INTERDISCIPLINARIETA' NELL'APPROCCIO DIAGNOSTICO-TERAPEUTICO DELLA SCLEROSI SISTEMICA

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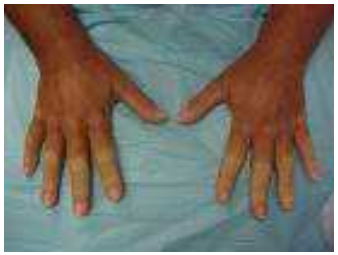
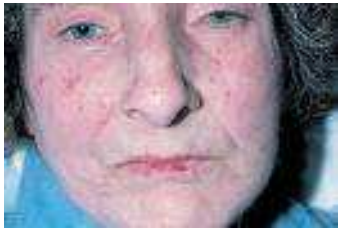
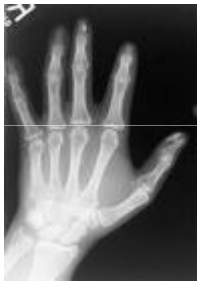
Systemic sclerosis (SSc)

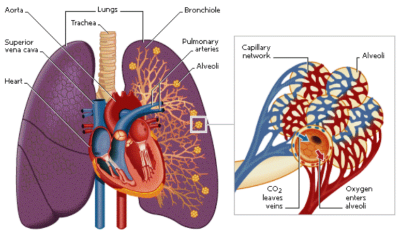
(Scleroderma, Scl; Progressive Systemic Sclerosis, SSp)

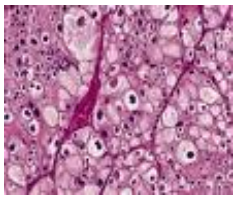


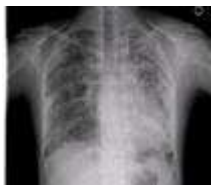


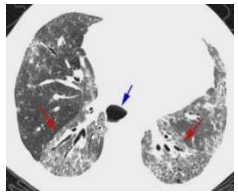


Systemic sclerosis is an acquired chronic connective tissue disease of unknown etiology characterized by immunity, vascular damage, and tissue fibrosis.

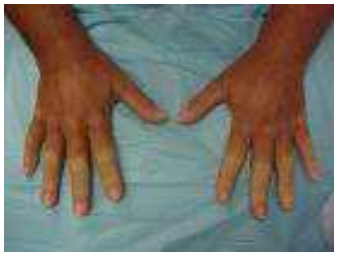


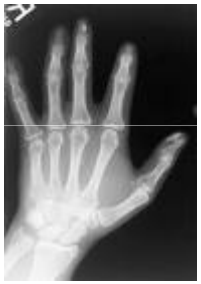


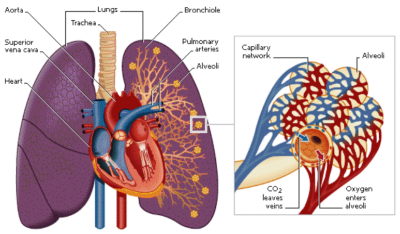




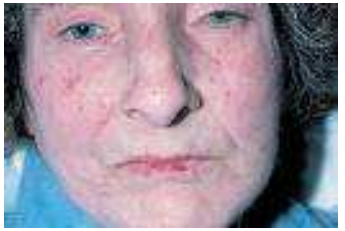
Systemic sclerosis (SSc)

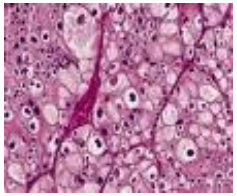


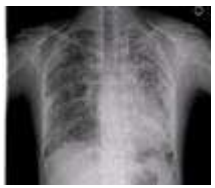


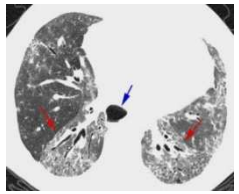


- Patients with SSc present a variety of symptoms and show considerable heterogeneity in clinical complications, autoantibody profiles, natural history, and prognosis.
- Raynaud phenomenon, skin thickening, esophageal problems, and pulmonary and cardiac fibrosis are common complications with no effective therapy.









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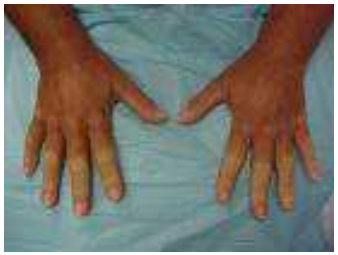
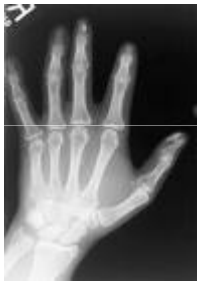
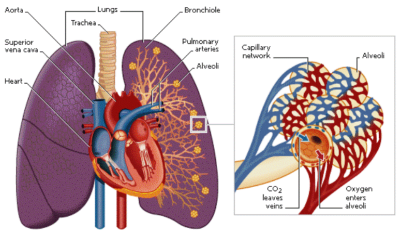
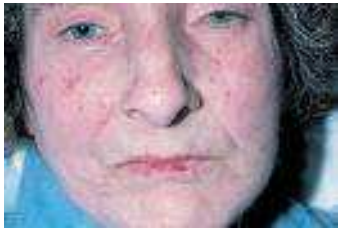
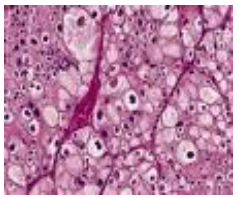


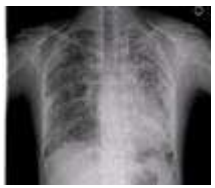


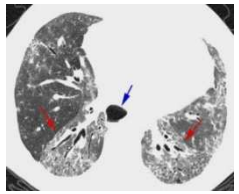


- Race, subtype, and antibody predict the course of the disease.
- Survival has improved in the past decade; the major cause of death is lung involvement.
- Scleroderma renal crisis and pulmonary hypertension are major complications that can be managed with current therapies.



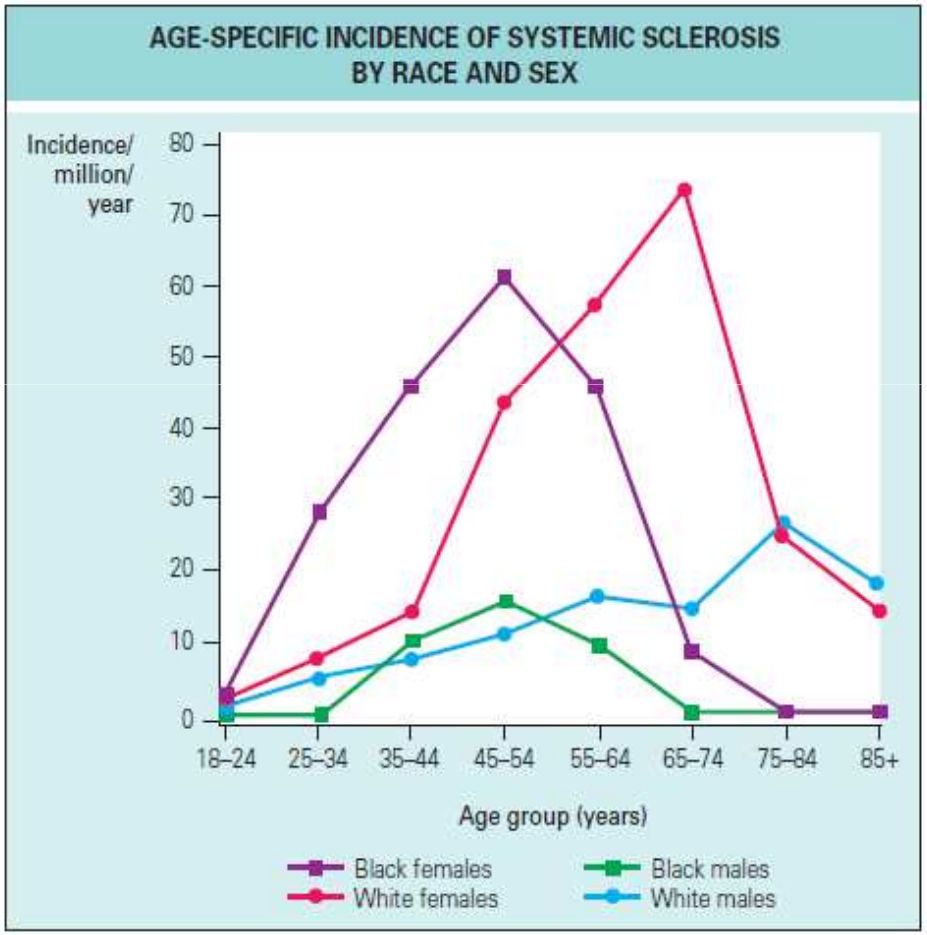






Systemic sclerosis (SSc)

- The incidence of SSc is reported at 20 cases per million population per year.
- More than 250 patients per million population are affected in the United States.



Prognosis

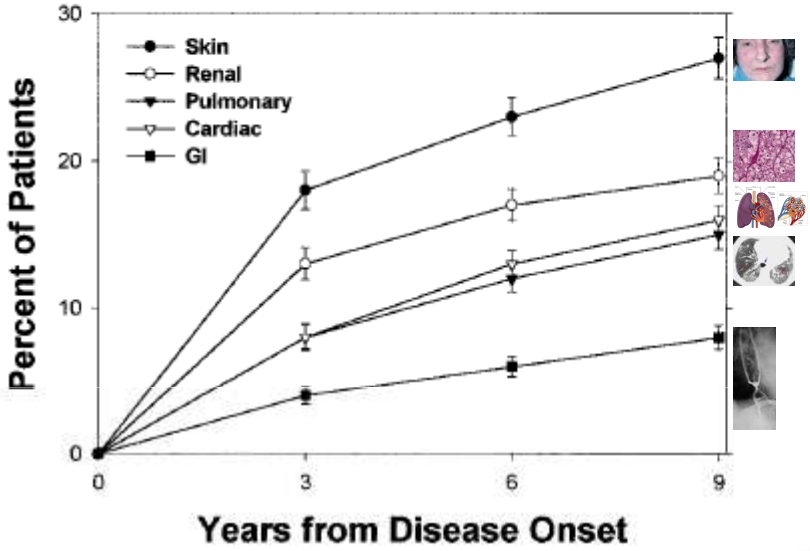


Figure 2. Cumulative frequency of severe organ system involvement in 953 patients with systemic sclerosis (SSc) and diffuse cutaneous involvement who developed severe organ system involvement during the time periods 0–3, 3–6, and 6–9 years after the onset of SSc. Values are the mean ± SEM. GI = gastrointestinal tract.

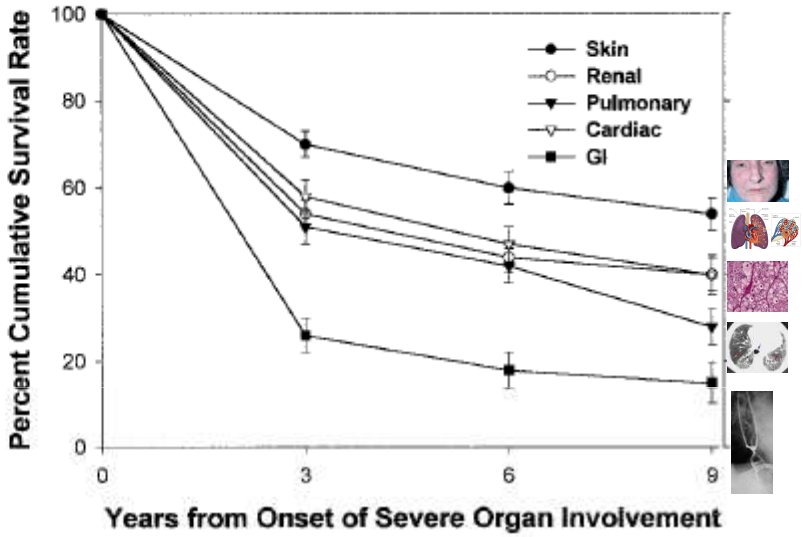


Figure 4. Cumulative survival rate, using the time of documentation of severe organ system involvement as the starting point, for patients with systemic sclerosis and diffuse cutaneous involvement who developed severe organ involvement during the time periods 0–3, 3–6, and 6–9 years. Values are the mean ± SEM. GI = gastrointestinal tract.

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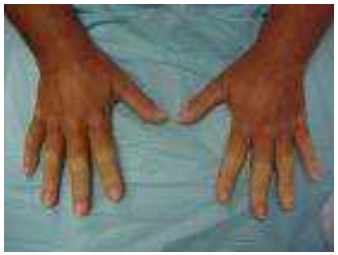
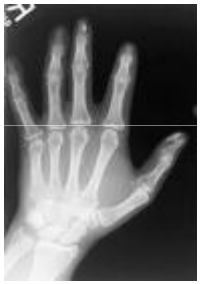
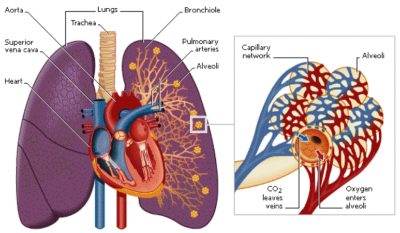
SEVERE ORGAN INVOLVEMENT IN SYSTEMIC SCLEROSIS WITH DIFFUSE SCLERODERMA

VIRGINIA D. STEEN and THOMAS A. MEDSGER, JR.

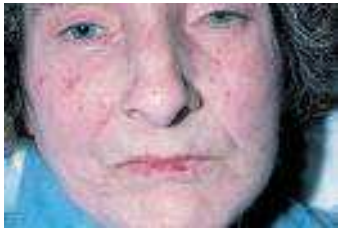
Systemic sclerosis (SSc)

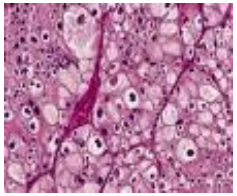


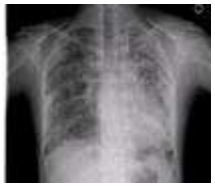


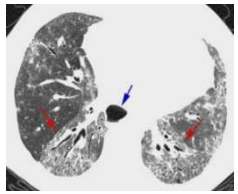


Systemic sclerosis is an acquired chronic connective tissue disease of unknown etiology characterized by **immunity**, **vascular damage**, and **tissue fibrosis**.









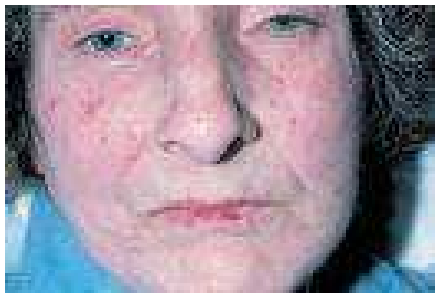
Etiology

Genetic Factors

Susceptibility

Clinical patterns

Enviromental Exposures, Drugs, Radiations



Chemicals
Silica
Heavy metals
Mercury
Organic chemicals
Vinyl chloride, Benzene, Toluene, Benzene, Trichloroethylene

Drugs
Bleomycin, Pentazocine, Taxol, Cocaine

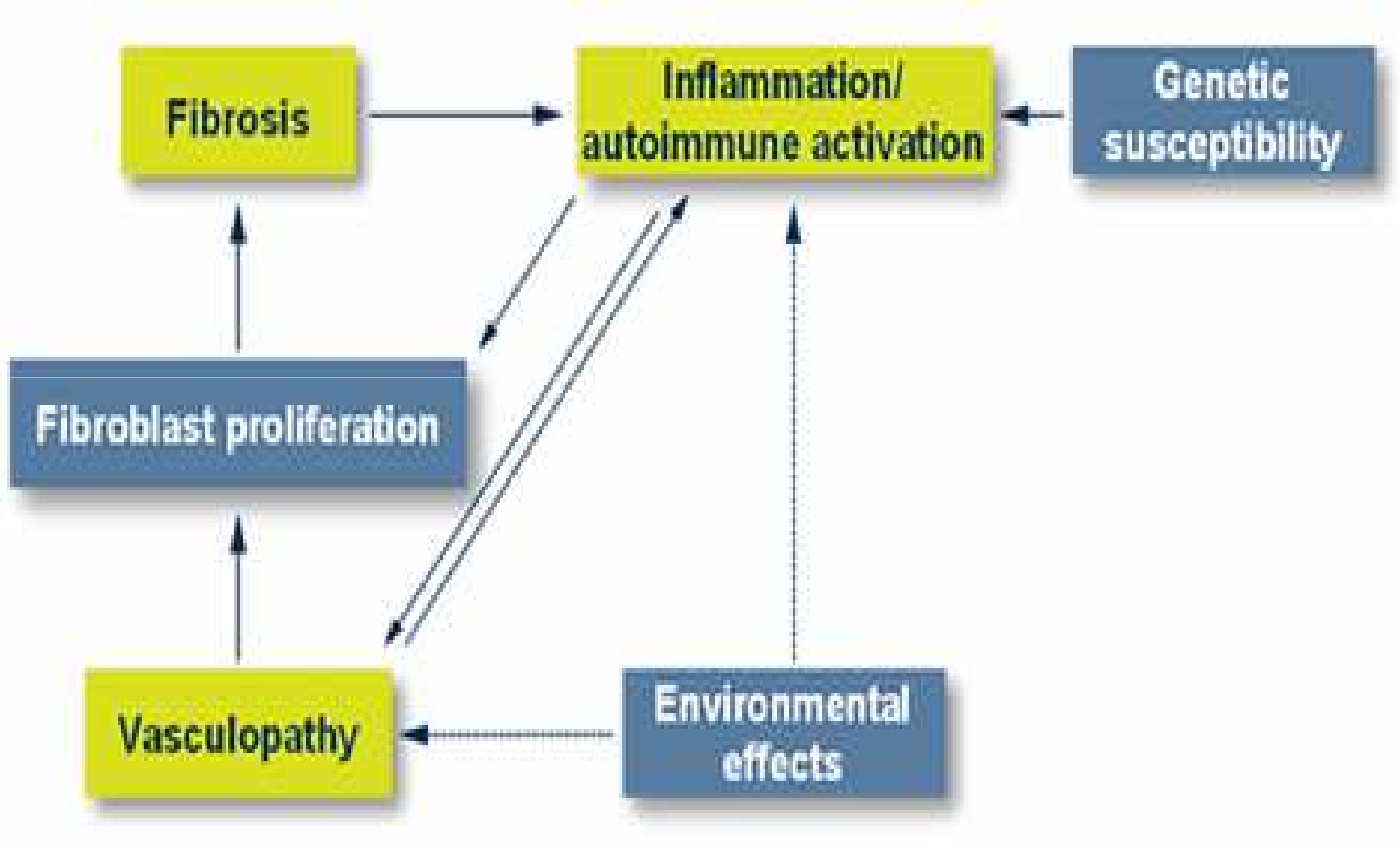
Dietary supplement/appetite suppressants
l-Tryptophan, Mazindol, Fenfluramine, Diethylpropion

