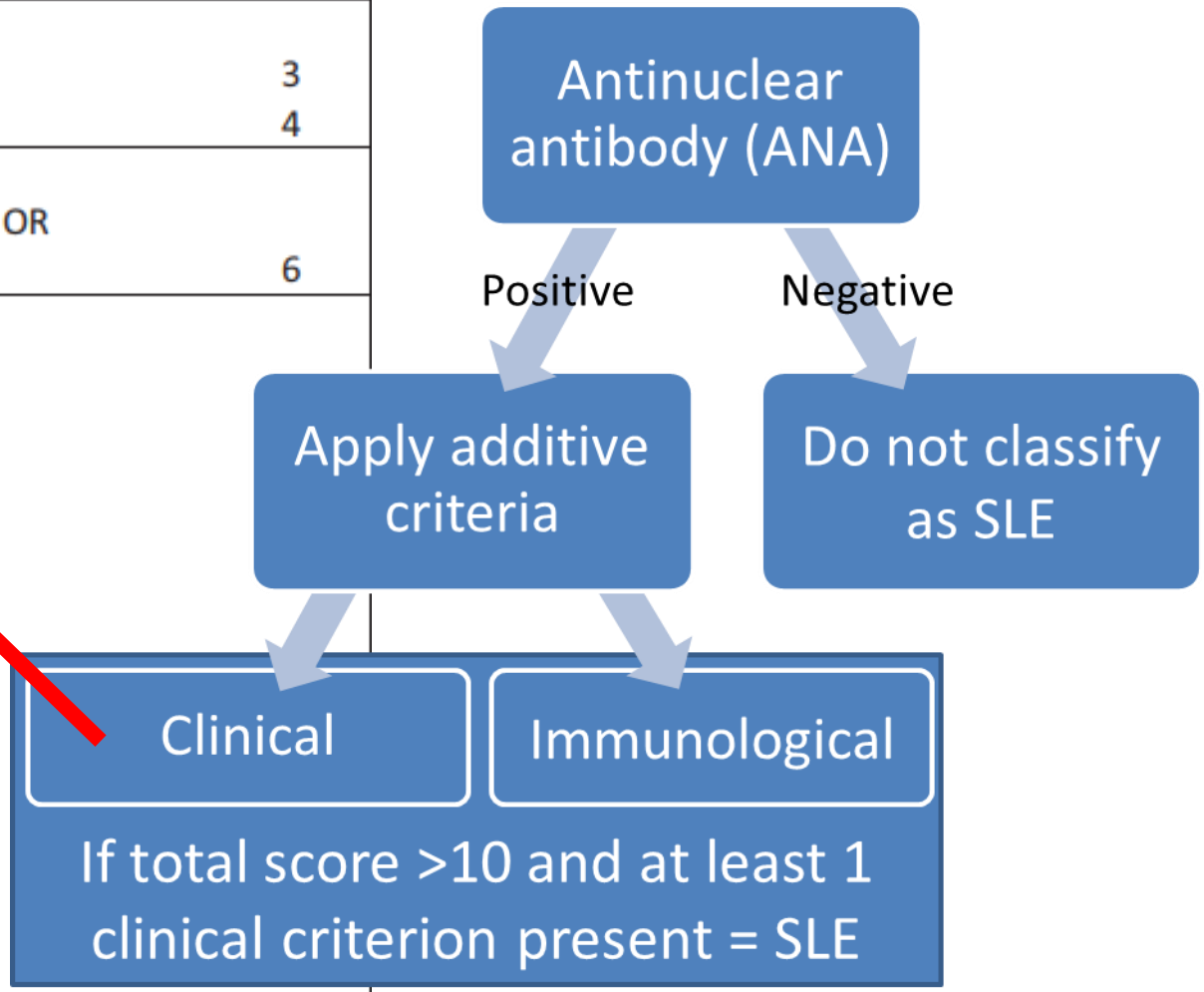


2019 EULAR / ACR Classification Criteria for SLE. Arthr. & Rheum. 2019, 71, 9, 1400–12

Classification criteria for SLE

Clinical criteria

Neuropsychiatric

- **Delirium –** Characterized by
  - 1) change in consciousness or level of arousal with reduced ability to focus,
  - 2) symptom development over hours to 2 days
  - 3) symptom fluctuation throughout the day,
  - 4) either
    - 4a) acute/subacute change in cognition (e.g., memory deficit or disorientation), or
    - 4b) change in behavior, mood, or affect (e.g., restlessness, reversal of sleep/wake cycle)

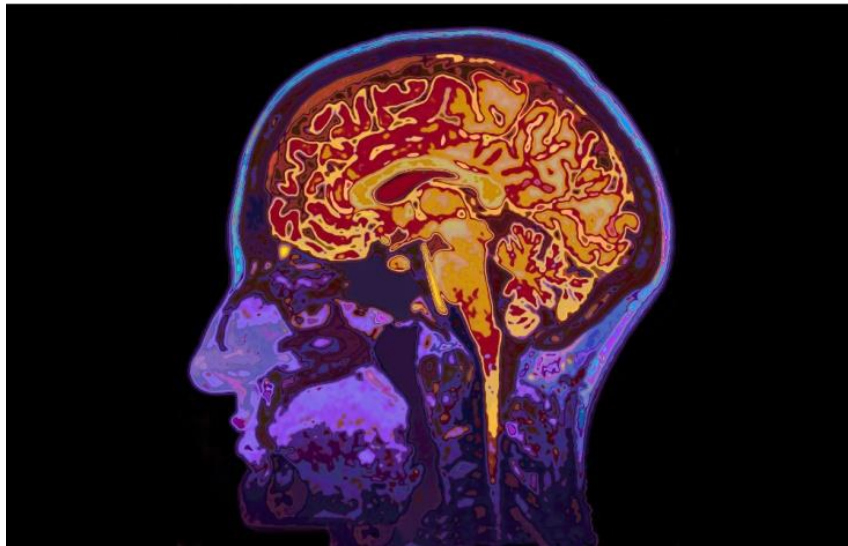
  – 3 points

- **Psychosis –** Characterized by
  - 1) delusions and/or hallucinations without insight and
  - 2) absence of delirium

  – 4 points

- **Seizure –** Primary generalized seizure or partial/focal seizure

  – 4 points



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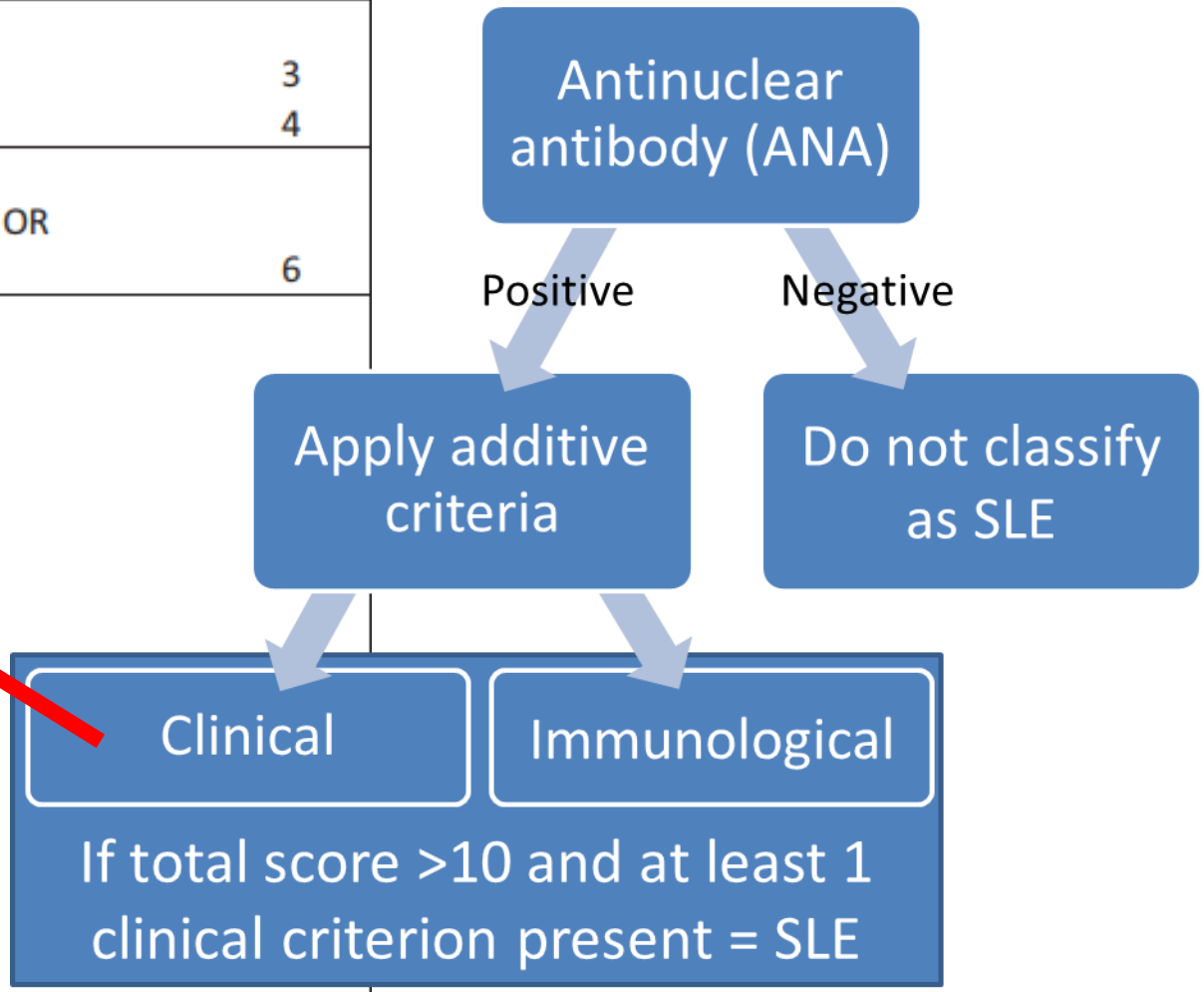


2019 EULAR / ACR Classification Criteria for SLE. Arthr. & Rheum. 2019, 71, 9, 1400–12

Classification criteria for SLE

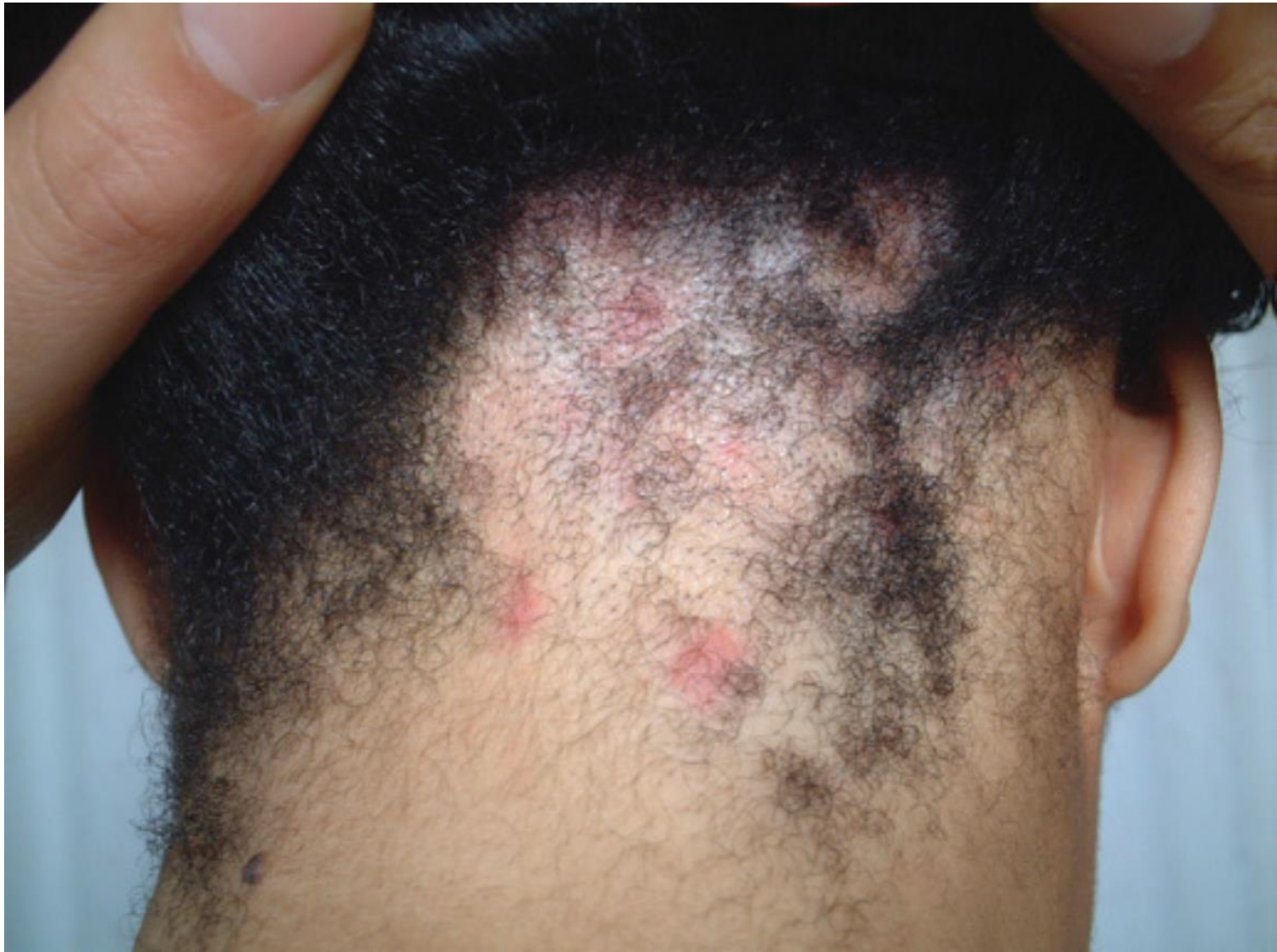
Clinical criteria

Mucocutaneous

- **Alopecia – 2 points**
- **Oral ulcers – 2 points**
- **Subacute cutaneous or discoid lupus – 4 points**
- **Acute cutaneous lupus** – 6 **points**

This may include physical examination or review of a photograph.

Alopecia - Non-scarring alopecia observed by a clinician



Classification criteria for SLE

Clinical criteria

Mucocutaneous

- **Alopecia – 2 points**
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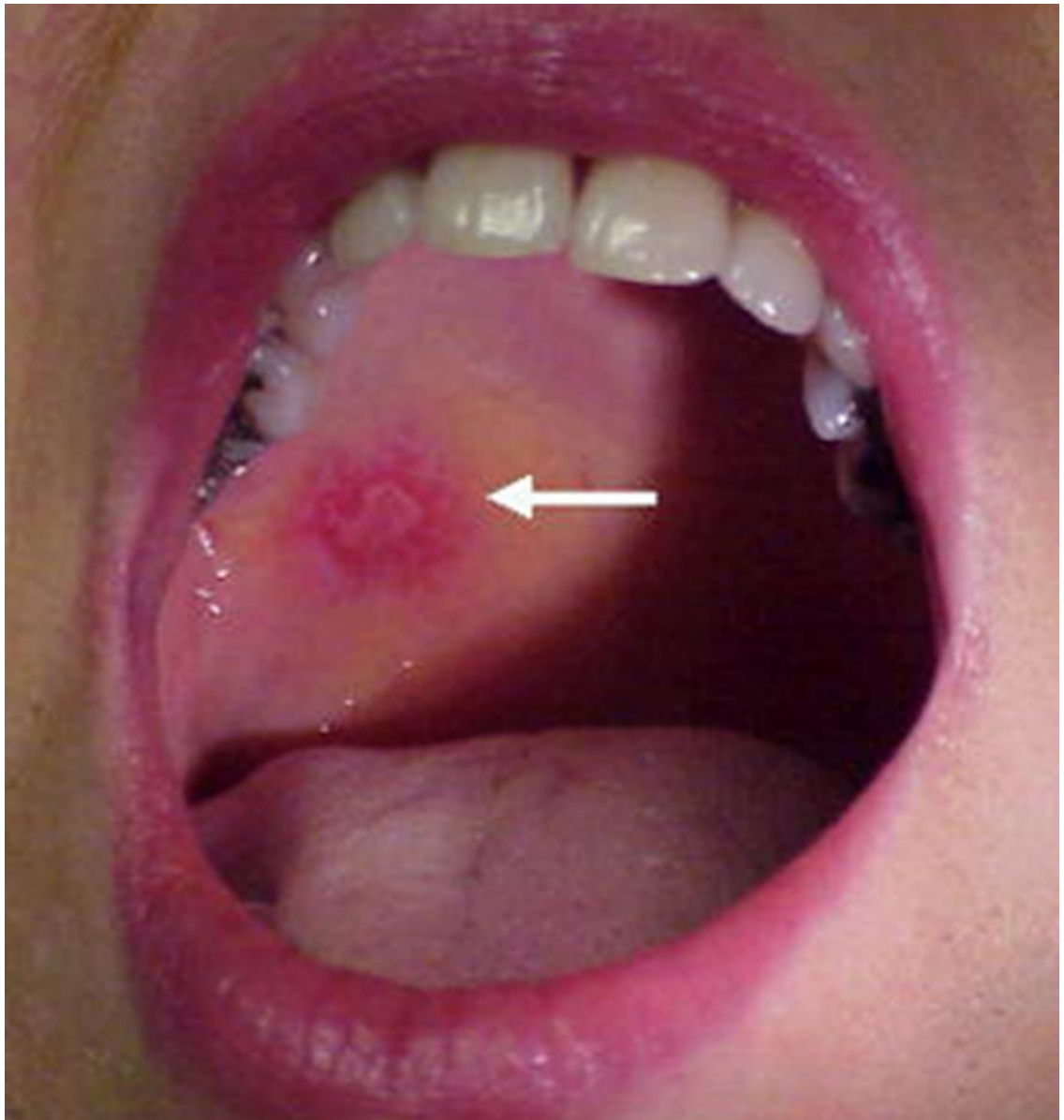
- **Acute cutaneous lupus** – 6 **points**

Oral ulcers – observed by a clinician



Classification criteria for SLE

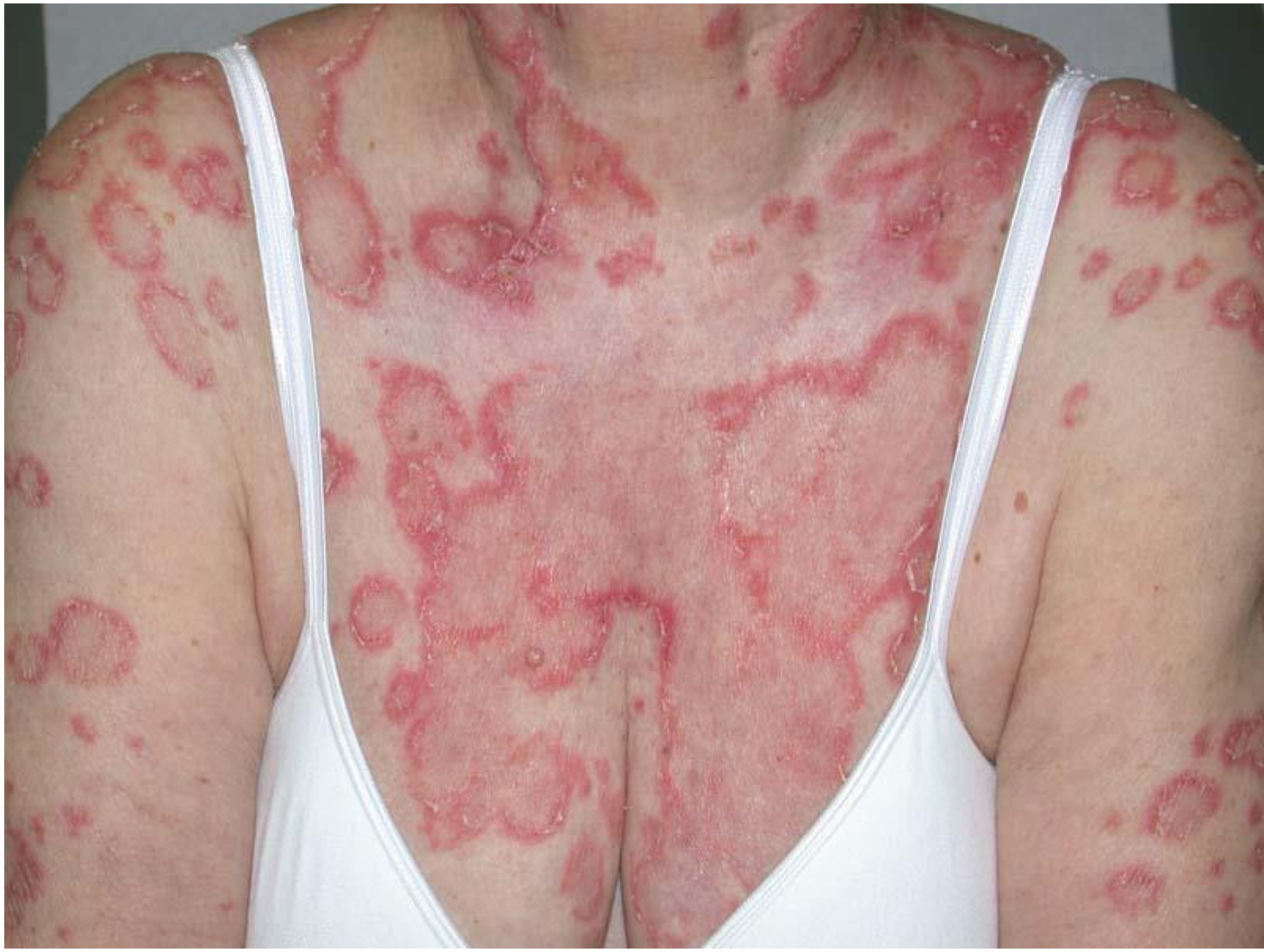
Clinical criteria

Mucocutaneous

- **Alopecia – 2 points**
- **Oral ulcers – 2 points**
- **Subacute cutaneous or discoid lupus – 4 points**
- **Acute cutaneous lupus** – 6 **points**

Subacute cutaneous lupus erythematosus – Annular or papulosquamous (psoriasiform) cutaneous eruption, usually photodistributed.

If skin biopsy is performed, typical changes must be present (interface vacuolar dermatitis consisting of a perivascular lymphohistiocytic infiltrate, often with dermal mucin noted).



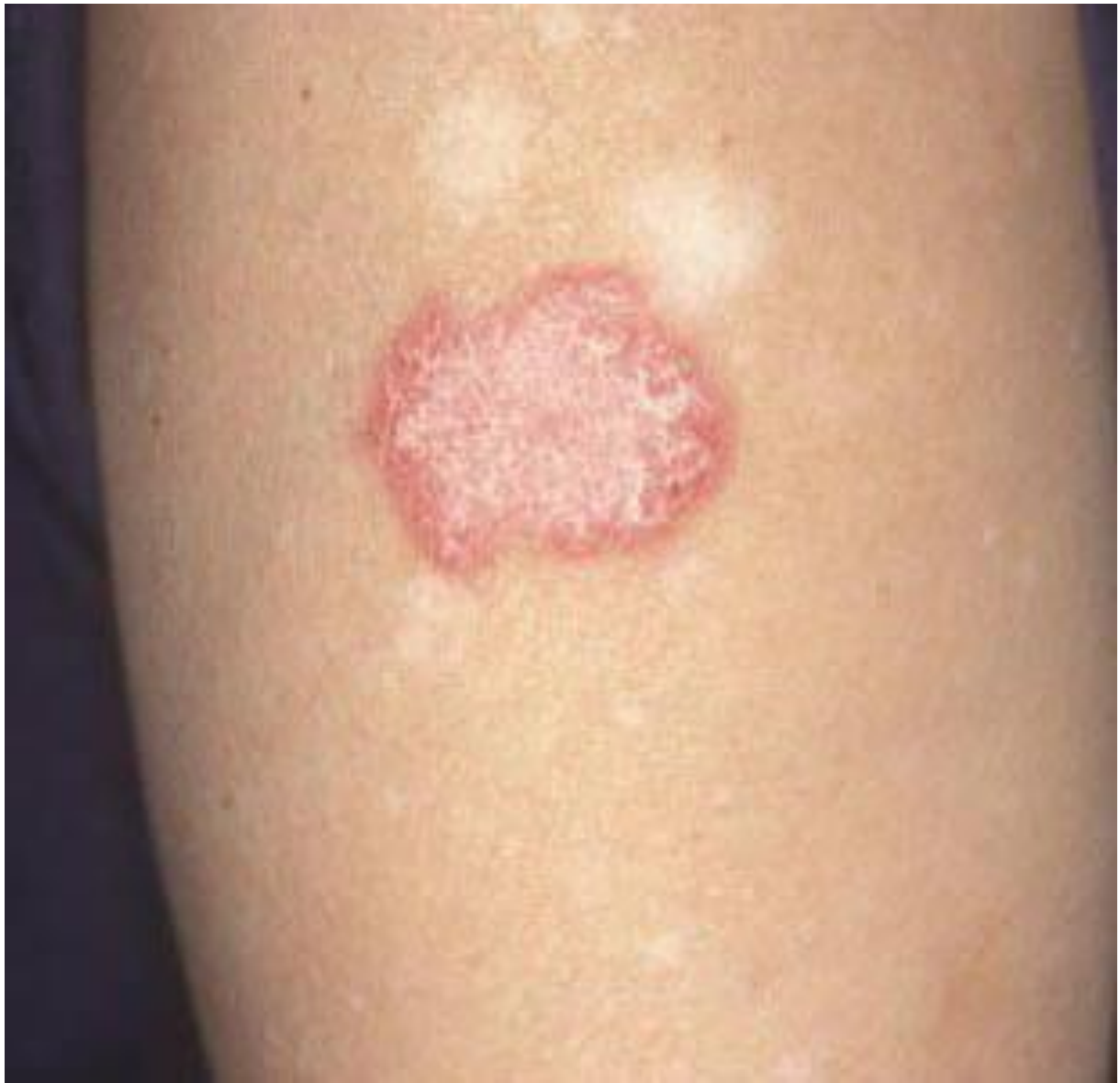
Classification criteria for SLE

Clinical criteria

Mucocutaneous

- **Alopecia** – **2 points**
- **Oral ulcers** – **2 points**
- **Subacute cutaneous or discoid lupus** – **4 points**
- **Acute cutaneous lupus** – 6 **points**

Discoid lupus erythematosus – Erythematous-violaceous cutaneous lesions with secondary changes of atrophic scarring, dyspigmentation, often follicular hyperkeratosis/plugging (scalp), leading to scarring alopecia on the scalp. If skin biopsy is performed, typical changes must be present (interface vacuolar dermatitis consisting of a perivascular and/or periappendageal lymphohistiocytic infiltrate. In the scalp, follicular keratin plugs may be seen. In longstanding lesions, mucin deposition may be noted)



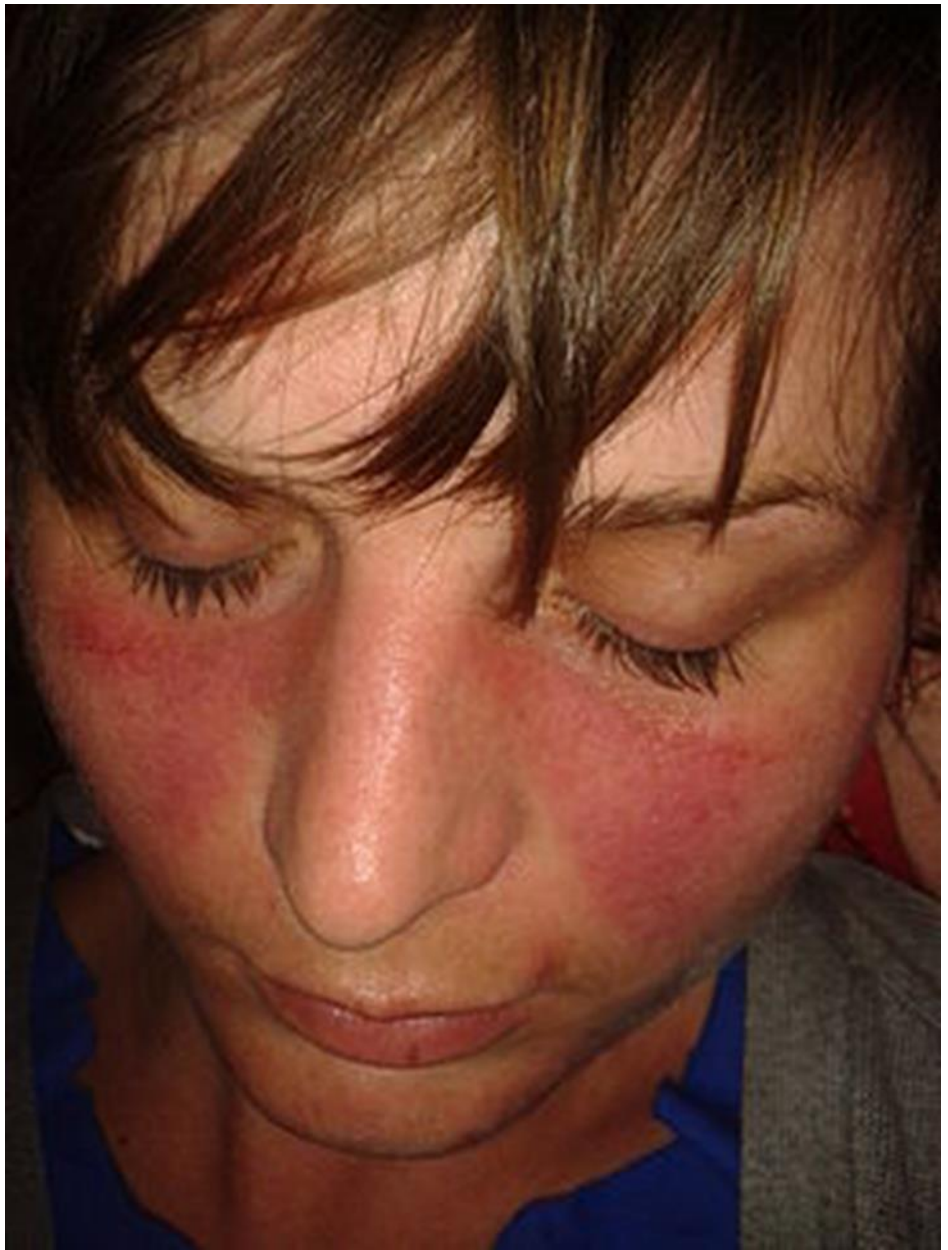
Classification criteria for SLE

Mucocutaneous

Clinical criteria

- **Alopecia** – **2 points**
- **Oral ulcers** – **2 points**
- **Subacute cutaneous or discoid lupus** – **4 points**
- **Acute cutaneous lupus** – 6 **points**

Acute cutaneous lupus – Malar rash (Fixed erythema, flat or raised, over the malar eminences, tending to spare the nasolabial folds) or generalized maculopapular rash observed by a clinician. If skin biopsy is performed, typical changes must be present (interface vacuolar dermatitis consisting of a perivascular lymphohistiocytic infiltrate, often with dermal mucin noted. Perivascular neutrophilic infiltrate may be present early in the course).



