Sclérodermie Systémique: bilan initial, examens de surveillance

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Epidemiology

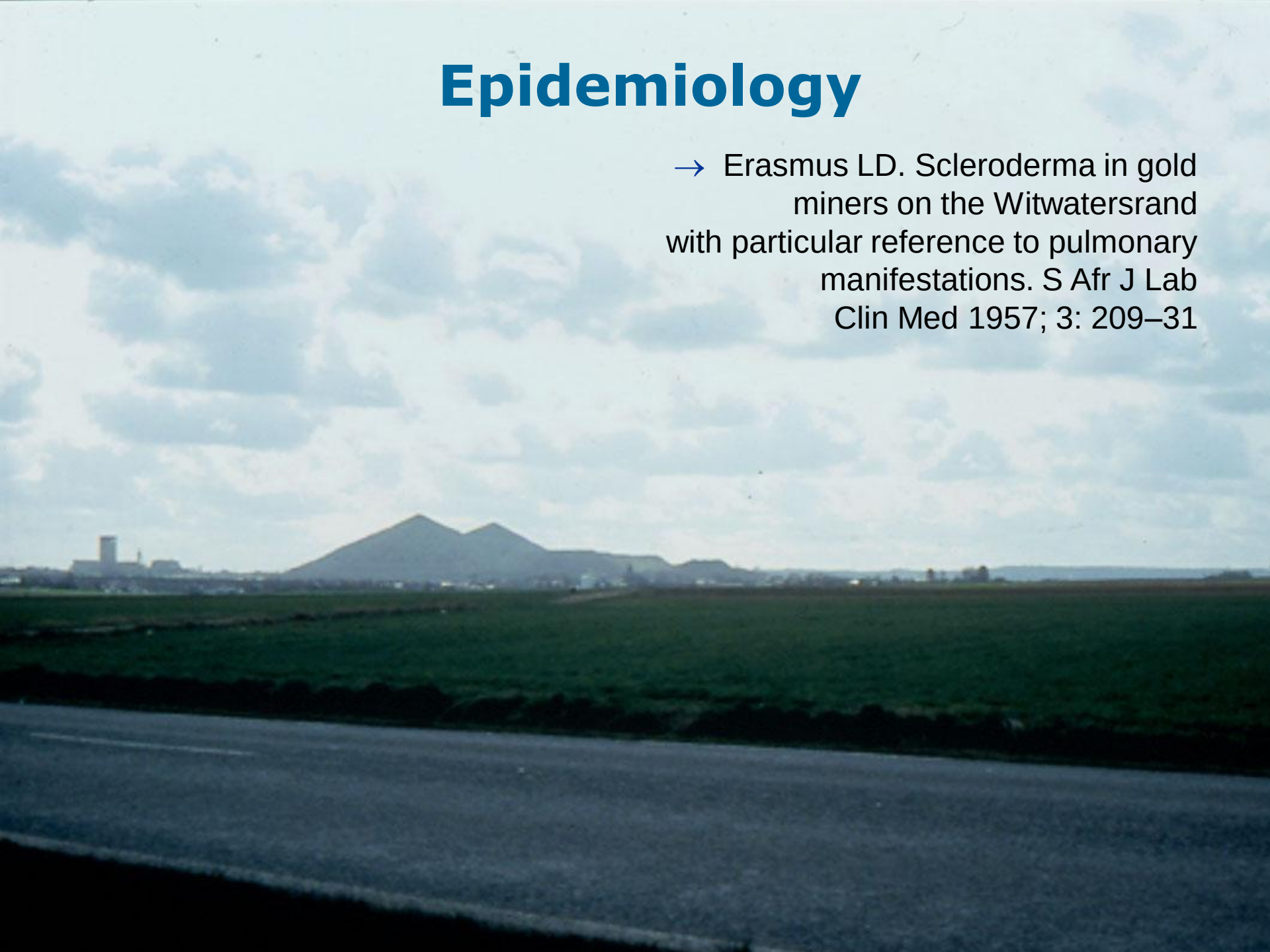
- Prévalence
  - USA : 260 millions d'habitants
  - UK : 13 à 48/million d'habitants
  - Australie : 86/million d'habitants
  - France (Seine-Saint-Denis) : 158/million d'adultes

  $\Rightarrow$ 6 à 8 000 SSc adultes en France

- Incidence aux USA et en Europe : 4,5 à 18,5 nouveaux cas/million d'habitants

Gaubitz M. Rheumatology 2006;45:ii3 Le Guern. Rheumatology 2004;43:1129

Epidemiology



→ Erasmus LD. Scleroderma in gold miners on the Witwatersrand with particular reference to pulmonary manifestations. S Afr J Lab Clin Med 1957; 3: 209–31

Epidemiology

Figure 2. Worker performing abrasive blasting at ground level.