Radiation Treatment

Infectious Agents

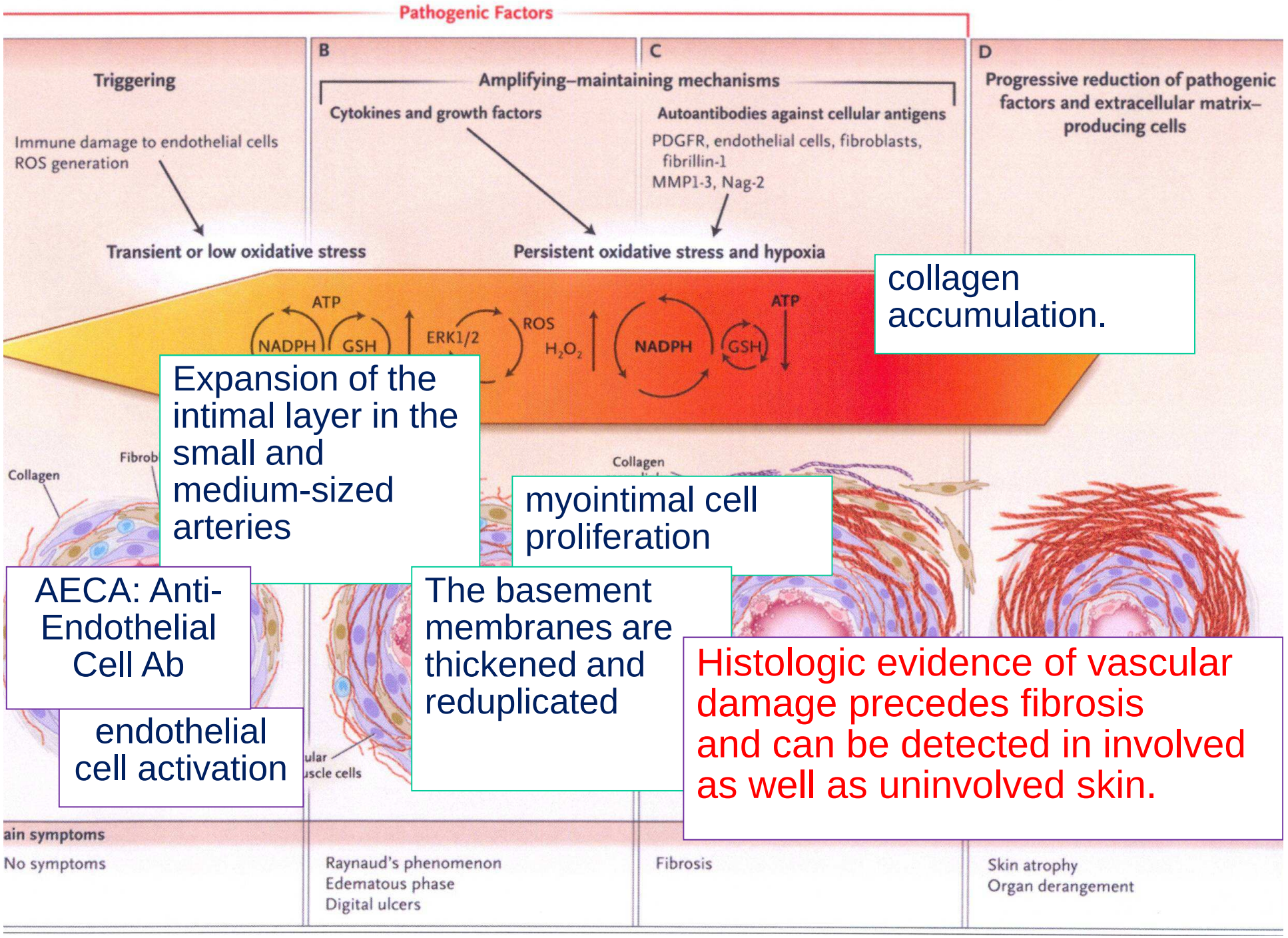
CMV?

Pathogenesis



The pathogenesis and cardinal features of SSc

[Adapted from Charles et al 2006]



collagen accumulation.

Expansion of the intimal layer in the small and medium-sized arteries

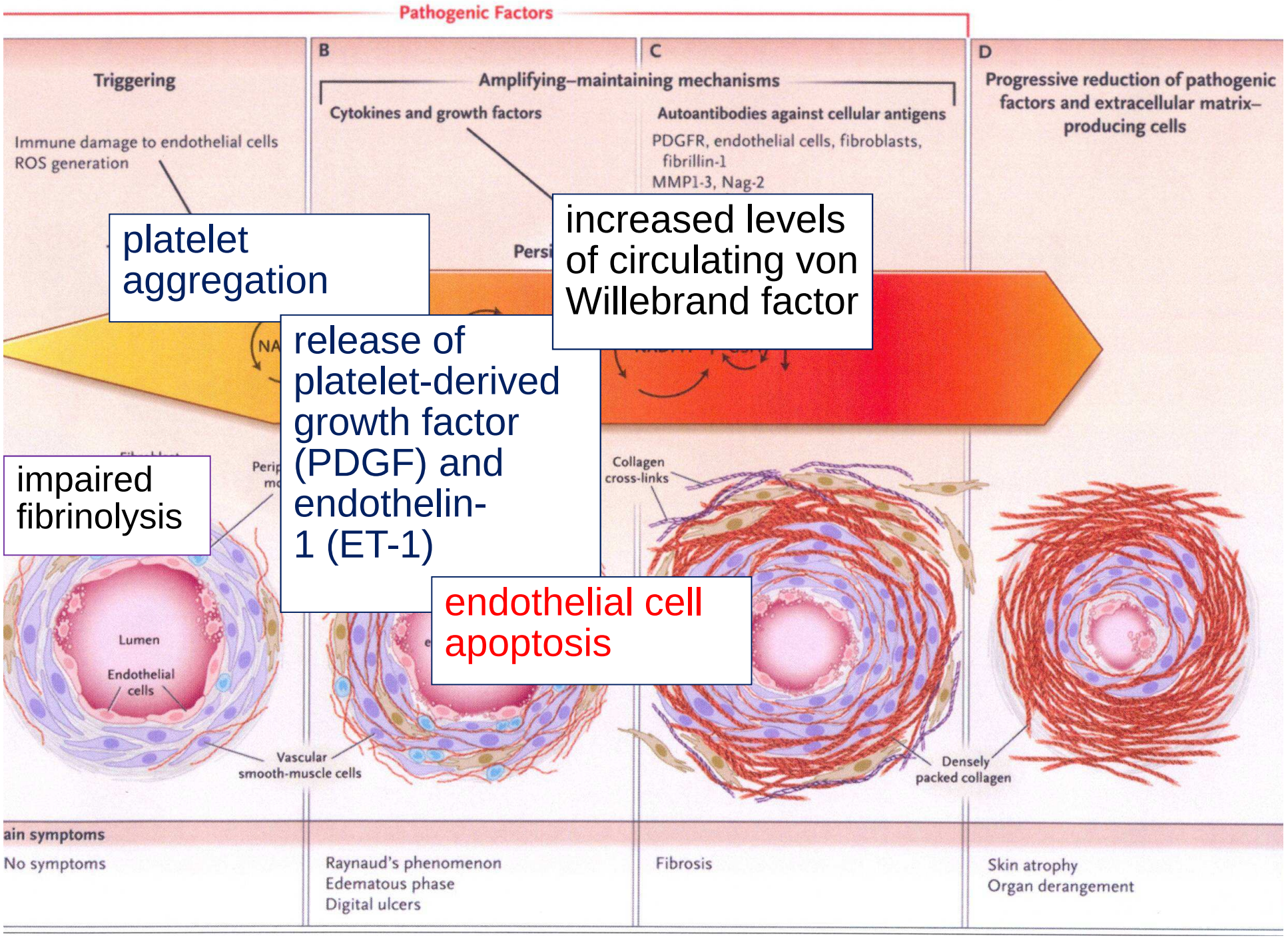
myointimal cell proliferation

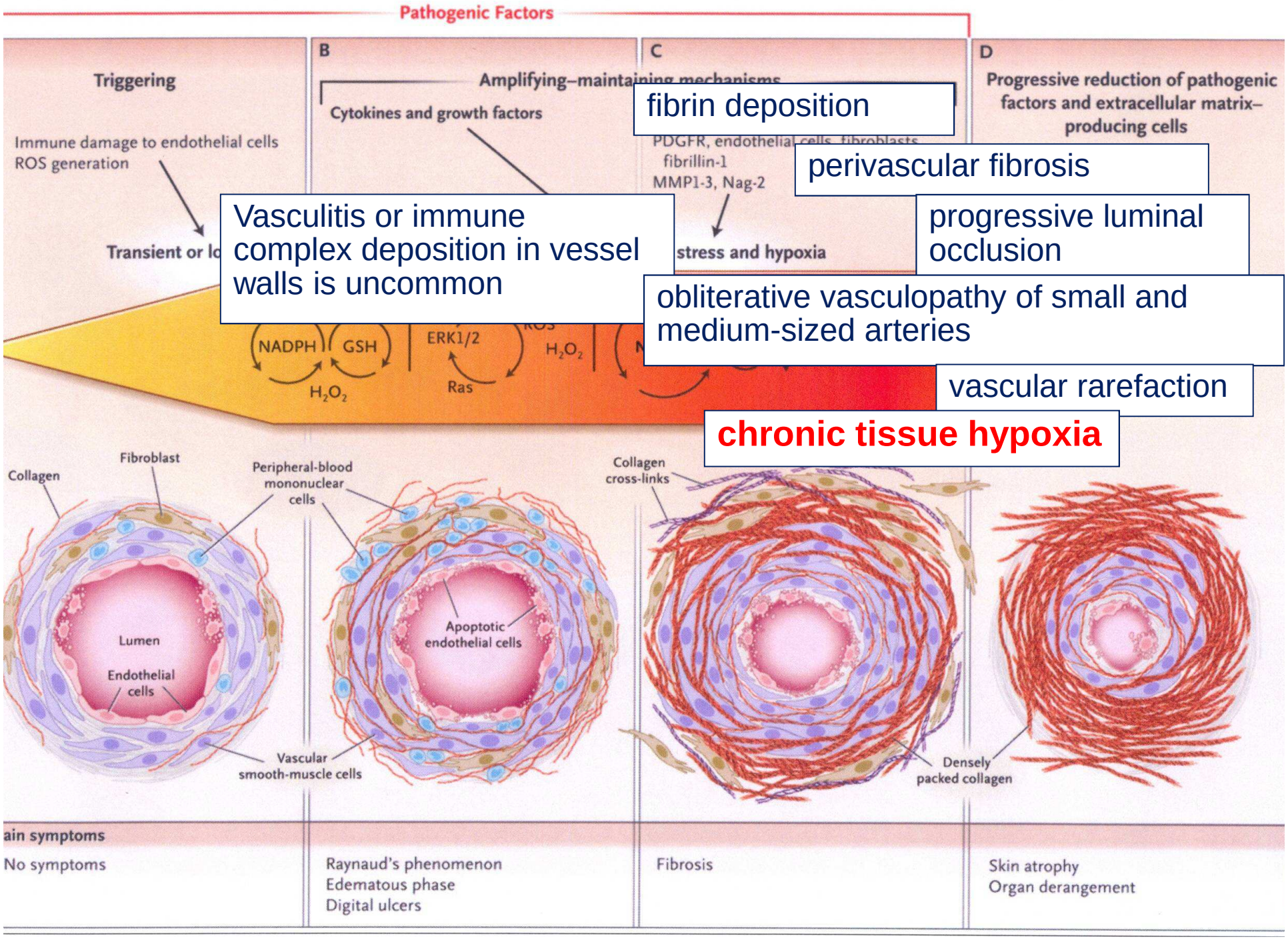
AECA: Anti-Endothelial Cell Ab

The basement membranes are thickened and reduplicated

endothelial cell activation

Histologic evidence of vascular damage precedes fibrosis and can be detected in involved as well as uninvolved skin.


Pathogenic Factors
Triggering
B
Amplifying–maintaining mechanisms
C
D
Progressive reduction of pathogenic factors and extracellular matrix–producing cells
Cytokines and growth factors
Autoantibodies against cellular antigens
Immune damage to endothelial cells
ROS generation
PDGFR, endothelial cells, fibroblasts, fibrillin-1
MMP1-3, Nag-2
platelet aggregation
increased levels of circulating von Willebrand factor
release of platelet-derived growth factor (PDGF) and endothelin-1 (ET-1)
impaired fibrinolysis
endothelial cell apoptosis
Collagen cross-links
Lumen
Endothelial cells
Vascular smooth-muscle cells
Densely packed collagen
ain symptoms
No symptoms
Raynaud's phenomenon
Edematous phase
Digital ulcers
Fibrosis
Skin atrophy
Organ derangement


Pathogenic Factors
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Progressive reduction of pathogenic factors and extracellular matrix–producing cells
Immune damage to endothelial cells
ROS generation
Cytokines and growth factors
PDGFR, endothelial cells, fibroblasts
fibrillin-1
MMP1-3, Nag-2
Transient or lo
stress and hypoxia
NADPH
GSH
ERK1/2
H_2O_2
Ras
fibrin deposition
perivascular fibrosis
Vasculitis or immune complex deposition in vessel walls is uncommon
progressive luminal occlusion
obliterative vasculopathy of small and medium-sized arteries
vascular rarefaction
chronic tissue hypoxia
Collagen
Fibroblast
Peripheral-blood mononuclear cells
Collagen cross-links
Lumen
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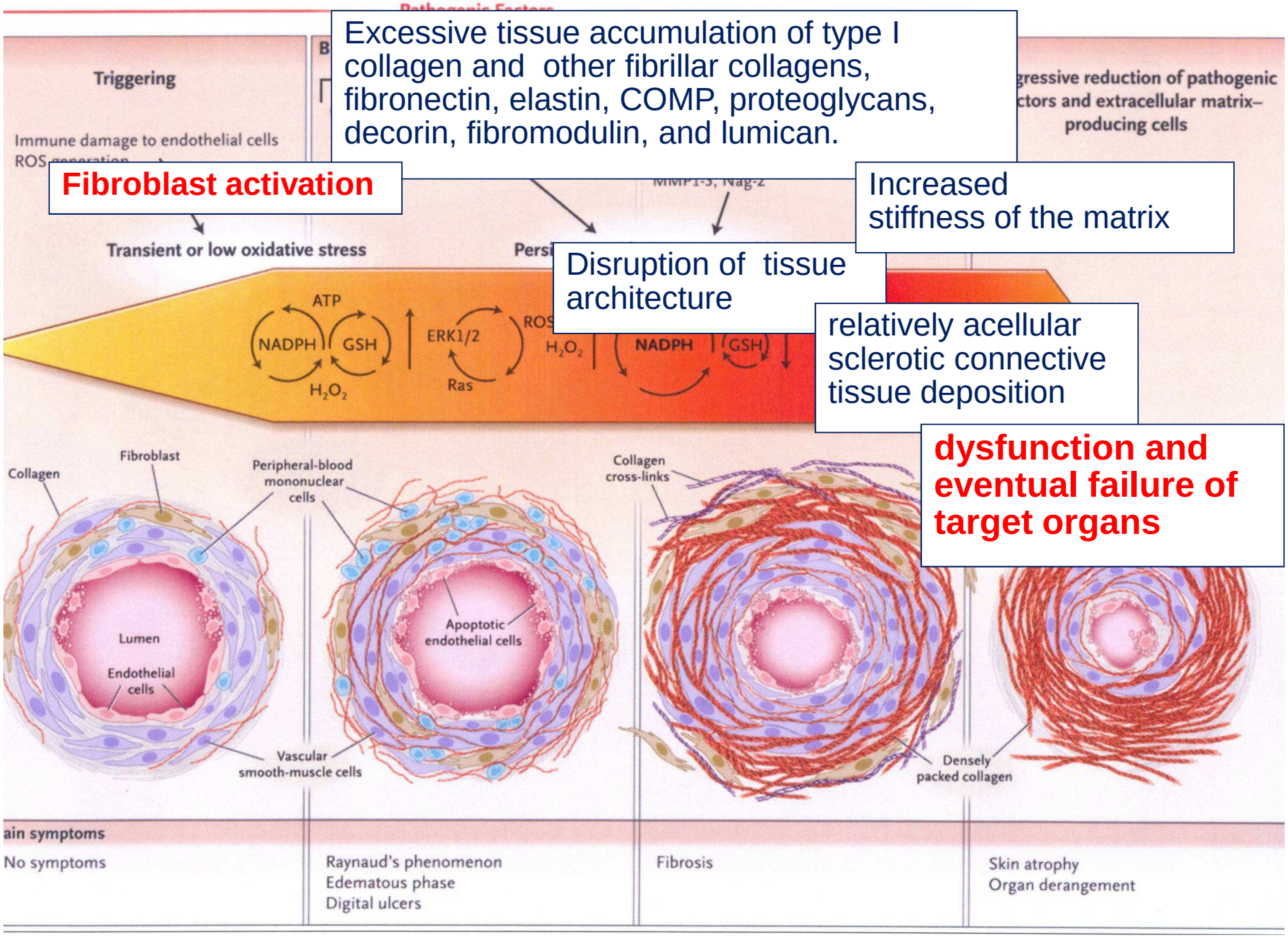
Excessive tissue accumulation of type I collagen and other fibrillar collagens, fibronectin, elastin, COMP, proteoglycans, decorin, fibromodulin, and lumican.
Fibroblast activation
Increased stiffness of the matrix
Disruption of tissue architecture
relatively acellular sclerotic connective tissue deposition
dysfunction and eventual failure of target organs
Triggering
Immune damage to endothelial cells
ROS generation
Transient or low oxidative stress
ATP
NADPH
GSH
H_2O_2
ERK1/2
Ras
ROS
H_2O_2
NADPH
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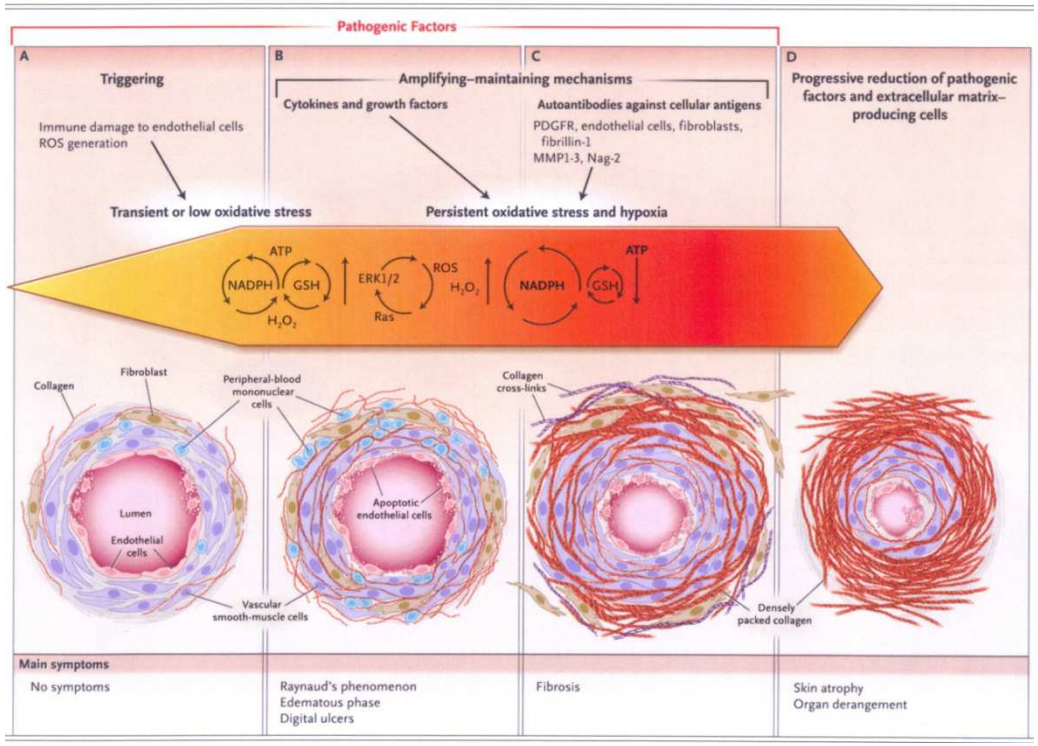
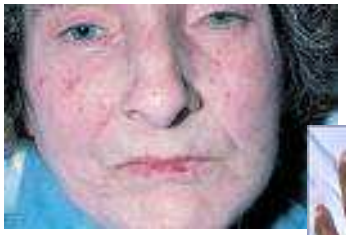
Densely packed collagen
No symptoms
Raynaud's phenomenon
Edematous phase
Digital ulcers
Fibrosis
Skin atrophy
Organ derangement