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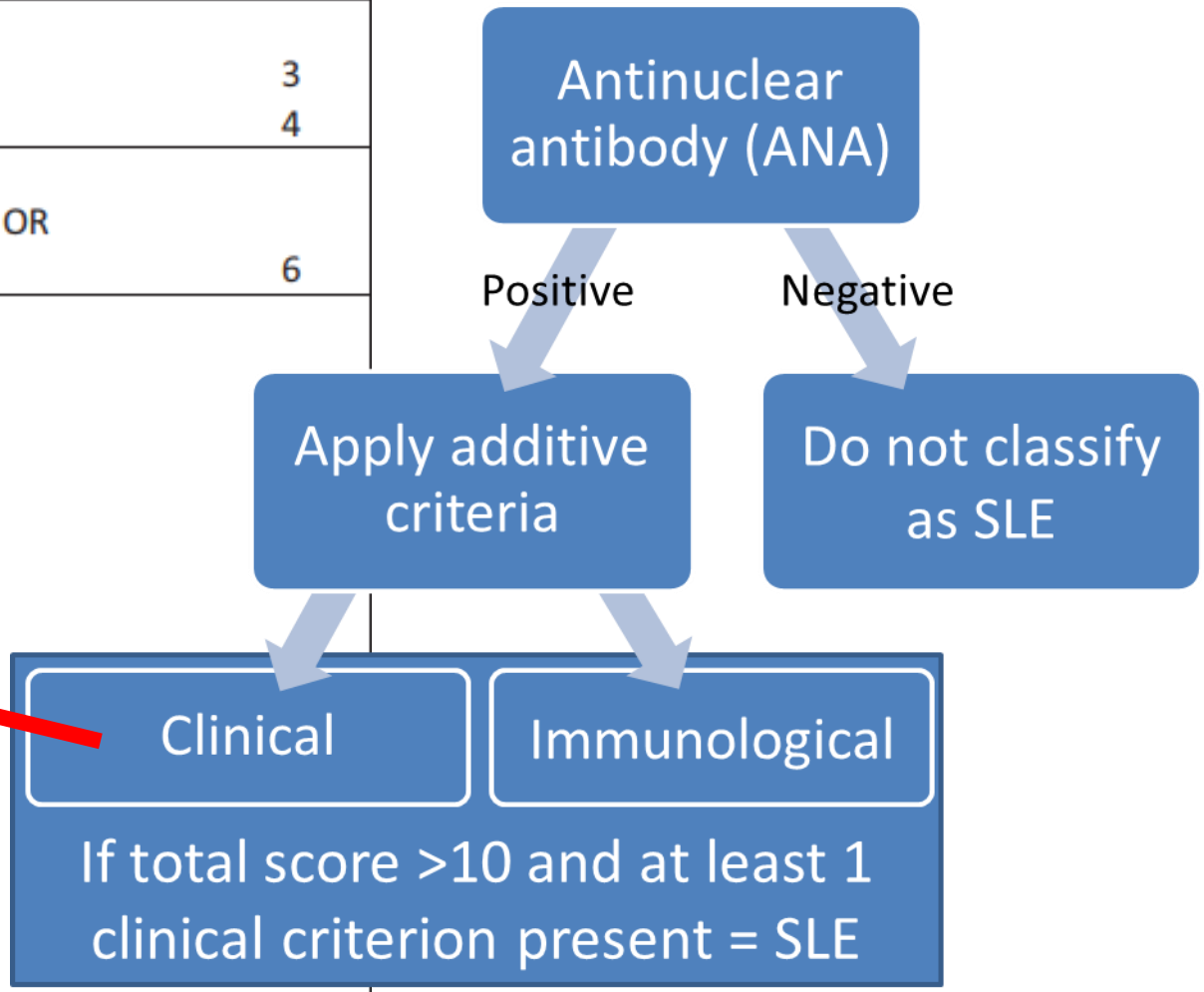


2019 EULAR / ACR Classification Criteria for SLE. Arthr. & Rheum. 2019, 71, 9, 1400–12

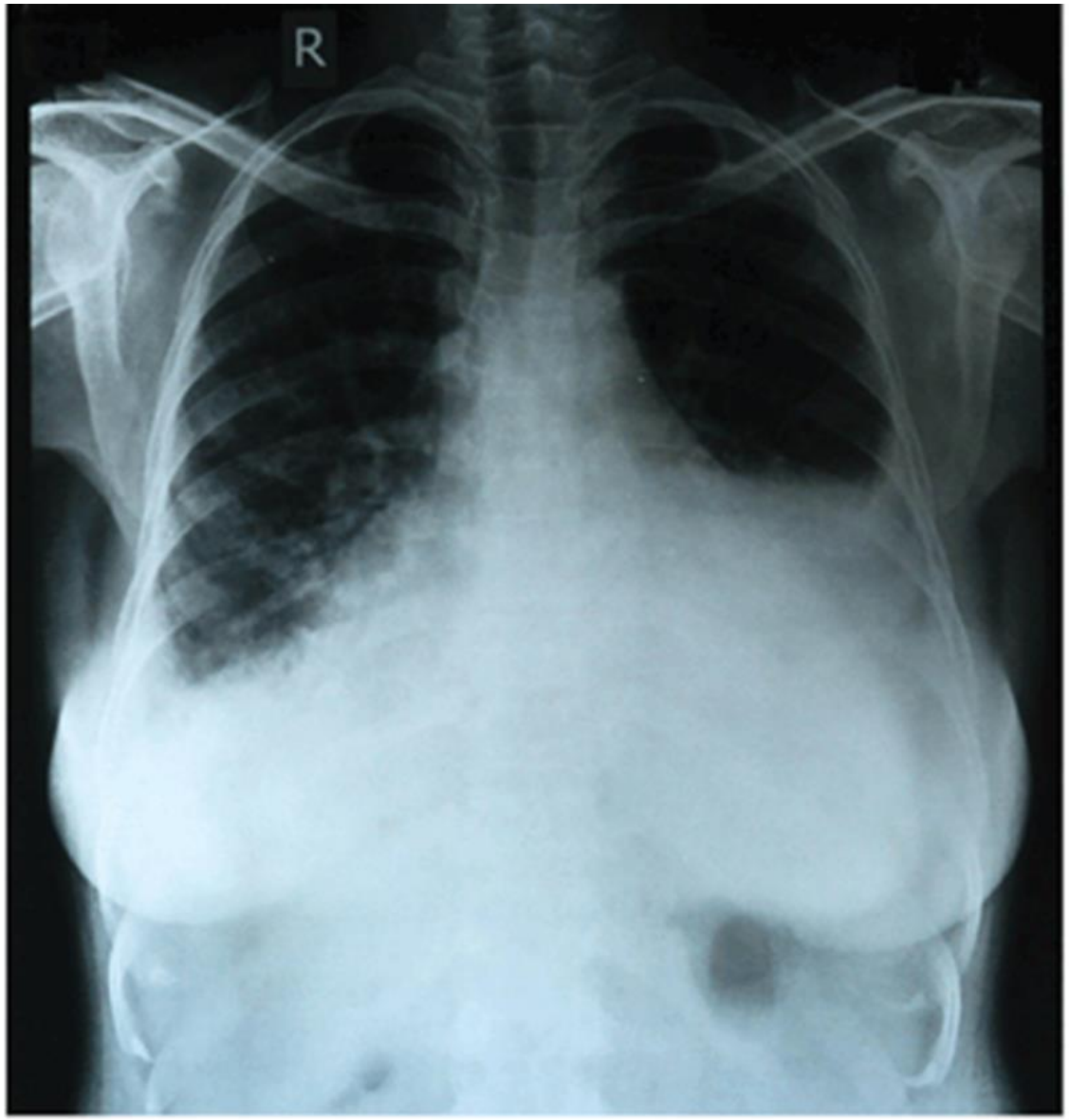
Classification criteria for SLE

Clinical criteria

Serosal

- **Pleural or pericardial effusion – 5 points**
- **Acute pericarditis – 6 points**

Pleural effusion – Imaging evidence (such as ultrasound, x-ray, CT scan, MRI) of pleural effusion



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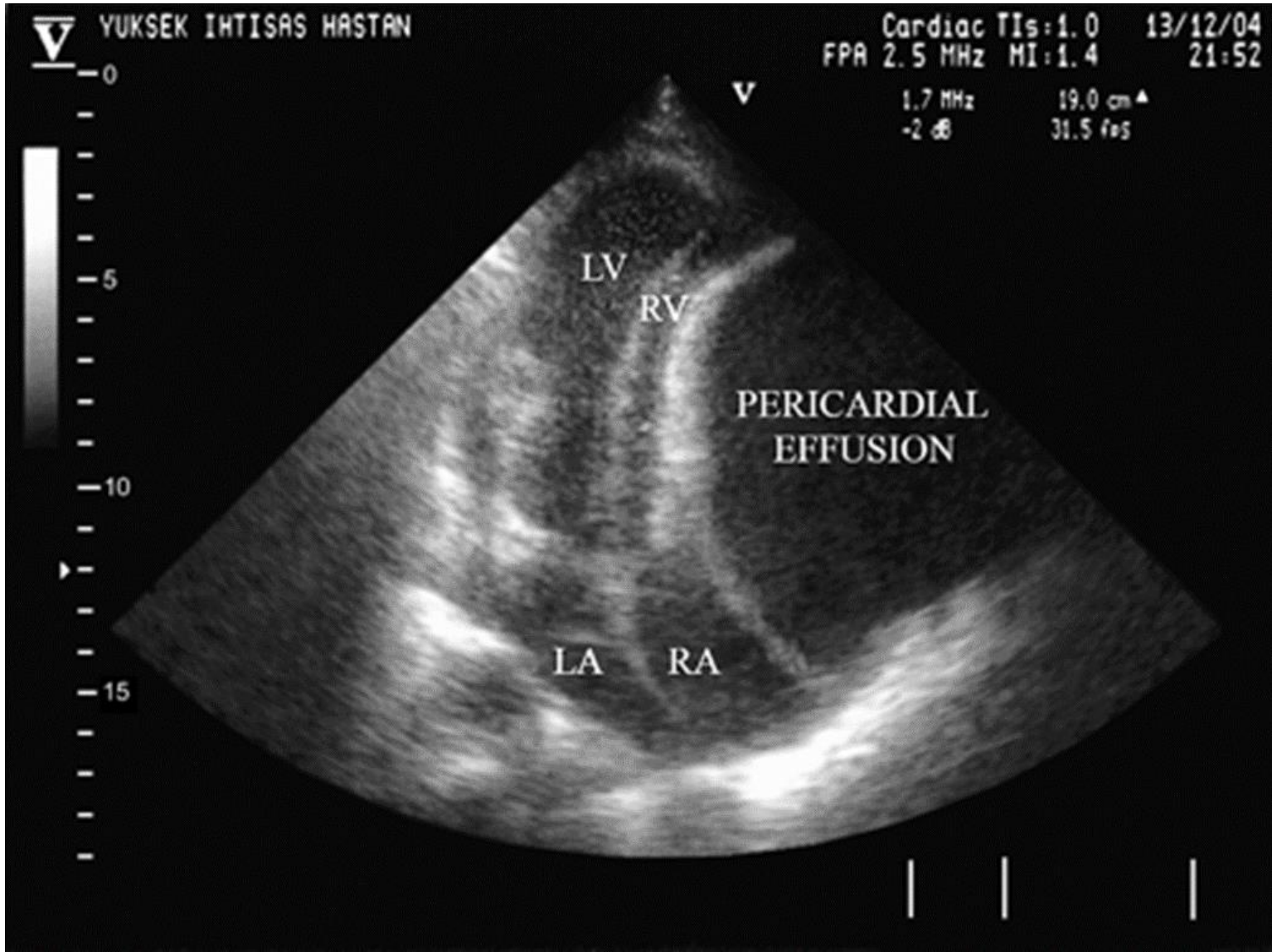

Classification criteria for SLE

Clinical criteria

Serosal

- **Pleural or pericardial effusion** – **5 points**
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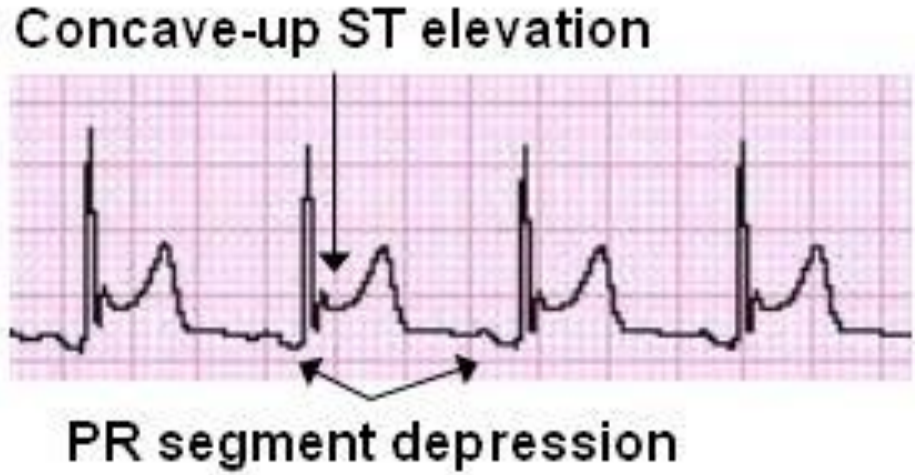
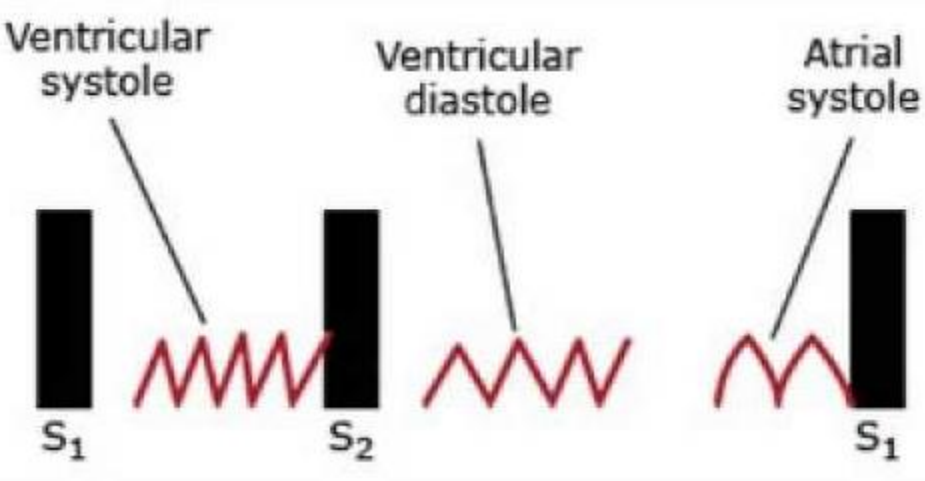
Acute pericarditis – ≥ 2 of:

1) pericardial chest pain (typically sharp, worse with inspiration, improved by leaning forward),
2) pericardial rub,
3) ECG with new widespread ST elevation or PR depression,
4) new or worsened pericardial effusion





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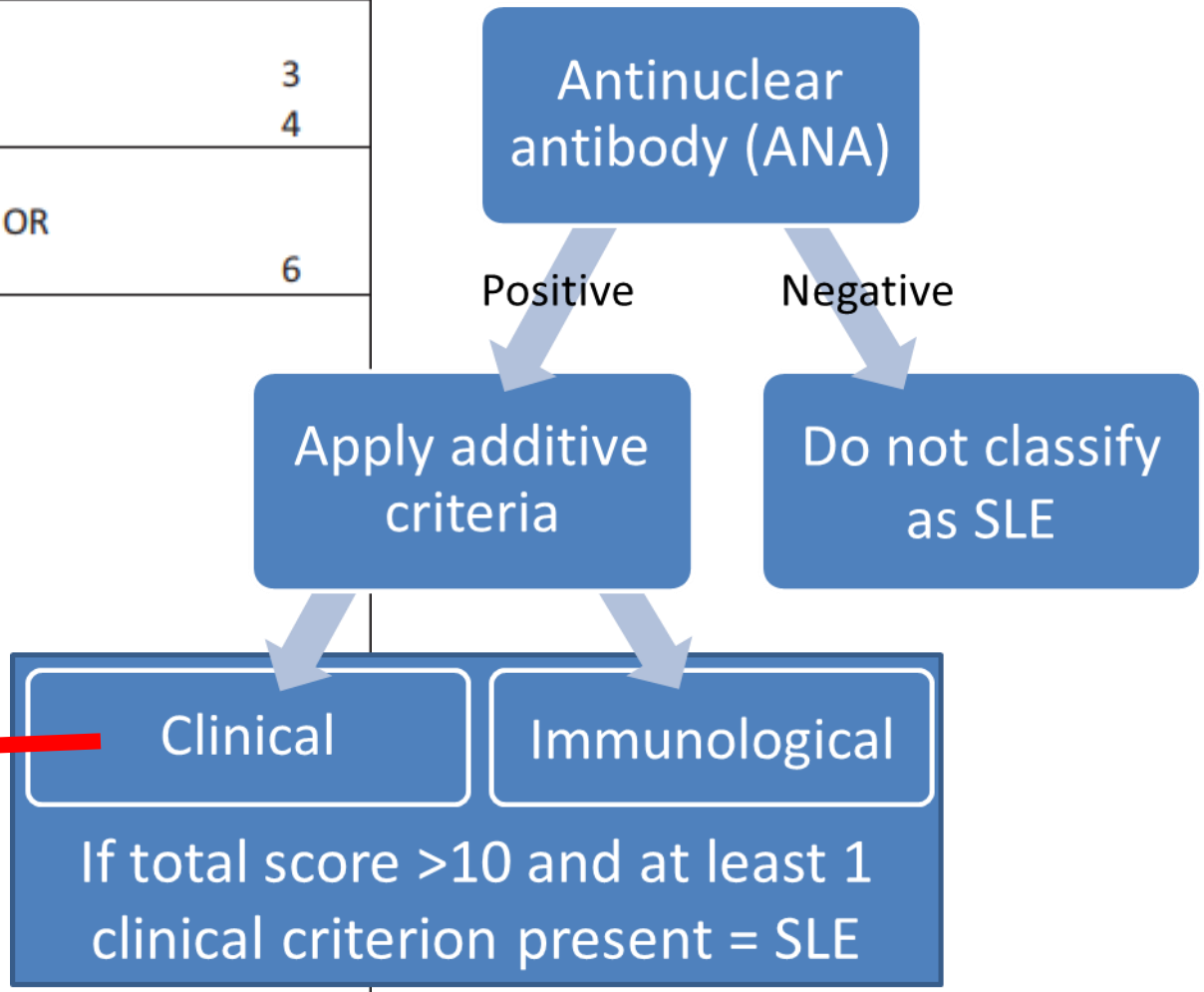

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Classification criteria for SLE

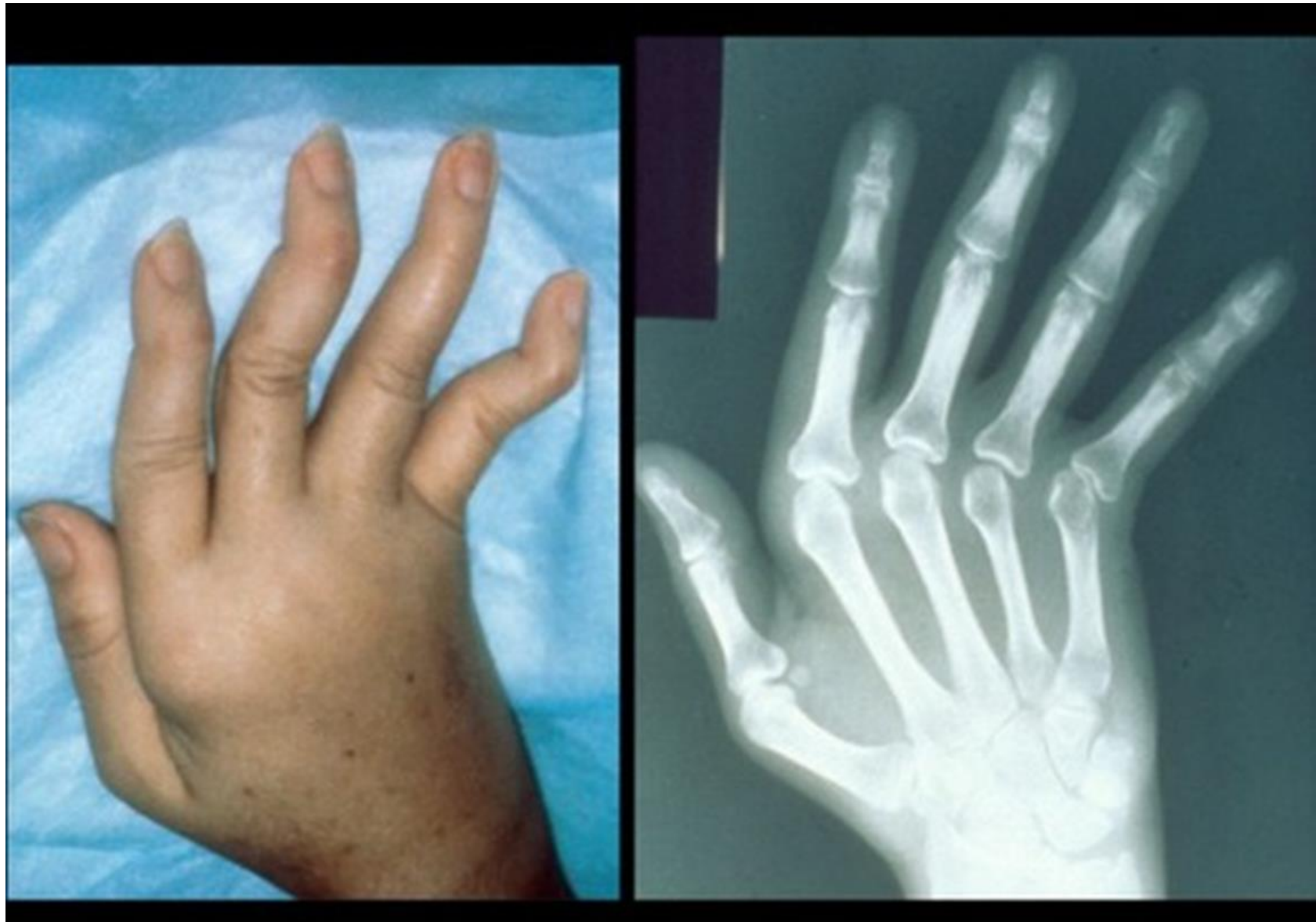
Clinical criteria

Musculoskeletal

Joint involvement -
EITHER

1) synovitis involving 2 or more joints characterized by swelling or effusion OR
2) tenderness in 2 or more joints and at least 30 minutes of morning stiffness

– **6 points**



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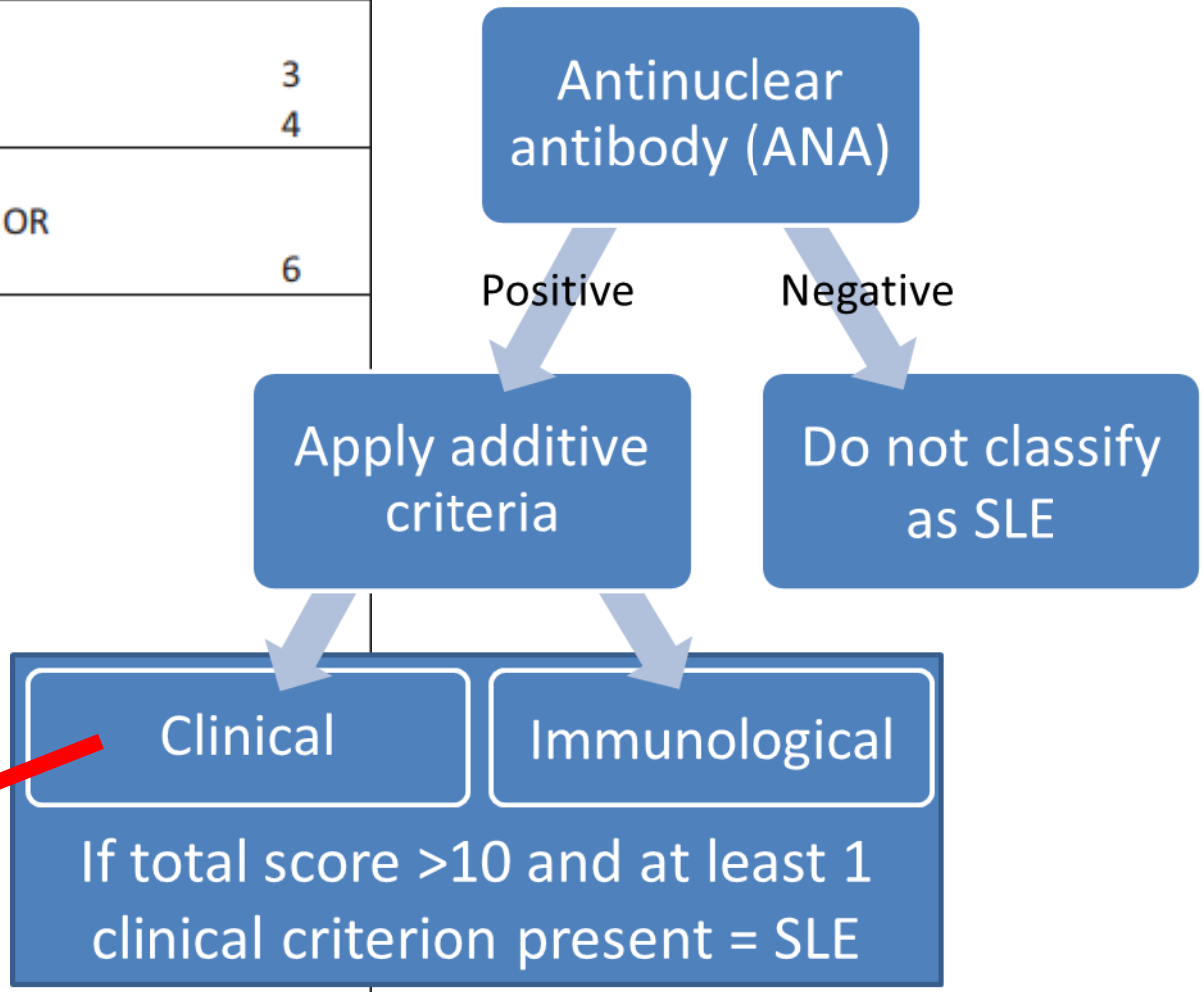

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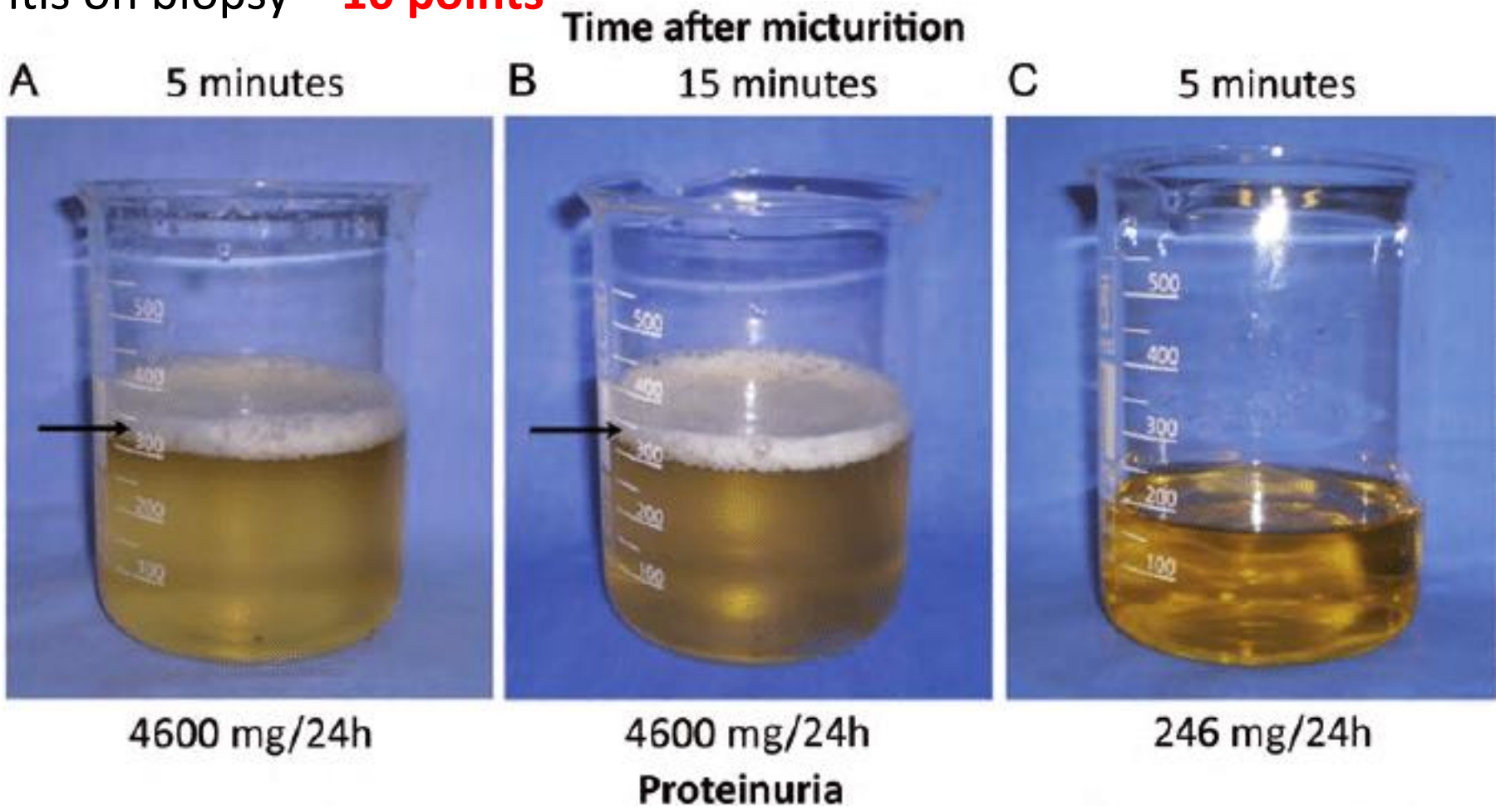
Renal

- Proteinuria – **4 points**
- Class II or V lupus nephritis on biopsy – **8 points**
- Class III or IV lupus nephritis on biopsy – **10 points**

Proteinuria

>0.5 g/24 hours by 24-hour urine or equivalent spot urine protein-to-creatinine ratio