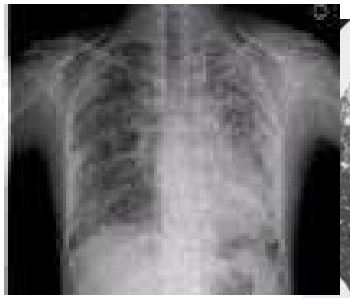
Vascular pathology

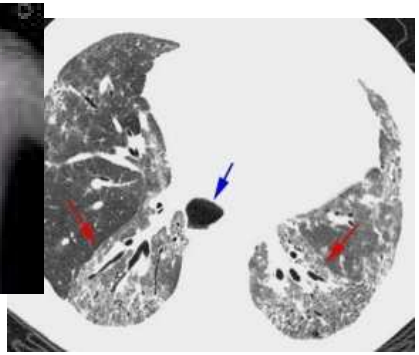


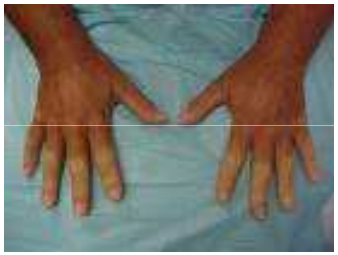
- Raynaud phenomenon
- Cutaneous telangiectasia
- Microscopic vascular changes at the nailfold,
- PAH
- Digital pit formation
- Gastric antral vascular ectasia
- Scleroderma renal crisis

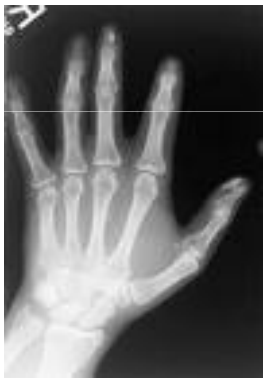
CLINICAL MANIFESTATIONS

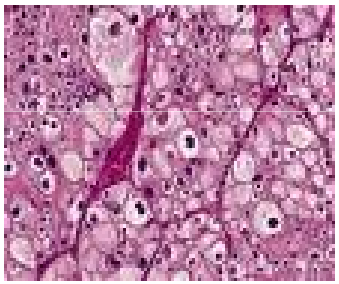


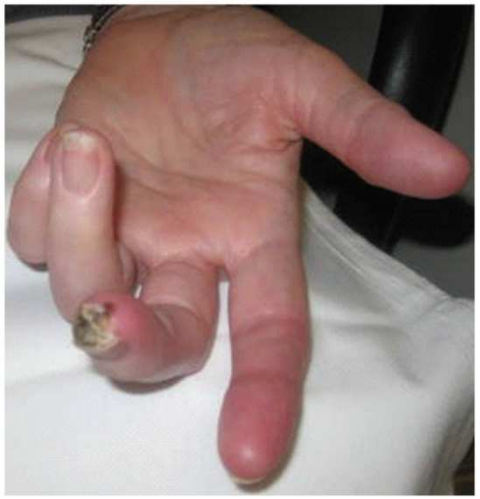


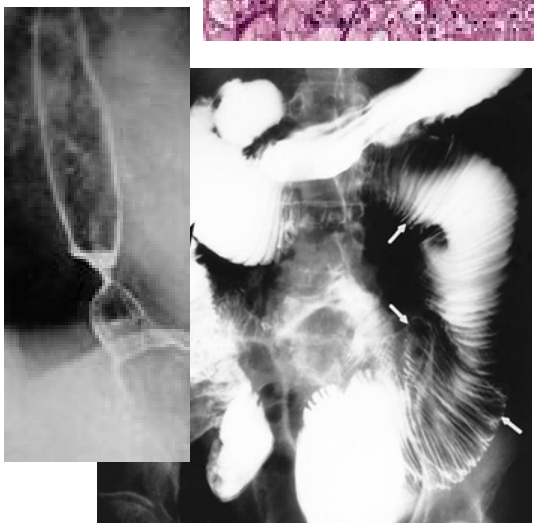


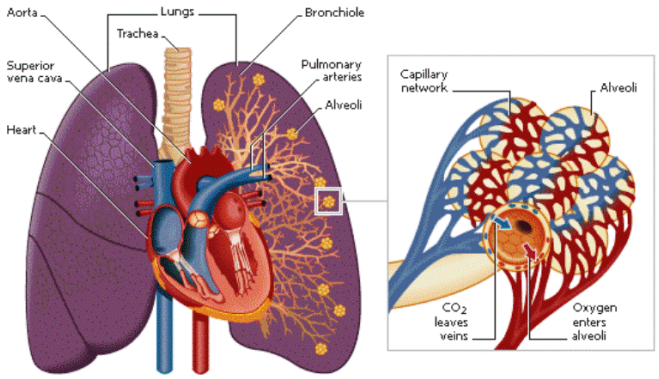






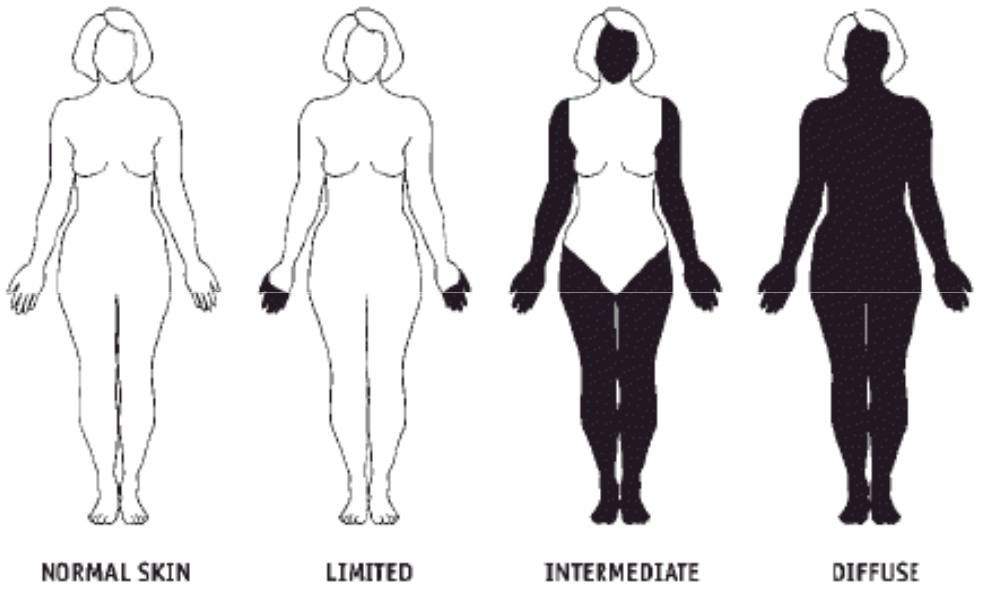






Clinical Subtypes

- Diffuse
- Limited
- Sine scleroderma
- Overlap
- UCTD- Undifferentiated Connective Tissue Disease

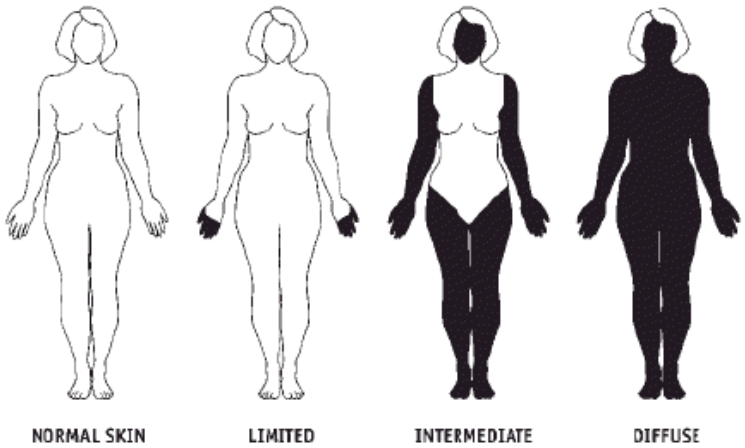


Diffuse

- TIME FROM RAYNAUD PHENOMENON TO OTHER MANIFESTATIONS
  < 1 YEAR
- DIFFUSE CUTANEOUS INVOLVEMENT
- TENDON FRICTION RUBS
- INTERNAL ORGAN INVOLVEMENT:

  EARLY AND OFTEN! (50% AT DIAGNOSIS)

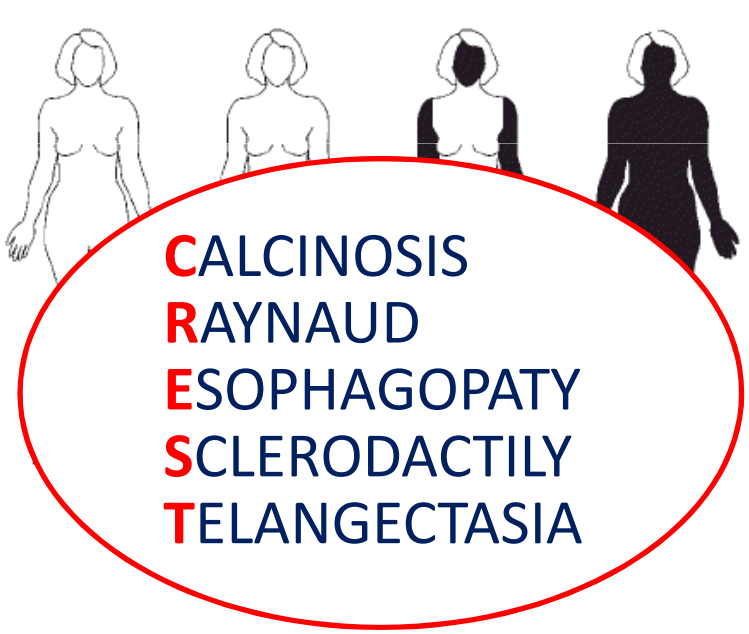
  - LUNG FIBROSIS
  - RENAL FAILURE
  - GI INVOLVEMENT
  - HEARTH INVOLVEMENT
- Ab SCL 70 positive (30%)



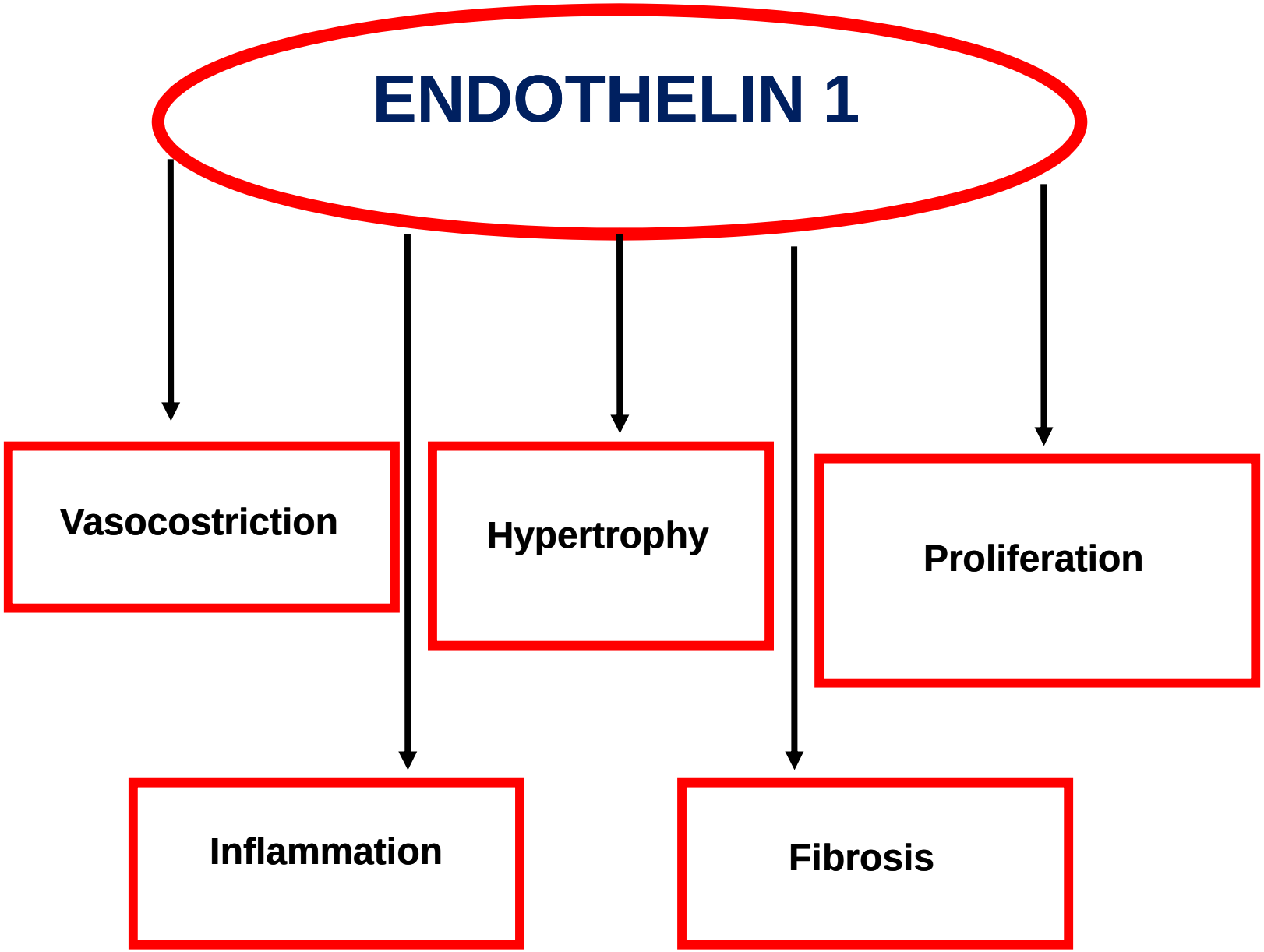
LeRoy EC et Al. Scleroderma. Classification, subset and Pathogenesis. J Rheumatol, 198815:202-205

Limited

- TIME FROM RAYNAUD PHENOMENON TO OTHER MANIFESTATIONS 10-15 years
- LIMITED CUTANEOUS INVOLVEMENT
  - CALCINOSIS
  - TELANGIECTASIA
  - DIGITAL ULCERS
- INTERNAL ORGAN INVOLVEMENT:
- GI INVOLVEMENT
- LUNG FIBROSIS (LATE)
- PAH (15%)
- PRIMITIVE BILIAR CIRRHOSIS
- Ab anti-Centromere (70-80%)



LeRoy EC et Al. Scleroderma. Classification, subset and Pathogenesis. J Rheumatol, 198815:202-205