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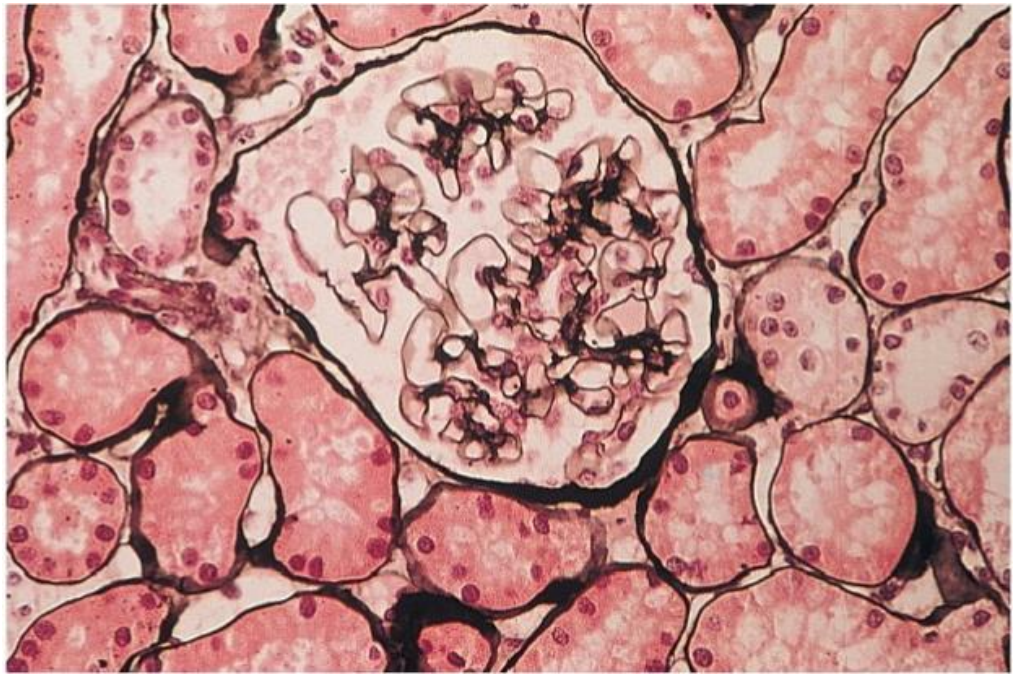
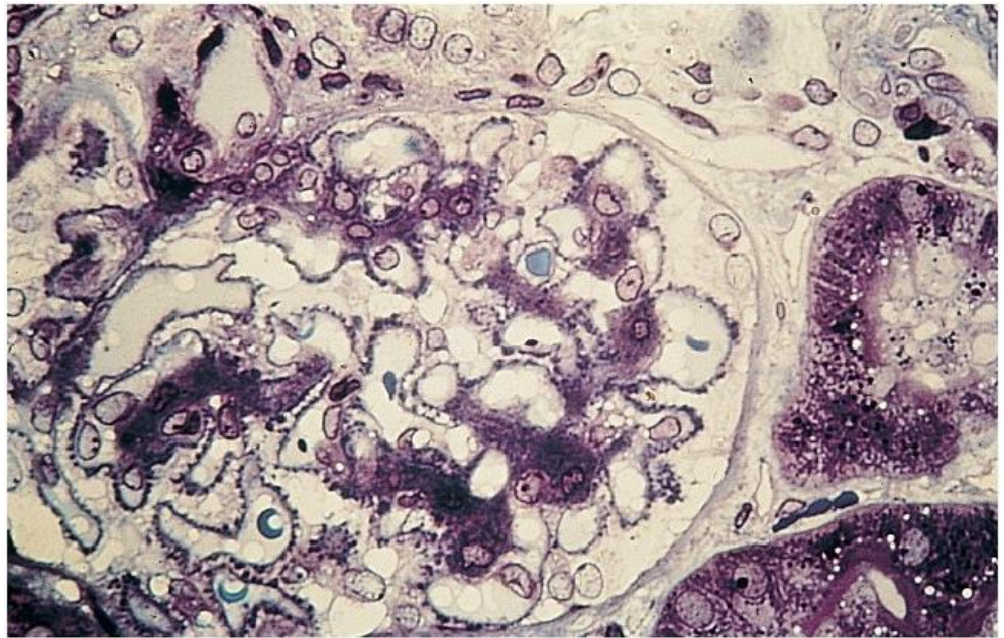


Class V: Membranous lupus nephritis: global or segmental subepithelial immune deposits or their morphologic sequelae by light microscopy and by immunofluorescence or electron microscopy, with or without mesangial alterations



Class II: Mesangial proliferative lupus nephritis: purely mesangial hypercellularity of any degree or mesangial matrix expansion by light microscopy, with mesangial immune deposit. A few isolated subepithelial or subendothelial deposits may be visible by immunofluorescence or electron microscopy, but not by light microscopy

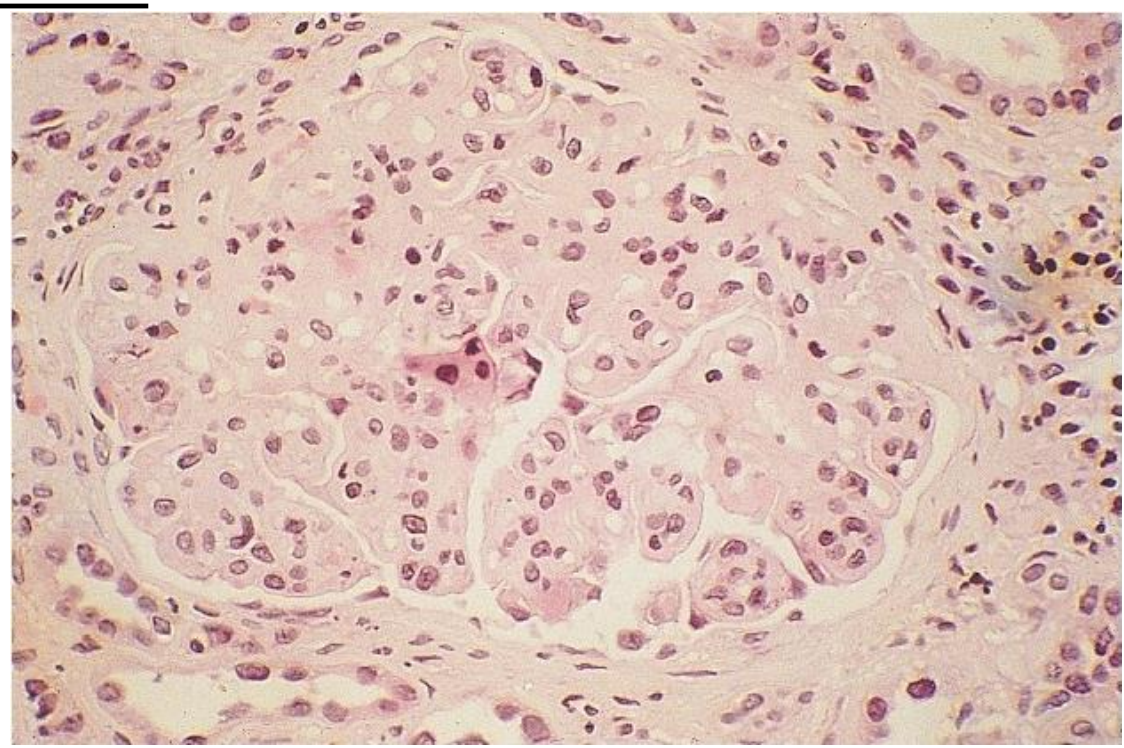
according to ISN/RPS 2003 classification

Classification criteria for SLE

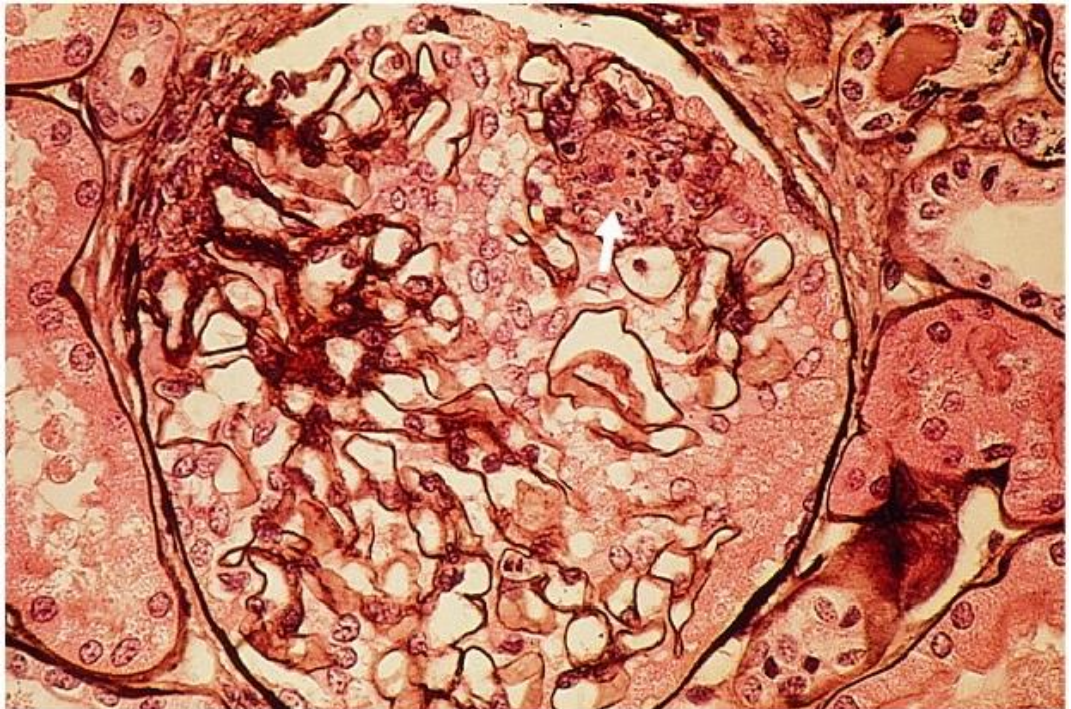
Renal

- Proteinuria – **4 points**
- Class II or V lupus nephritis on biopsy – **8 points**
- Class III or IV lupus nephritis on biopsy – **10 points**

Clinical criteria



Class III: Focal lupus nephritis: active or inactive focal, segmental, or global endocapillary or extracapillary glomerulonephritis involving <50% of all glomeruli, typically with focal subendothelial immune deposits, with or without mesangial alterations



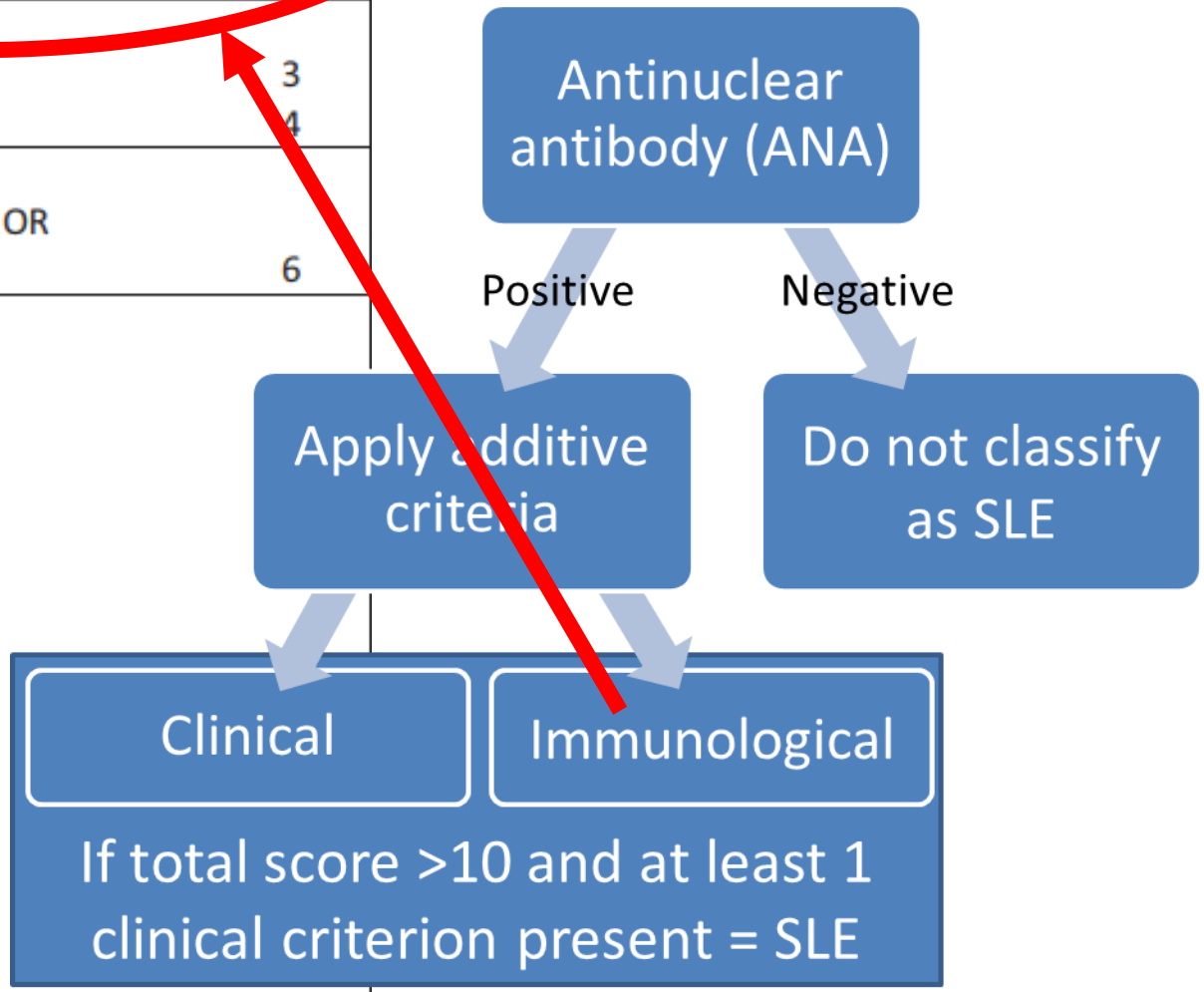
Class IV: Diffuse lupus nephritis: active or inactive diffuse, segmental, or global endocapillary or extracapillary glomerulonephritis involving ≥50% of all glomeruli, typically with diffuse subendothelial immune deposits, with or without mesangial alterations. This class includes cases with diffuse wire loop deposits but with little or no glomerular proliferation

according to ISN/RPS 2003 classification

Classification criteria for SLE

Constitutional	
Fever	2
Hematologic	
Leukopenia	3
Thrombocytopenia	4
Autoimmune hemolysis	4
Neuropsychiatric	
Delirium	2
Psychosis	3
Seizure	5
Mucocutaneous	
Non-scarring alopecia	2
Oral ulcers	2
Subacute cutaneous OR discoid lupus	4
Acute cutaneous lupus	6
Serosal	
Pleural or pericardial effusion	5
Acute pericarditis	6
Musculoskeletal	
Joint involvement	6
Renal	
Proteinuria >0.5g/24h	4
Renal biopsy Class II or V lupus nephritis	8
Renal biopsy Class III or IV lupus nephritis	10

Antiphospholipid antibodies	
Anti-cardiolipin antibodies OR	
Anti-β2GP1 antibodies OR	
Lupus anticoagulant	2
Complement proteins	
Low C3 OR low C4	3
Low C3 AND low C4	4
SLE-specific antibodies	
Anti-dsDNA antibody* OR	
Anti-Smith antibody	6



2019 EULAR / ACR Classification Criteria for SLE. Arthr. & Rheum. 2019, 71, 9, 1400–12

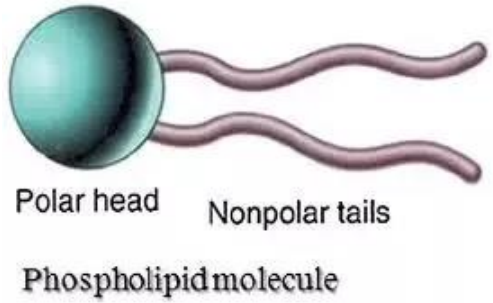
Classification criteria for SLE

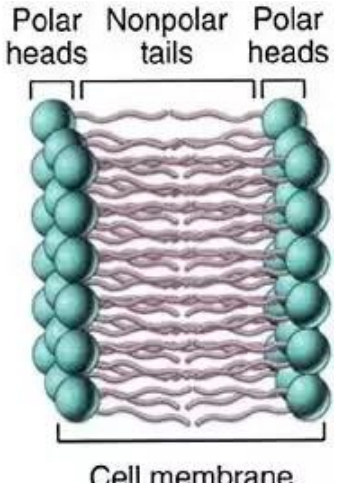
Immunological criteria

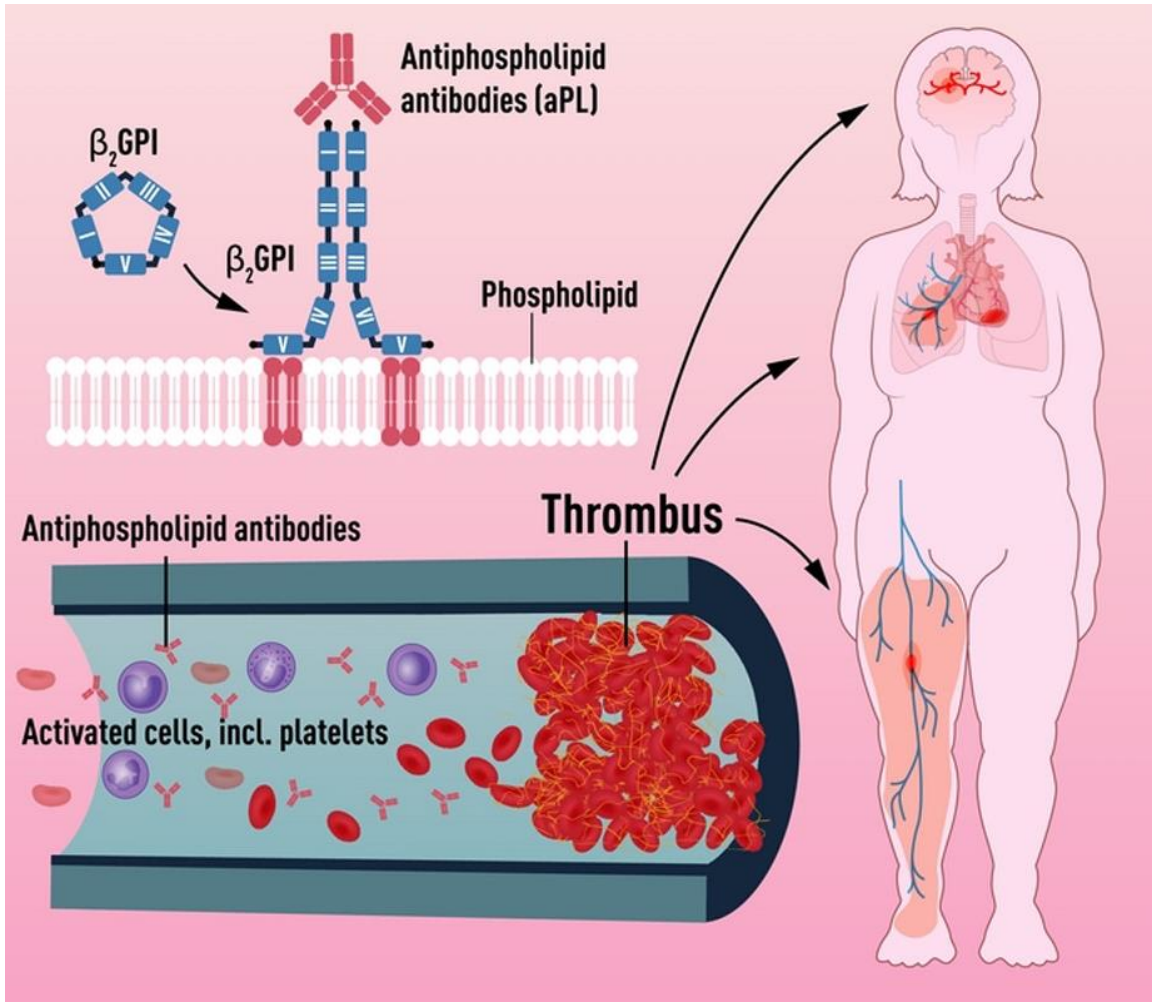
Antiphospholipid antibodies

- Anticardiolipin antibodies (IgA, IgG, or IgM) at medium or high titer OR
- Positive anti-β2GPI antibodies (IgA, IgG, or IgM) OR
- Positive lupus anticoagulant

– **2 points**







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Fever	2
Hematologic	
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Autoimmune hemolysis	4
Neuropsychiatric	
Delirium	2
Psychosis	3
Seizure	5
Mucocutaneous	
Non-scarring alopecia	2
Oral ulcers	2
Subacute cutaneous OR discoid lupus	4
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Serosal	
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Renal	
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Complement proteins	
Low C3 OR low C4	3
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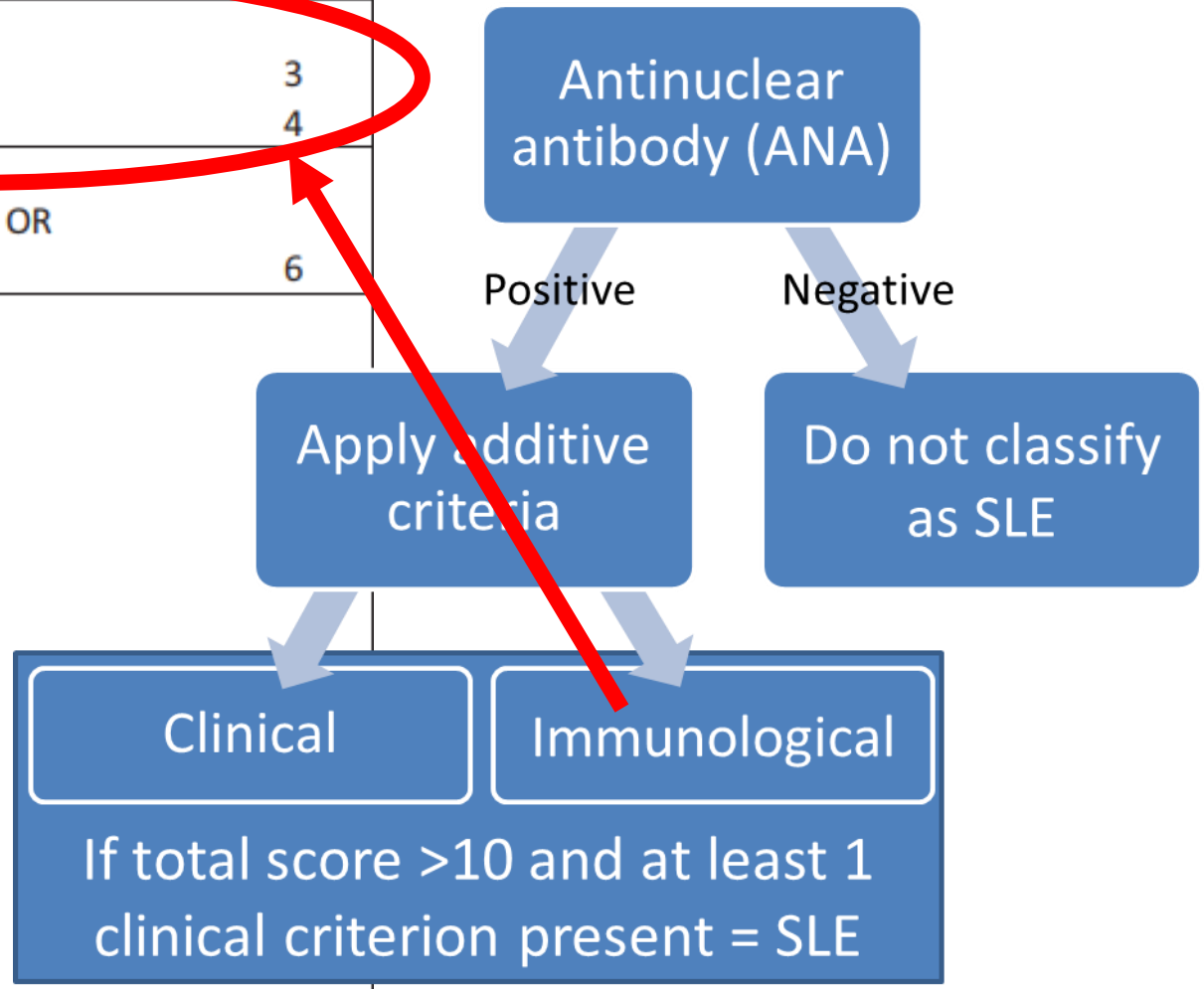


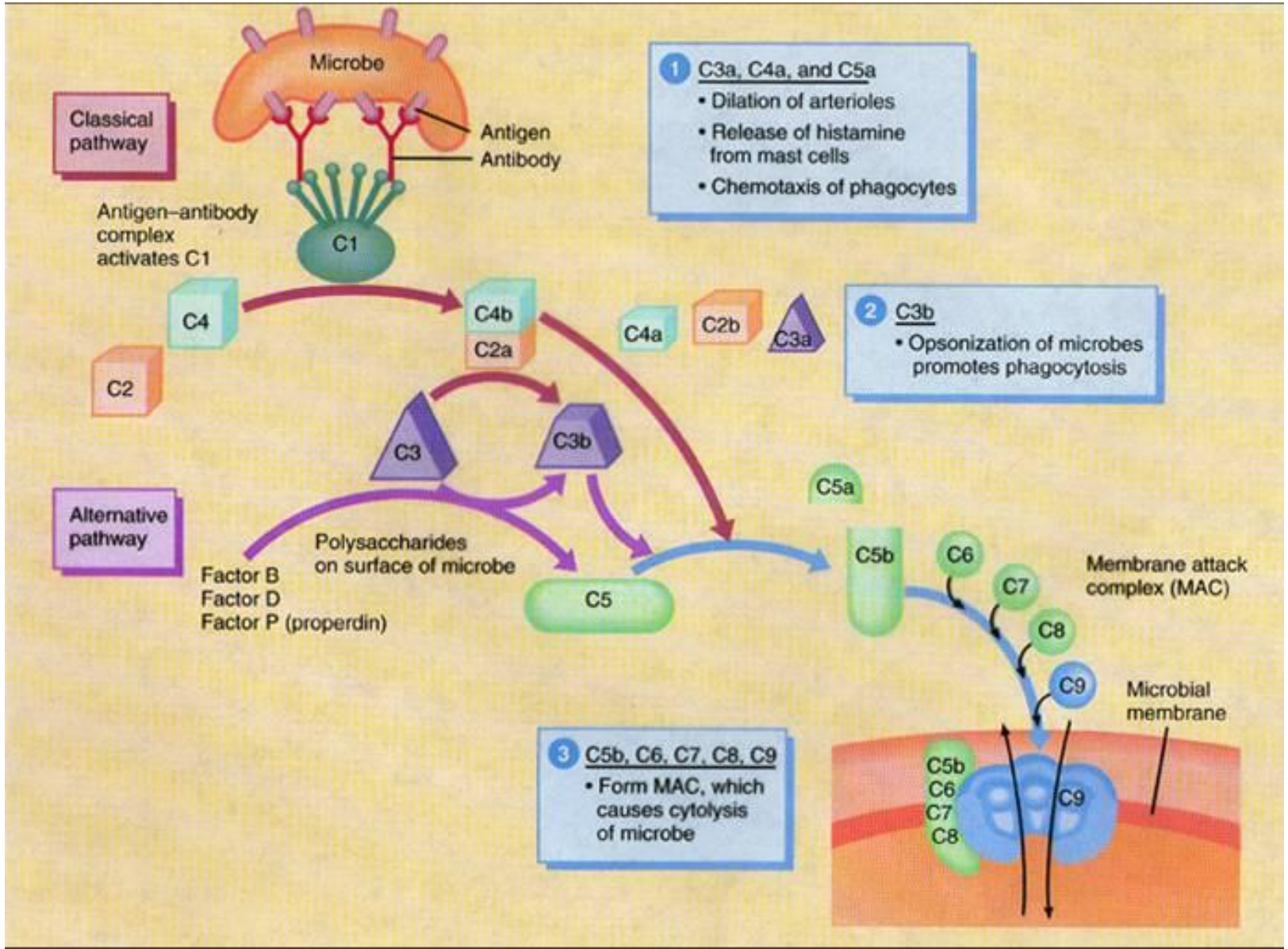
2019 EULAR / ACR Classification Criteria for SLE. Arthr. & Rheum. 2019, 71, 9, 1400–12

Classification criteria for SLE

Immunological criteria

Complement proteins

- Low C3 – **3 points**
- Low C4 – **3 points**
- Low C3 and C4 – **4 points**



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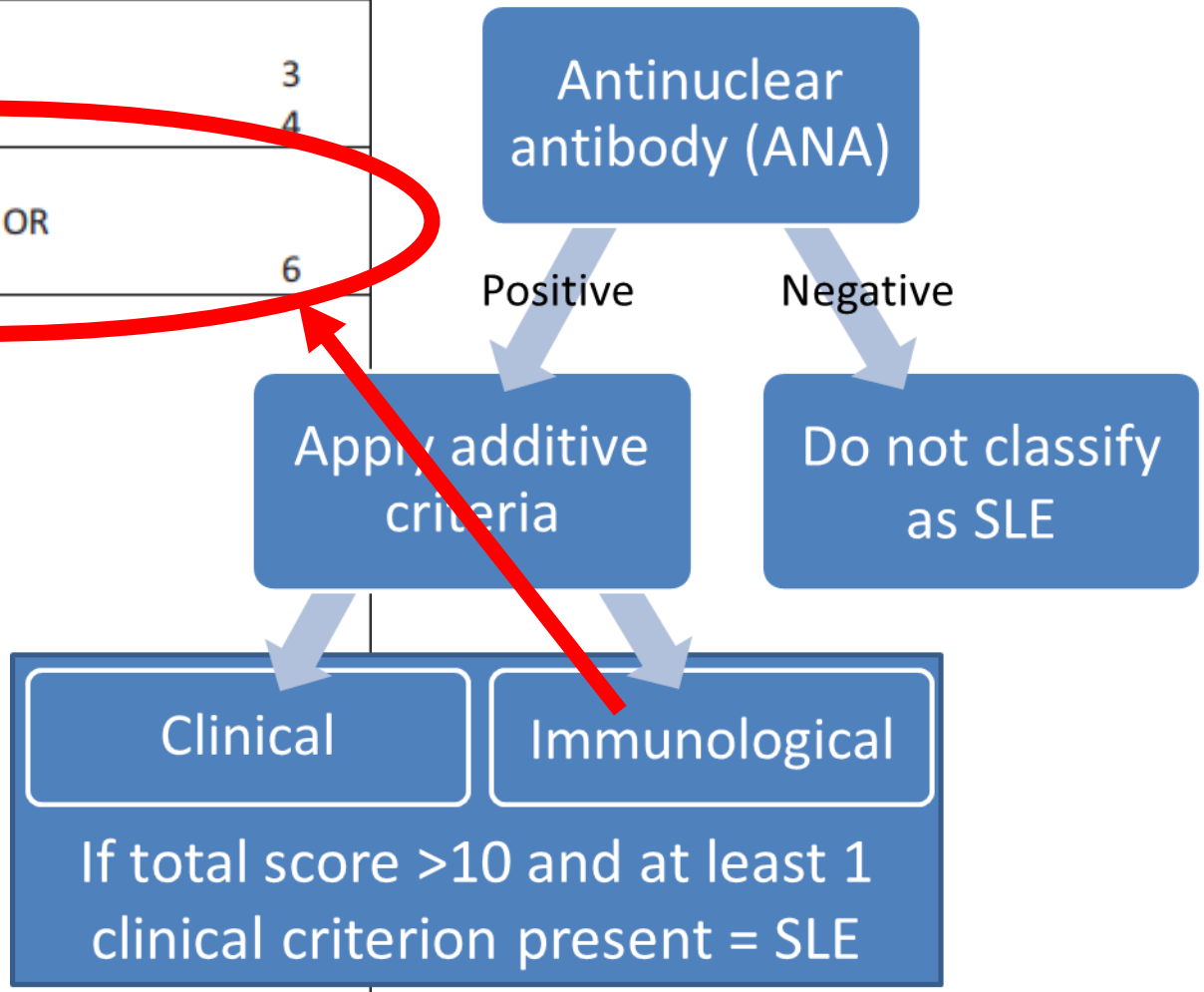