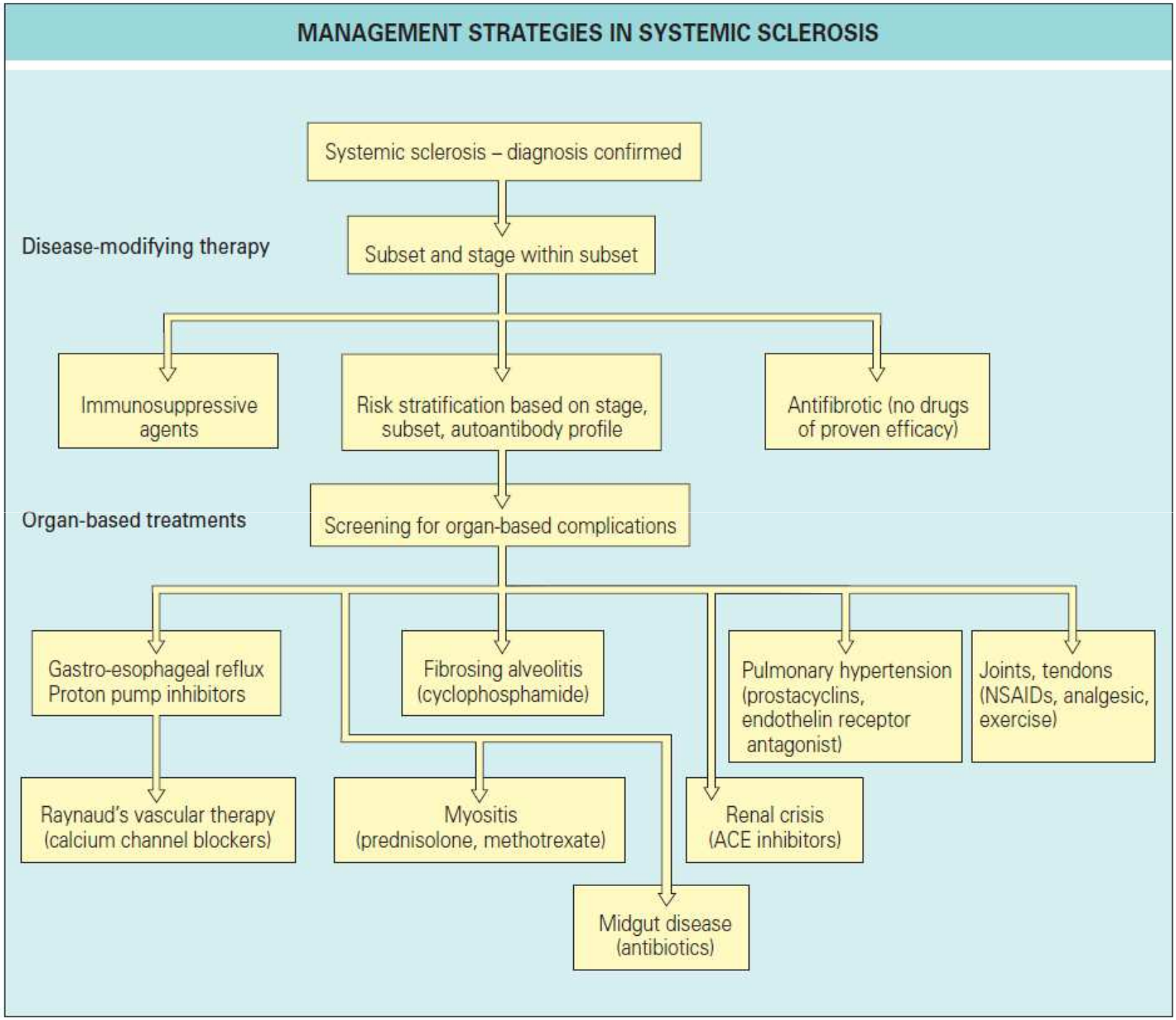

ENDOTHELIN 1
Vasocostriction
Hypertrophy
Proliferation
Inflammation
Fibrosis

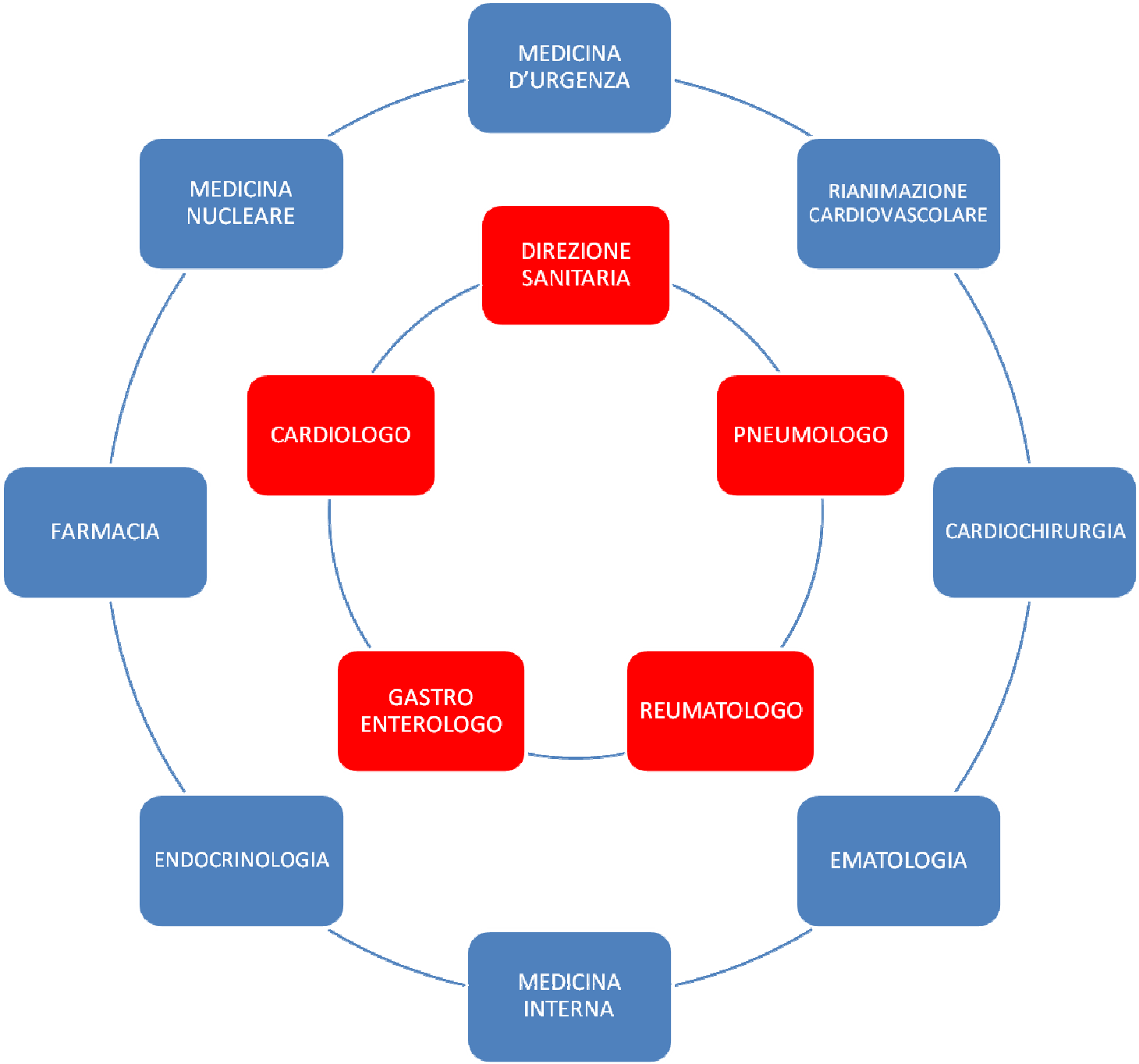
- Thrombin, epinephrine, TNF-α, TGF-β, angiotensin II, and hypoxia can all stimulate ET-1 release from endothelial cells.

- Increased plasma ET-1 levels have been associated with Raynaud phenomenon and SSc, particularly the diffuse cutaneous subset with associated PAH, pulmonary fibrosis, and scleroderma renal crisis.

- The critical role that ET-1 plays in the pathogenesis of SSc vascular disease is illustrated by the efficacy of the dual endothelin receptor antagonist bosentan in the prevention of ischemic digital ulcers and in improvement of symptoms of PAH.

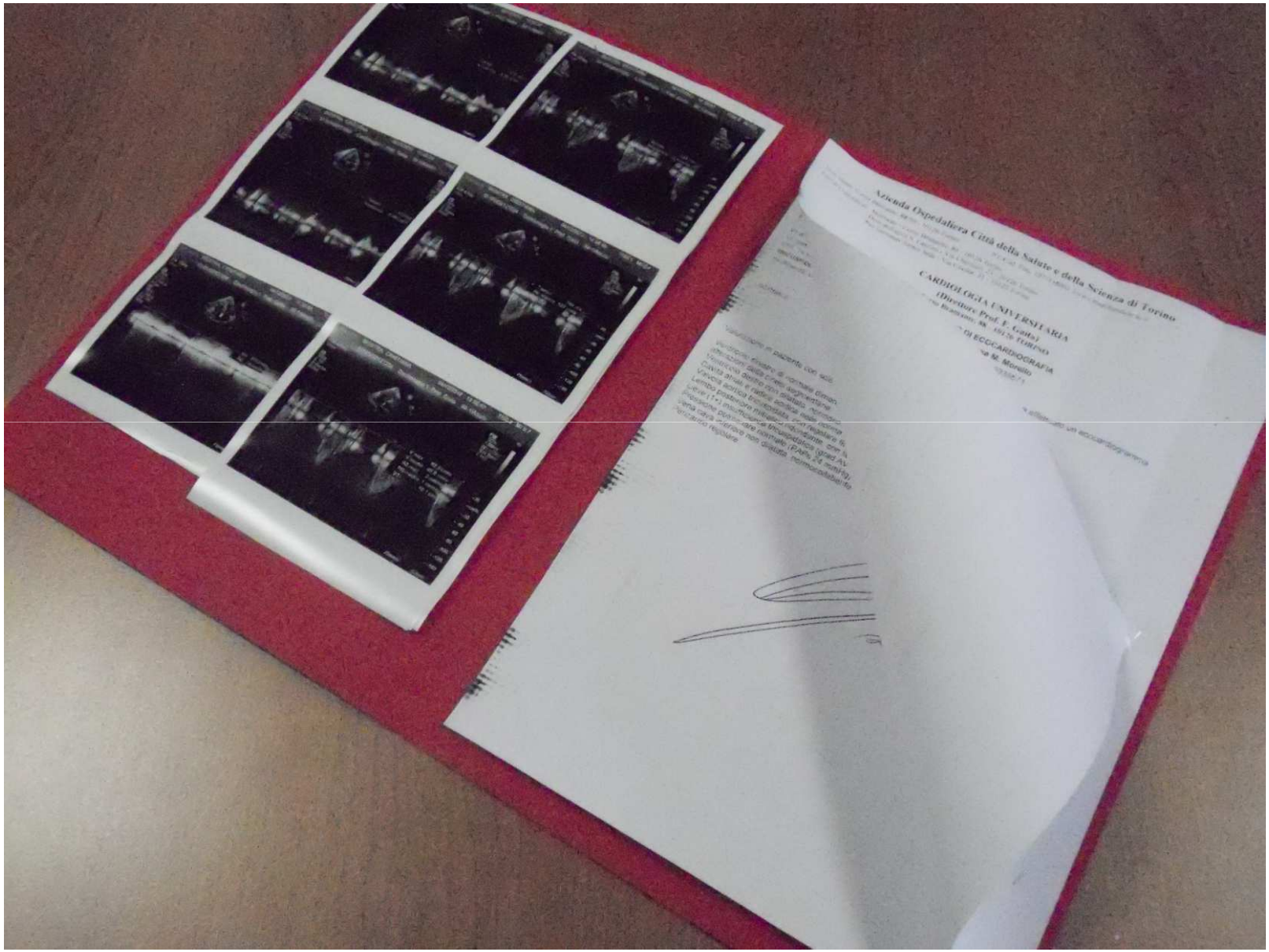
- ET-1 also enhances fibroblast proliferation and synthesis of types I and III collagens and decreases expression of collagenase (MMP-1).


MANAGEMENT STRATEGIES IN SYSTEMIC SCLEROSIS
Systemic sclerosis – diagnosis confirmed
Disease-modifying therapy
Subset and stage within subset
Immunosuppressive agents
Risk stratification based on stage, subset, autoantibody profile
Antifibrotic (no drugs of proven efficacy)
Organ-based treatments
Screening for organ-based complications
Gastro-esophageal reflux Proton pump inhibitors
Fibrosing alveolitis (cyclophosphamide)
Pulmonary hypertension (prostacyclins, endothelin receptor antagonist)
Joints, tendons (NSAIDs, analgesic, exercise)
Raynaud's vascular therapy (calcium channel blockers)
Myositis (prednisolone, methotrexate)
Renal crisis (ACE inhibitors)
Midgut disease (antibiotics)


MEDICINA D'URGENZA
RIANIMAZIONE CARDIOVASCOLARE
CARDIOCHIRURGIA
EMATOLOGIA
MEDICINA INTERNA
ENDOCRINOLOGIA
FARMACIA
MEDICINA NUCLEARE
DIREZIONE SANITARIA
CARDIOLOGO
PNEUMOLOGO
GASTRO ENTEROLOGO
REUMATOLOGO

GRUPPO IPERTENSIONE POLMONARE
AOU CITTA' DELLA SALUTE E DELLA SCIENZA DI TORINO

Cardiologia Universitaria	F.Gaita; W.Grosso Marra; P.Omedè' M. Capriolo; M.Cannillo; J.Perversi
Cardiologia Ospedaliera	S. Marra; L.Checco ; M.Giorgi ; PL. Sbarra
Reumatologia	E.Fusaro; CL.Peroni; R.De Giovanni; S.Parisi
Pneumologia	C.Bucca D.Libertucci L.Mercante
Gastroenterologia	A.Ottobrelli
Direzione Sanitaria Molinette	R.Arione; MC.Azzolina; N.Bosco
Med. Urgenza	C. Moiraghi: F.Bonino
Rianimazione Cardiovascolare	M.Lupo: D.Pasero
Cardiochirurgia	M.Rinaldi
SSCVD Centro malattie trombotiche ed emorragiche:	PC.Schinco; A.Borchiellini; E.Beggiato
Medicina Prof. Montrucchio:	L.Brussino
Endocrinologia	E. Ghigo; R.Rossetto
Farmacia Molinette	S.Stecca; D.Cestino; P.Crosasso
Medicina Nucleare:	G. Bisi; M.Baccega; R.Casoni


Azienda Ospedaliera Città della Salute e della Scienza di Torino
CARDIOLOGIA UNIVERSITARIA
(Direttore Prof. F. Gaita)
ECOCARDIOGRAFIA

2007-2008 **OPERAZIONE ECOCARDIOGRAMMA**

2008 PRIMO NUCLEO CARDIOLOGO-PNEUMOLOGO-GASTROENTEROLOGO-REUMATOLOGO-DIREZIONE SANITARIA

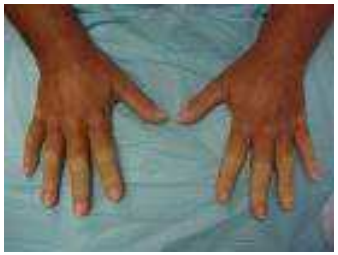
2008 CATETERISMO CARDIACO DESTRO CON TEST DI VASOREATTIVITA'

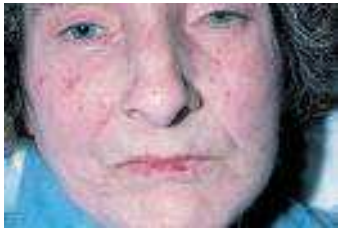
2009 VALUTAZIONI CLINICHE COLLEGIALI

2009 ESTENSIONE DEL GRUPPO DI LAVORO

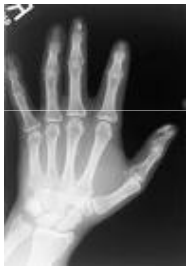
DEFINIZIONE DI PERCORSI CLINICO-ASSISTENZIALI, AMMINISTRATIVI E DI COMUNICAZIONE

Organ Involvement in Systemic sclerosis

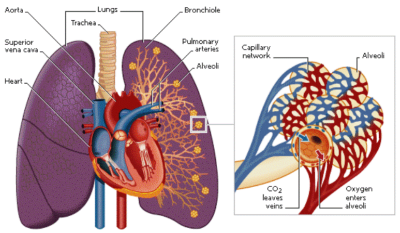


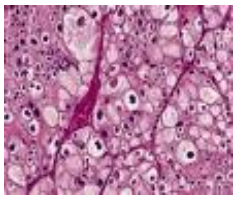


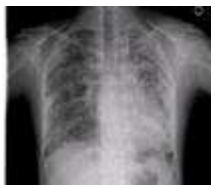
- Patients with SSc present a variety of symptoms and show considerable heterogeneity in clinical complications, autoantibody profiles, natural history, and prognosis.

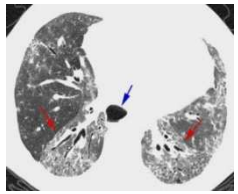


- Raynaud phenomenon, skin thickening, esophageal problems, and pulmonary and cardiac fibrosis are common complications with no effective therapy.



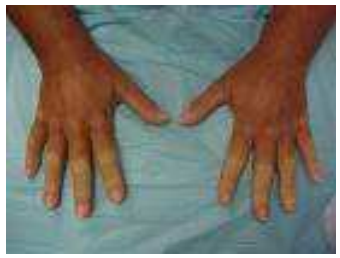






Organ Involvement in Systemic sclerosis

Raynaud phenomenon



- Present in greater than 95% of patients
- Raynaud phenomenon is cold-induced and, less commonly, stress-induced
- Three pathophysiologic mechanisms:

1) Neurogenic mechanisms (sympathetic nervous system; α 2A/D, α2C, β1, β2, and β3 receptors; release of nitric oxide NO)

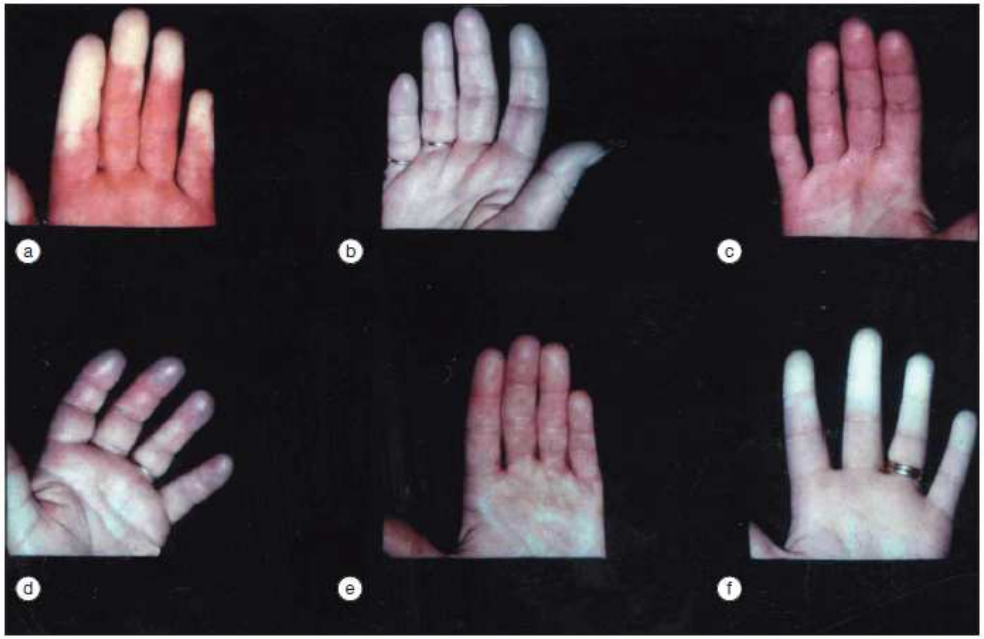
2) blood and blood vessel wall interactions

3) abnormalities of the inflammatory and immune responses.

Triphasic color changes:

1) Constriction of the digital vessels leads to pallor of the digits
2) Cyanosis secondary to deoxygenation of static venous blood
3) Reactive hyperemic stage with resulting erythema.

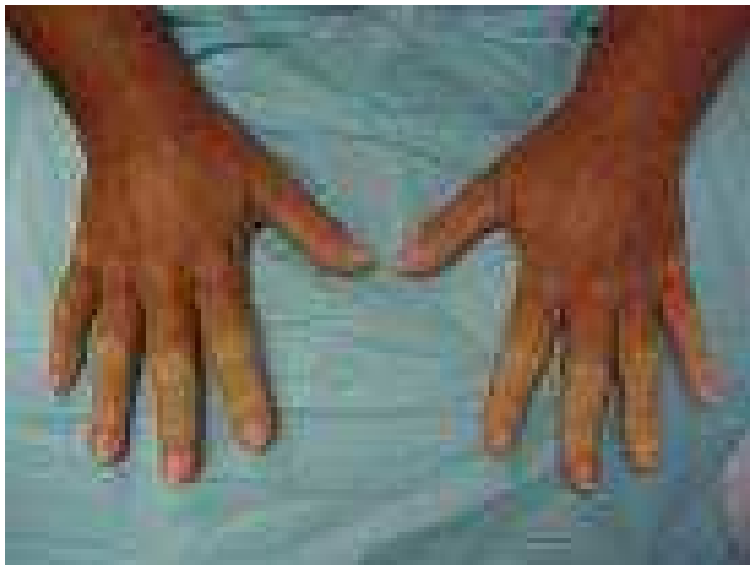
RP may involve digits, nose, tongue, ear lobes and nipples, as well as other organs.