2019 EULAR / ACR Classification Criteria for SLE. Arthr. & Rheum. 2019, 71, 9, 1400–12

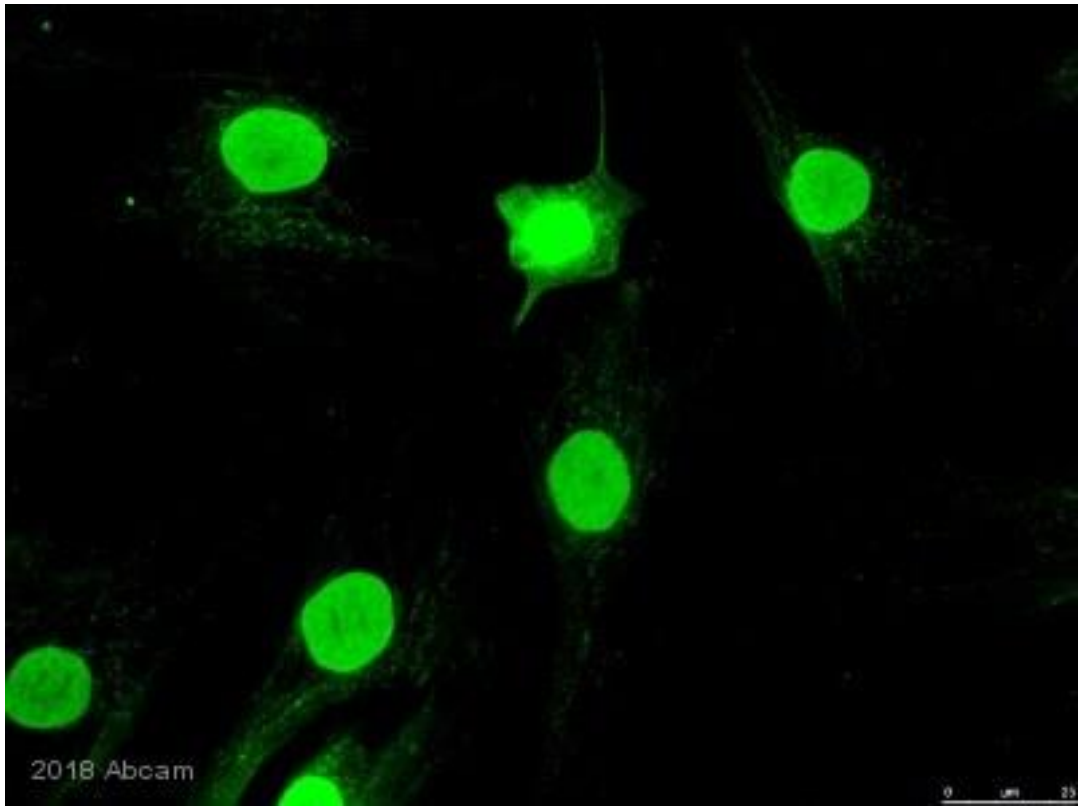
Classification criteria for SLE

Immunological criteria

SLE-specific antibodies

- Anti-dsDNA antibodies in an immunoassay with demonstrated ≥90% specificity for SLE against relevant disease controls OR
- anti-Sm antibodies

– **6 points**



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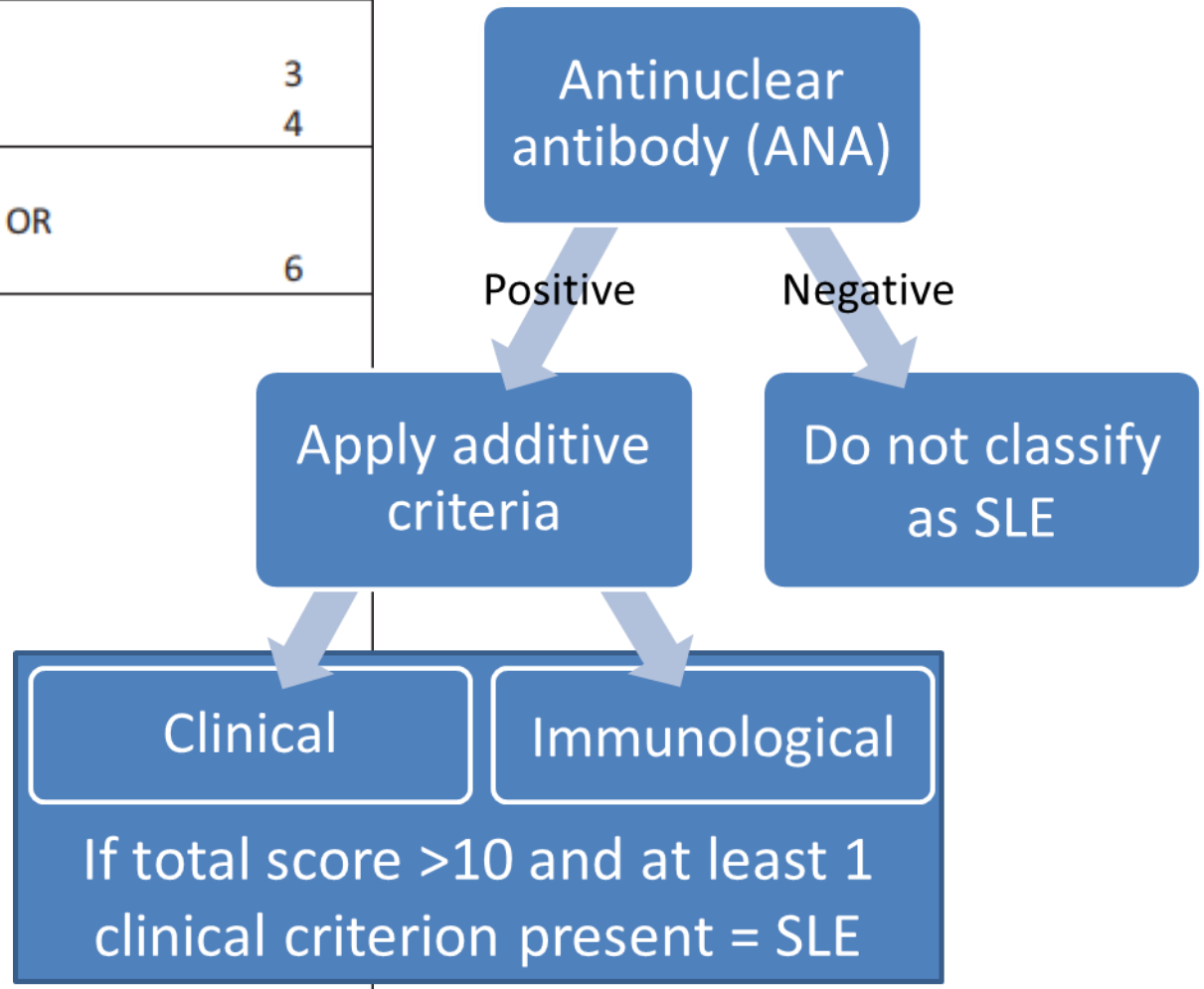


2019 EULAR / ACR Classification Criteria for SLE. Arthr. & Rheum. 2019, 71, 9, 1400–12

Treatment of SLE

- SLE care is multidisciplinary, based on a shared patient-physician decision, and should consider individual, medical and societal costs.
- Treatment of organ-threatening / life-threatening SLE includes an initial period of high-intensity immunosuppressive therapy to control disease activity, followed by a longer period of less intensive therapy to consolidate response and prevent relapses.
- Treatment goals include long-term patient survival, prevention of organ damage and optimization of health-related quality of life.

EULAR 2019 Guidelines

Goals of Treatment

- Treatment in SLE should aim at remission or low disease activity and prevention of flares in all organs, maintained with the lowest possible dose of glucocorticoids.
- Flares of SLE can be treated according to the severity of organ(s) involvement by adjusting ongoing therapies (glucocorticoids, immunomodulating agents) to higher doses, switching or adding new therapies.

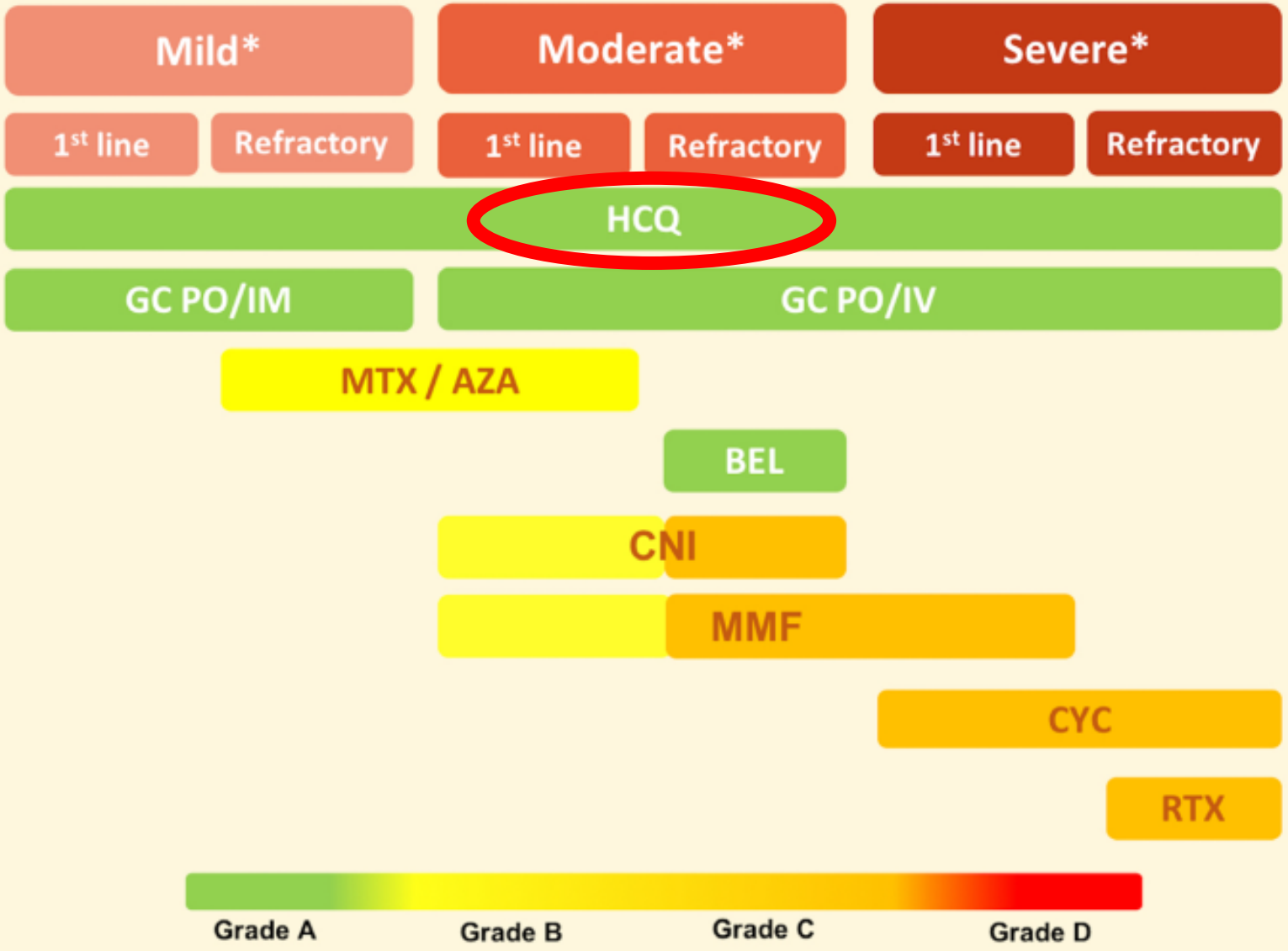
EULAR 2019 Guidelines

Treatment of non-renal Systemic Lupus Erythematosus

Adjunct:

Sun protection
Vaccinations
Exercise
No smoking
Body weight
Blood pressure
Lipids
Glucose

Antiplatelets
anti-coagulants
(in aPL- positive
patients)



Target

Remission
SLEDAI = 0
HCQ
No GC

or

Low disease activity
SLEDAI ≤ 4
HCQ
Pre ≤ 7.5 mg/d
Immunosuppressives
(in stable doses and
well-tolerated)

2019 EULAR recommendations for SLE, Fanouriakis A. et al., Ann.Rheum.Dis. 2019;78:736–745.

Hydroxychloroquine

- Recommended for all patients with SLE, unless contraindicated
- Dose not exceeding 5 mg/kg (real body weight)
- Ophthalmological screening should be performed at baseline, after 5 years, and yearly thereafter

EULAR 2019 Guidelines

Treatment of non-renal Systemic Lupus Erythematosus

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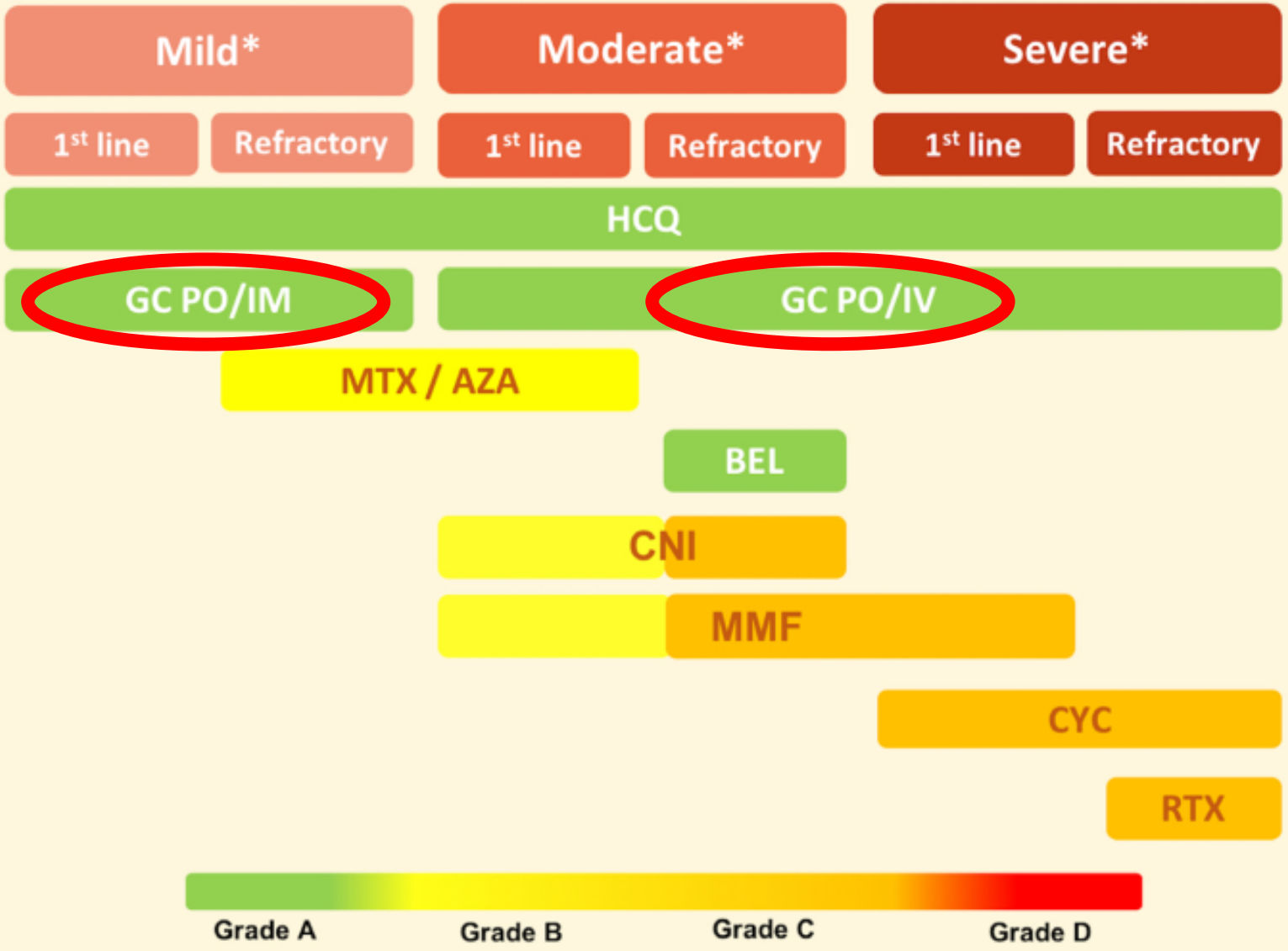

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2019 EULAR recommendations for SLE, Fanouriakis A. et al., Ann.Rheum.Dis. 2019;78:736–745.

Glucocorticisteroids

- Can be used at doses and route of administration that depend on the type and severity of organ involvement
- Pulses of i/v m.p. (250–1000 mg/day, for 1–3 days) provide immediate therapeutic effect and enable the use of lower starting dose of oral GC
- For chronic treatment, GC should be minimised to less than 7.5 mg/day and, when possible, withdrawn.
- Prompt initiation of immunomodulatory agents can expedite the tapering/discontinuation of GC

EULAR 2019 Guidelines

Treatment of non-renal Systemic Lupus Erythematosus

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Blood pressure
Lipids
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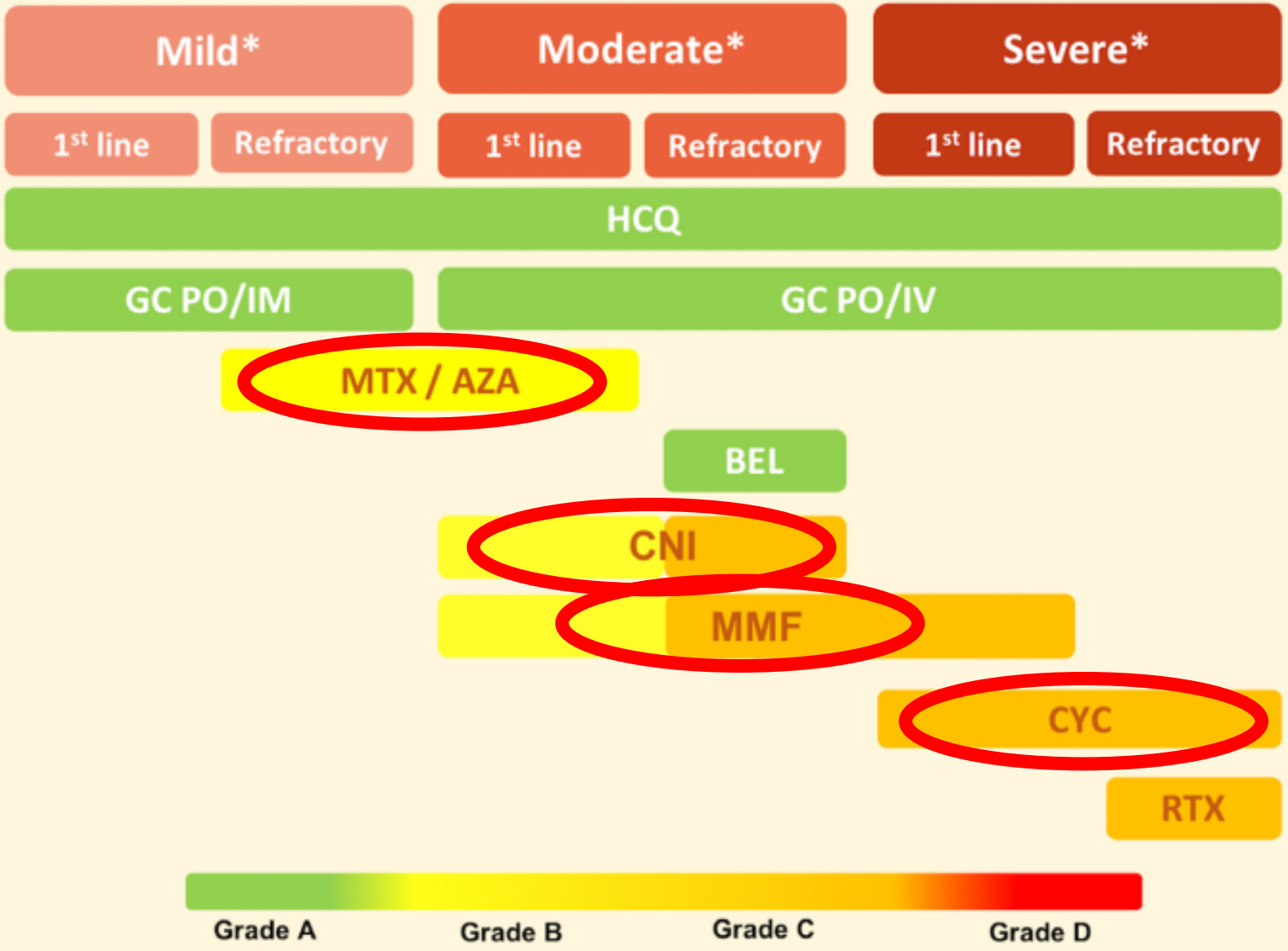

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Immunosuppressives
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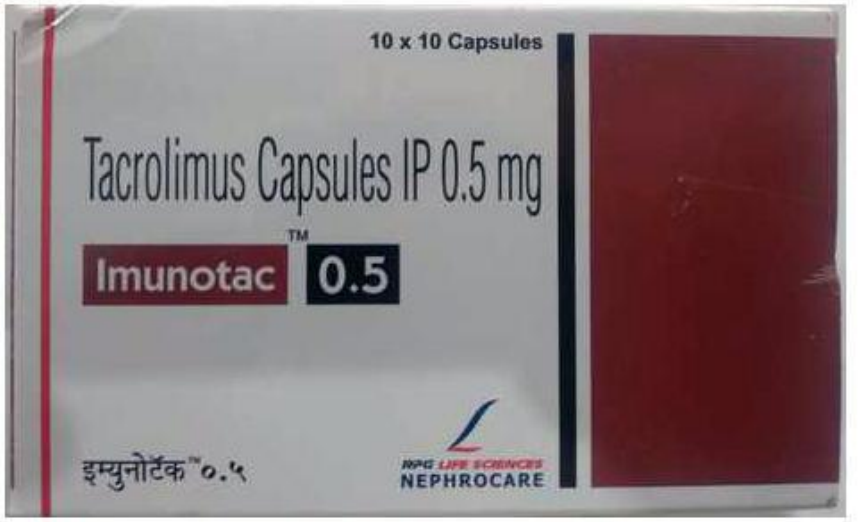
2019 EULAR recommendations for SLE, Fanouriakis A. et al., Ann.Rheum.Dis. 2019;78:736–745.

Immunomodulating / immunosuppressive agents

- In pts not responding to HCQ (alone or in comb. with GC) or pts unable to reduce GC below doses acceptable for chronic use, addition of MTX, AZP or MMF should be considered.
- It can be included in the initial therapy in cases of organ-threatening disease
- Cyclophosphamide can be used for severe organ-threatening or life-threatening SLE as well as ‘rescue’ therapy in patients not responding to other immunosuppressive agents

EULAR 2019 Guidelines

Immunomodulating / immunosuppressive agents



- **Calcineurin inhibitors** alone or in combination with MMF may be considered as second-line agents for induction or maintenance therapy mainly in membranous LN, podocytopathy, or in proliferative disease with refractory nephrotic syndrome, despite standard-of-care within 3–6 months
- First-line treatment of skin disease includes topical agents (GC and/or CNIs)

EULAR 2019 Guidelines

Treatment of non-renal Systemic Lupus Erythematosus

Adjunct:

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Vaccinations
Exercise
No smoking
Body weight
Blood pressure
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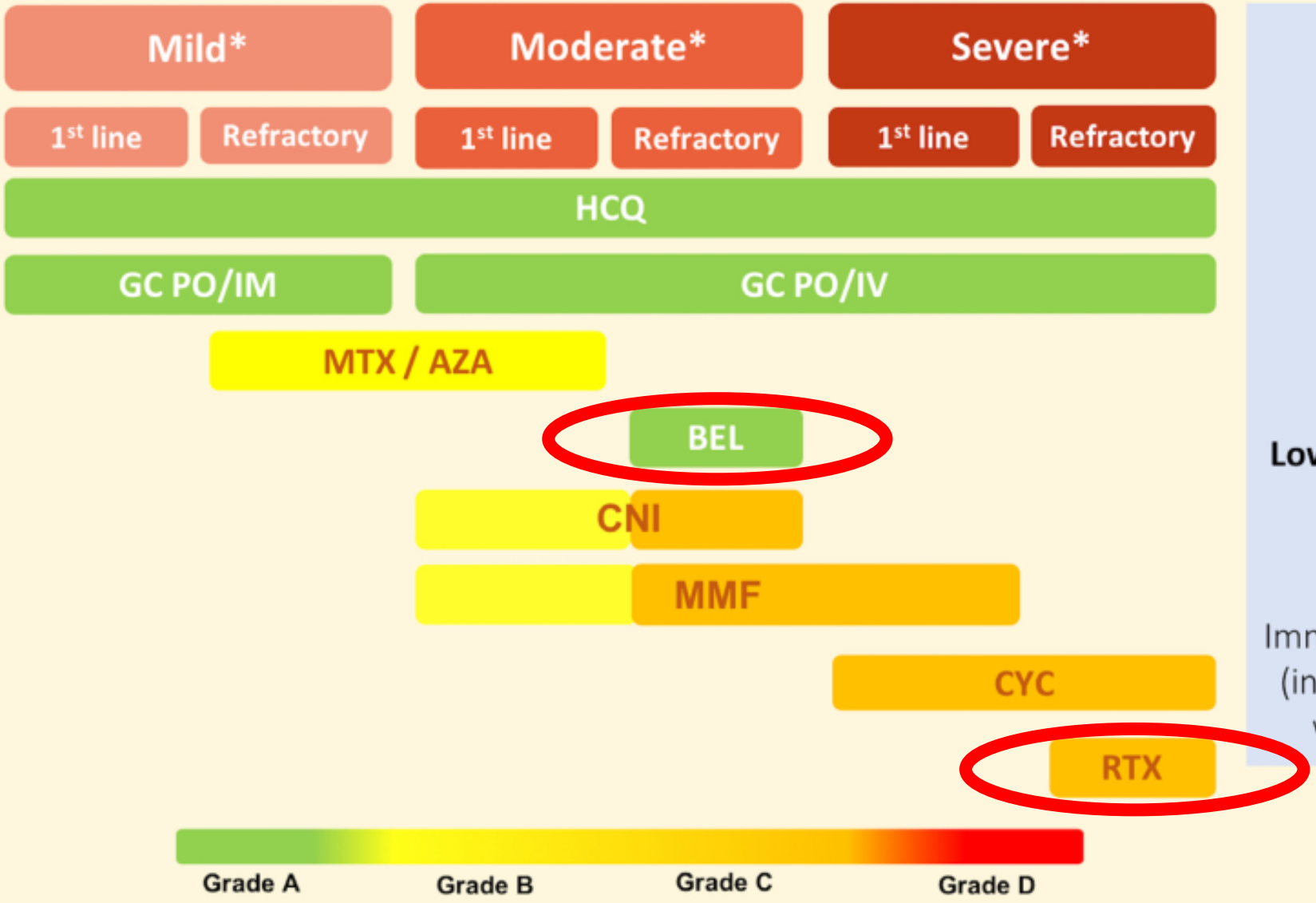

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No GC

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Low disease activity
SLEDAI ≤ 4
HCQ
Pre ≤ 7.5 mg/d
Immunosuppressives
(in stable doses and
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2019 EULAR recommendations for SLE, Fanouriakis A. et al., Ann.Rheum.Dis. 2019;78:736–745.

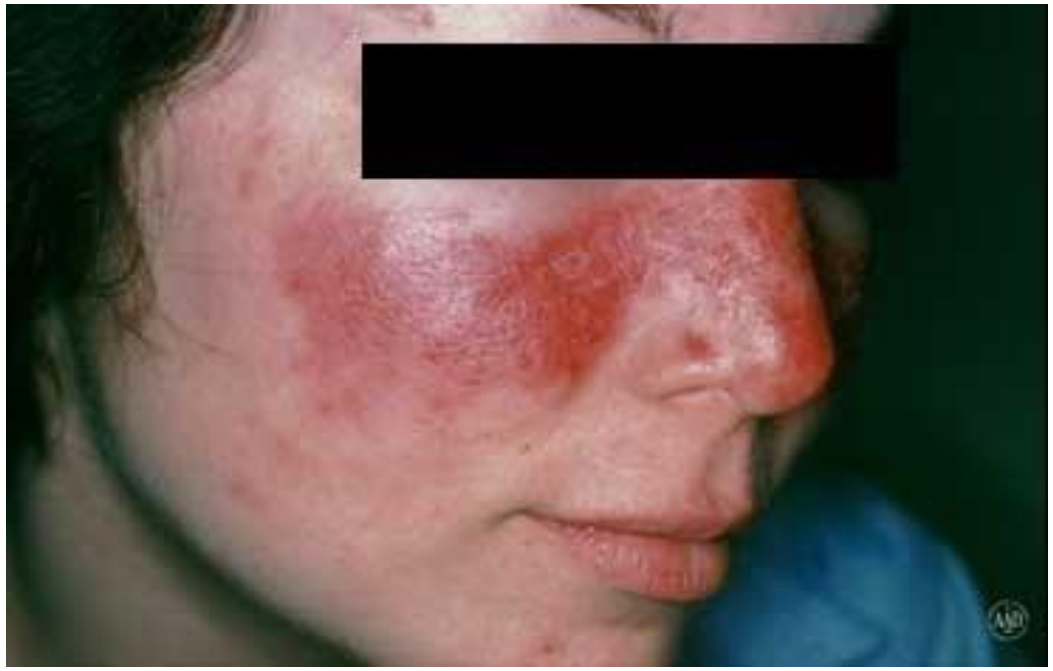
Biologics

- In patients with inadequate response to standard-of-care (combinations of HCQ and GC with or without immunosuppressive agents), defined as residual disease activity not allowing tapering of glucocorticoids and/or frequent relapses, add-on treatment with belimumab should be considered
- In organ-threatening disease refractory or with intolerance/contraindications to standard immunosuppressive agents, rituximab can be considered

EULAR 2019 Guidelines

Treatment of specific manifestation

Skin disease



- First-line treatment includes:
  - topical agents (GC, calcineurin inhibitors),
  - antimalarials (HCQ, quinacrine)
  - and/or systemic GC

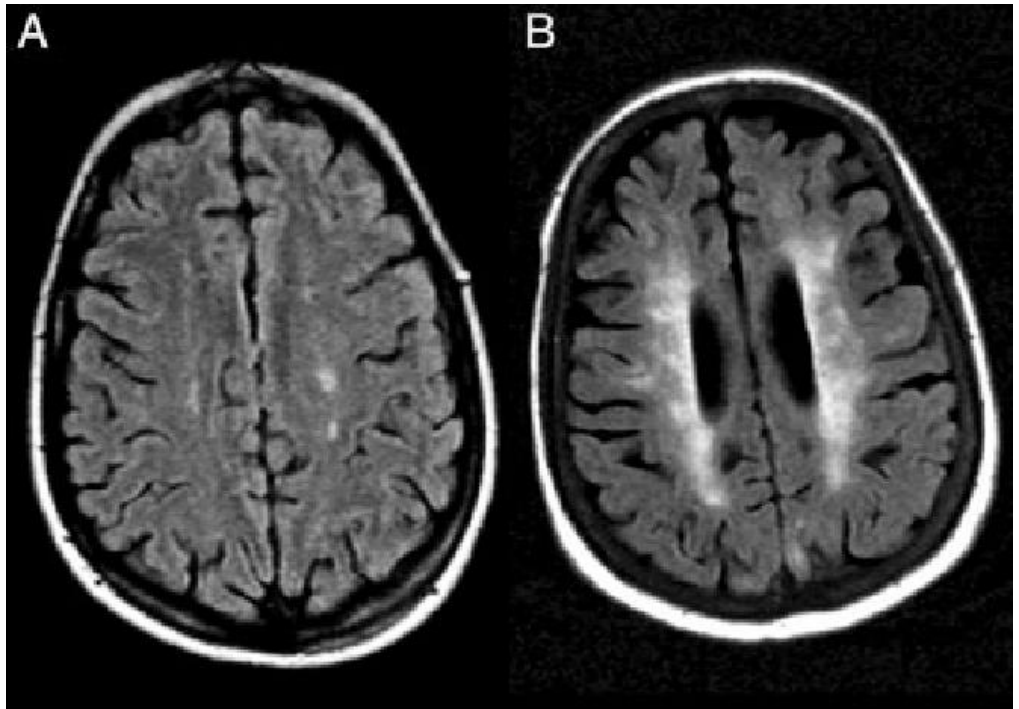
- In non-responsive cases or cases requiring high-dose GC, methotrexate, retinoids, dapsone or mycophenolate can be added.

EULAR 2019 Guidelines

Treatment of specific manifestation

Neuropsychiatric disease

- Treatment includes GC/immunosuppressive agents for manifestations considered to reflect an inflammatory process, and antiplatelet/anticoagulants for atherothrombotic/aPL-related manifestations



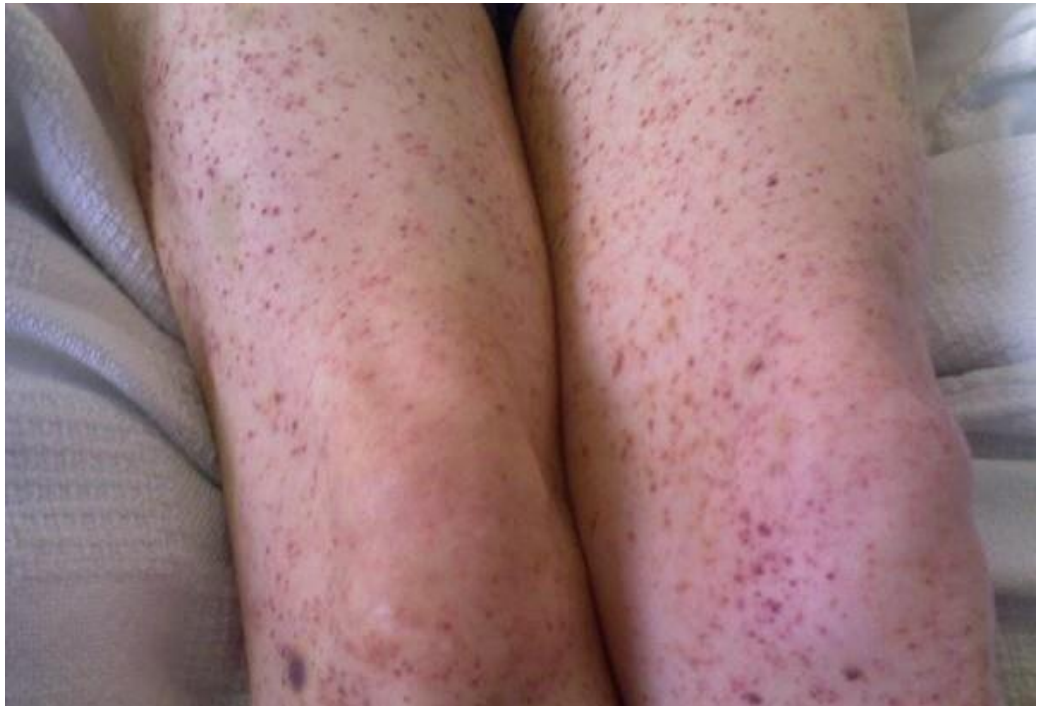
It can be facilitated by neuroimaging, investigation of cerebrospinal fluid, consideration of risk factors and exclusion of confounding factors

EULAR 2019 Guidelines

Treatment of specific manifestation

Haematological disease

- Acute treatment of lupus thrombocytopenia includes:
  - high-dose GC (including pulses)
  - and/or i.v. IgG
- For maintenance of response, immunosuppressive/GC-sparing agents such as MMF, AZP or cyclosporine can be used



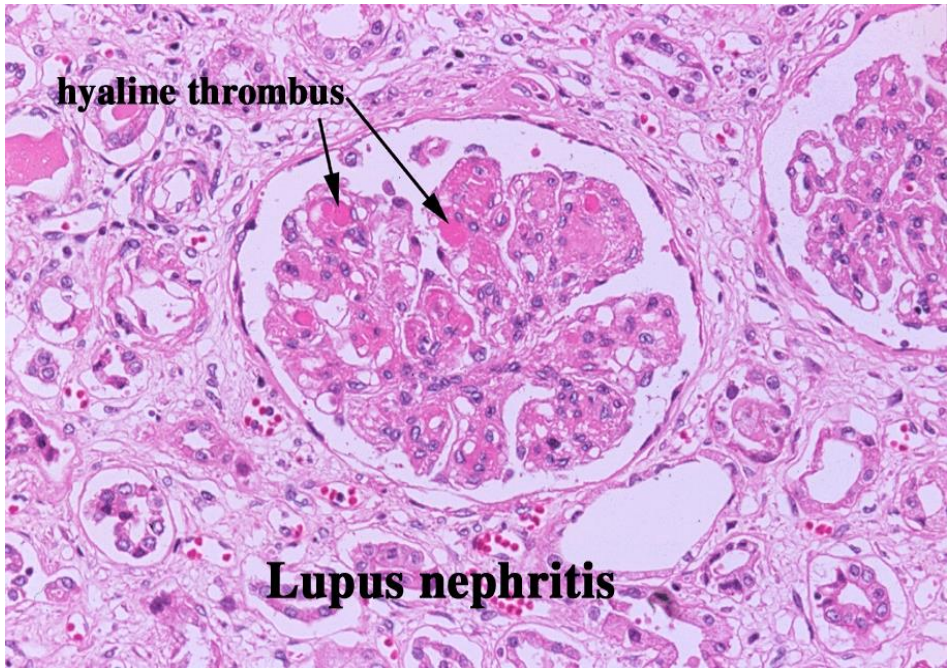
- Refractory cases can be treated with rituximab or cyclophosphamide.

EULAR 2019 Guidelines

Treatment of specific manifestation

Renal disease

- Early recognition of renal involvement and performance of renal biopsy are essential to ensure optimal outcomes
- MMF or low-dose i.v. cyclophosphamide are recommended as initial (induction) treatment.
- In pts at high risk for renal failure, similar regimens may be considered but high-dose i.v. cyclophosphamide can also be used

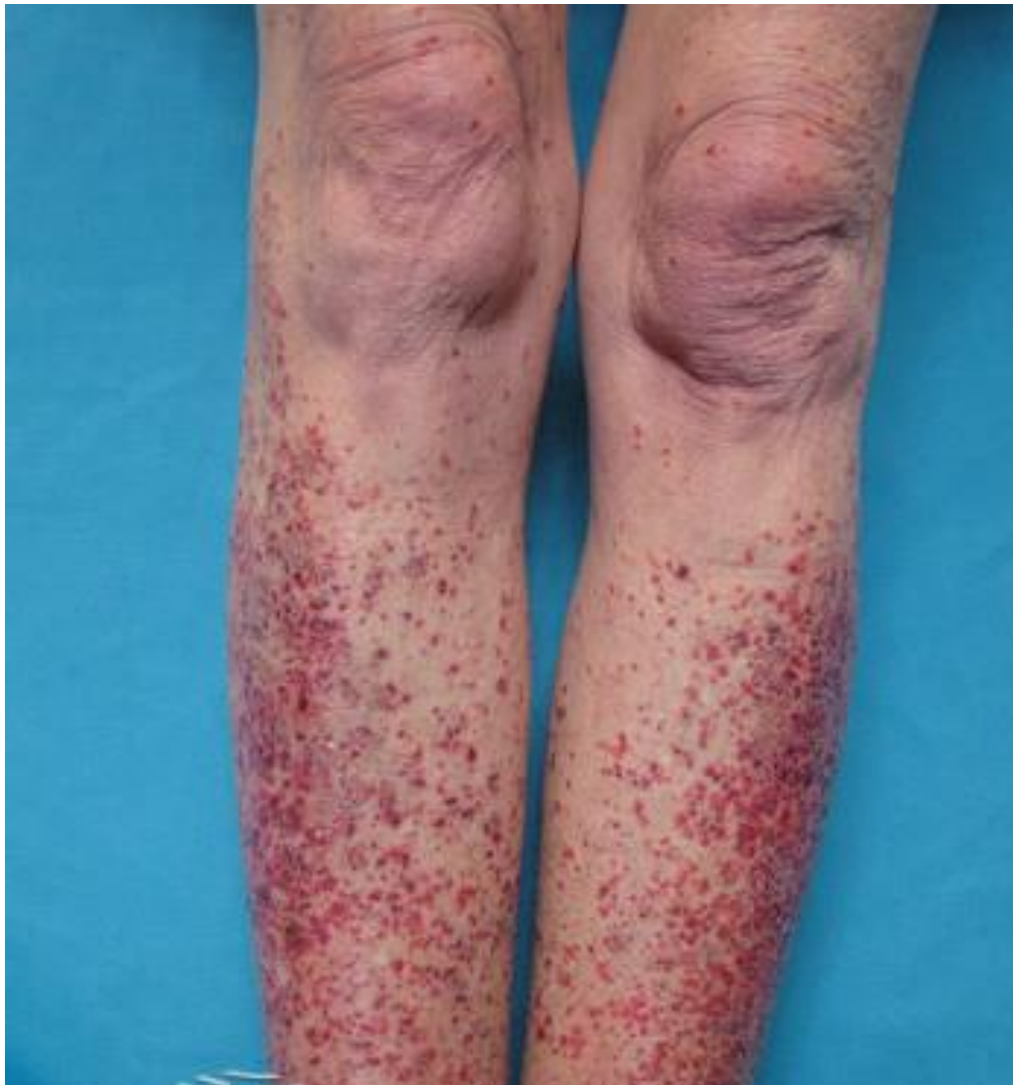


- For maintenance therapy, MMF or AZP should be used.
- MMF may be combined with low dose of a calcineurin inhibitor in severe nephrotic syndrome or incomplete renal response.

EULAR 2019 Guidelines

Drug-induced lupus

- **Drugs**: procainamide, hydralazine, penicillamine, minocycline, isoniazid, methyldopa, quinidine, chlorpromazine, diltiazem, anti-TNF
- **Clinical**: generally milder disease with predominantly arthritis and serositis
- **Laboratory**:
  - (+) anti-histone (95%);
  - (–) anti-ds-DNA
  - (–) anti-Sm;
  - normal complement levels
- **Course**: usually reversible w/in 4–6 wk after stopping medication



SYSTEMIC SCLEROSIS AND SCLERODERMA

DEFINITION

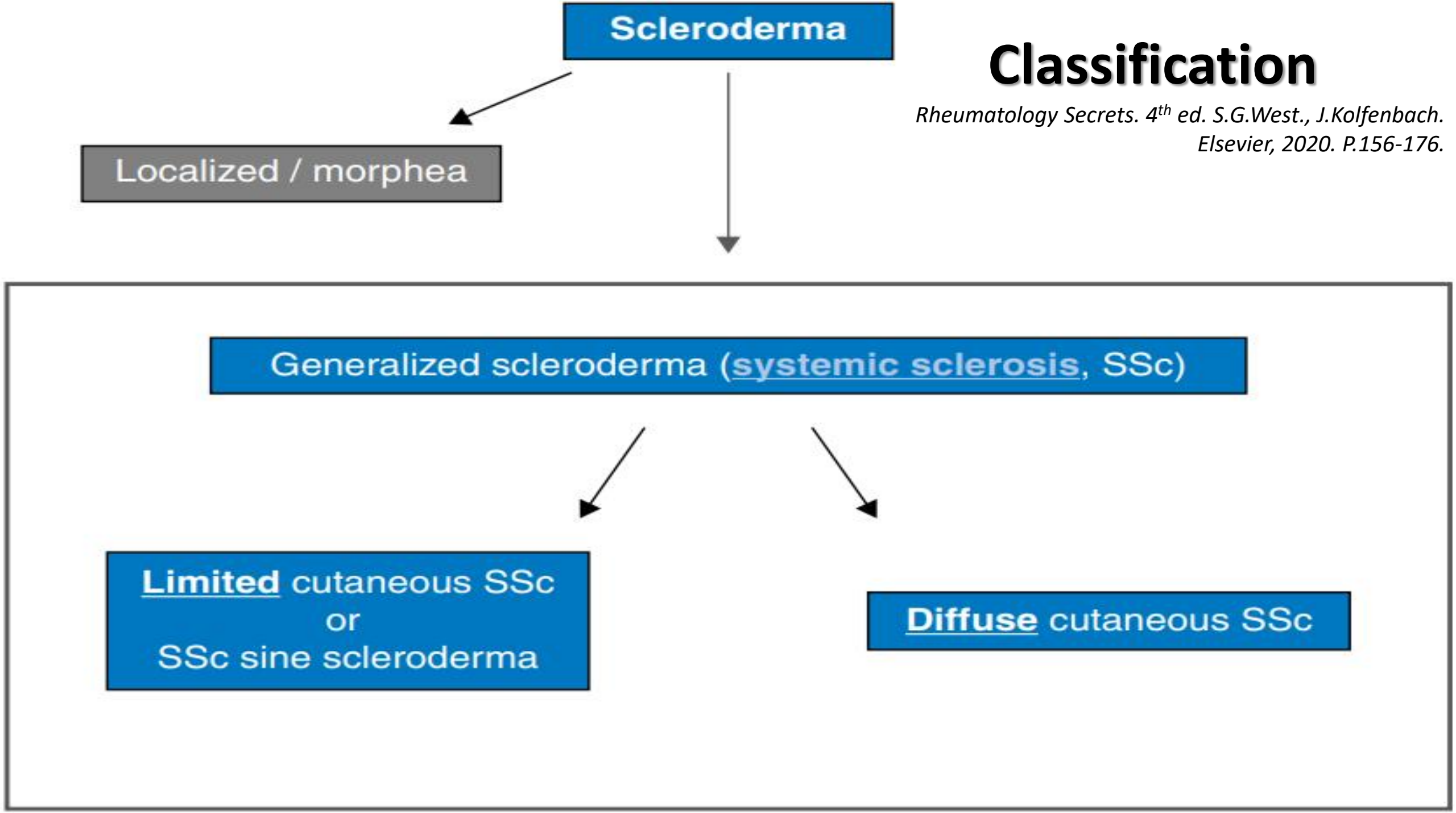
- **Scleroderma** is a group of autoimmune diseases that may result in changes to the skin, blood vessels, muscles, and internal organs.
- The disease can be either localized to the skin or involve other organs as well.
- Symptoms may include areas of thickened skin, stiffness, feeling tired, and poor blood flow to the fingers or toes with cold exposure.

EPIDEMIOLOGY

- Peak onset of SSc between **ages 30–60**;
- More common in **women** than men – **5-7 : 1**
- 10–20 new SSc cases per 1,000,000 people per year in the U.S.
- 3,7–19 new SSc cases per 1,000,000 people per year in the Ukraine.

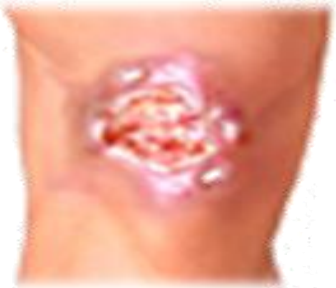
Classification

Rheumatology Secrets. 4th ed. S.G.West., J.Kolfenbach. Elsevier, 2020. P.156-176.



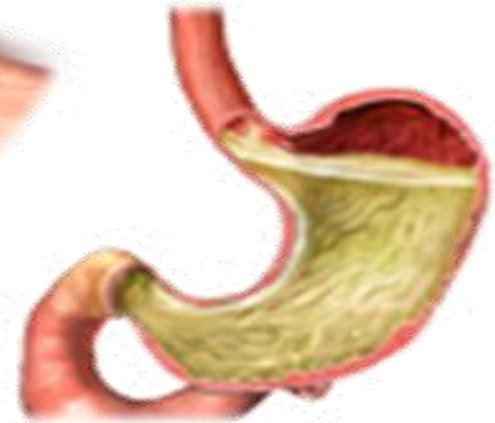
The limited symptoms of scleroderma are referred to as CREST

Calcinosis- calcium deposits in the skin



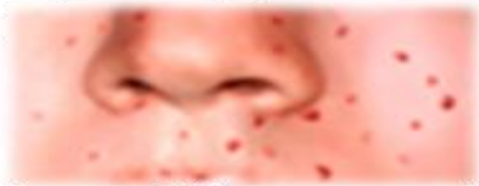
Raynaud's phenomenon- spasm of blood vessels in response to cold or stress

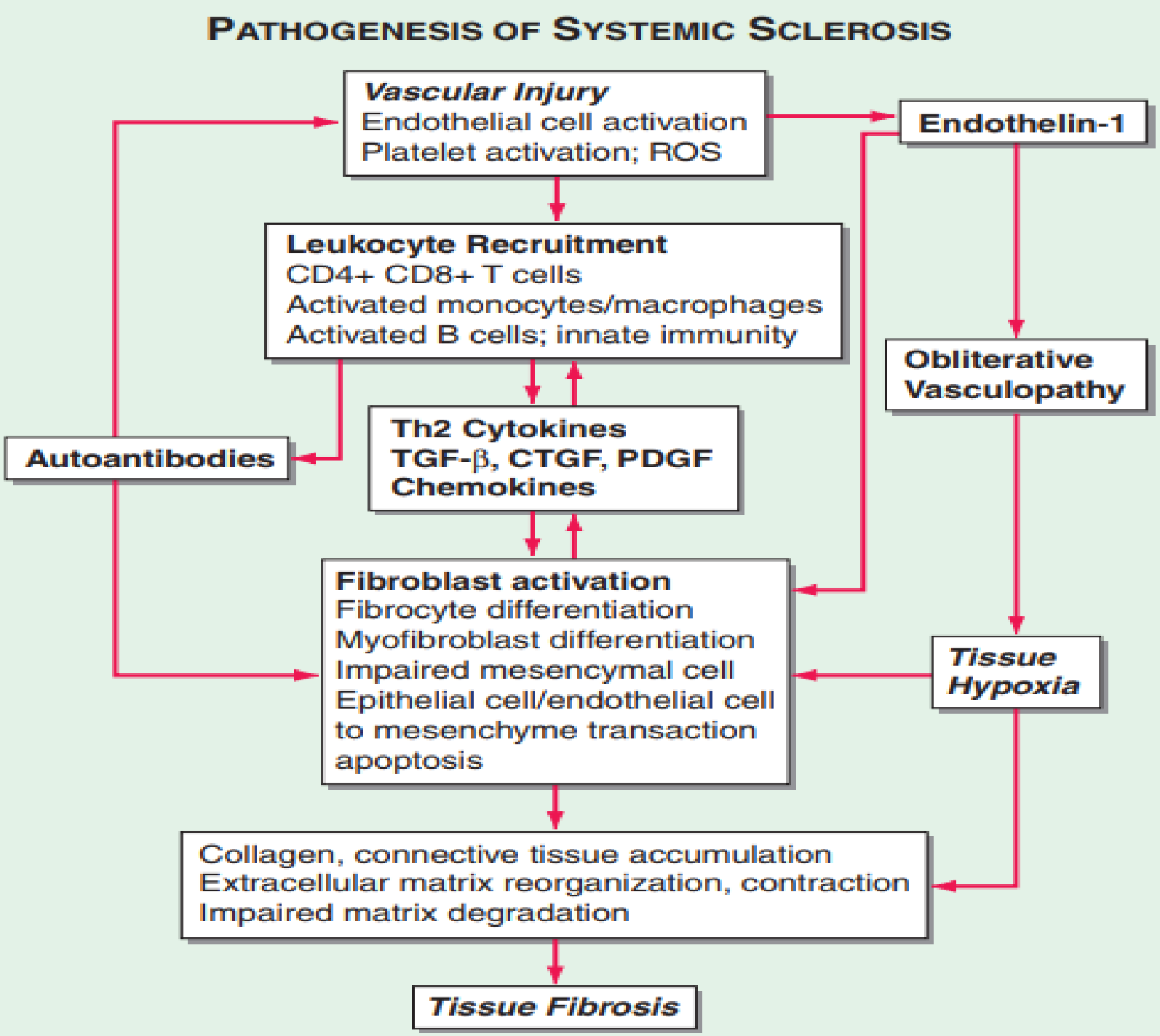
Esophageal dysfunction- acid reflux and decrease in motility of esophagus



Sclerodactyly- thickening and tightening of the skin on the fingers and hands

Telangiectasias- dilation of capillaries causing red marks on surface of skin





- ROS - reactive oxygen species
- TGF-β - transforming growth factor β
- CTGF - connective tissue growth factor
- PDGF - platelet-derived growth factor

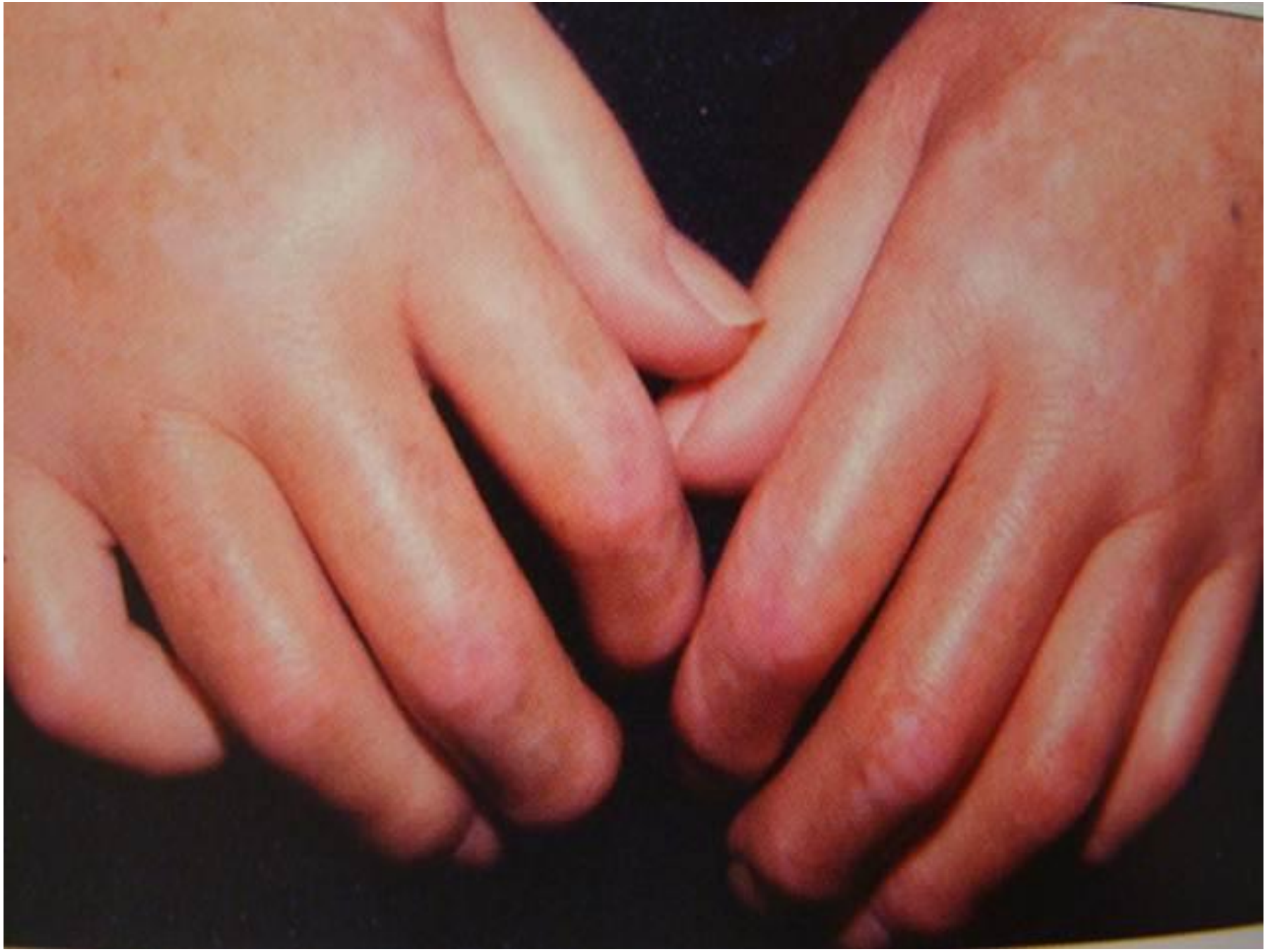
Harrison's Rheumatology 3rd edition / A.S.Fauci, C.A. Langford, R.C. Basner / McGrawHill Education, 2013, C.113-129.

Diagnostic criteria for SSc (ACR & EULAR, 2013)

≥ 9 → definite SSc

Items	Sub-items	Weight
Skin thickening of fingers of both hands extending proximal to metacarpophalangeal (MCP) joints		9
Skin thickening of fingers (only count the highest score)	Puffy fingers Whole finger, distal to MCP	2 4
Fingertip lesions (only count the highest score)	Digital tip ulcers Pitting scars	2 3
Telangiectasia		2
Abnormal nailfold capillaries		2
Pulmonary arterial hypertension and/or interstitial lung disease		2
Raynaud's phenomenon		3
Scleroderma-related antibodies (any of anti-centromere, anti-topoisomerase I [anti-ScL 70], anti-RNA polymerase III)		3
Patients with a total score of ≥9 are classified as having definite systemic sclerosis (sensitivity 91%, specificity 92%)		

2013 Classification criteria for SSc. Vanden Hoogen F, et al. Arthritis Rheum 2013;65:2737-47



Diagnostic criteria for SSc (ACR & EULAR, 2013)

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Telangiectasia		2
Abnormal nailfold capillaries		2
Pulmonary arterial hypertension and/or interstitial lung disease		2
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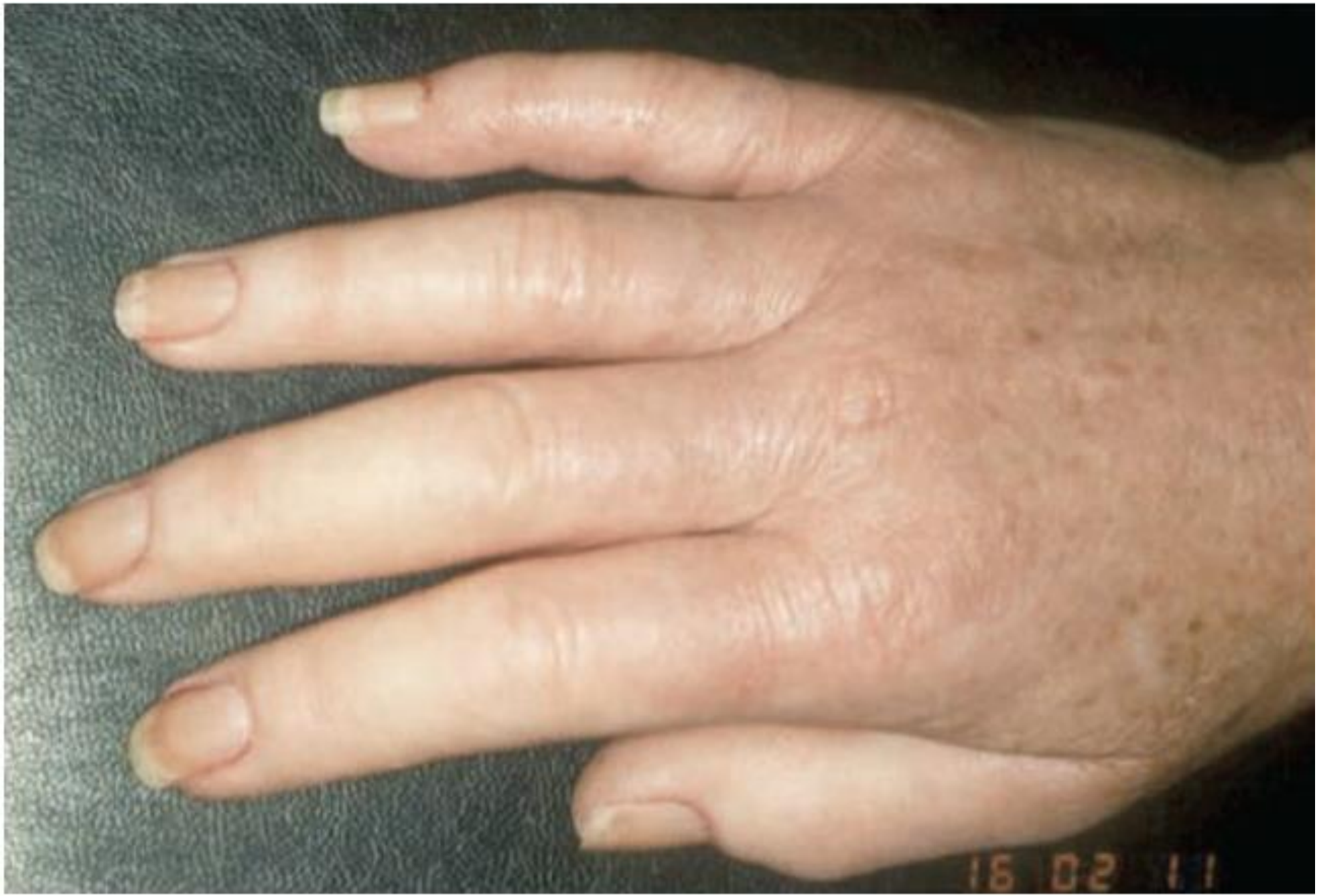

Sclerodactyly. Note skin induration on the fingers, and fixed flexion contractures at the proximal interphalangeal joints in a patient with limited cutaneous systemic sclerosis (SSc).

Harrison's Rheumatology 3rd edition / A.S.Fauci, C.A. Langford, R.C. Basner / McGrawHill Education, 2013, C.113-129.