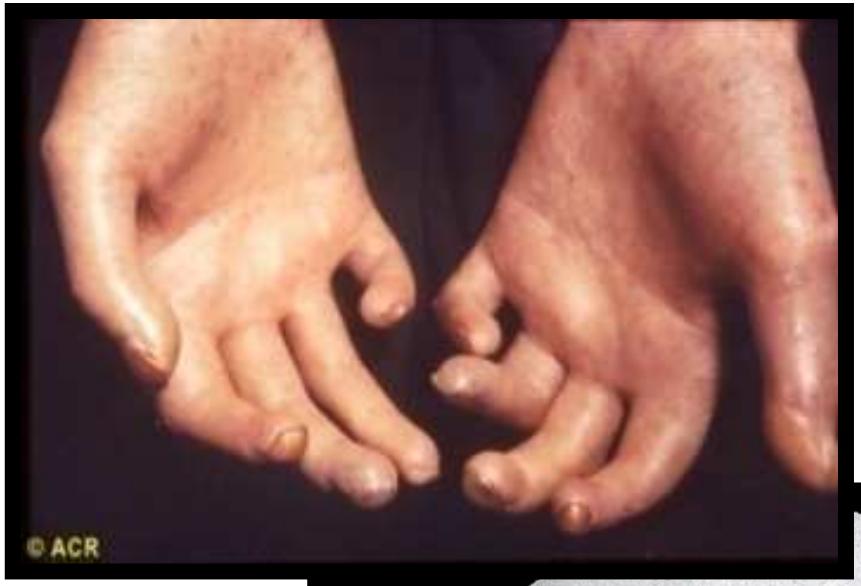


RAYNAUD PHENOMENON

Primary Raynaud's phenomenon is an exaggerated response to stimuli, with no known underlying cause

Secondary Raynaud's phenomenon is usually caused by diffuse connective tissue diseases, more rarely by haematological and occlusive arterial diseases and patients are more likely to develop tissue damage

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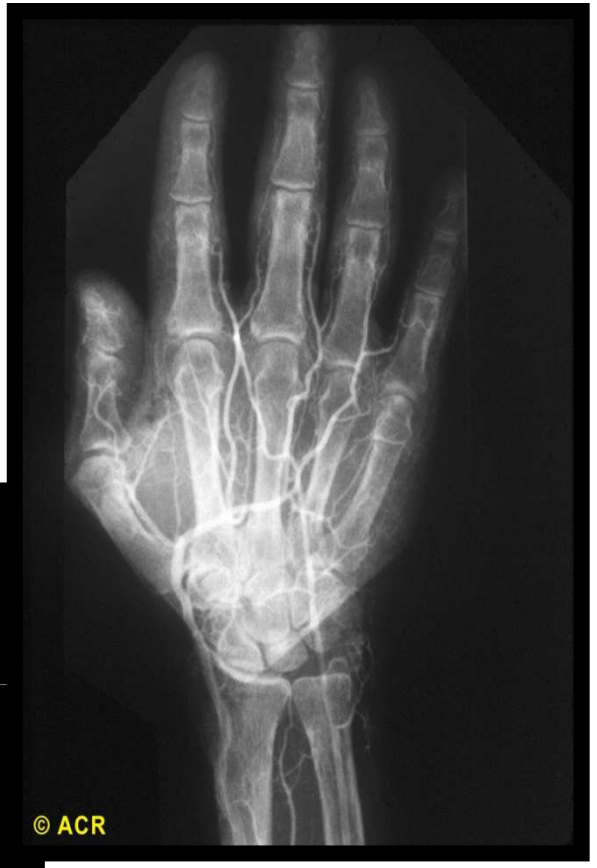
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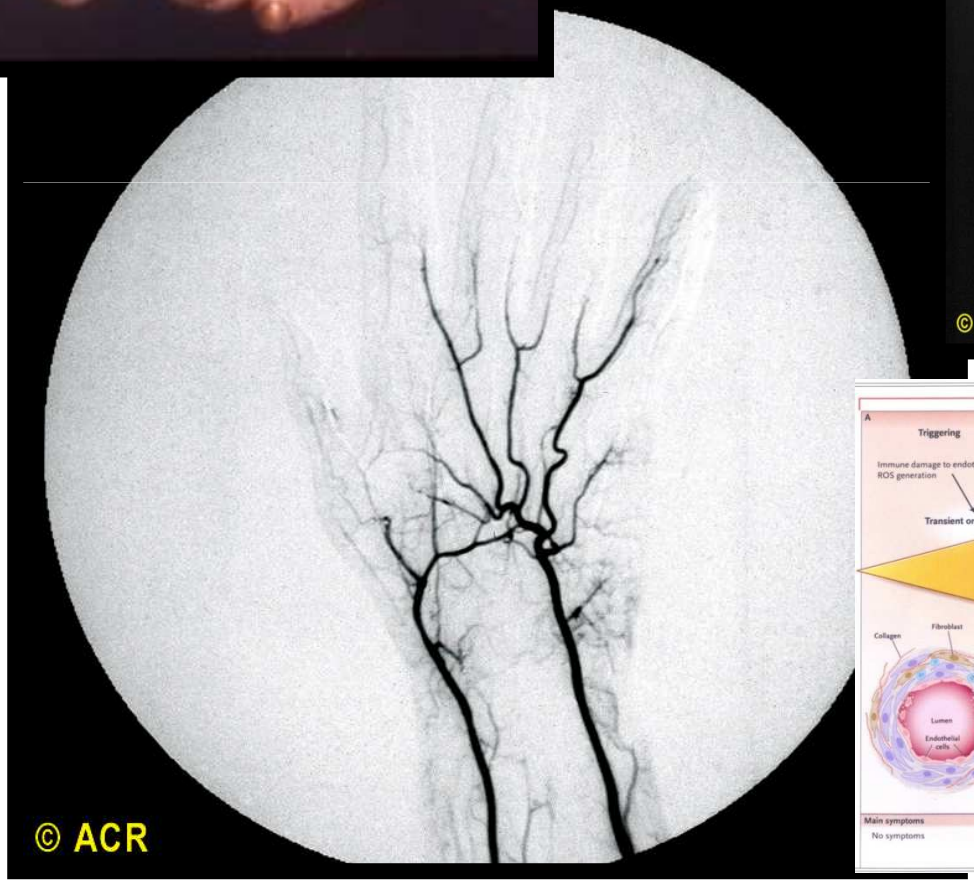
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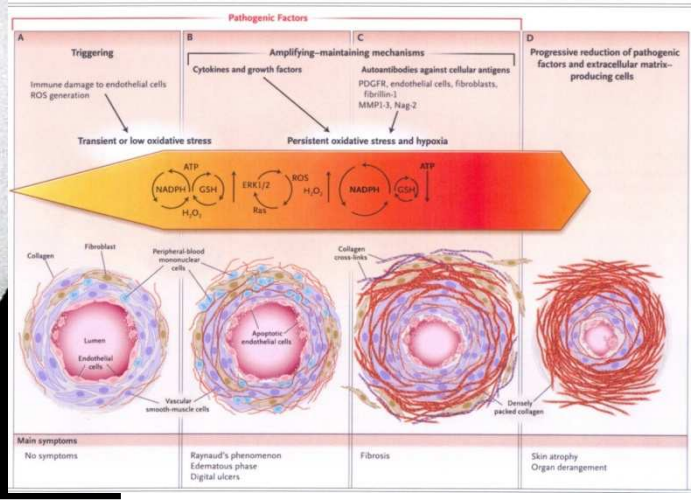
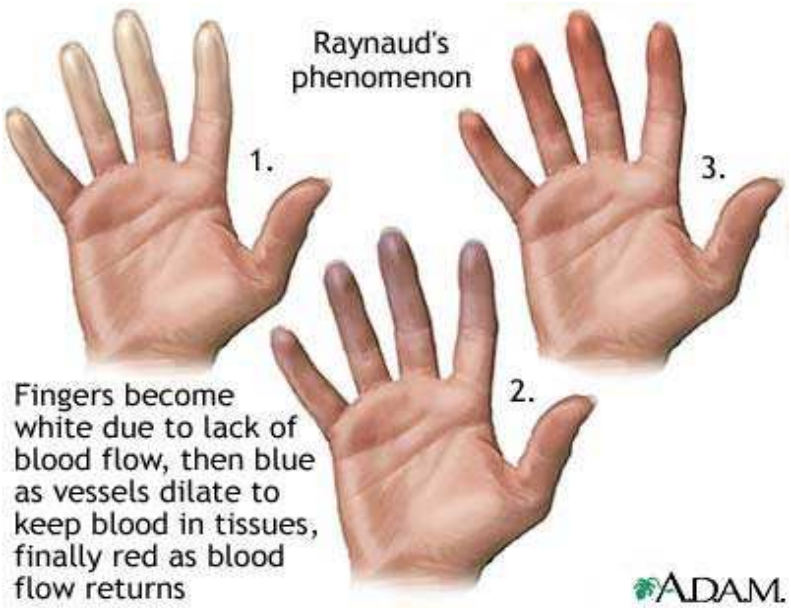

Pathogenic Factors
A
Triggering
Immune damage to endothelial cells
ROS generation
B
Amplifying–maintaining mechanisms
Cytokines and growth factors
C
Autoantibodies against cellular antigens
PDGFR, endothelial cells, fibroblasts, fibrillin-1
MMP1-3, Nag-2
D
Progressive reduction of pathogenic factors and extracellular matrix–producing cells
Transient or low oxidative stress
Persistent oxidative stress and hypoxia
ATP
NADPH
GSH
ERK1/2
ROS
H_2O_2
Ras
Collagen
Fibroblast
Peripheral-blood mononuclear cells
Collagen cross-links
Lumen
Endothelial cells
Apoptotic endothelial cells
Vascular smooth-muscle cells
Densely packed collagen
Main symptoms
No symptoms
Raynaud's phenomenon
Edematous phase
Digital ulcers
Fibrosis
Skin atrophy
Organ derangement

RAYNAUD PHENOMENON

- *DIAGNOSIS* -

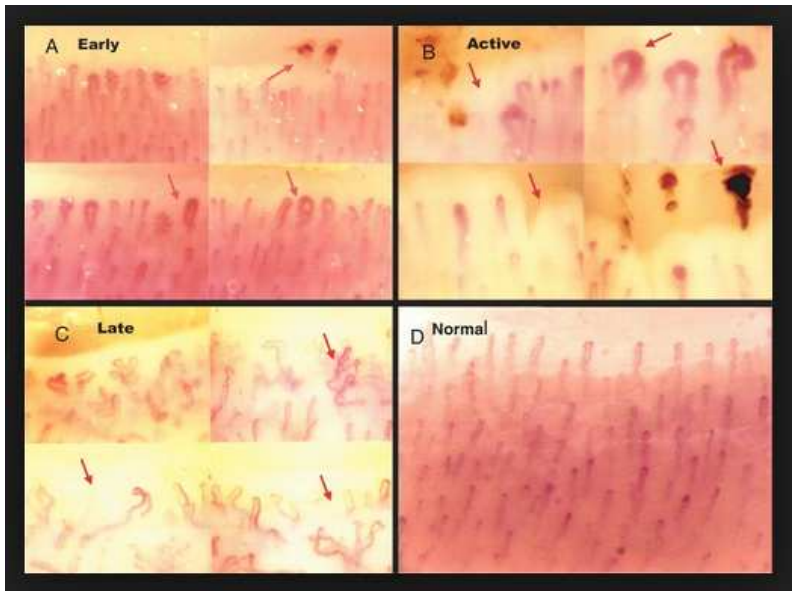
1. Clinical findings
2. Nailfold capillaroscopy



RAYNAUD PHENOMENON

-*DIAGNOSIS* -

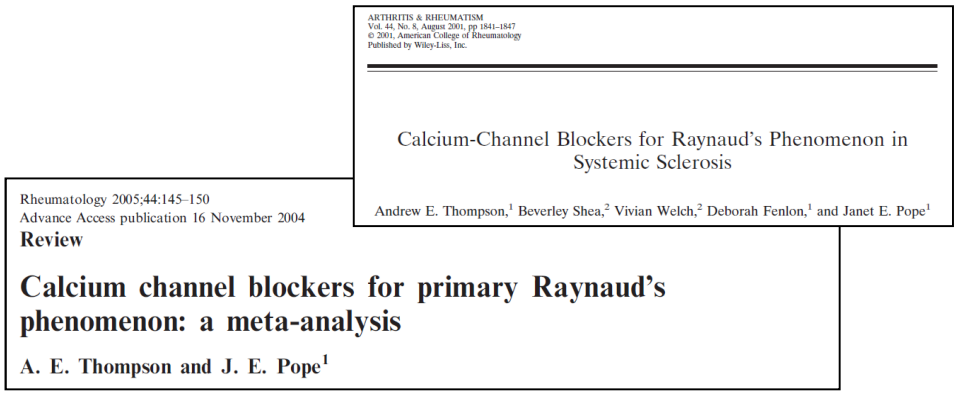
1. Clinical findings
2. nailfold capillaroscopy



Therapy

- Cold protecting
- Stopping smoking

- Nifedipine (or Amlodipine or Lercanidipine)
- Iloprost, Alprostidil
- Bosentan, Ambristentan
- Sindenafil, Tadalafil
- Transdermal glyceryl trinitrate
- Aminaftone
- Fluoxetine
- Surgery



ARTHRITIS & RHEUMATISM
Vol. 44, No. 8, August 2001, pp 1841–1847
© 2001, American College of Rheumatology
Published by Wiley-Liss, Inc.

Calcium-Channel Blockers for Raynaud's Phenomenon in Systemic Sclerosis

Andrew E. Thompson,[1] Beverley Shea,[2] Vivian Welch,[2] Deborah Fenlon,[1] and Janet E. Pope[1]

Rheumatology 2005;44:145–150
Advance Access publication 16 November 2004

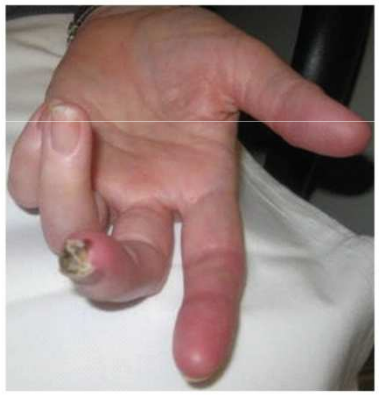
Review

Calcium channel blockers for primary Raynaud's phenomenon: a meta-analysis

A. E. Thompson and J. E. Pope[1]

ULCERE DIGITALI

LESIONI NECROTICHE CUTANEE
DELLE PARTI DISTALI DELLE DITA



RESPONSABILI DI:

- DOLORE
- DISABILITA’
- RICADUTE SOCIALI
- POSSIBILI INFEZIONI
- PERDITA DI TESSUTO - AMPUTAZIONI

ULCERE DIGITALI

CIRCA IL 75% DEI PAZIENTI CON SSc PRESENTANO ULCERE ENTRO 5 ANNI DAL PRIMO SINTOMO NON-RAYNAUD

TENDENZA ALLA RECIDIVA:

- 66% DEI PAZIENTI HANNO PIU' DI UN EPISODIO
- 50% DEI PAZIENTI NE HANNO 2 (NONOSTANTE I VASODILATATORI)

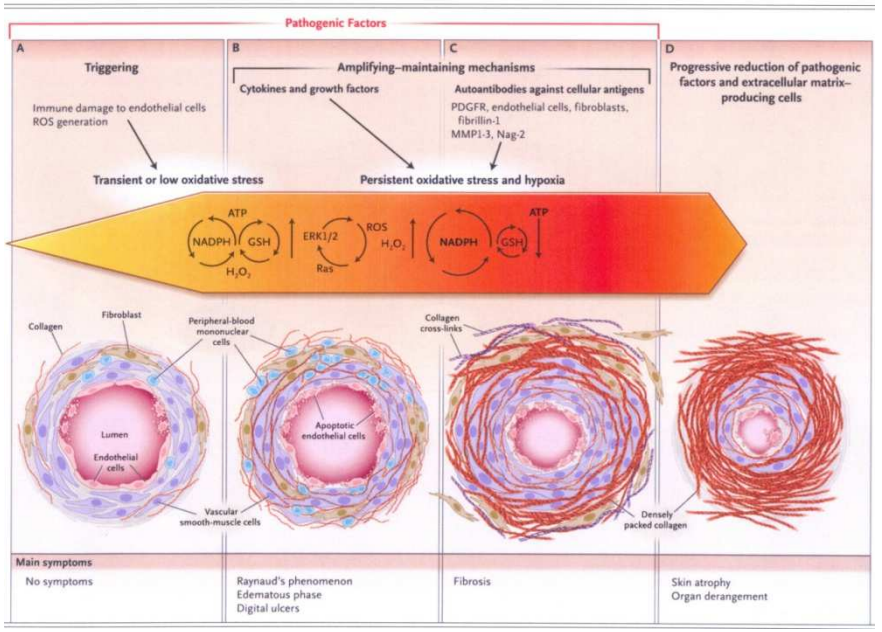
IL 7% SUBISCE UN'AMPUTAZIONE

[14] E. Hachulla, P. Clerson, D. Launay et al., "Natural history of ischemic digital ulcers in systemic sclerosis: single-center retrospective longitudinal study," *The Journal of Rheumatology*, vol. 34, no. 12, pp. 2423–2430, 2007.

ULCERE DIGITALI

ESPRESSIONE DI:

- DANNO STRUTTURALE (PROLIFERAZIONE INTIMALE)
- DANNO FUNZIONALE (> PRODUZIONE DI AGENTI VASOCOSTRITTORI)
- TROMBOSI ENDOLUMINALE



ULCERE DIGITALI

EZIOLOGIA MULTIFATTORIALE

ISCHEMICA
MECCANICA
INFIAMMATORIA

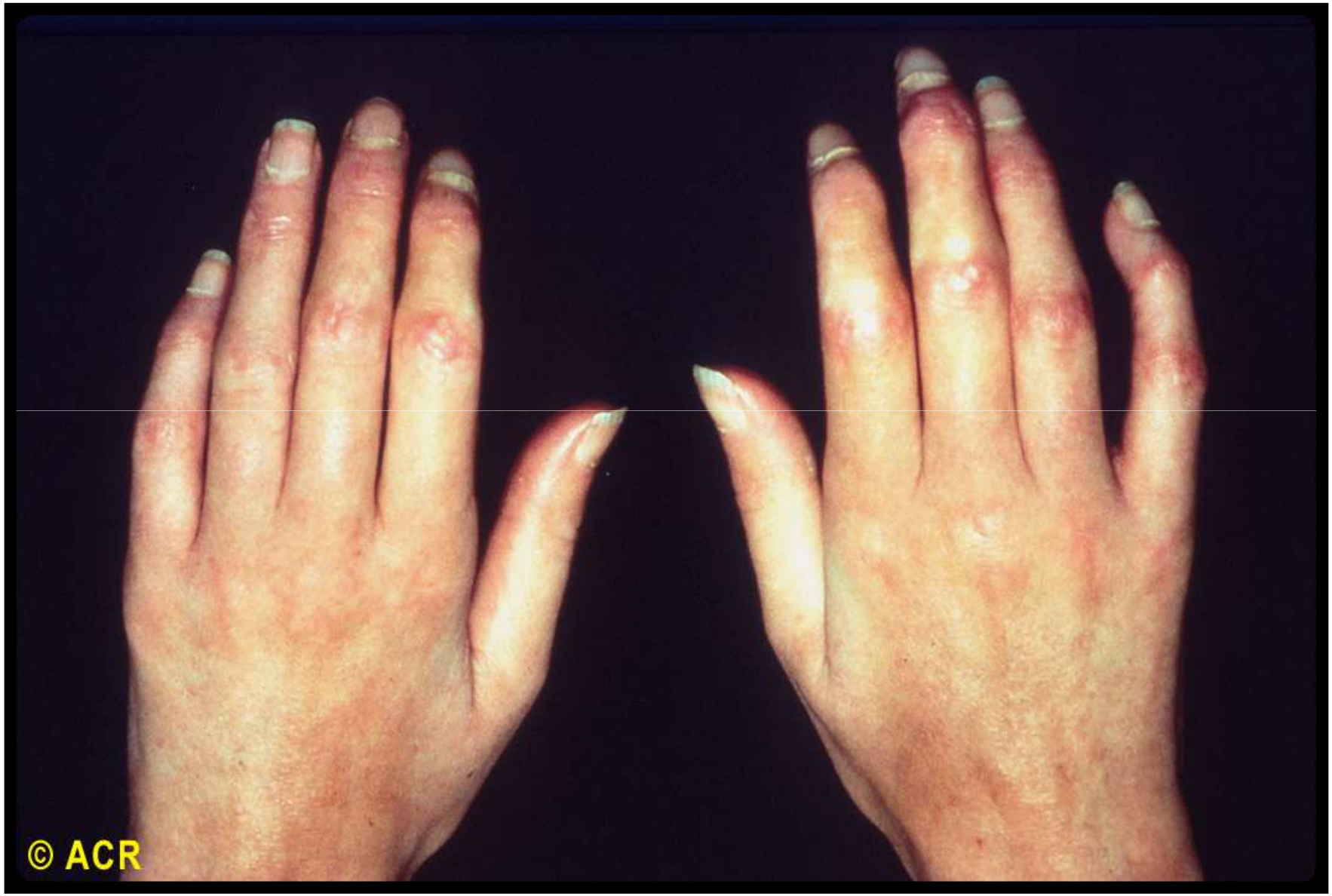
TRE TIPI DI LESIONE

ULCERA ACRALE
SUP. ESTENSORIE
CALCINOSI

ULCERE DIGITALI

FATTORI DI RISCHIO:

- SESSO MASCHILE
- PRESENZA DI IPERTENSIONE ARTERIOSA POLMONARE O RIDUZIONE DELLA DLCO
- FORMA DIFFUSA
- ESORDIO PRECOCE DELLA SSc
- PRESENZA DI Ac anti TOPOISOMERASI I
- FUMO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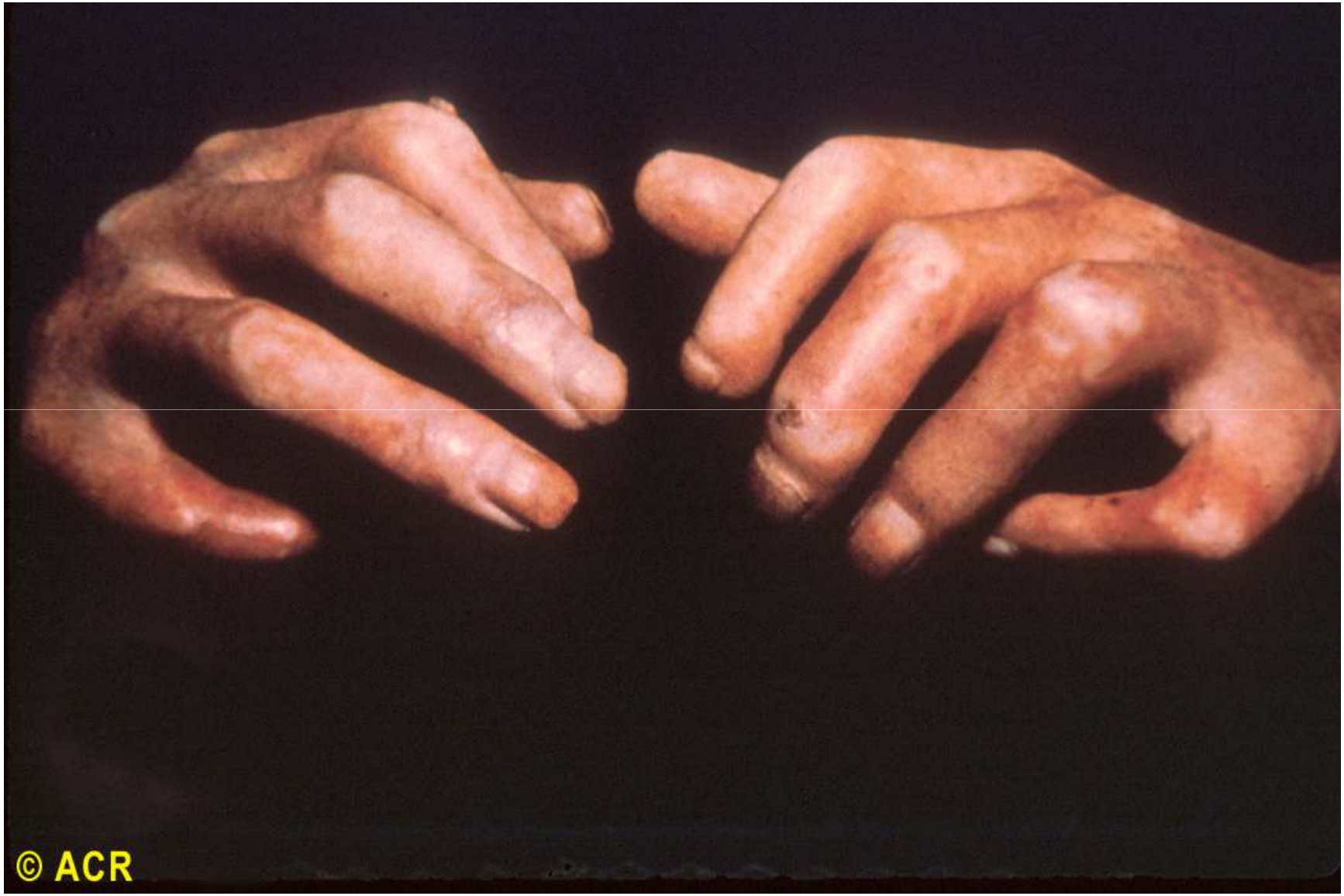
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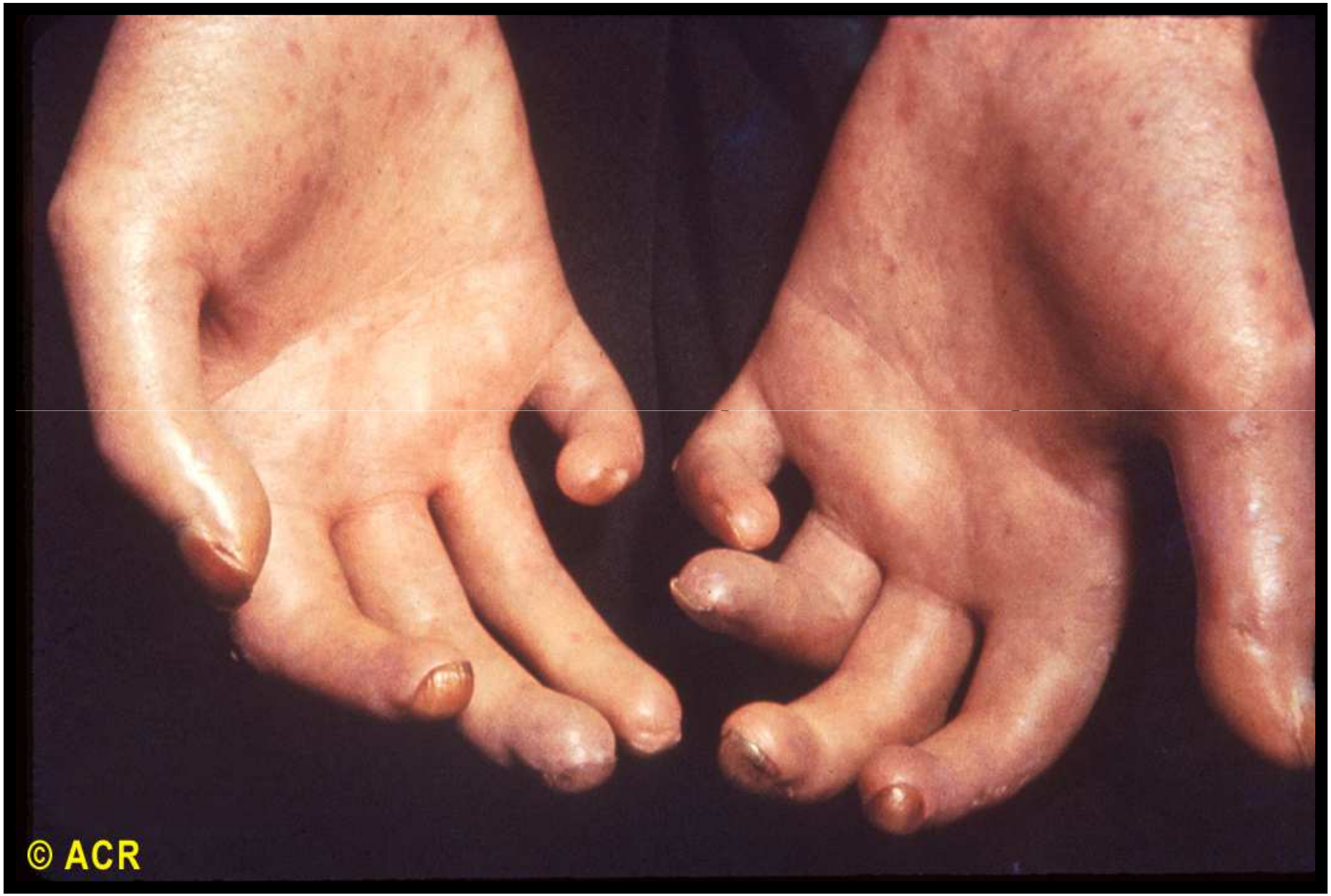
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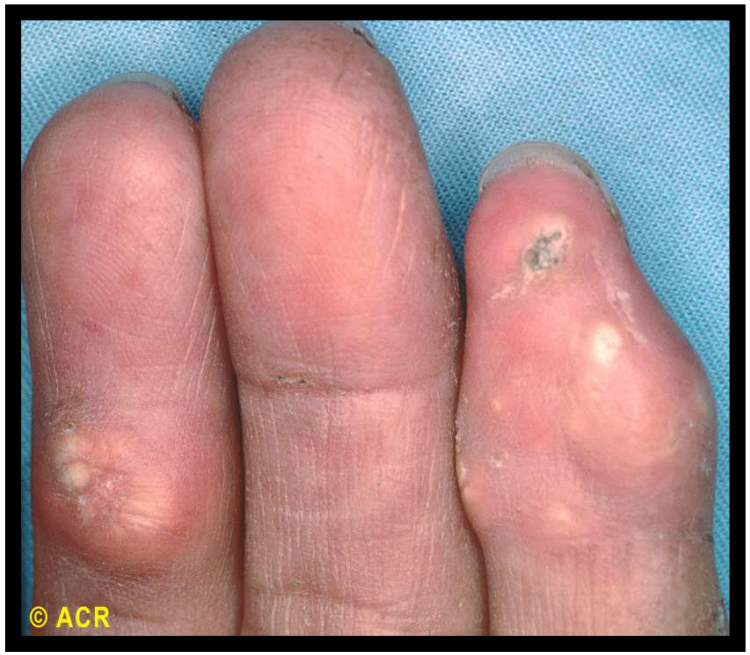
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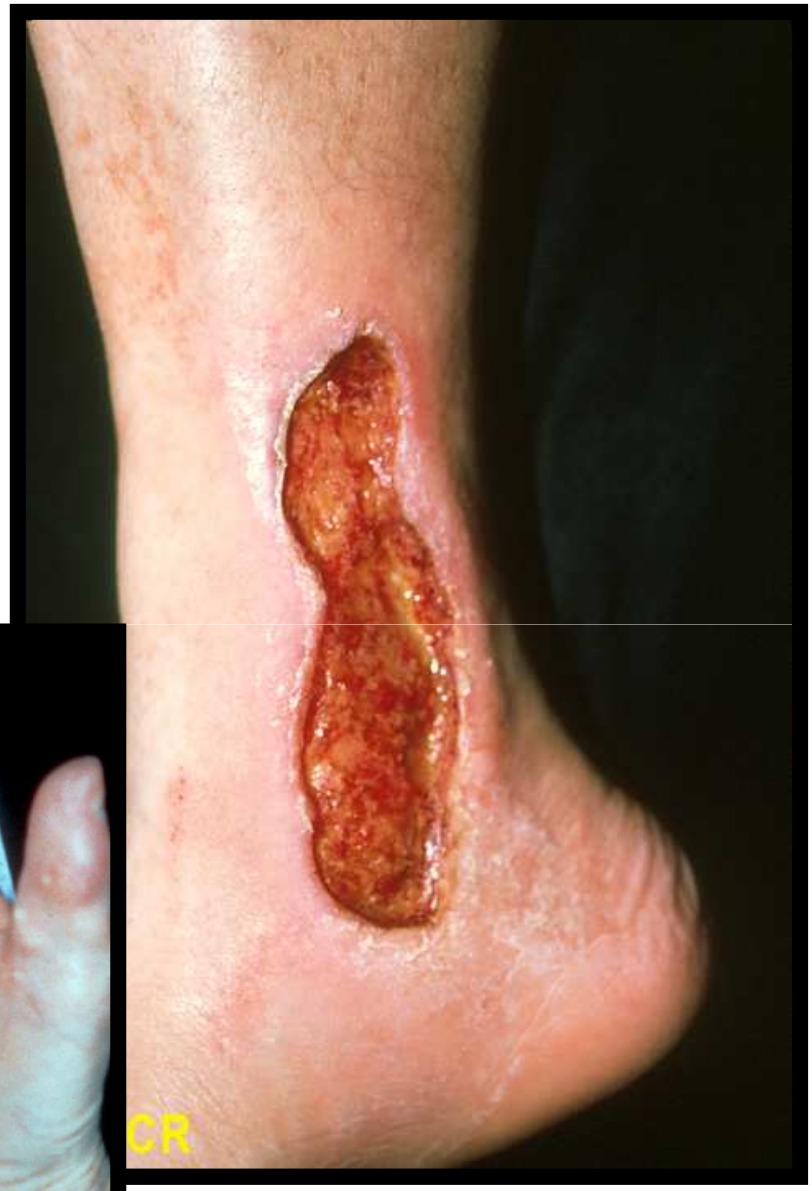
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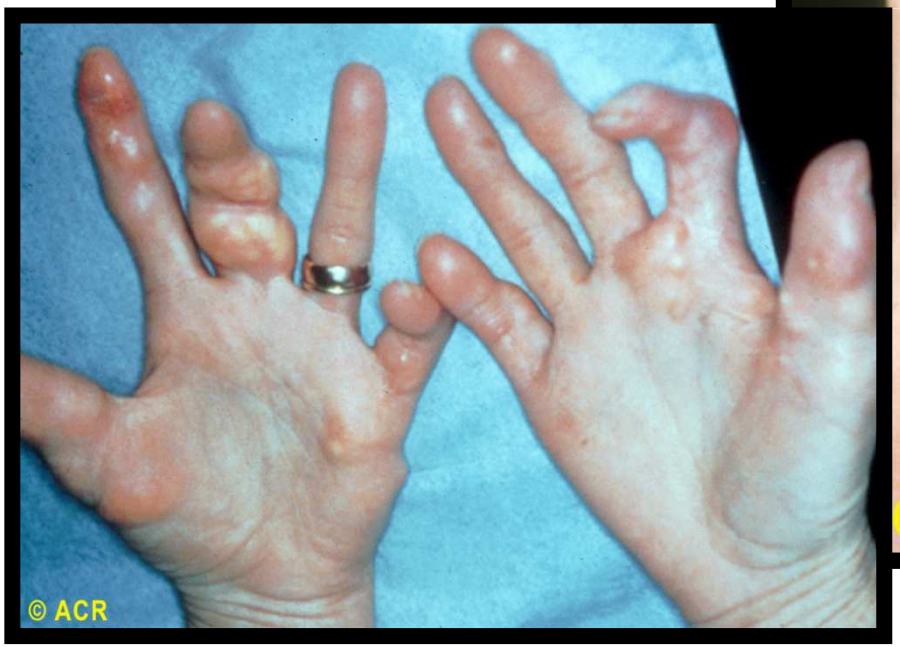
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Therapy

- Cold protecting
- Stopping smoking

- Nifedipine (or Amlodipine or Lercanidipine)
- Iloprost, Alprostidil
- Bosentan, Ambristentan
- Sindenafil, Tadalafil
- Transdermal glyceryl trinitrate
- Aminaftone
- Fluoxetine
- Surgery

Beta-bloccanti

Emivita	Farmaci
Lunga	Atenololo, Bisoprololo, Nebivololo
Intermedia	Metoprololo
Breve	Propanololo

Affinità Recettoriale B1	Farmaci
Scarsamente Selettivi	Atenololo, Metoprololo, Propanololo
Selettivi	Bisopololo, Nadololo

Mohokum M et al. The Association of Raynaud's Syndrome with B-blockers: a meta-analysis. Angiology 2012 Oct; 63(7): 535-40.