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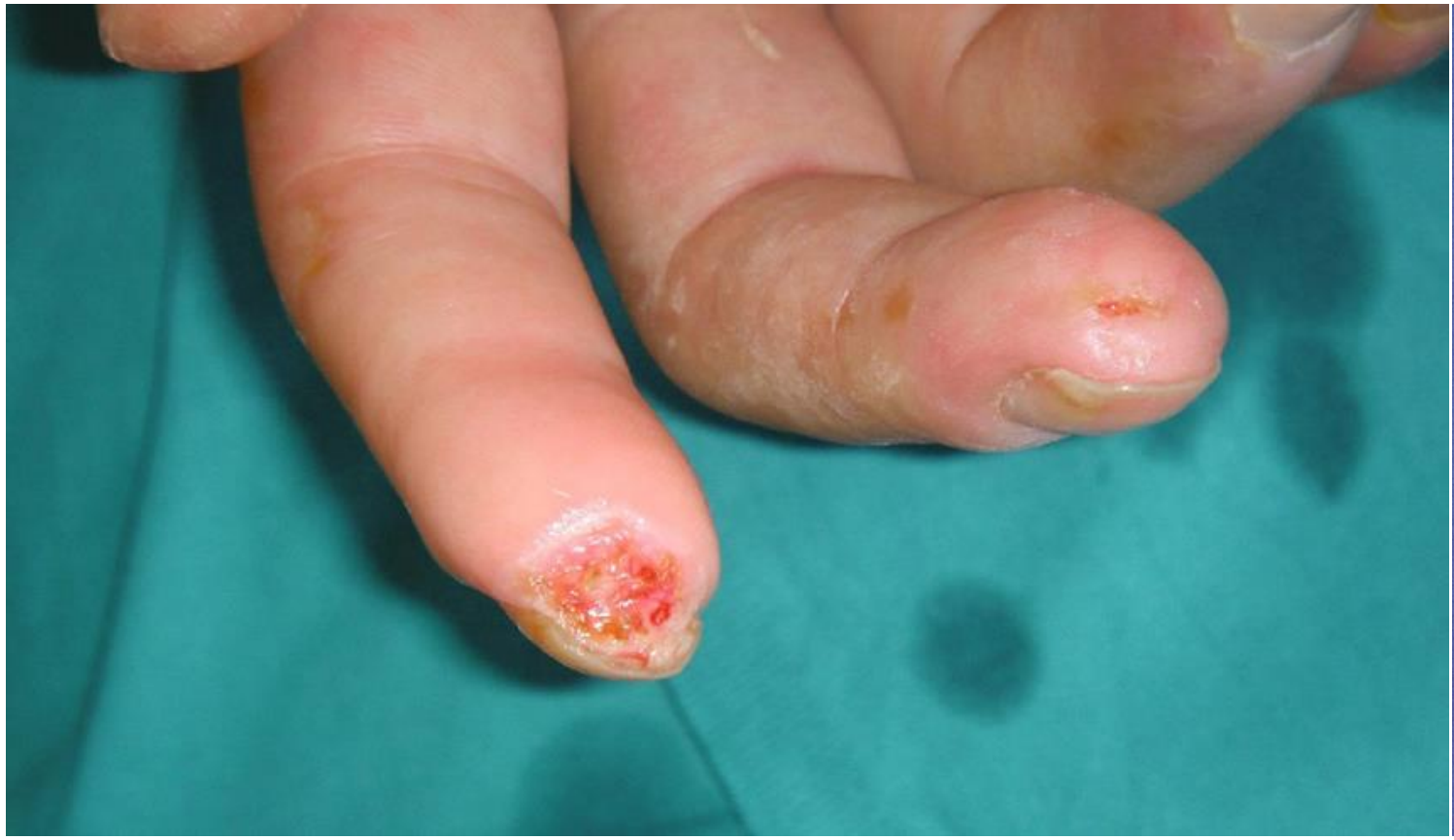
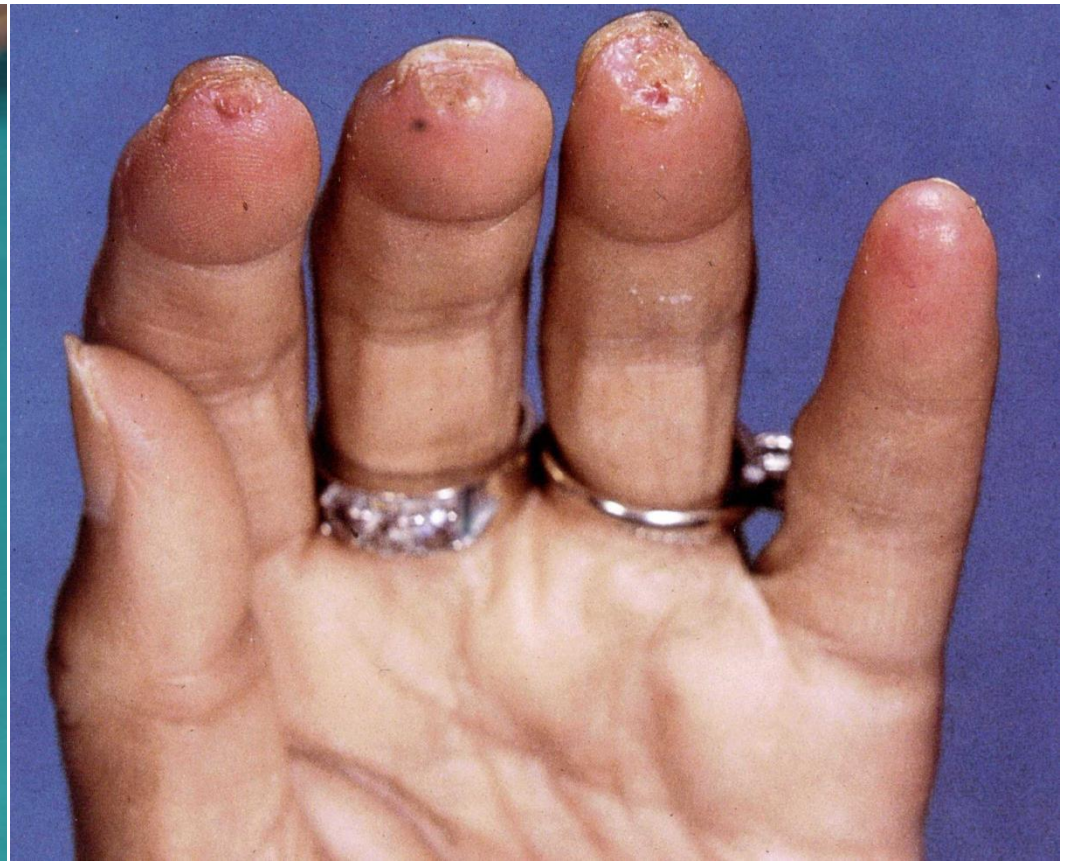
2013 Classification criteria for SSc. Vanden Hoogen F, et al. Arthritis Rheum 2013;65:2737-47

Digital tip ulcers and pitting scars





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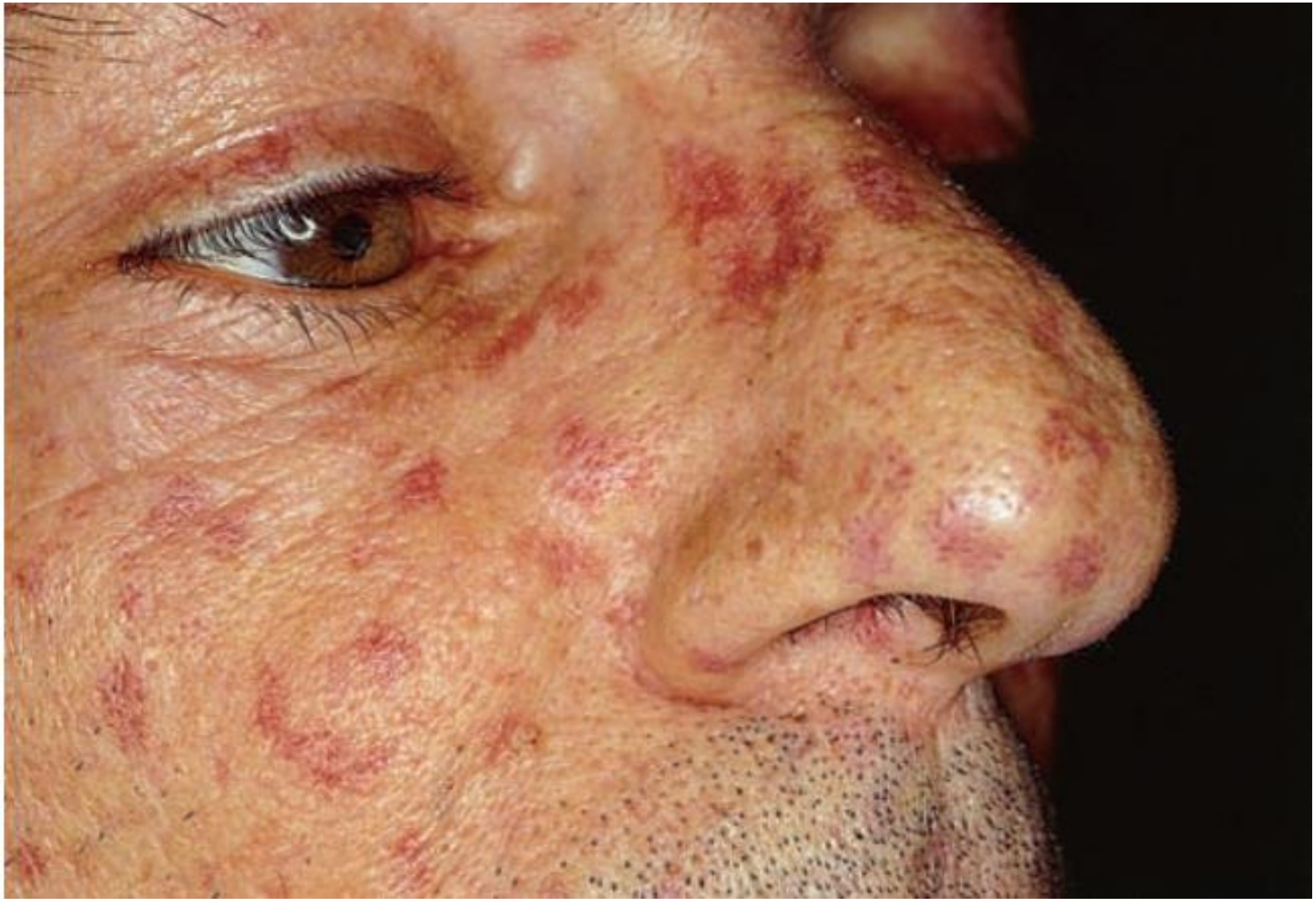

Cutaneous vascular changes. Telangiectasia on the face.

Harrison's Rheumatology 3rd edition / A.S.Fauci, C.A. Langford, R.C. Basner / McGrawHill Education, 2013, C.113-129.

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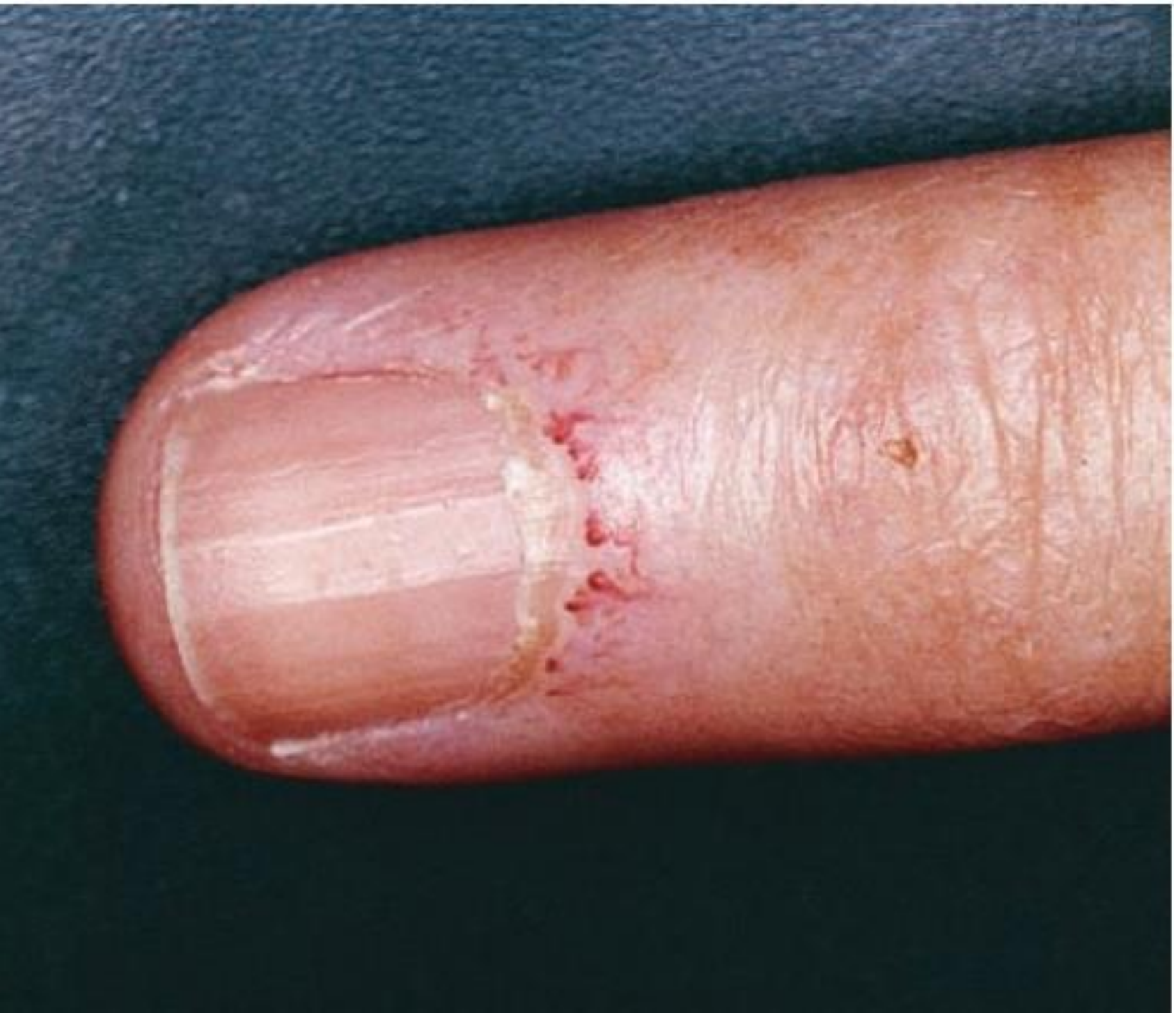
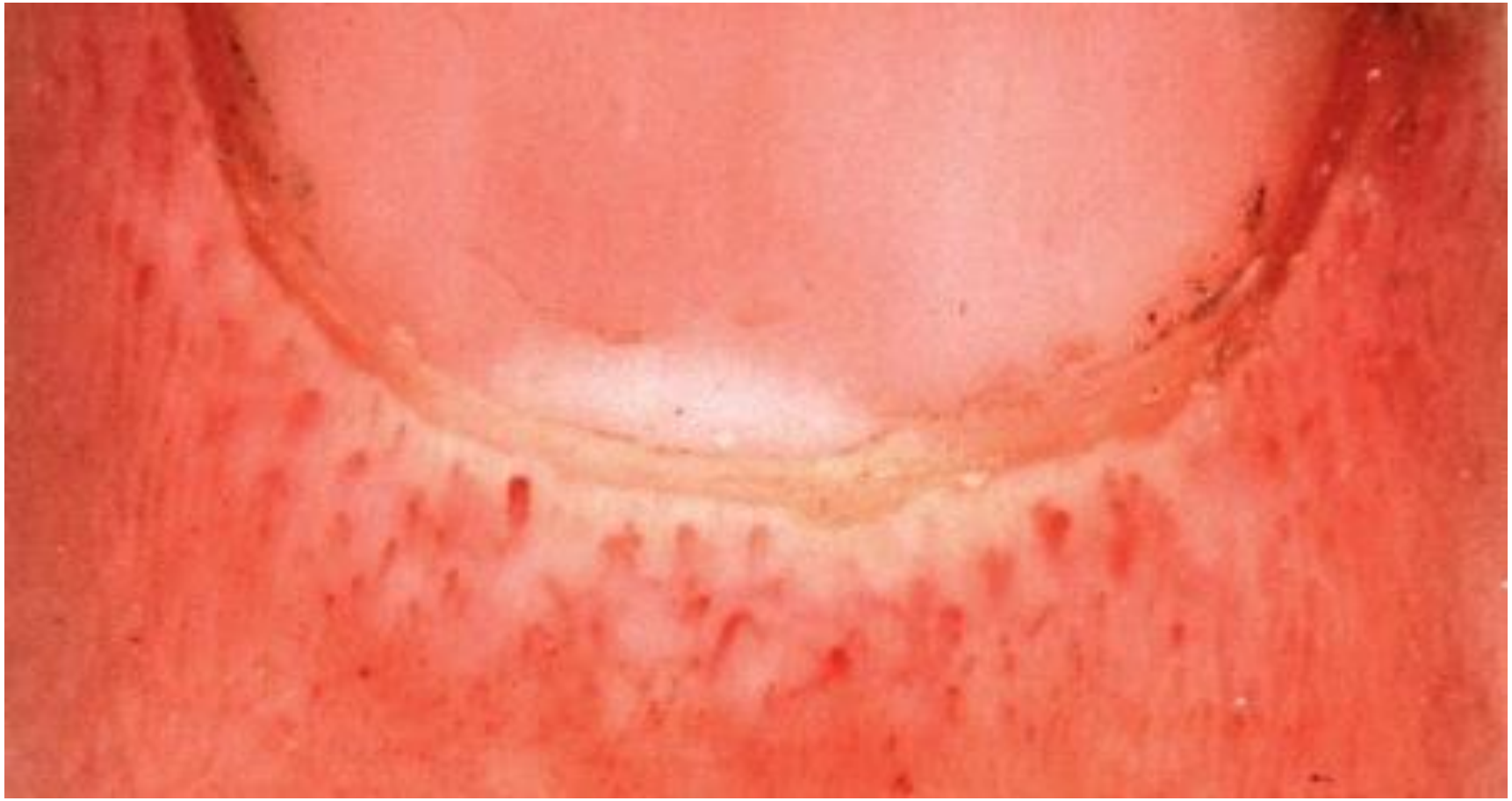


Cutaneous vascular changes. Capillary changes at the nailfold in a patient with limited cutaneous systemic sclerosis (lcSSc).

Harrison's Rheumatology 3rd edition / A.S.Fauci, C.A. Langford, R.C. Basner / McGrawHill Education, 2013, C.113-129.

ANBORMAL NAILFOLD CAPILLARIES



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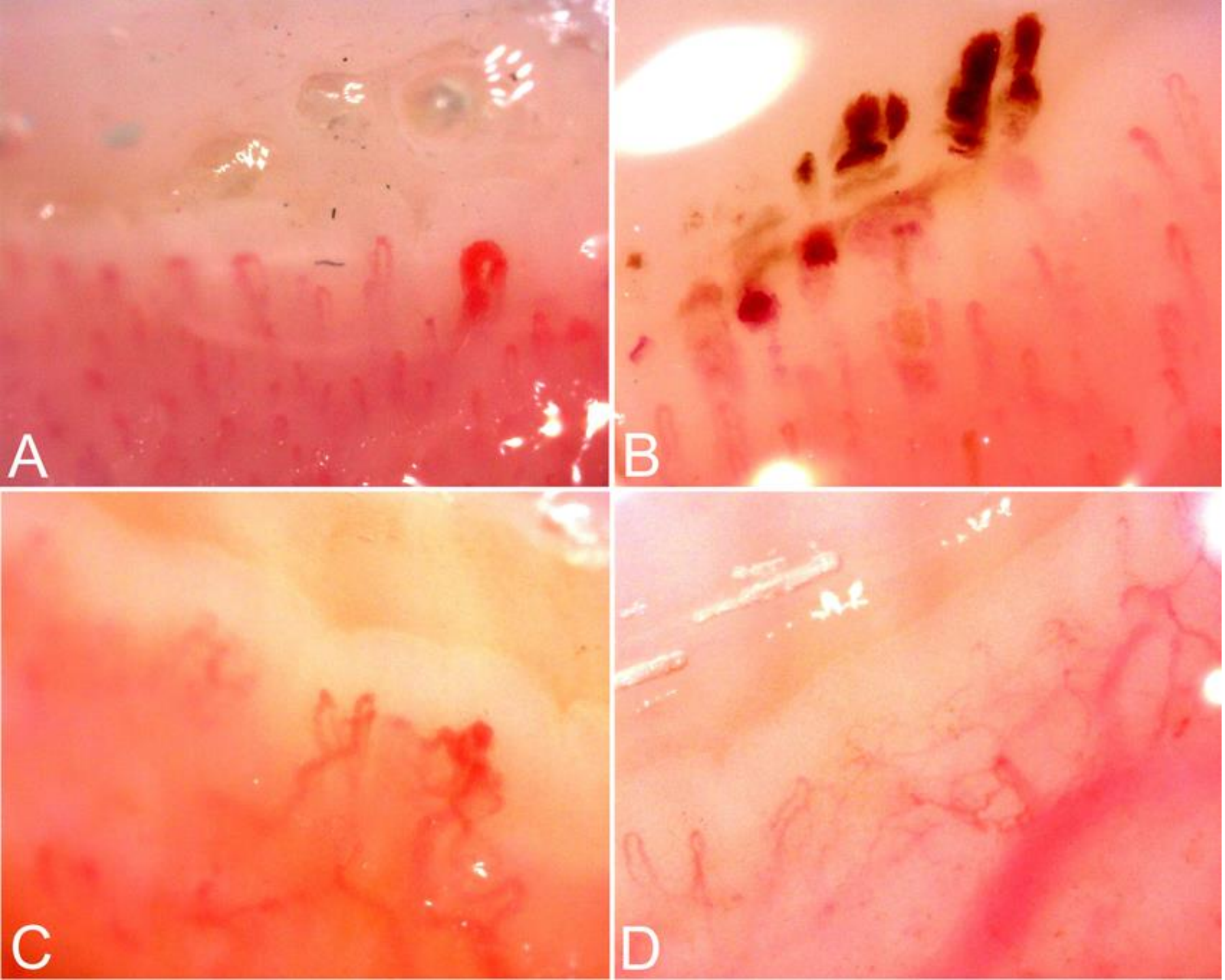

Capillaroscopy.
Scleroderma pattern.
Early (A),
active (B)
and late (C, D)
patterns.

Capillaroscopy – a role in modern rheumatology. M.M. Chojnowski et al. Reumatologia 2016; 54, 2: 67–72

Diagnostic criteria for SSc (ACR & EULAR, 2013)

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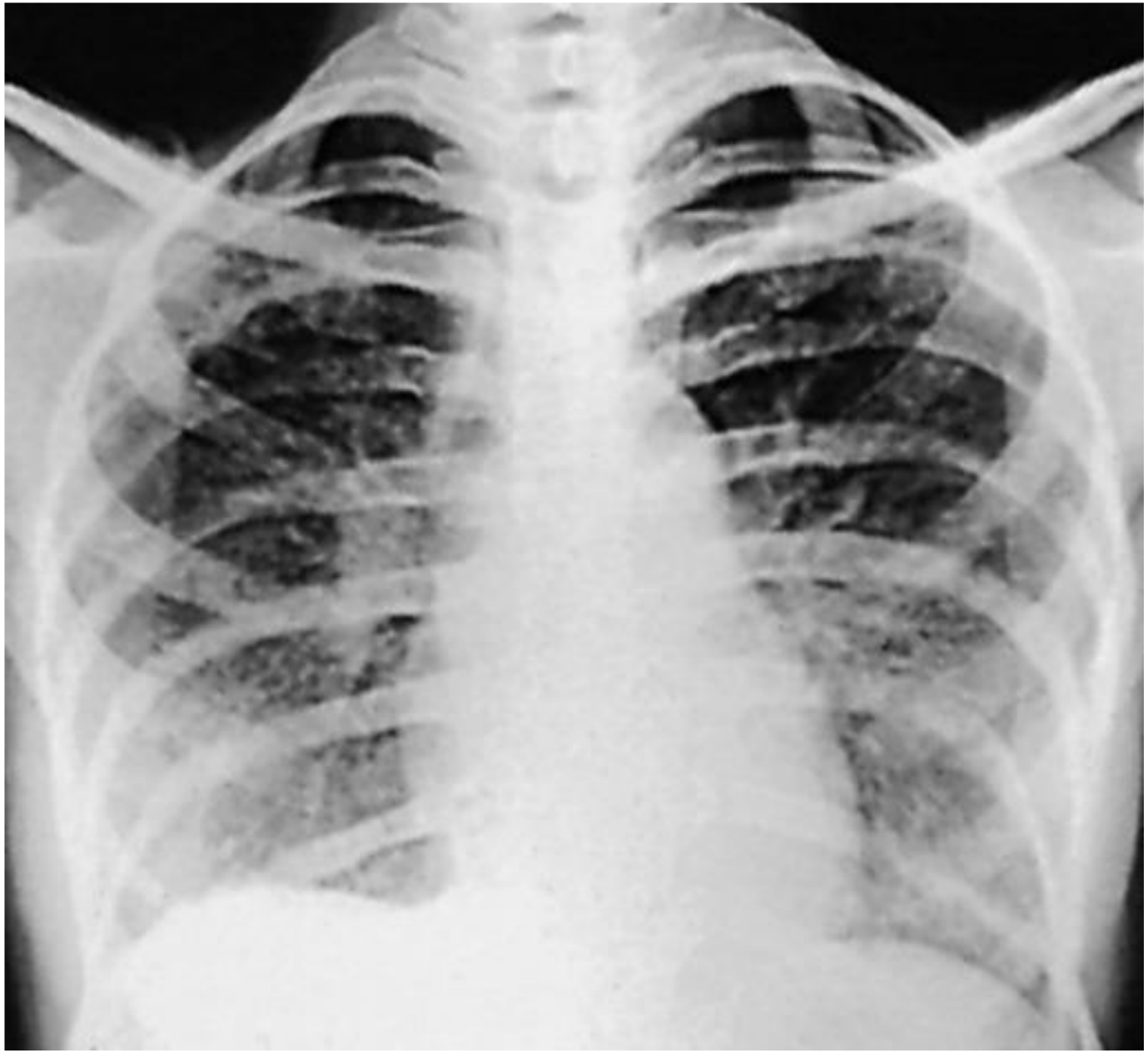
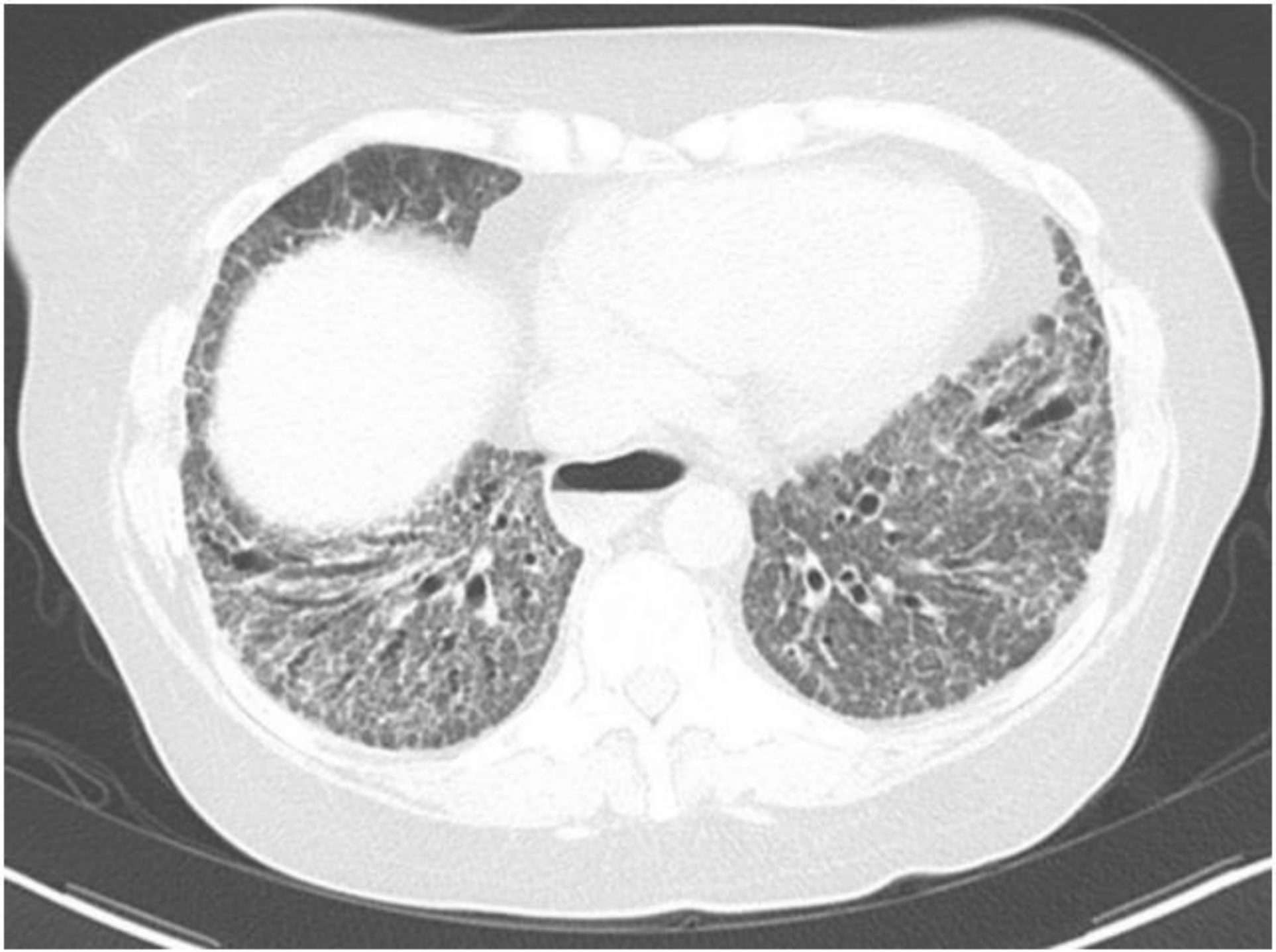


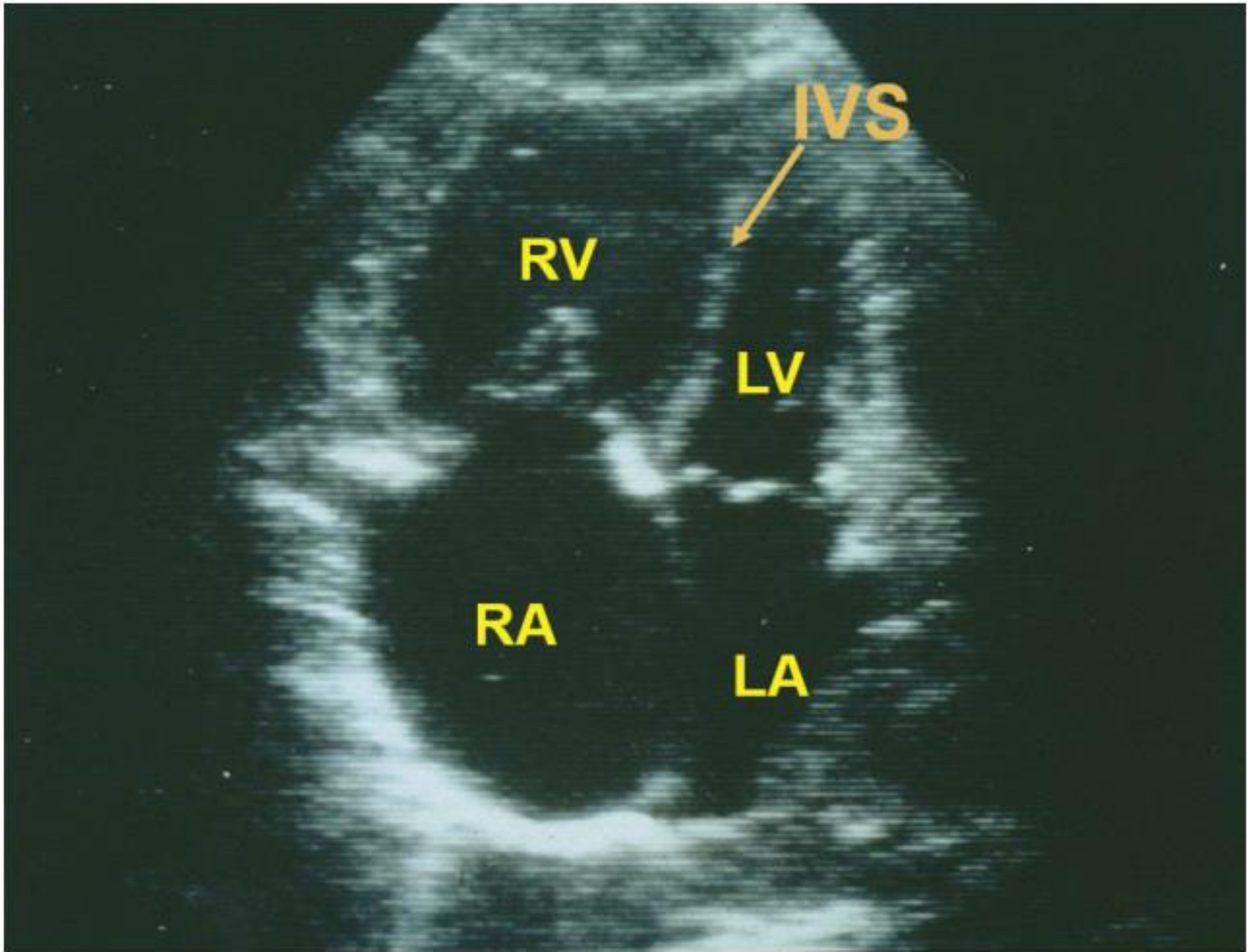
Scleroderma.
Chest X-ray

- Interstitial lung fibrosis



- High-resolution CT image with bibasilar fibrotic interstitial lung disease characteristic of systemic sclerosis.
- Note also the dilated, fluid-filled esophagus.

Rheumatology Secrets. 4th ed. S.G.West., J.Kolfenbach. Elsevier, 2020. P.156-176.



- Echocardiographic features of pulmonary AH: dilated RA, RV, flattening of the interventricular septum.
- IVS - interventricular septum;
- LA - left atrium;
- LV - left ventricle;
- RA - right atrium;
- RV - right ventricle.

Rheumatology Secrets. 4th ed. S.G.West., J.Kolfenbach. Elsevier, 2020. P.156-176.