Microvascular Research 82 (2011) 84–87

Contents lists available at ScienceDirect

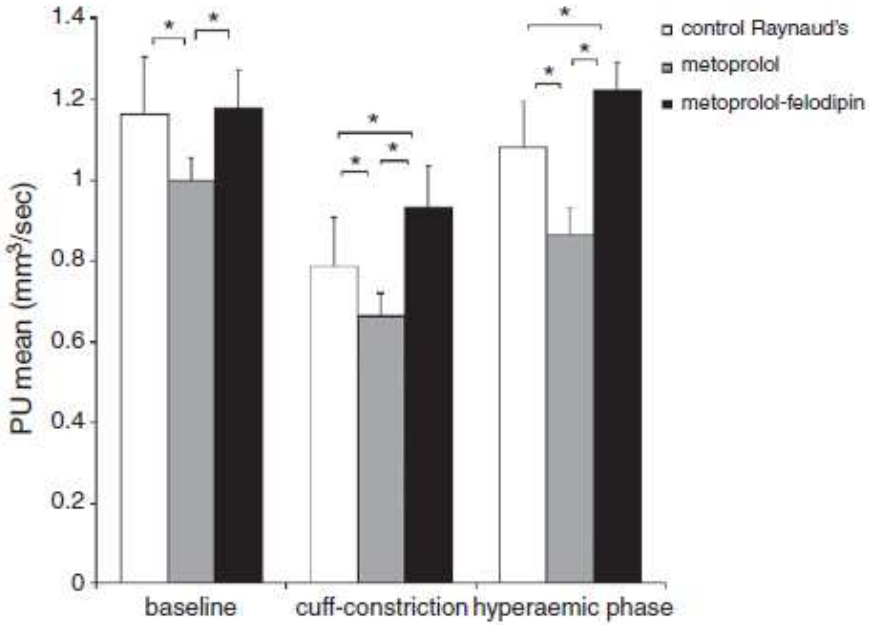
Microvascular Research

journal homepage: www.elsevier.com/locate/ymvre

Regular Article

The effect of metoprolol alone and combined metoprolol–felodipin on the digital microcirculation of patients with primary Raynaud's syndrome

Zoltan Csiki [a,*], Ildiko Garai [c], Amir H. Shemirani [b], Gabor Papp [a], Katalin S. Zsori [d], Csilla Andras [e], Margit Zeher [a]



Scleroderma Renal Crisis

- A proliferative obliterative vasculopathy with concentric ‘onion skin’ narrowing of arterioles and glomerular ischemia. The glomeruli do not show inflammatory changes or immune deposits. These pathologic findings, along with the presence of marked hyperreninemia, suggest that altered perfusion of the juxtaglomerular apparatus triggering renin-driven hypertension may be a driver of SRC.

- Corticosteroid use (>15 mg prednisone per day) predispose to the development of renal crisis.

- Patients at increased risk, particularly with early diffuse cutaneous disease, should be educated to monitor their blood pressure regularly.

Scleroderma Renal Crisis

- New-onset hypertension, often markedly elevated, with retinopathy, microangiopathic hemolytic anemia (MAHA), and other signs of end-organ damage, including blood and protein in the urine, are signs of a life-threatening illness.

- Early use of ACE inhibitors has clearly improved survival rate.

- Prognosis of scleroderma renal crisis is still not adequate.

RHEUMATOLOGY

Rheumatology 2012;51:460–467
doi:10.1093/rheumatology/ker271
Advance Access publication 15 November 2011

Original article

Scleroderma renal crisis: a retrospective multicentre study on 91 patients and 427 controls

Loïc Guillevin[1], Alice Bérezné[1], Raphaèle Seror[1], Luis Teixeira[1], Jacques Pourrat[2], Alfred Mahr[1], Eric Hachulla[3], Christian Agard[4], Jean Cabane[5], Philippe Vanhille[6], Jean-Robert Harle[7], Isabelle Deleveaux[8] and Luc Mouthon[1]

- 'Prophylactic' ACEi do not reduce the risk of SRC; they are associated with worse outcome and increased likelihood of requiring permanent dialysis.

CURRENT OPINION

Renal disease in scleroderma: an update on evaluation, risk stratification, pathogenesis and management

Victoria K. Shanmugam and Virginia D. Steen

Curr Opin Rheumatol 2012, 24:669–676

Seminars in Arthritis and Rheumatism ∎ (2013) ∎∎–∎∎∎

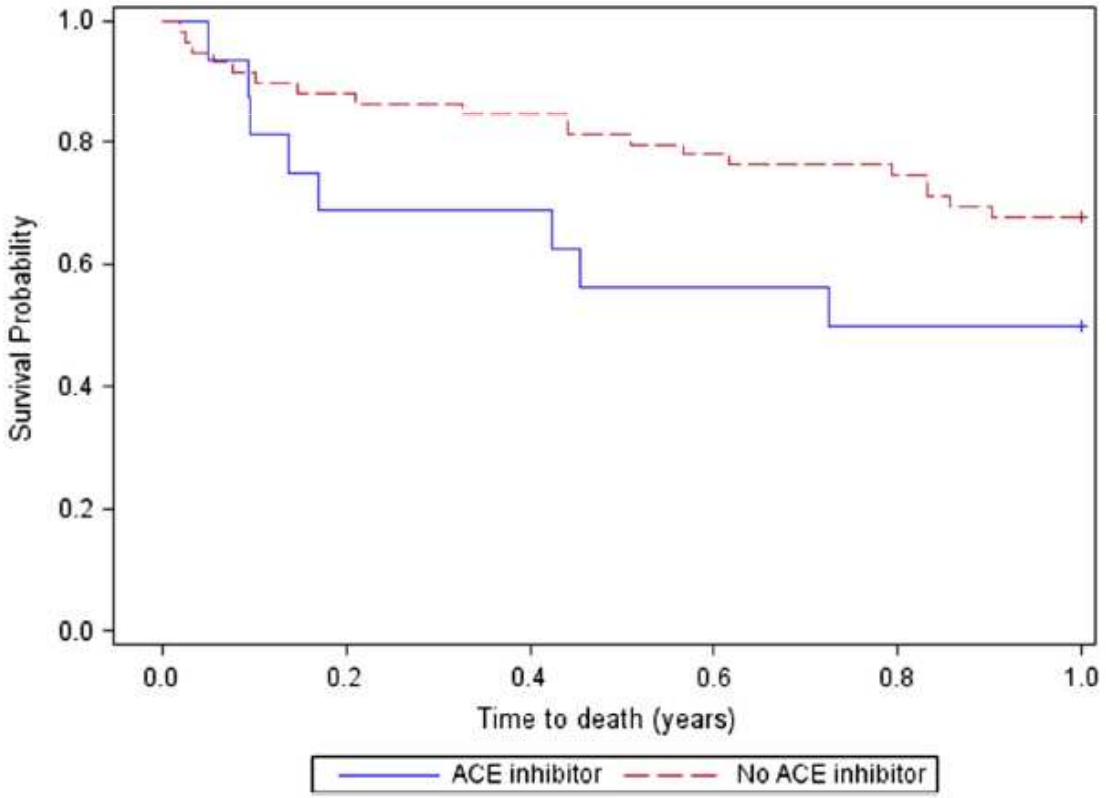
Contents lists available at ScienceDirect

Seminars in Arthritis and Rheumatism

journal homepage: www.elsevier.com/locate/semarthrit

Exposure to ACE inhibitors prior to the onset of scleroderma renal crisis —Results from the International Scleroderma Renal Crisis Survey☆

Marie Hudson, MD, MPH[a,b,*], Murray Baron, MD[a,b], Solène Tatibouet, MSc[a], Daniel E. Furst, MD[c], Dinesh Khanna, MD, MS[d], International Scleroderma Renal Crisis Study Investigators[1]



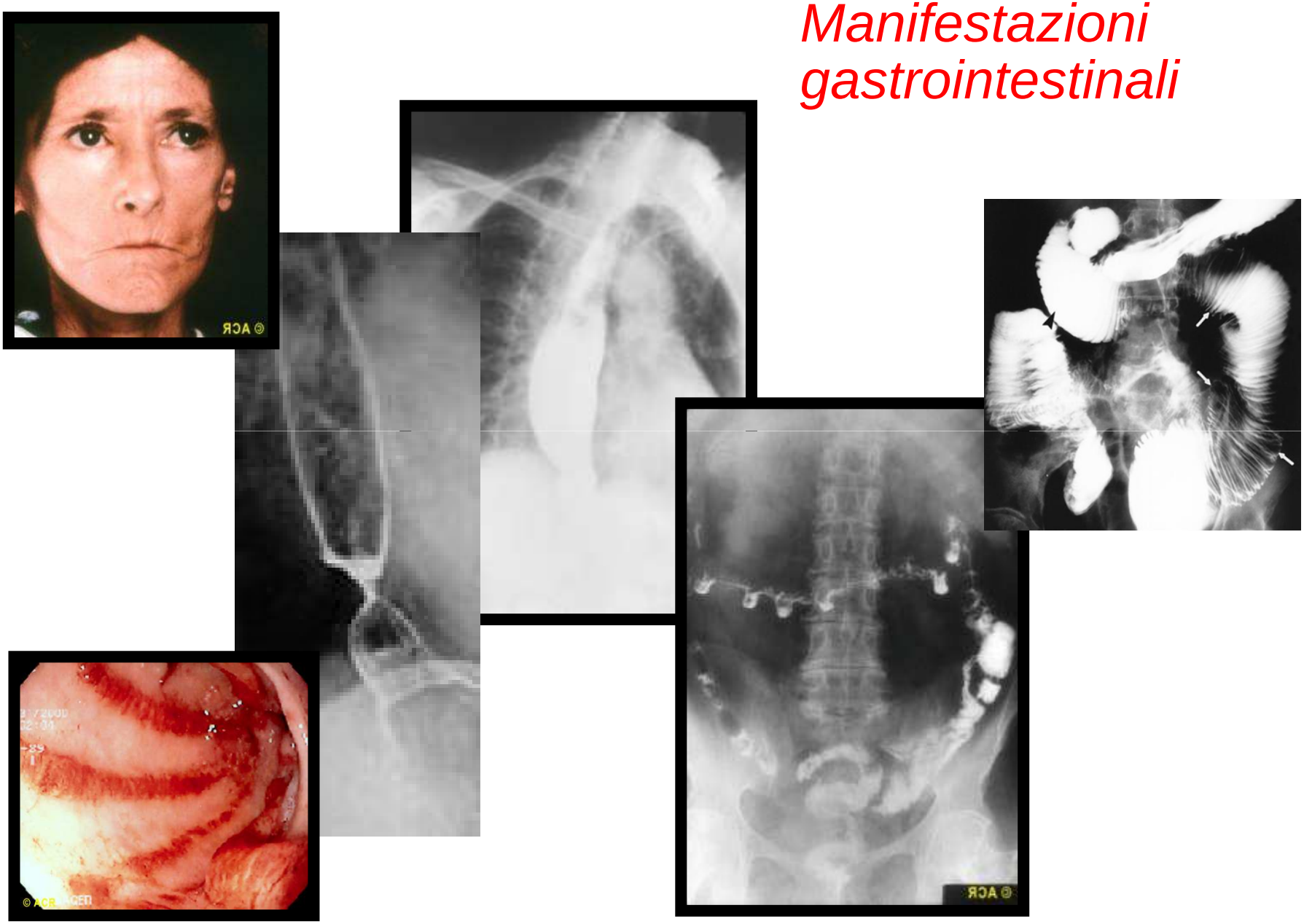
EULAR recommendations for the treatment of systemic sclerosis: a report from the EULAR Scleroderma Trials and Research group (EUSTAR)

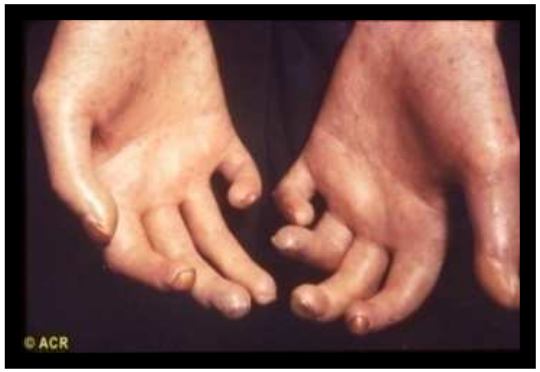
O Kowal-Bielecka,[1] R Landewé,[2] J Avouac,[3] S Chwiesko,[1] I Miniati,[4] L Czirjak,[5] P Clements,[6] C Denton,[7] D Farge,[8] K Fligelstone,[9] I Földvari,[10] D E Furst,[6] U Müller-Ladner,[11] J Seibold,[12] R M Silver,[13] K Takehara,[14] B Garay Toth,[15] A Tyndall,[16] G Valentini,[17] F van den Hoogen,[18] F Wigley,[19] F Zulian,[20] Marco Matucci-Cerinic,[4] and the EUSTAR co-authors

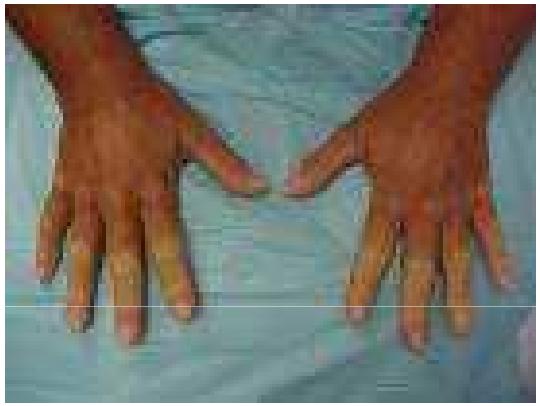
Box 1 Research agenda

1. Evaluation of the efficacy and safety of cyclophosphamide in the treatment of early diffuse SSc
2. Evaluation of the efficacy and safety of mycophenolate mofetil and azathioprine in the treatment of SSc
3. Evaluation of the efficacy and safety of sildenafil in the treatment of SSc-RP and digital ulcers
4. Evaluation of the efficacy and safety of ACE inhibitors in the prevention of SRC
5. Evaluation of calcium antagonists in the prevention of SSc-PAH

Manifestazioni gastrointestinali







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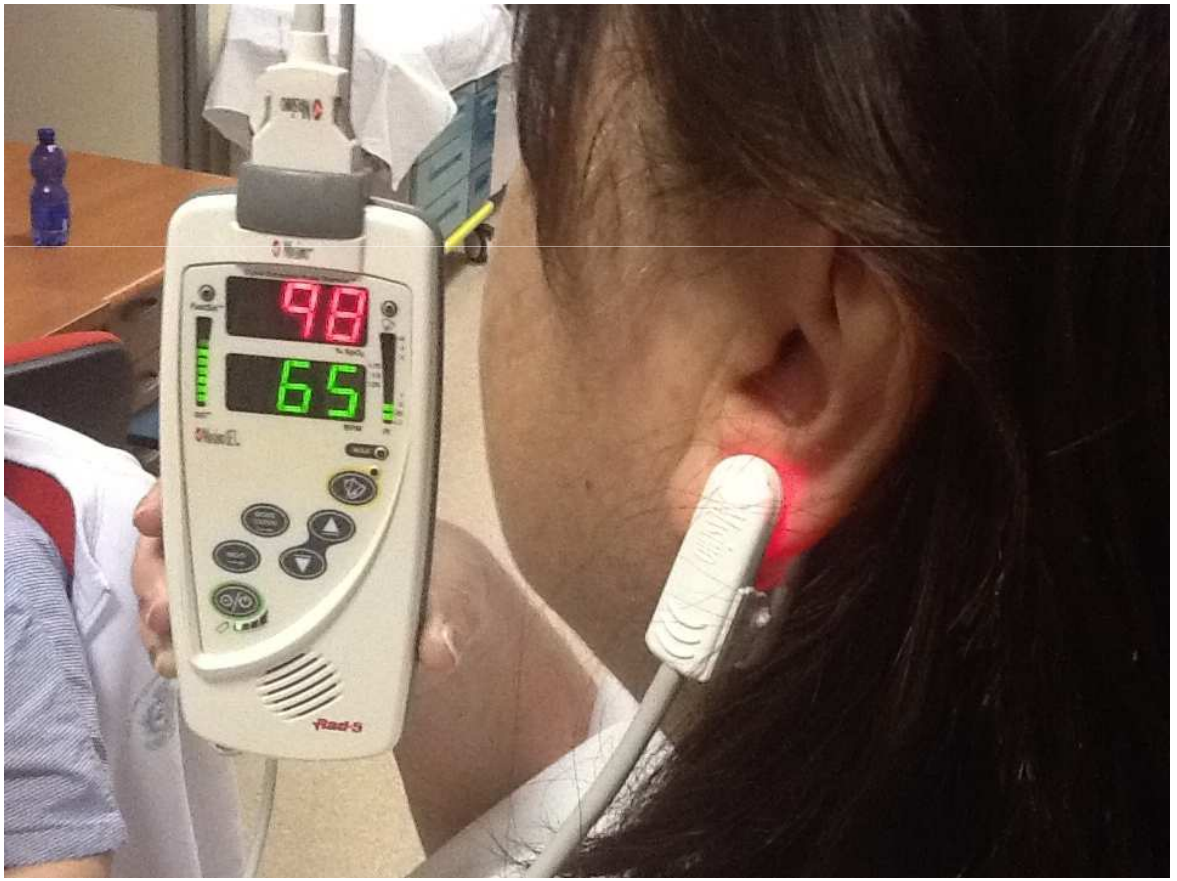

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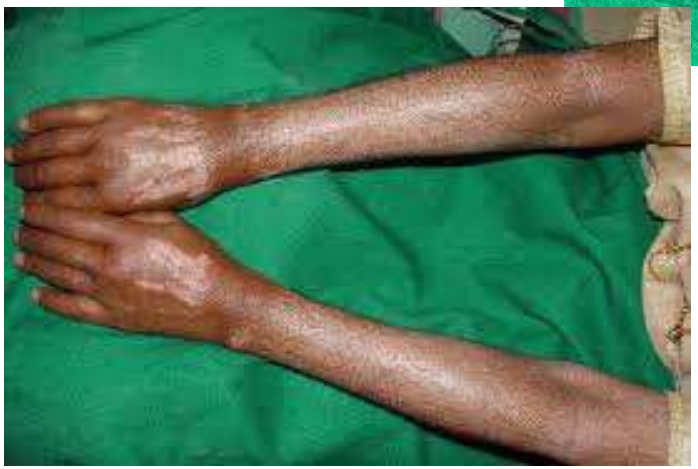