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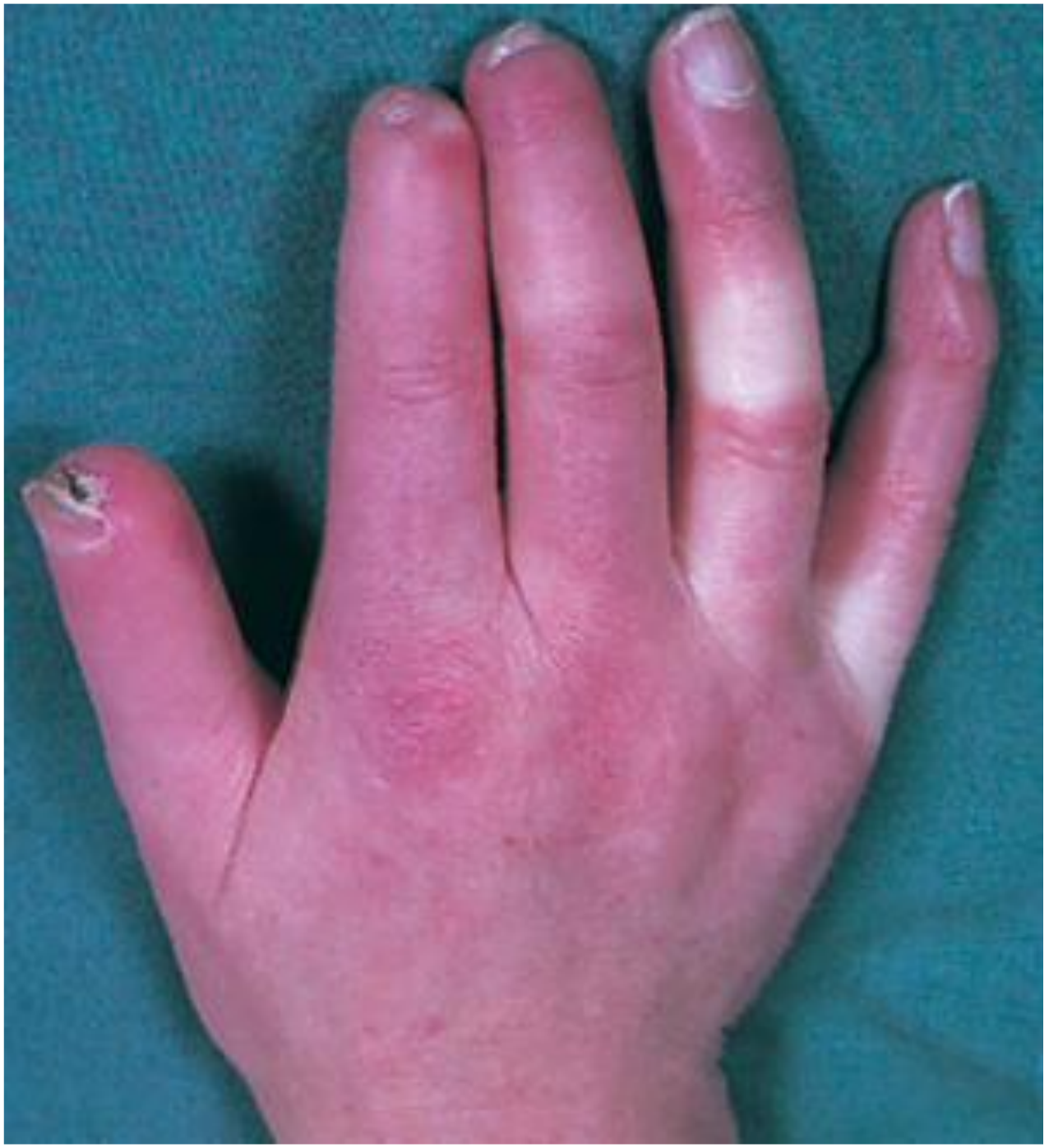
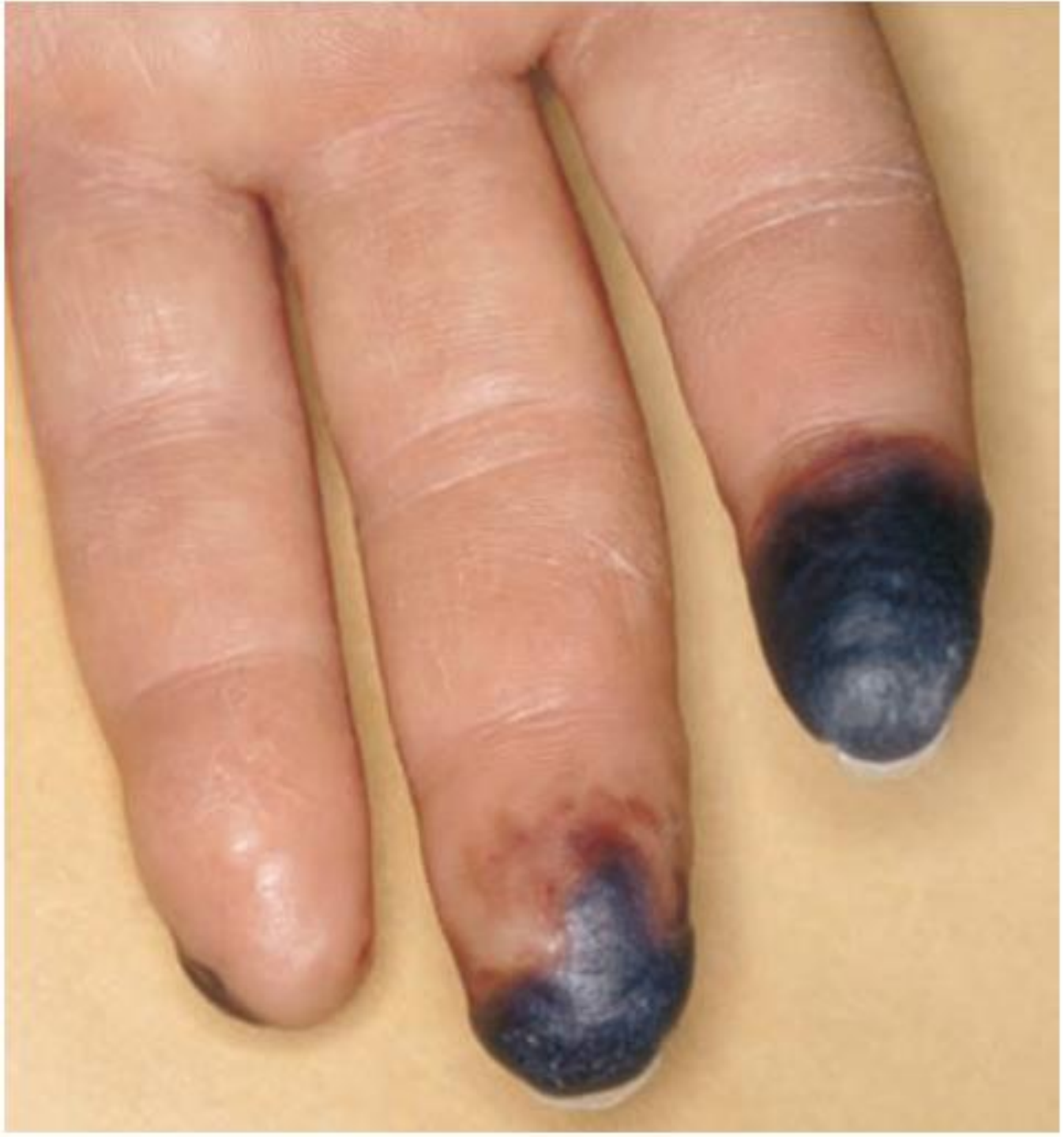


Limited cutaneous scleroderma

- Puffy fingers,
- tight skin,
- Raynaud ' s phenomenon,
- loss of distal digits and
- ulceration of tips of digits.



Digital necrosis. Sharply demarcated necrosis of the fingertip in a patient with limited cutaneous systemic sclerosis (SSc) associated with severe Raynaud's phenomenon.

Harrison's Rheumatology 3rd edition / A.S.Fauci, C.A. Langford, R.C. Basner / McGrawHill Education, 2013, C.113-129.

Diagnostic criteria for SSc (ACR & EULAR, 2013)

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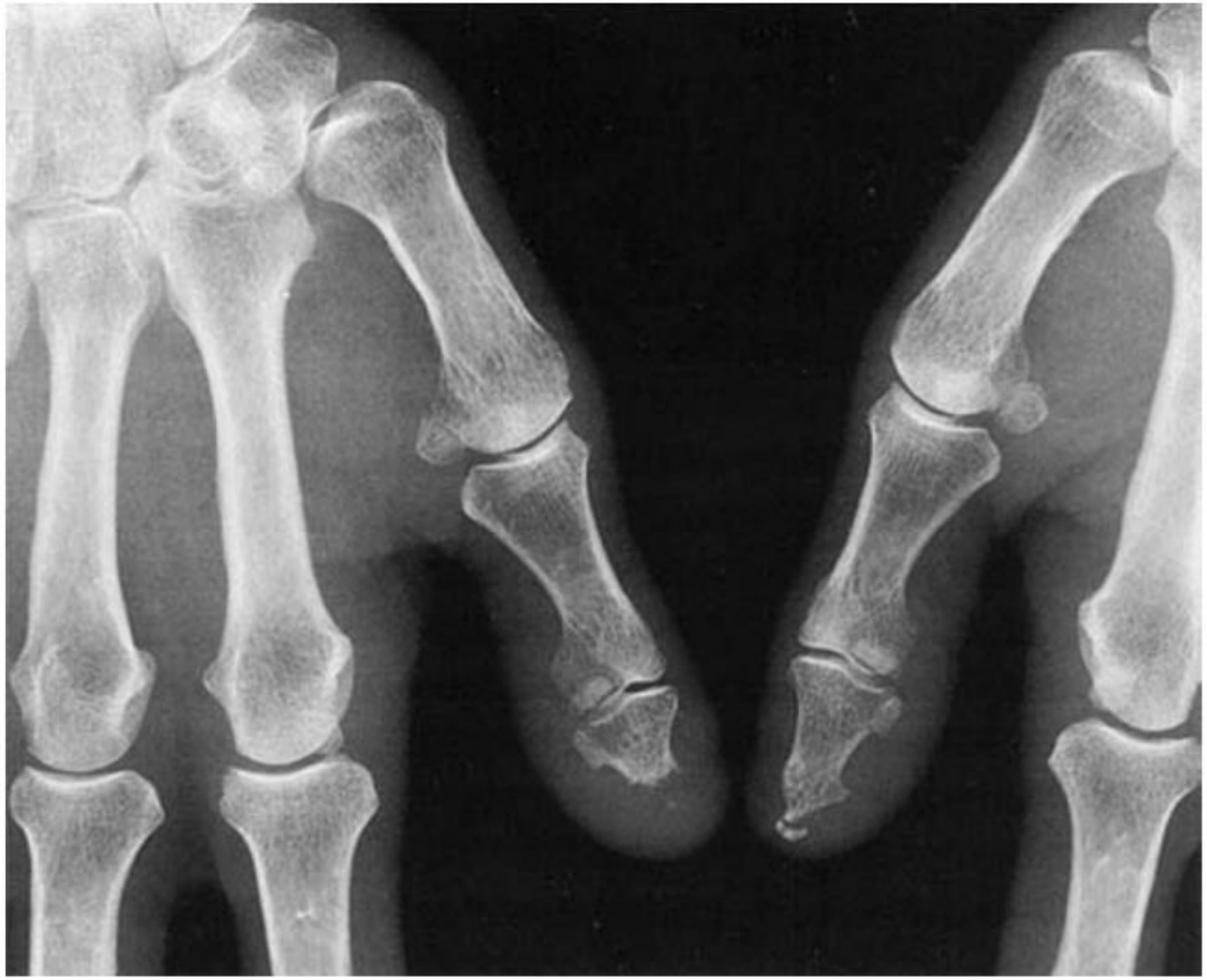
2013 Classification criteria for SSc. Vanden Hoogen F, et al. Arthritis Rheum 2013;65:2737-47

AUTOANTIBODIES AND ASSOCIATED FEATURES IN SYSTEMIC SCLEROSIS (SSc)

TARGET ANTIGEN	SSc SUBSET	CHARACTERISTIC CLINICAL ASSOCIATION
Topoisomerase-I	dcSSc	Tendon friction rubs, ILD, cardiac involvement, scleroderma renal crisis
Centromere proteins	lcSSc	Digital ischemia, calcinosis, isolated PAH; renal crisis rare
RNA polymerase III	dcSSc	Extensive skin, tendon friction rubs, renal crisis
U3-RNP	dcSSc	PAH, ILD, scleroderma renal crisis, myositis
Th/T0	lcSSc	ILD, PAH
PM/Scl	lcSSc	Calcinosis, myositis
U1-RNP	MCTD	PAH

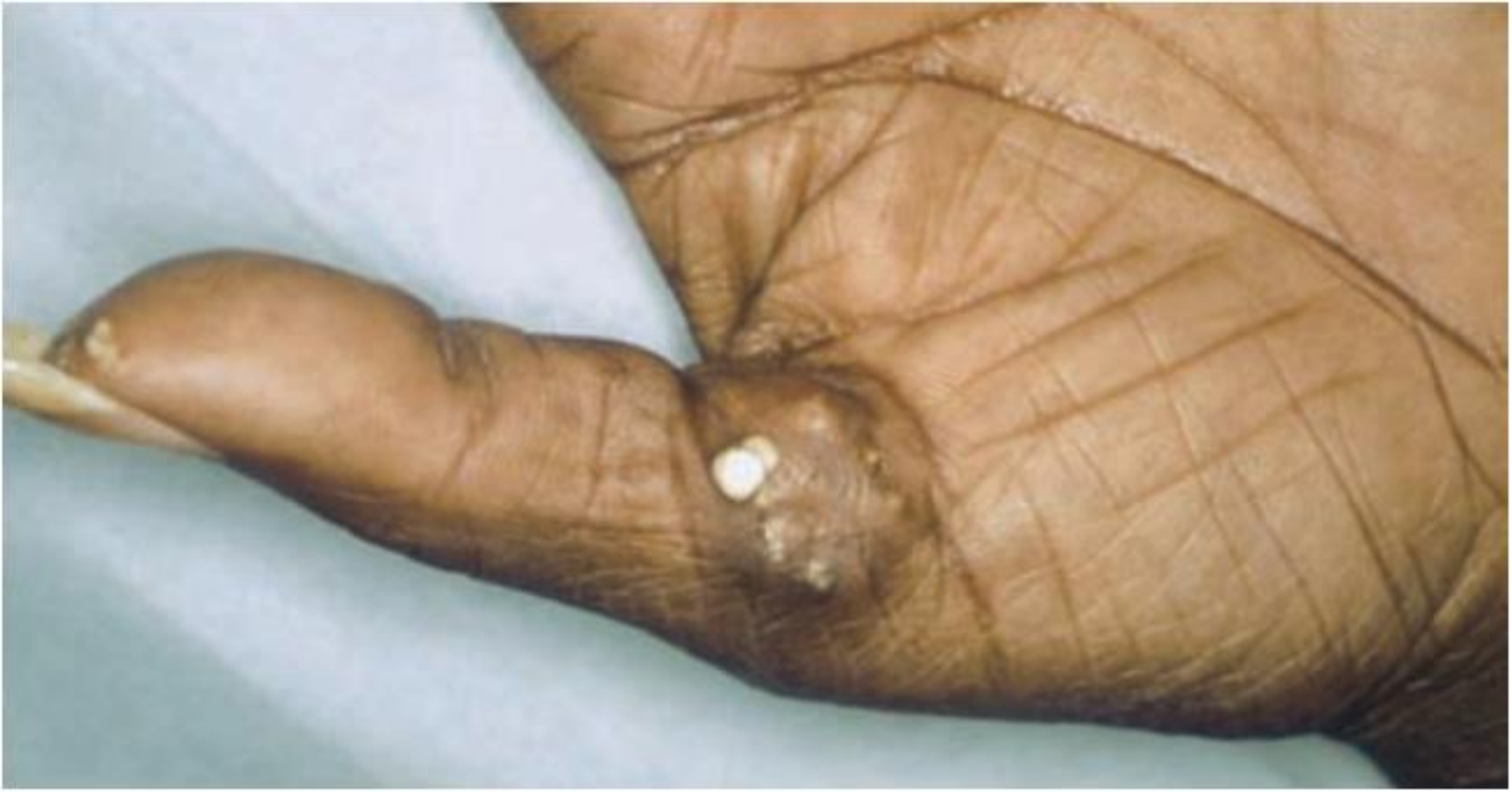
- dcSSc – diffuse cutaneous SSc;
- ILD – interstitial lung disease;
- lcSSc – limited cutaneous SSc;
- MCTD – mixed connective tissue disease;
- PAH – pulmonary arterial hypertension

Harrison's Rheumatology 3rd edition / A.S.Fauci, C.A. Langford, R.C. Basner / McGrawHill Education, 2013, C.113-129.



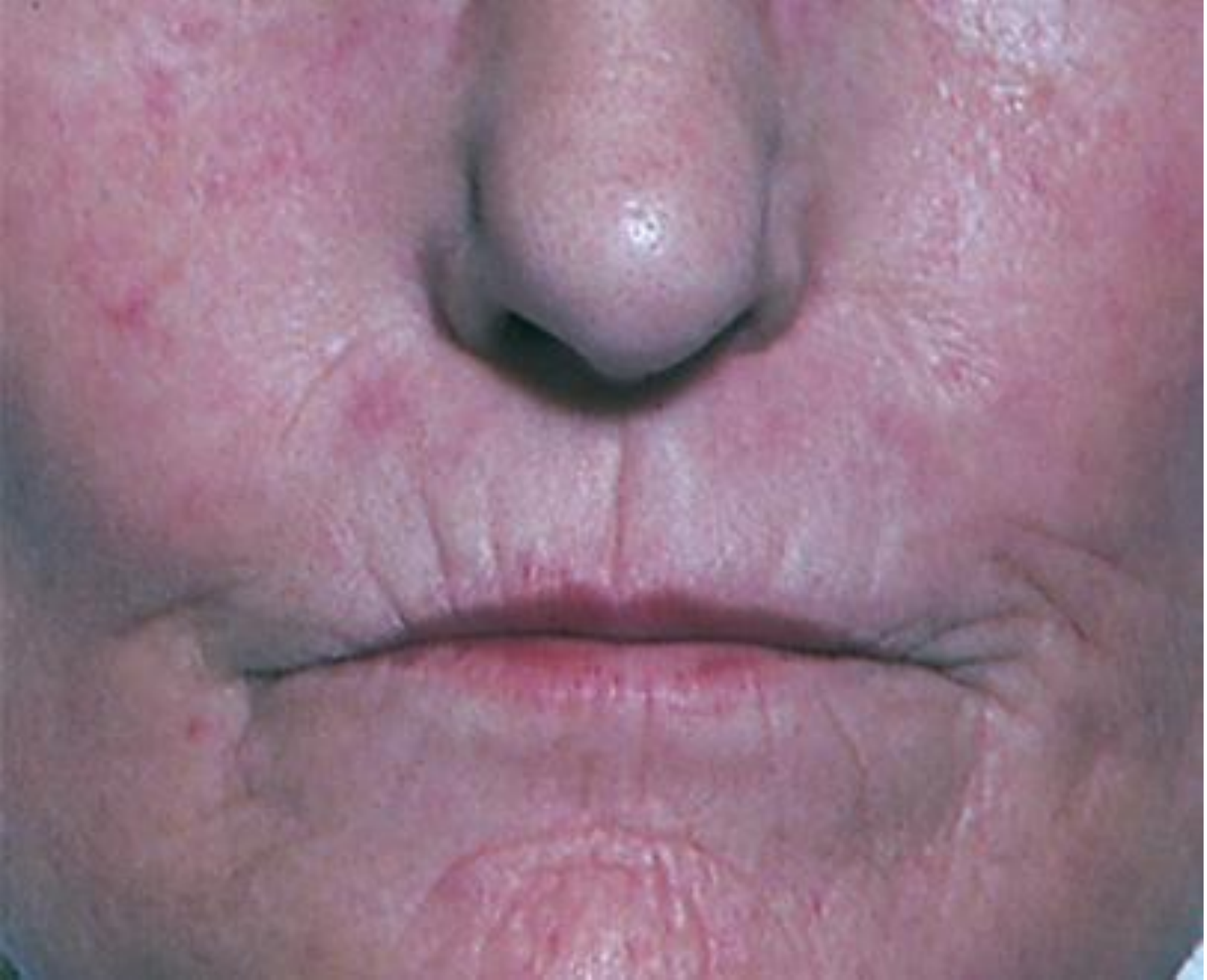
Acro-osteolysis. Note dissolution of terminal phalanges in a patient with long-standing limited cutaneous systemic sclerosis (lcSSc) and Raynaud's phenomenon.

Harrison's Rheumatology 3rd edition / A.S.Fauci, C.A. Langford, R.C. Basner / McGrawHill Education, 2013, C.113-129.



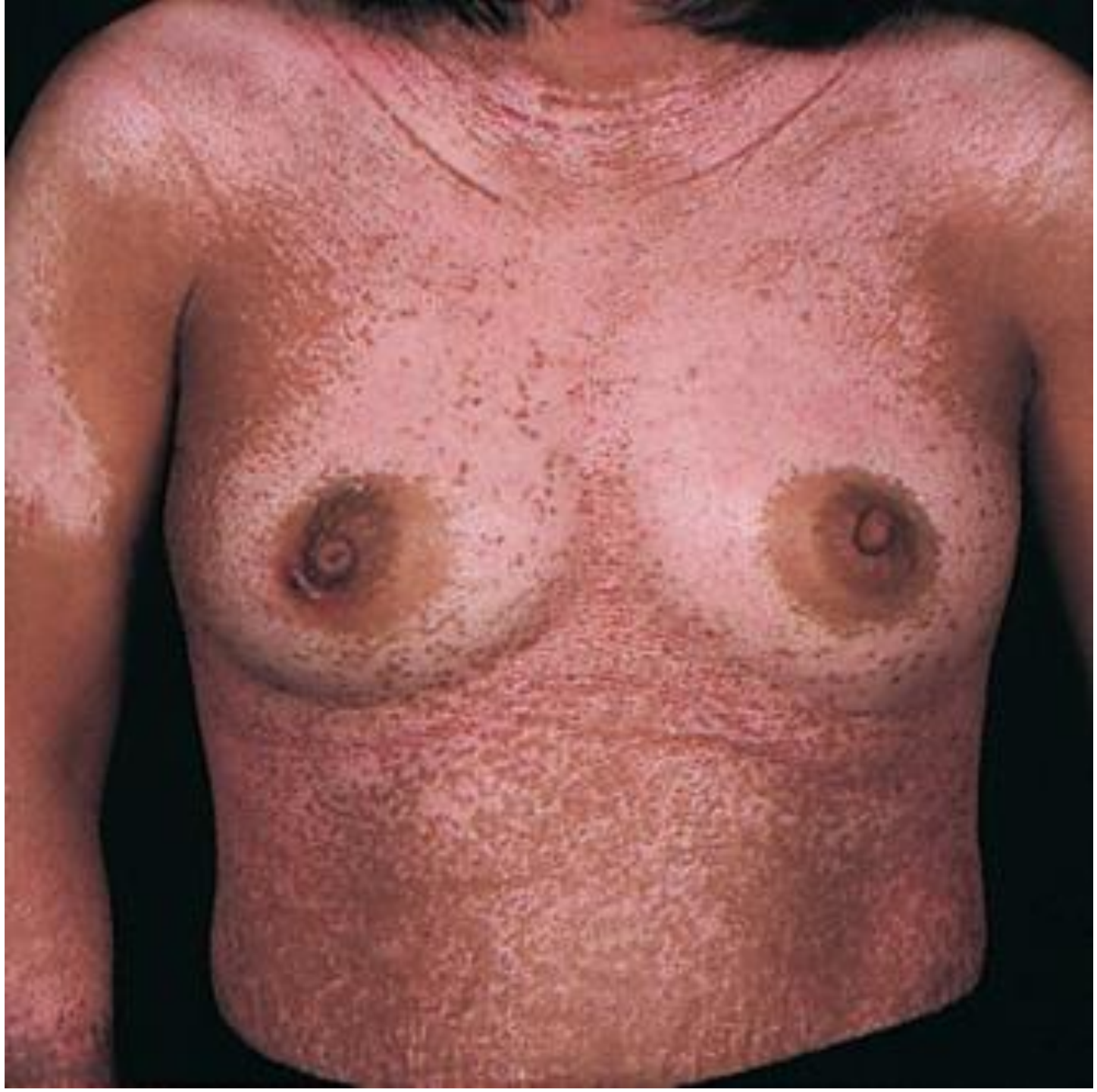
Calcinosis cutis. Note large calcific deposit breaking through the skin in a patient with limited cutaneous systemic sclerosis (lcSSc).

Harrison's Rheumatology 3rd edition / A.S.Fauci, C.A. Langford, R.C. Basner / McGrawHill Education, 2013, C.113-129.



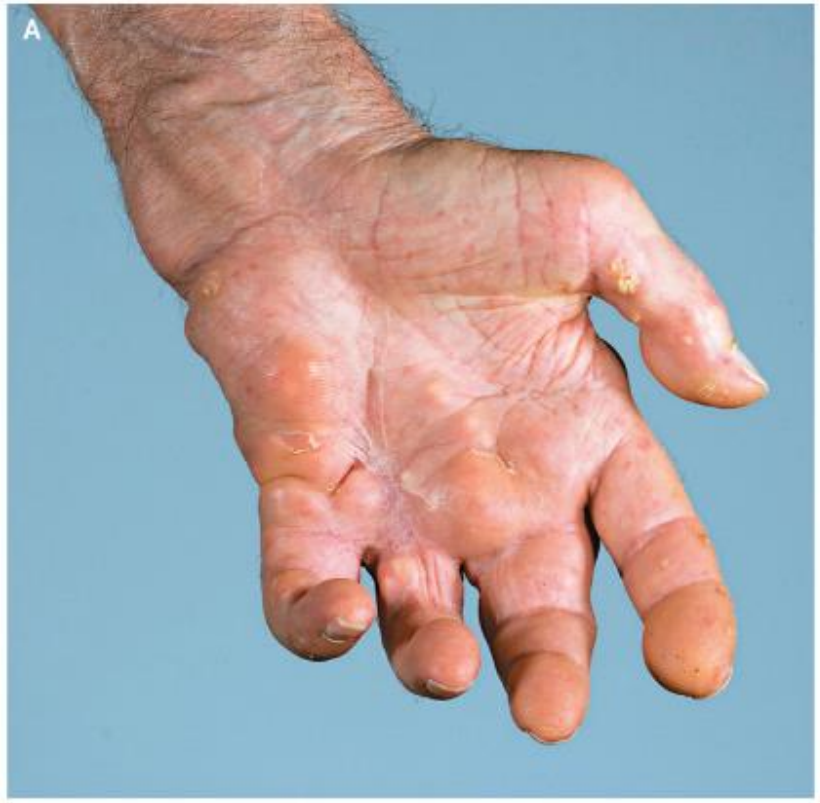
Limited cutaneous scleroderma

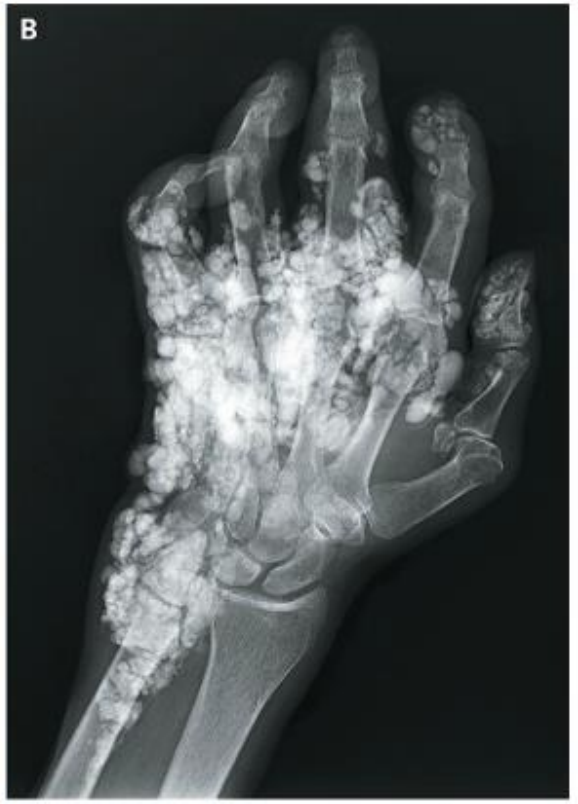
- Microstomia
- telangiectasia

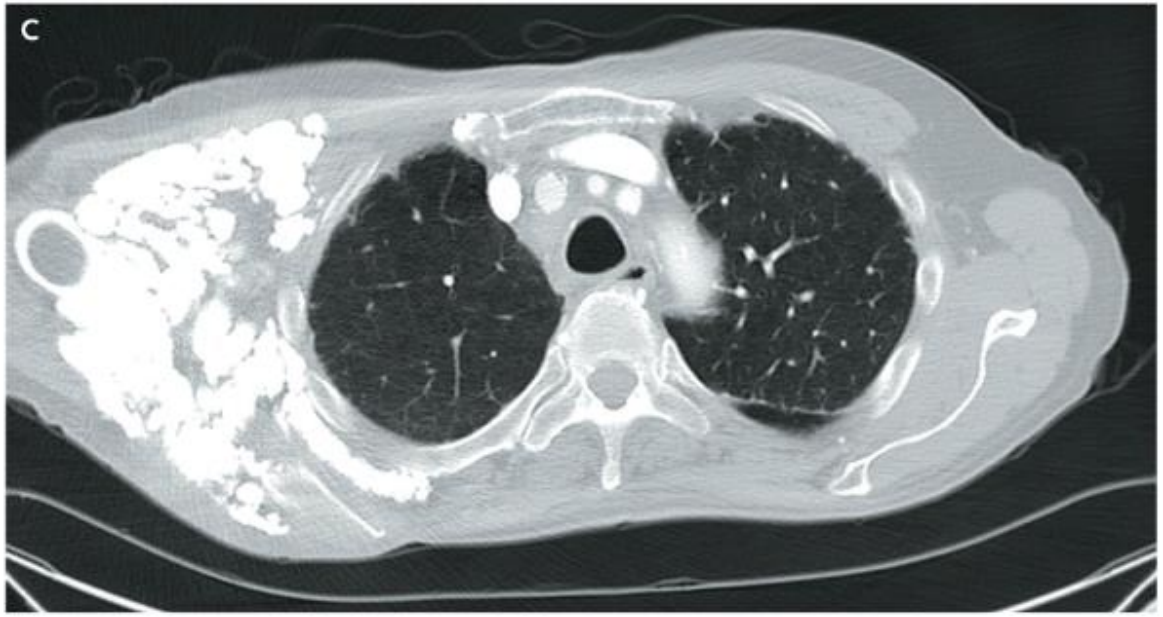


Diffuse cutaneous scleroderma

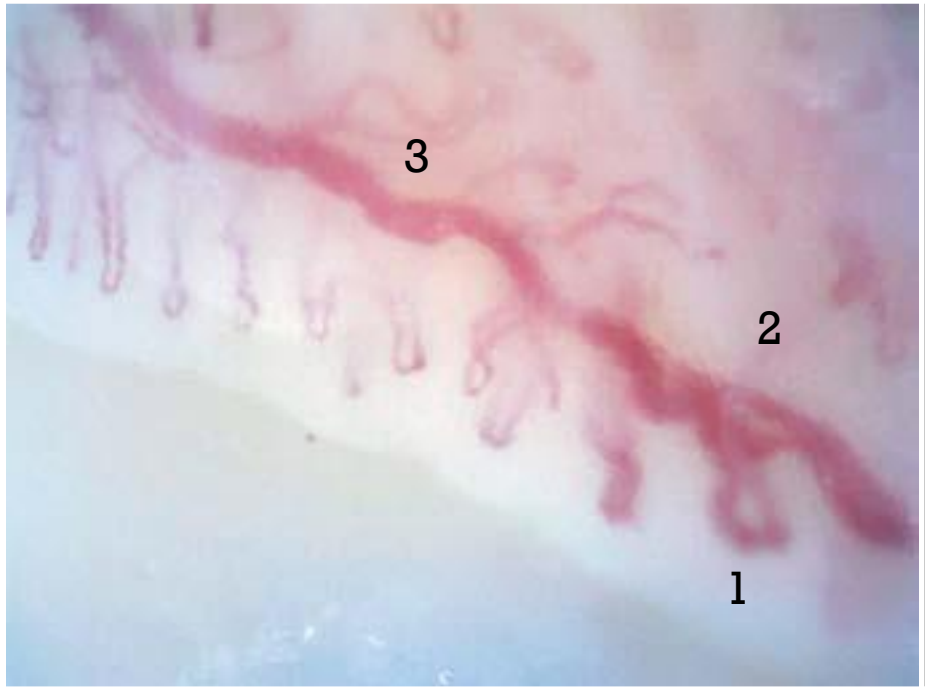
- Hypo-pigmentation
- Hyper-pigmentation
- “Salt and pepper”

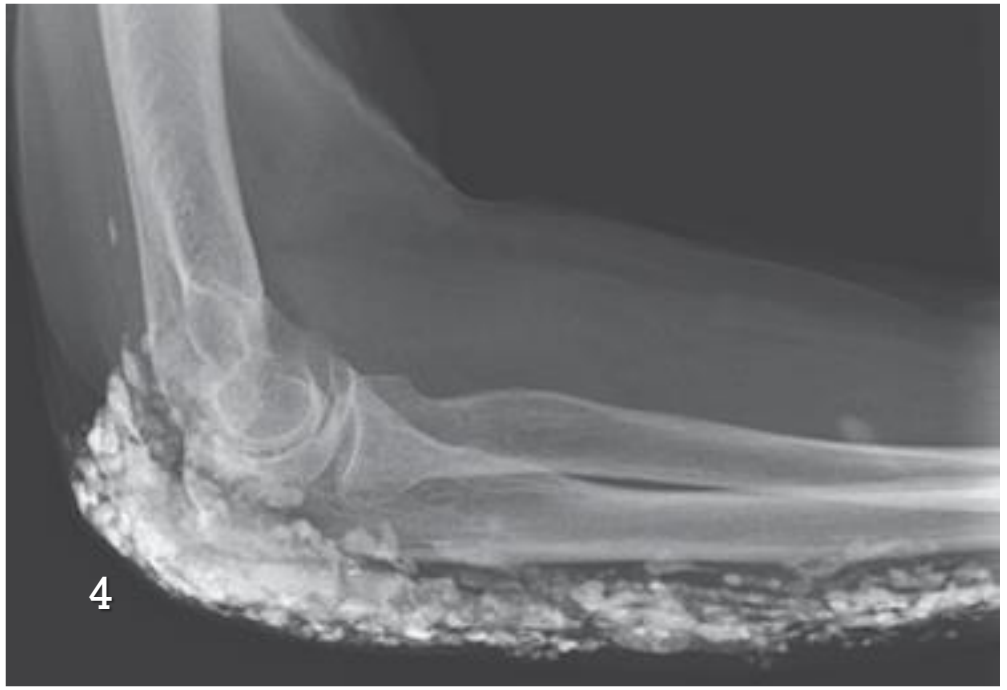




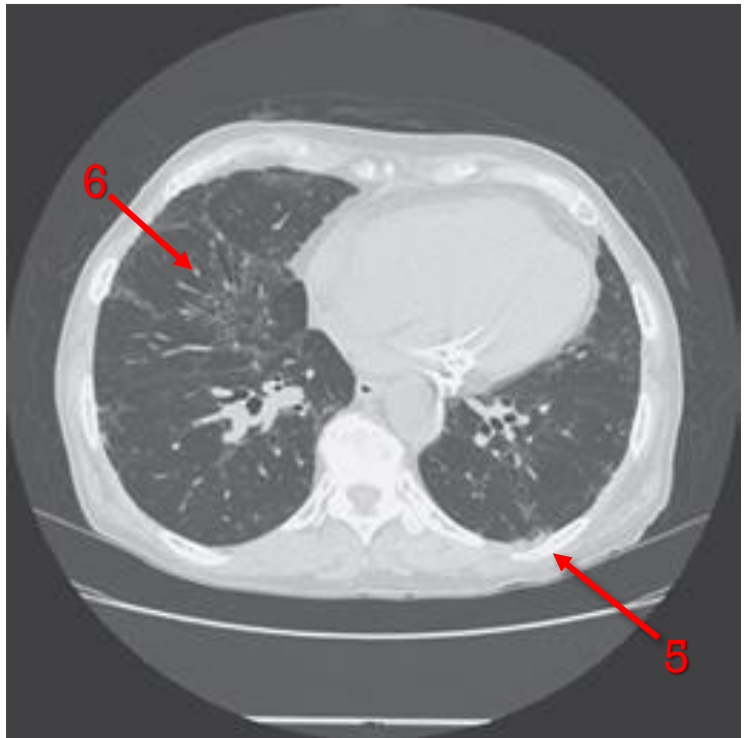


- A 74-year-old man with 16-year history of systemic sclerosis. Extensive calcinosis cutis was observed on plain radiographs of the hands and on axial computed tomographic images of the chest.

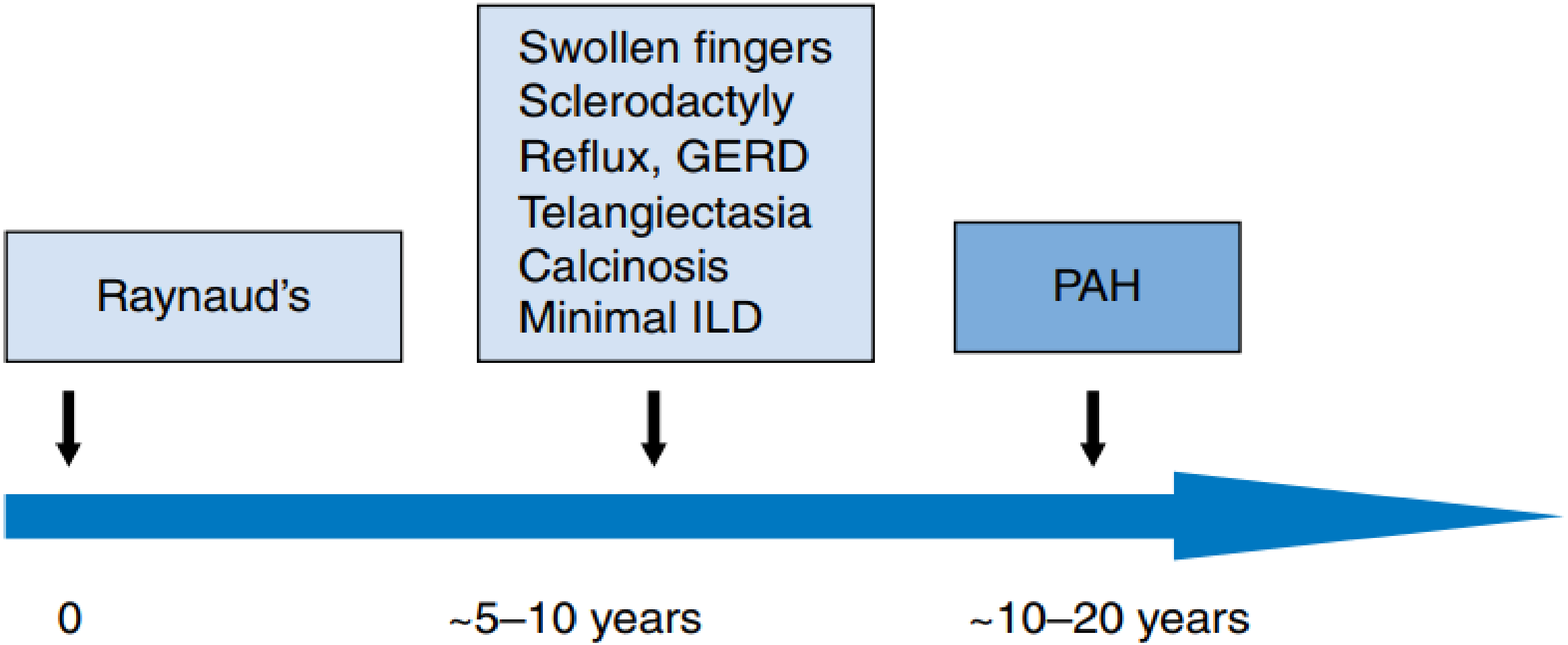




- 75-year-old woman with scleroderma.
- Nailfold videocapillaroscopy showed dilated and tortuous capillary loops (1), severe capillary loss (2), and neovascularization (3)
- Arm X-ray confirmed exuberant calcinosis cutis (4)
- An axial CT of the chest showed bilateral basilar reticular fibrosis (5), with ground-glass opacities suggesting an active alveolitis within the lung parenchyma (6)



Classic presentation of centromere positive Limited SSc



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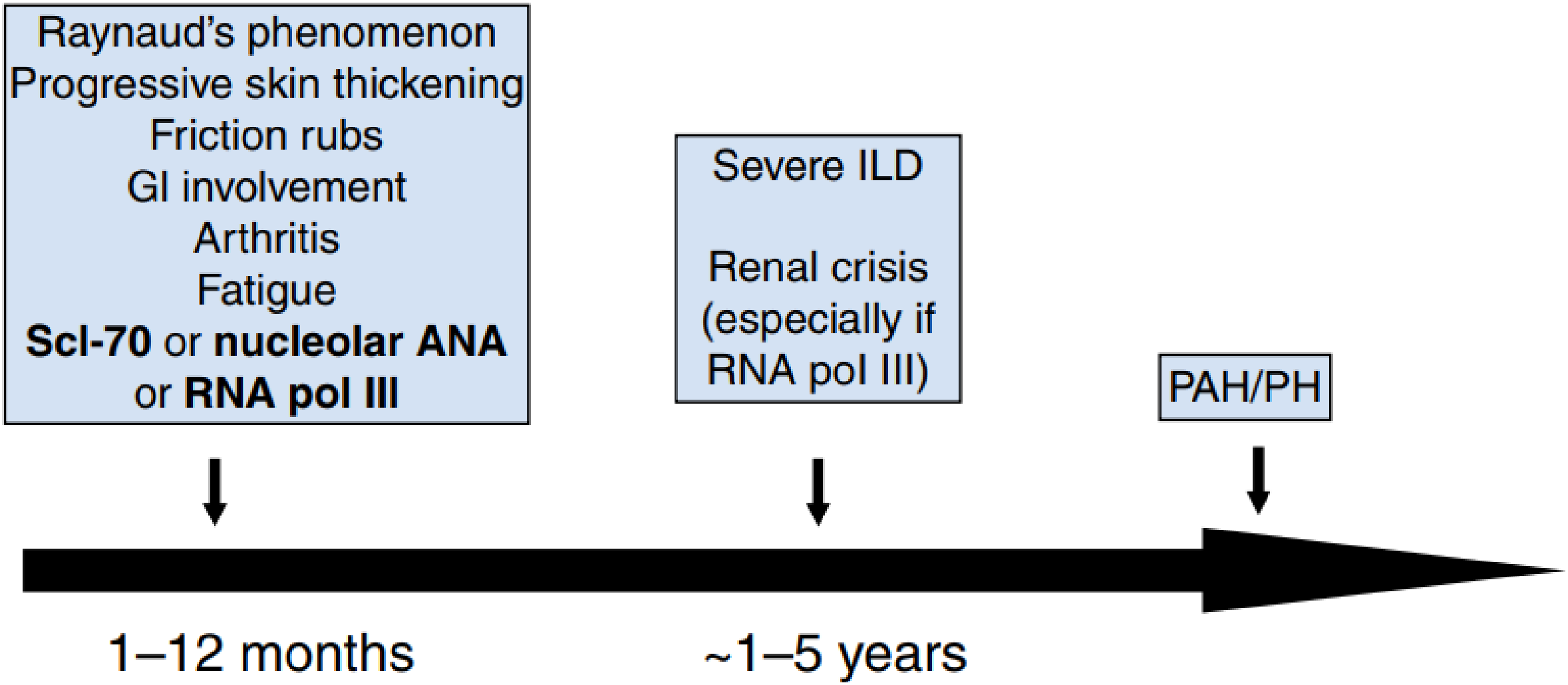
Classic presentation of Diffuse SSc



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Treatment of SSc, according to the organ involvement

Raynaud's phenomenon (RP)

- ***Dihydropyridine-type calcium antagonists***, usually oral **Nifedipine** – first-line therapy
- ***PDE-5 inhibitors (Sildenafil) –*** oral
- ***Prostanoids*** – i.v. **Iloprost** – for severe SSc-RP after oral therapy
- ***Selective serotonin reuptake inhibitor*** – oral **Fluoxetine** might improve SSc-RP attacks (limited data)

Update of EULAR recommendations for the treatment of systemic sclerosis. Kowal-Bielecka O, et al. Ann Rheum Dis 2017;76:1327–1339.

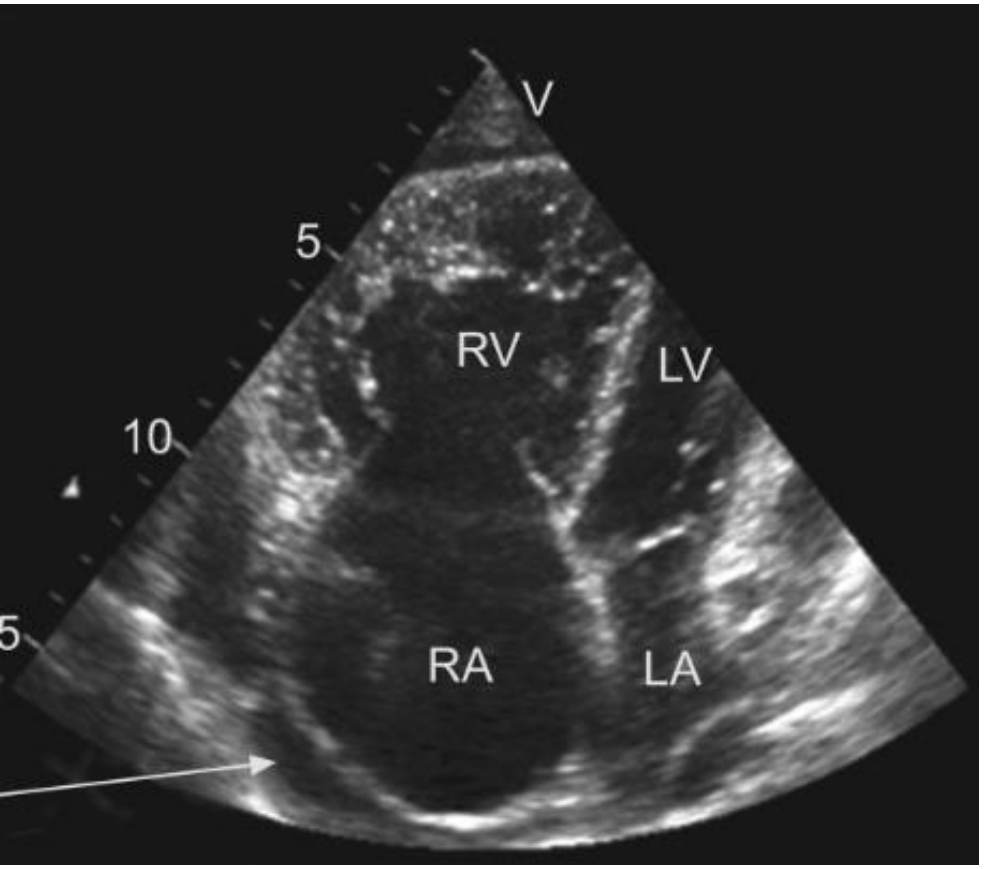
Treatment of SSc, according to the organ involvement

Digital ulcers (DU)

- ***Prostanoids*** – i.v. **Iloprost** is efficacious in healing DU in pts with SSc
- ***PDE-5 inhibitors (Sildenafil) –*** oral – improve healing of DU and may prevent development of new DU in pts with SSc
- ***Dual endothelin receptor antagonist*** (**Bosentan**) – reduce the number of new DU (especially in pts with multiple DU despite use of CCB, PDE-5 inhibitors or iloprost therapy)

Update of EULAR recommendations for the treatment of systemic sclerosis. Kowal-Bielecka O, et al. Ann Rheum Dis 2017;76:1327–1339.

Treatment of SSc, according to the organ involvement

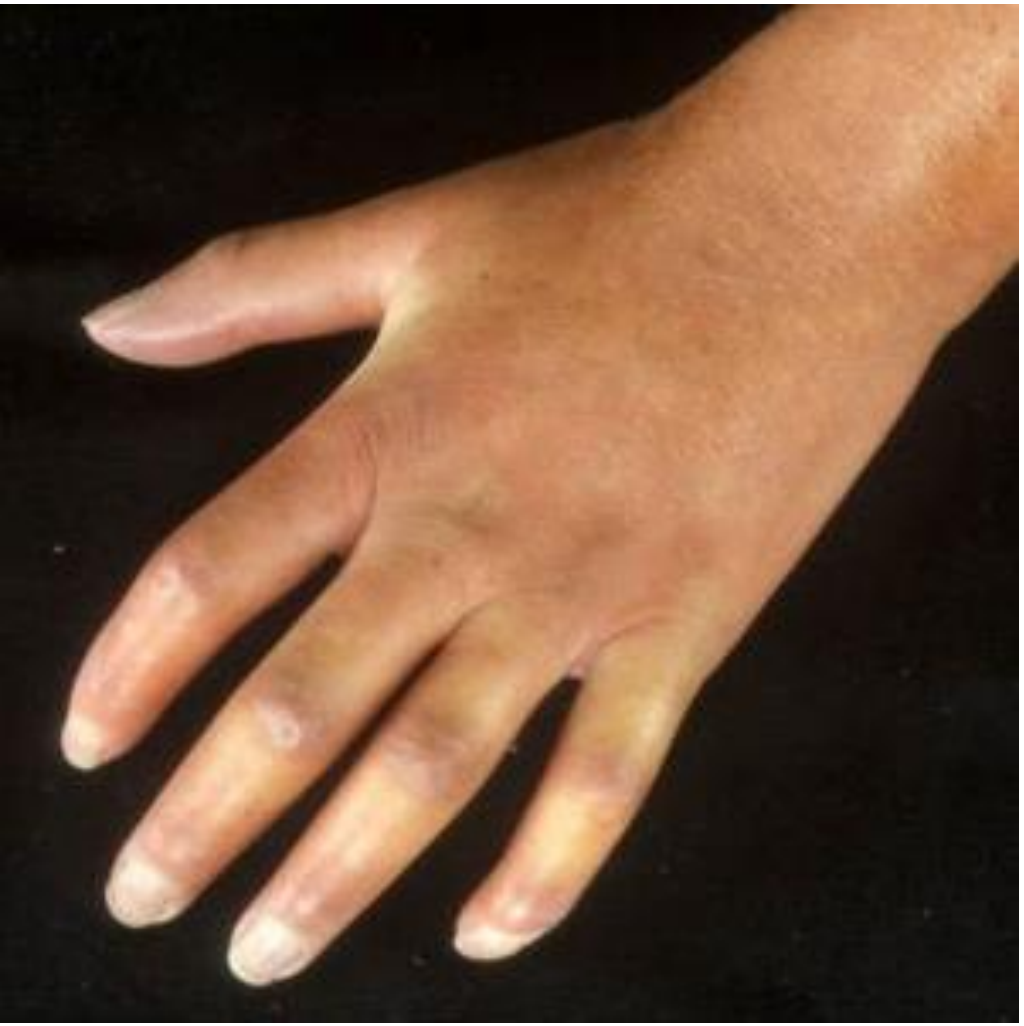


Update of EULAR recommendations for the treatment of systemic sclerosis. Kowal-Bielecka O, et al. Ann Rheum Dis 2017;76:1327–1339.

Pulmonary arterial hypertension (PAH)

- ***Endothelin receptor antagonists*** (**Ambrisentan, Bosentan, Macitentan**)
- ***PDE-5 inhibitors (*****Sildenafil, Tadalafil*****)***
- ***Stimulator of soluble guanylate cyclase (*****Riociguat*****)*** - novel oral drug for the treatment of PAH
- ***Prostanoids*** - i.v. **Epoprostenol, Iloprost, Treprostinil** – improves exercise capacity, functional class and haemodynamic measures in SSc-PAH and should be considered for the pts with severe SSc-PAH (class III and IV)

Treatment of SSc, according to the organ involvement

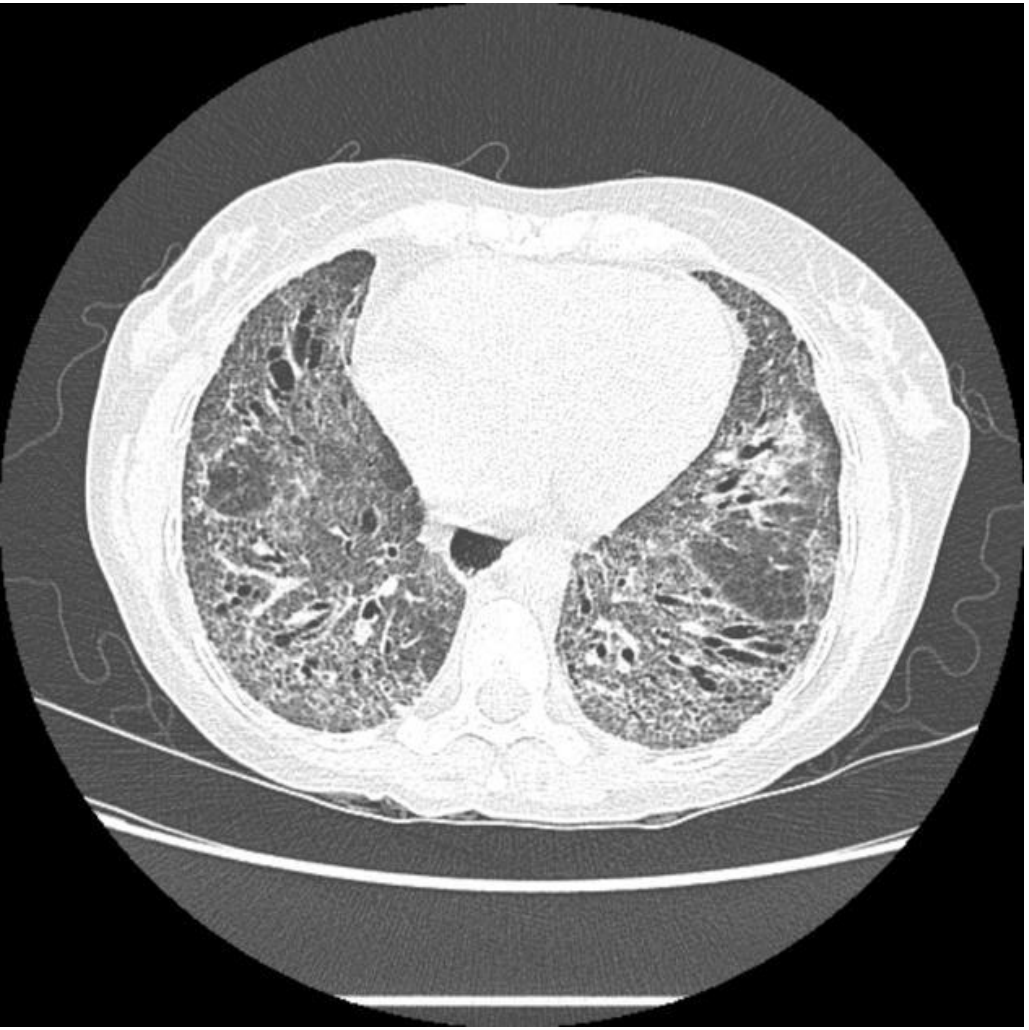


Skin injury

- **Methotrexate** may be considered for treatment of skin manifestations of early diffuse SSc.
- **Haematopoietic stem cell transplantation** – should be considered for treatment of selected patients with rapidly progressive SSc at risk of organ failure

Update of EULAR recommendations for the treatment of systemic sclerosis. Kowal-Bielecka O, et al. Ann Rheum Dis 2017;76:1327–1339.

Treatment of SSc, according to the organ involvement

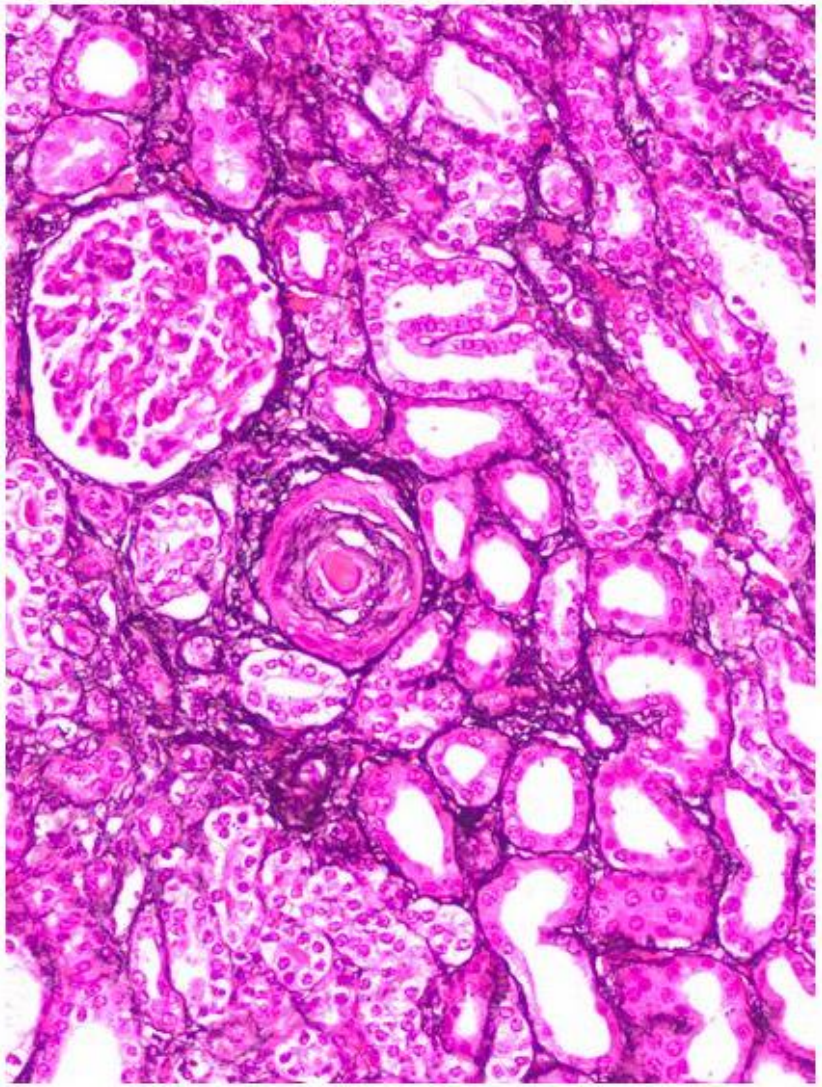


Interstitial lung disease (ILD)

- **Cyclophosphamide** should be considered for treatment of patients with SSc with progressive ILD.
- **Haematopoietic stem cell transplantation** – should be considered for stabilisation of lung function of selected patients with rapidly progressive SSc at risk of organ failure

Update of EULAR recommendations for the treatment of systemic sclerosis. Kowal-Bielecka O, et al. Ann Rheum Dis 2017;76:1327–1339.

Treatment of SSc, according to the organ involvement

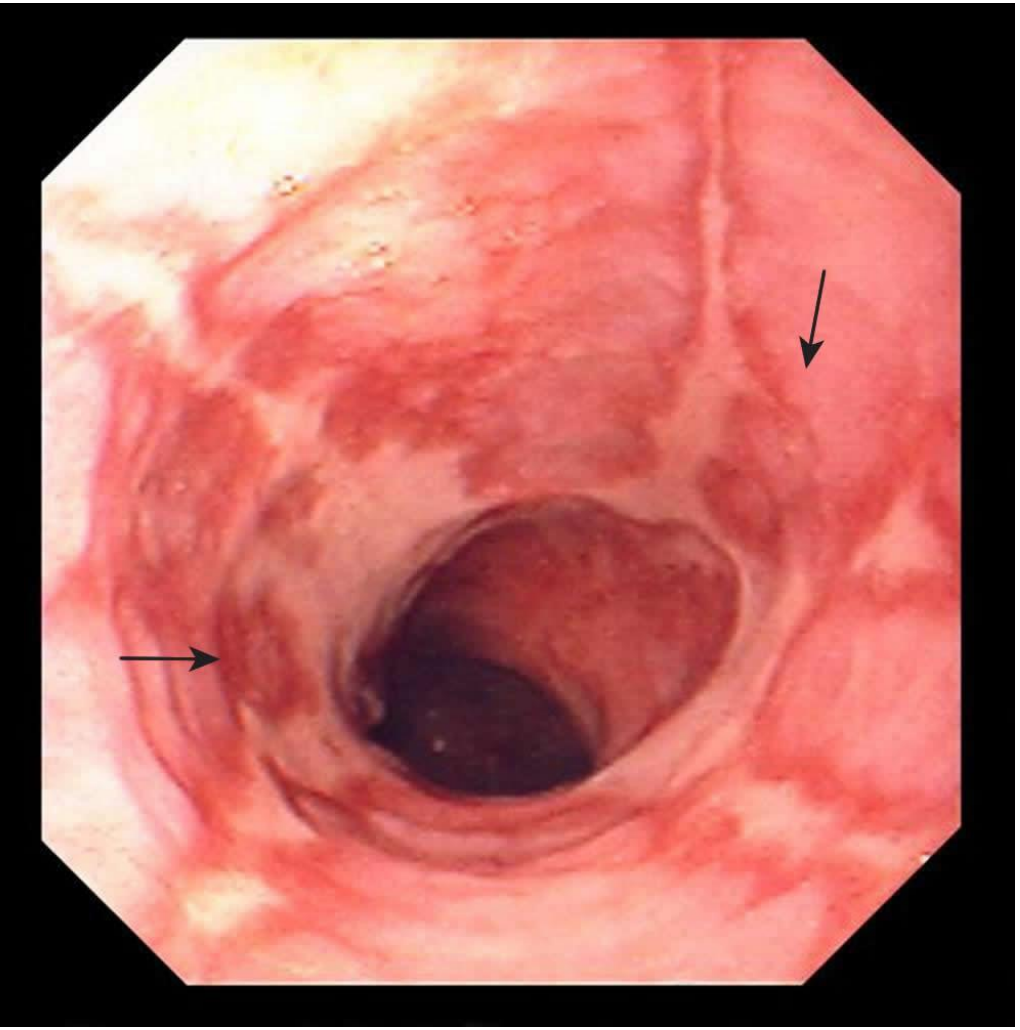


Scleroderma renal crisis (SRC)

- Several cohort studies showed benefit in survival with use of ***ACE inhibitors*** in patients with SRC. Experts recommend immediate use of ***ACE inhibitors*** in the treatment of SRC.
- ***Glucocorticoids*** are associated with a higher risk of SRC. BP and renal function should be carefully monitored in patients with SSc treated with ***glucocorticoids***.

Update of EULAR recommendations for the treatment of systemic sclerosis. Kowal-Bielecka O, et al. Ann Rheum Dis 2017;76:1327–1339.

Treatment of SSc, according to the organ involvement



Gastrointestinal disease

- ***PPI*** – for SSc-related GERD and prevention of oesophageal ulcers and strictures
- ***Prokinetic drugs*** – for SSc-related symptomatic motility disturbances (dysphagia, GERD, early satiety, bloating, pseudo-obstruction, etc).
- Intermittent or rotating ***antibiotics*** to treat symptomatic small intestine bacterial overgrowth in patients with SSc

Update of EULAR recommendations for the treatment of systemic sclerosis. Kowal-Bielecka O, et al. Ann Rheum Dis 2017;76:1327–1339.

THANK YOU FOR YOUR ATTENTION