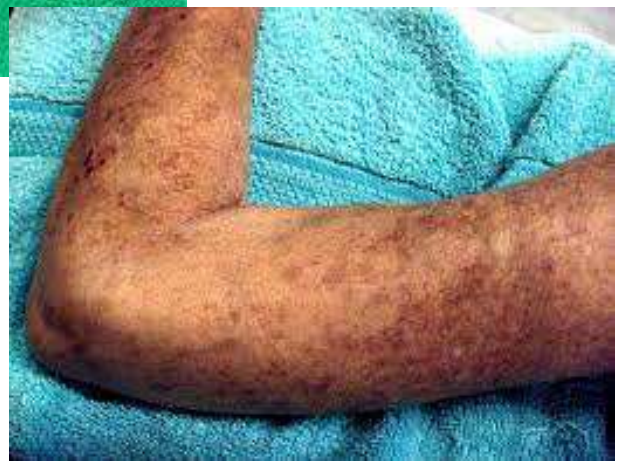

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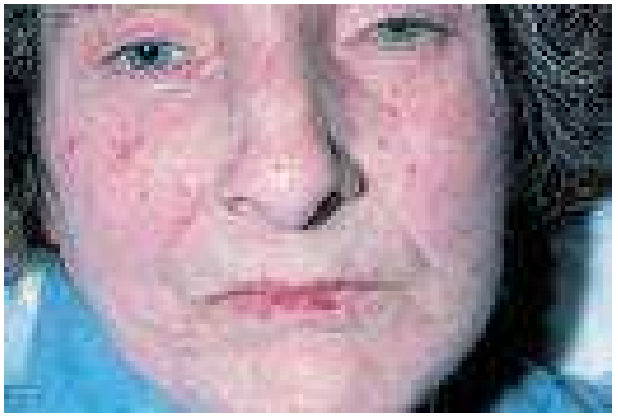
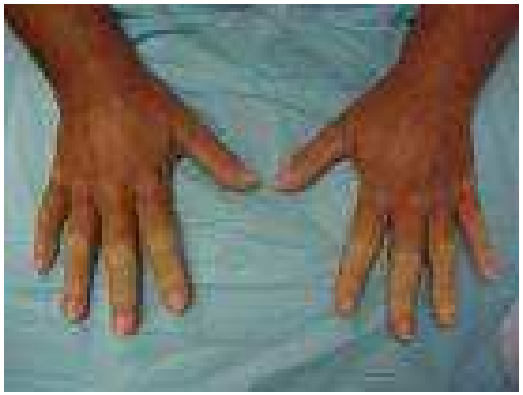
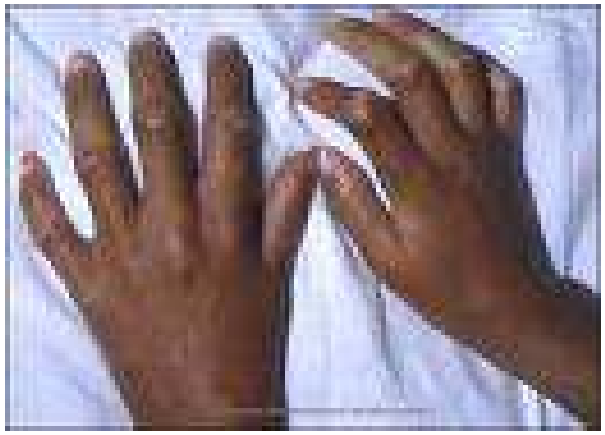
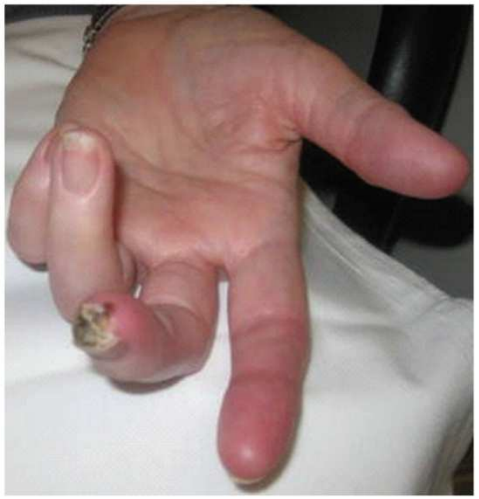




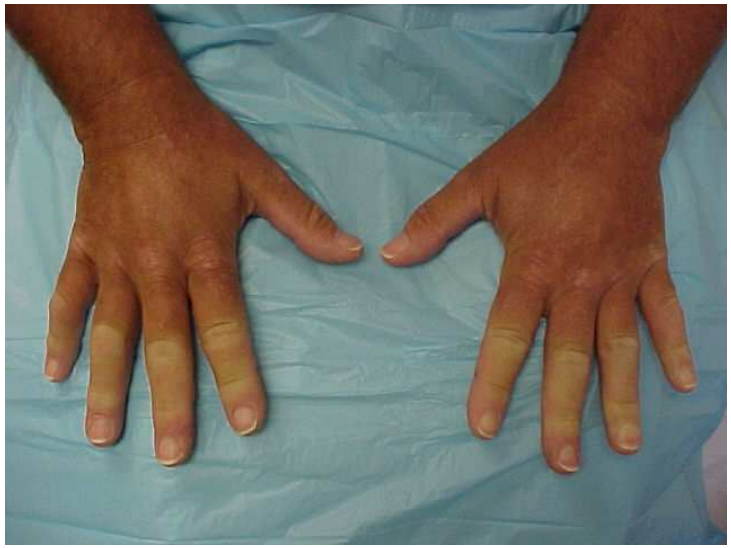




EPIDEMIOLOGY

	INCIDENCE	PREVALENCE
RAYNAUD PHENOMENON		4-15% (40.000-150.000/1.000.000)
SYSTEMIC SCLEROSIS	0,6-19/1.000.000	125-250/1.000.000

1 PATIENT
WITH RAYNAUD PHENOMENON
ON 320-600 DEVELOPS SSc
WITHIN 1-15 YEARS



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International consensus criteria for the diagnosis of Raynaud's phenomenon

Emanual Maverakis [a,b,*], Forum Patel [a], Daniel G. Kronenberg [a], Lorinda Chung [c], David Fiorentino [c,d], Yannick Allanore [e], Serena Guiducci [f], Roger Hesselstrand [g], Laura K. Hummers [h], Chris Duong [a], Bashar Kahaleh [i], Alexander Macgregor [j], Marco Matucci-Cerinic [k], Frank A. Wollheim [g], Maureen D. Mayes [l], M. Eric Gershwin [m]

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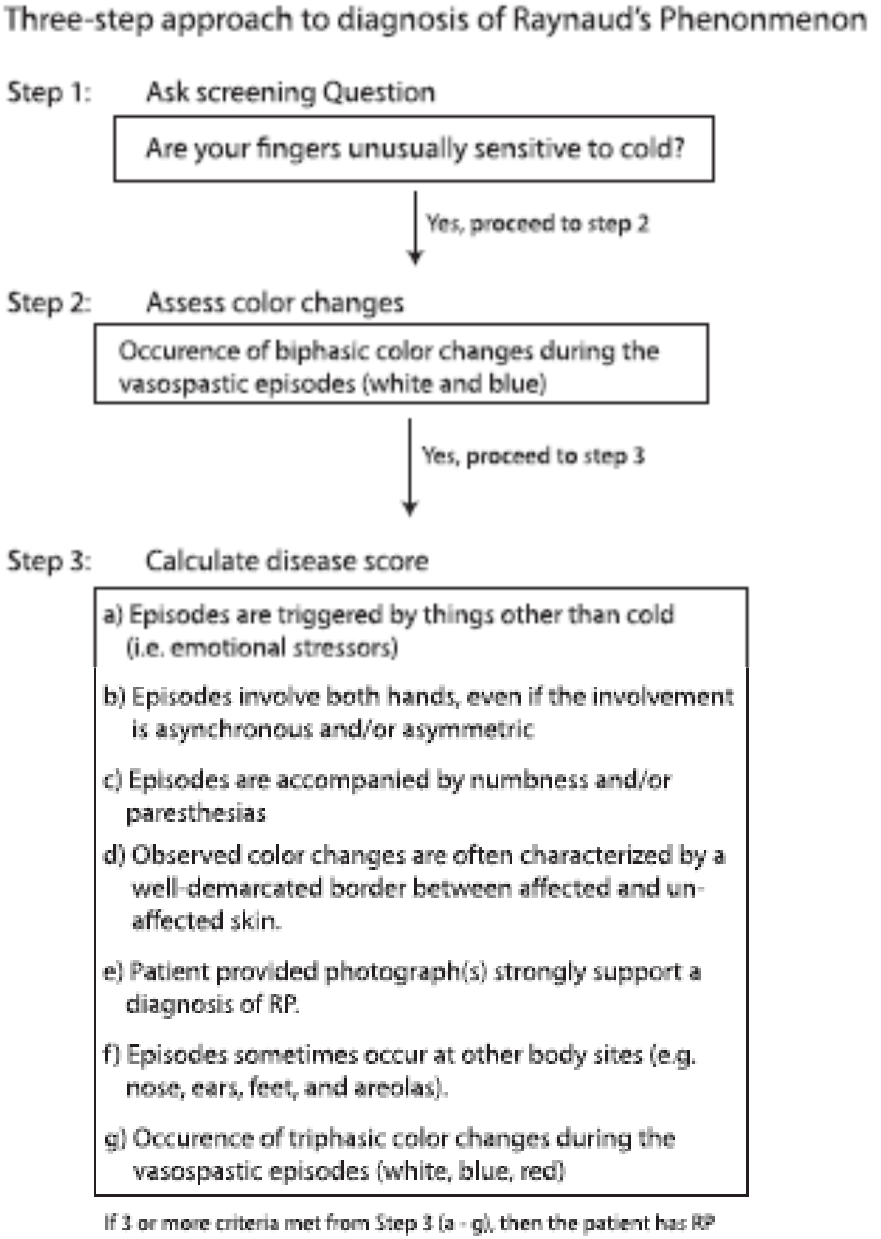

Fig. 2. Three step outline for newly proposed diagnostic method

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International consensus criteria for the diag phenomenon

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Diagnostic criteria for primary Raynaud's phenomenon.

- Meets 3 step criteria for diagnosis of Raynaud's phenomenon
- Normal capillaroscopy (e.g. clusters 1 and 2, which were described as "normal" and "perfect normal" by Ingegnoli et al.)
- Physical examination is negative for findings suggestive of secondary causes, (e.g. ulcerations, tissue necrosis or gangrene, sclerodactyly, calcinosis, or skin fibrosis)
- No history of existing connective tissue disease
- Negative or low titer ANA (e.g. 1:40 by indirect immunofluorescence)

Three-step approach to diagnosis of Raynaud's Phenonmenon

Step 1: Ask screening Question

Are your fingers unusually sensitive to cold?

Yes, proceed to step 2

Step 2: Assess color changes

Occurence of biphasic color changes during the vasospastic episodes (white and blue)

Yes, proceed to step 3

Step 3: Calculate disease score

a) Episodes are triggered by things other than cold (i.e. emotional stressors)

b) Episodes involve both hands, even if the involvement is asynchronous and/or asymmetric

c) Episodes are accompanied by numbness and/or paresthesias

nges are often characterized by a
order between affected and un-

iotograph(s) strongly support a

s occur at other body sites (e.g.
areolas).

sic color changes during the
es (white, blue, red)

If 3 or more criteria met from Step 3 (a - g), then the patient has RP

Fig. 2. Three step outline for newly proposed diagnostic method

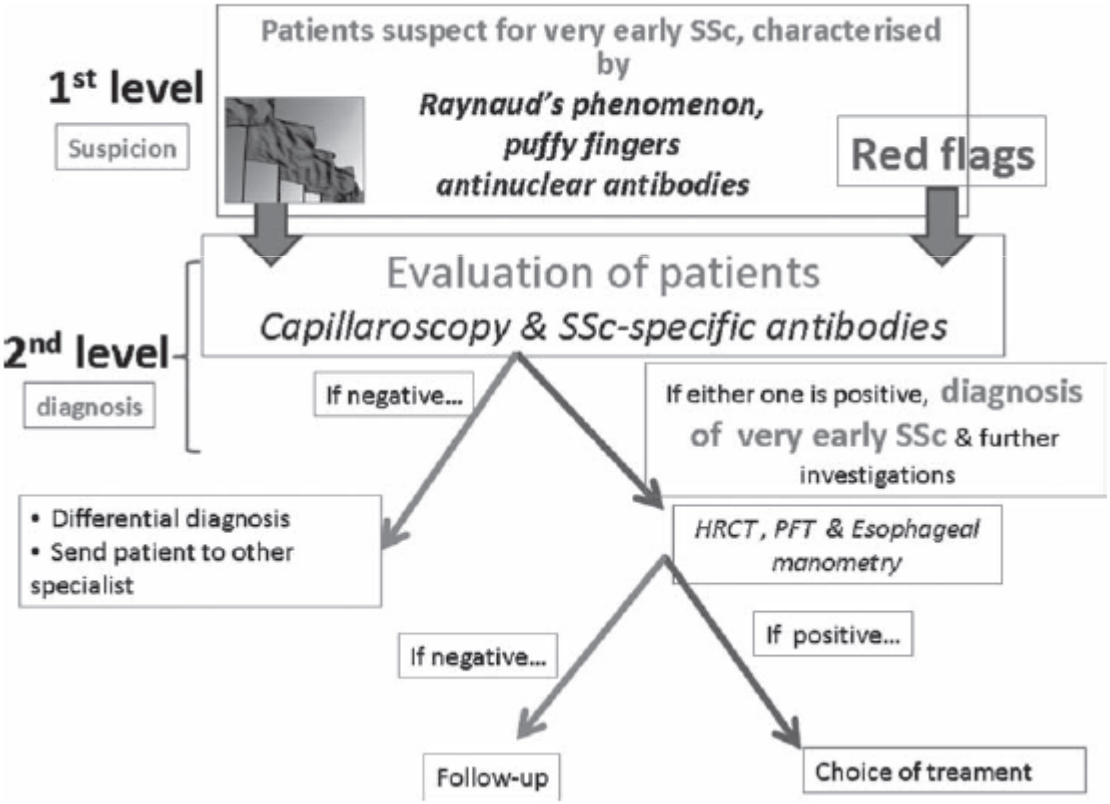
Preliminary criteria for the very early diagnosis of systemic sclerosis: results of a Delphi Consensus Study from EULAR Scleroderma Trials and Research Group

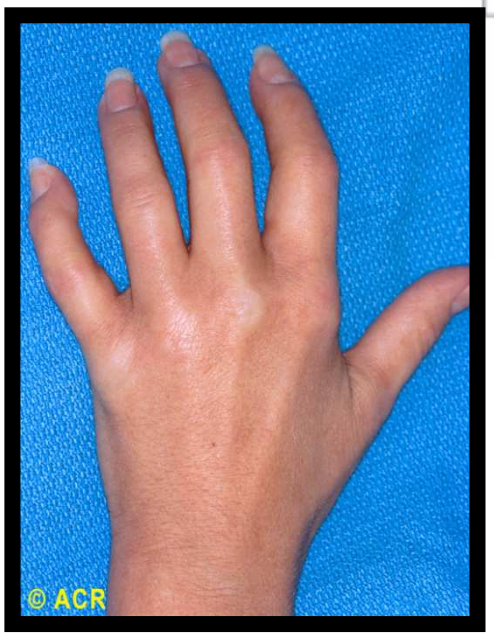
J Avouac,[1] J Fransen,[2] UA Walker,[3] V Riccieri,[4] V Smith,[5] C Muller,[6] I Miniati,[7] H Tarner,[3] S Balbanda Pandone,[4] M Cutolo,[8] Y Allanore,[1] O Distler,[14] G Valentini,[11] L Czirjak,[12] UM Kowal-Bielecka,[13] DE Furst,[12] A Tyndall,[2] M Matucci-Cerinic,[7] EUSTAR Group

Ann Rheum Dis 2011;**70**:476–481. doi:10.1136/ard.2010.136929

	Criteria selected by experts
Criteria considered as having a high clinical relevance for the very early diagnosis of SSc	Raynaud's phenomenon Puffy swollen digits turning into sclerodactily Abnormal capillaroscopy with scleroderma pattern Positive anticentromere antibodies Positive anti-topoisomerase-1 antibodies
Criteria considered as leading to an early referral	Raynaud's phenomenon Puffy fingers Positive antinuclear antibodies

EUSTAR, European League Against Rheumatism Scleroderma Trial and Research; SSc, systemic sclerosis.





1st level

Suspicion

Patients suspect for very early SSc, characterised by

Raynaud's phenomenon,
puffy fingers
antinuclear antibodies

Red flags

2nd level

diagnosis

Evaluation of patients

Capillaroscopy & SSc-specific antibodies

If negative...

- Differential diagnosis
- Send patient to other specialist

If either one is positive, diagnosis of very early SSc & further investigations

HRCT, PFT & Esophageal manometry

If negative...

Follow-up

If positive...

Choice of treament

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EUSTAR, European League Against Rheumatism Scleroderma Trial and Research; SSC, systemic sclerosis.

REVIEW

Annals of the RHEUMATIC DISEASES The EULAR Journal

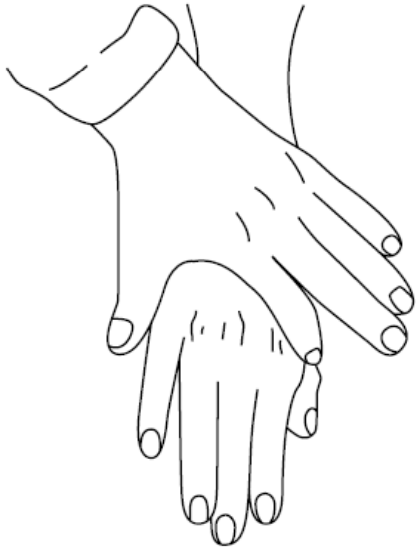
Early referral recommendation for newly diagnosed rheumatoid arthritis: evidence based development of a clinical guide

P Emery, F C Breedveld, M Dougados, J R Kalden, M H Schiff, J S Smolen

Rapid referral to a rheumatologist advised in the event of *clinical suspicion of RA*, which may be supported by the presence of any of the following (grade C evidence):

- ≥3 articolazioni colpite
- Compromissione delle metacarpofalangee e/o delle metatarsofalangee (***Squeeze test*** positivo)
- Rigidità mattutina ≥ 30 min

Manovra della Gronda



submitted)

- Patients with RA have been shown to have an improved long term outcome, when treated by a rheumatologist (grade C evidence)
- There is evidence that a delay >12 weeks in treatment results in a missed opportunity to improve long term outcome (grade C evidence)
- RF positivity, raised acute phase response, and erosions on *x* ray are associated with poor outcome. Their absence at presentation should not preclude diagnosis or referral (grade C evidence)
- NSAIDs can mask signs and symptoms at presentation (grade D evidence)
- Corticosteroids should not be prescribed without an accurate diagnosis (grade D evidence)

Early referral algorithm for newly diagnosed RA.

APPROCCI INTERDISCIPUNARI IN REUMATOLOGIA

3a Edizione

DIAGNOSTICA PER IMMAGINI ED APPROCCI INTERVENTISTICI IN REUMATOLOGIA PASSATO, PRESENTE E FUTURO

TORINO, 17 e 18 aprile 2015

GRAZIE E ....

.... ARRIVEDERCI AL PROSSIMO ANNO!

Enrico Fusaro

S.C. Reumatologia AO Città della Salute e della Scienza di Torino

Azienda Ospedaliera Città della Salute e della Scienza di Torino

2013 Classification Criteria for Systemic Sclerosis

An American College of Rheumatology/European League Against Rheumatism Collaborative Initiative

Item	Sub-item(s)	Weight/score†
Skin thickening of the fingers of both hands extending proximal to the metacarpophalangeal joints *(sufficient criterion)*	–	9
Skin thickening of the fingers *(only count the higher score)*	Puffy fingers	2
	Sclerodactyly of the fingers (distal to the metacarpophalangeal joints but proximal to the proximal interphalangeal joints)	4
Fingertip lesions *(only count the higher score)*	Digital tip ulcers	2
	Fingertip pitting scars	3
Telangiectasia	–	2
Abnormal nailfold capillaries	–	2
Pulmonary arterial hypertension and/or interstitial lung disease *(maximum score is 2)*	Pulmonary arterial hypertension	2
	Interstitial lung disease	2
Raynaud's phenomenon	–	3
SSc-related autoantibodies (anticentromere, anti–topoisomerase I [anti–Scl-70], anti–RNA polymerase III) *(maximum score is 3)*	Anticentromere Anti–topoisomerase I Anti–RNA polymerase III	3

≥ 9

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