→ Erasmus LD. Scleroderma in gold miners on the Witwatersrand with particular reference to pulmonary manifestations. S Afr J Lab Clin Med 1957; 3: 209–31

Epidemiology

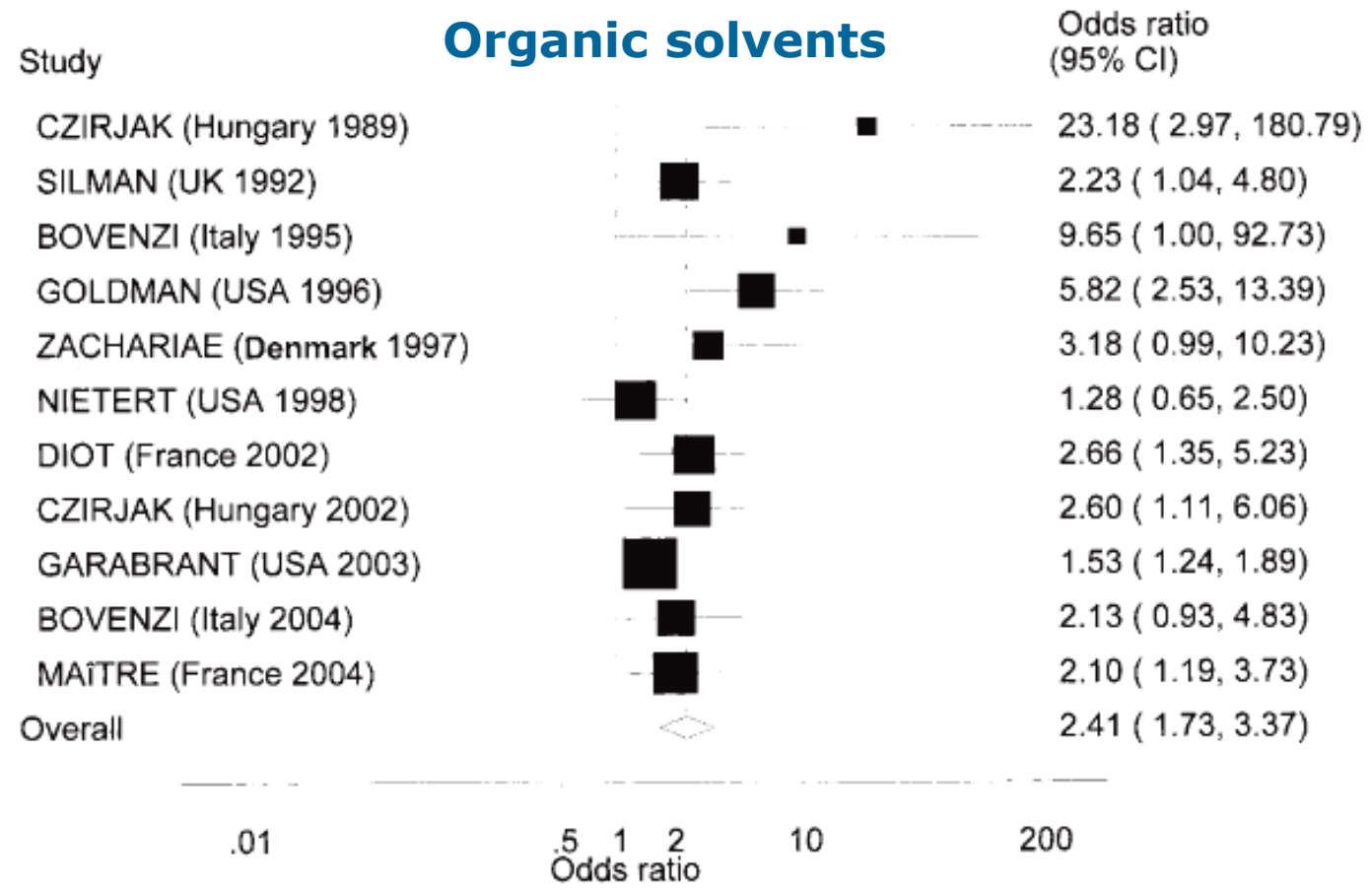
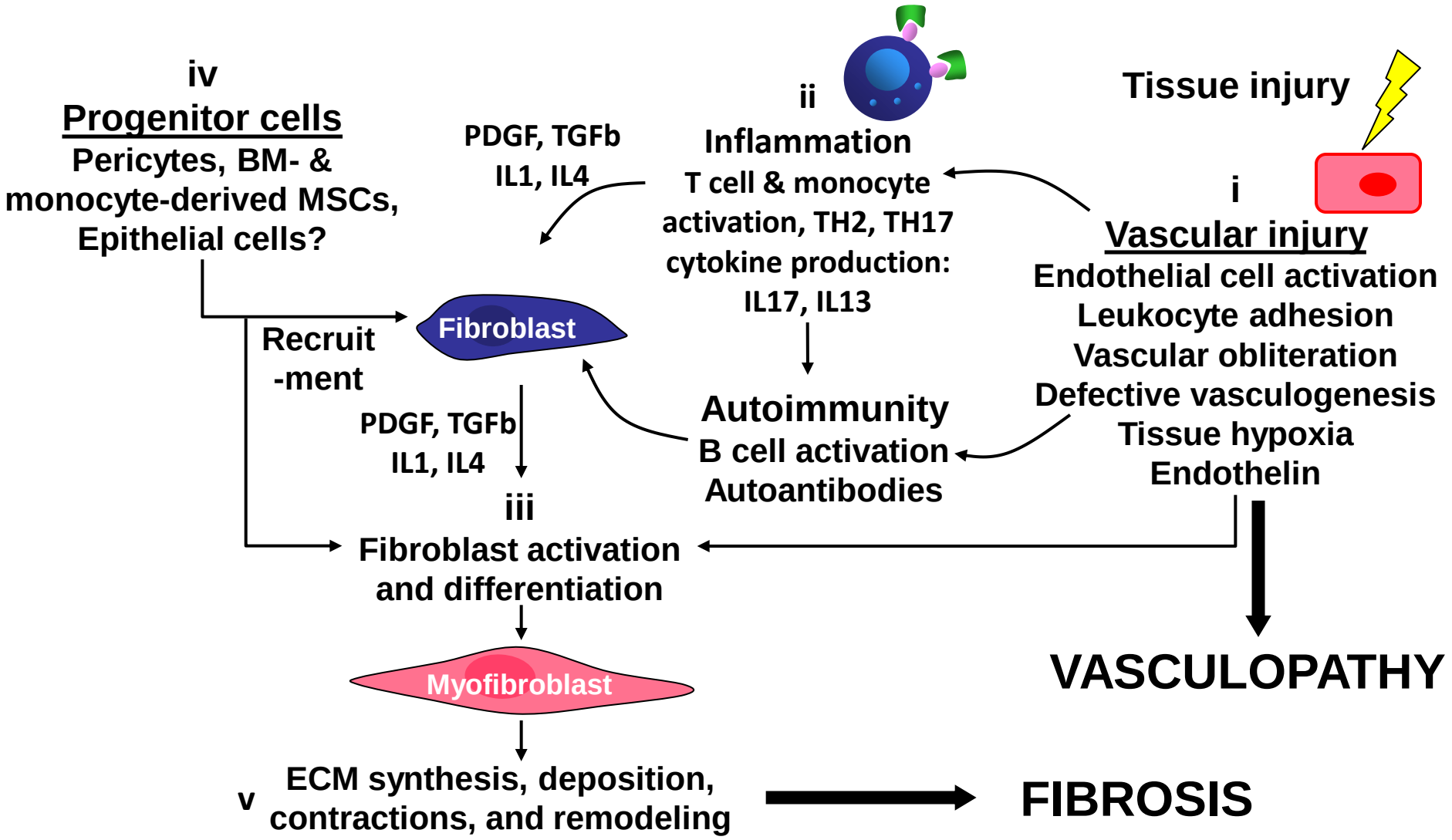


Figure 1. Exposure to any or any organic solvent and the risk of systemic sclerosis (SSc) in the whole sample. Points and overall (diamond) estimates are given as odds ratios (OR) with 95% CI. The size of each box is roughly proportional to the weight of the corresponding study in the metaanalysis.

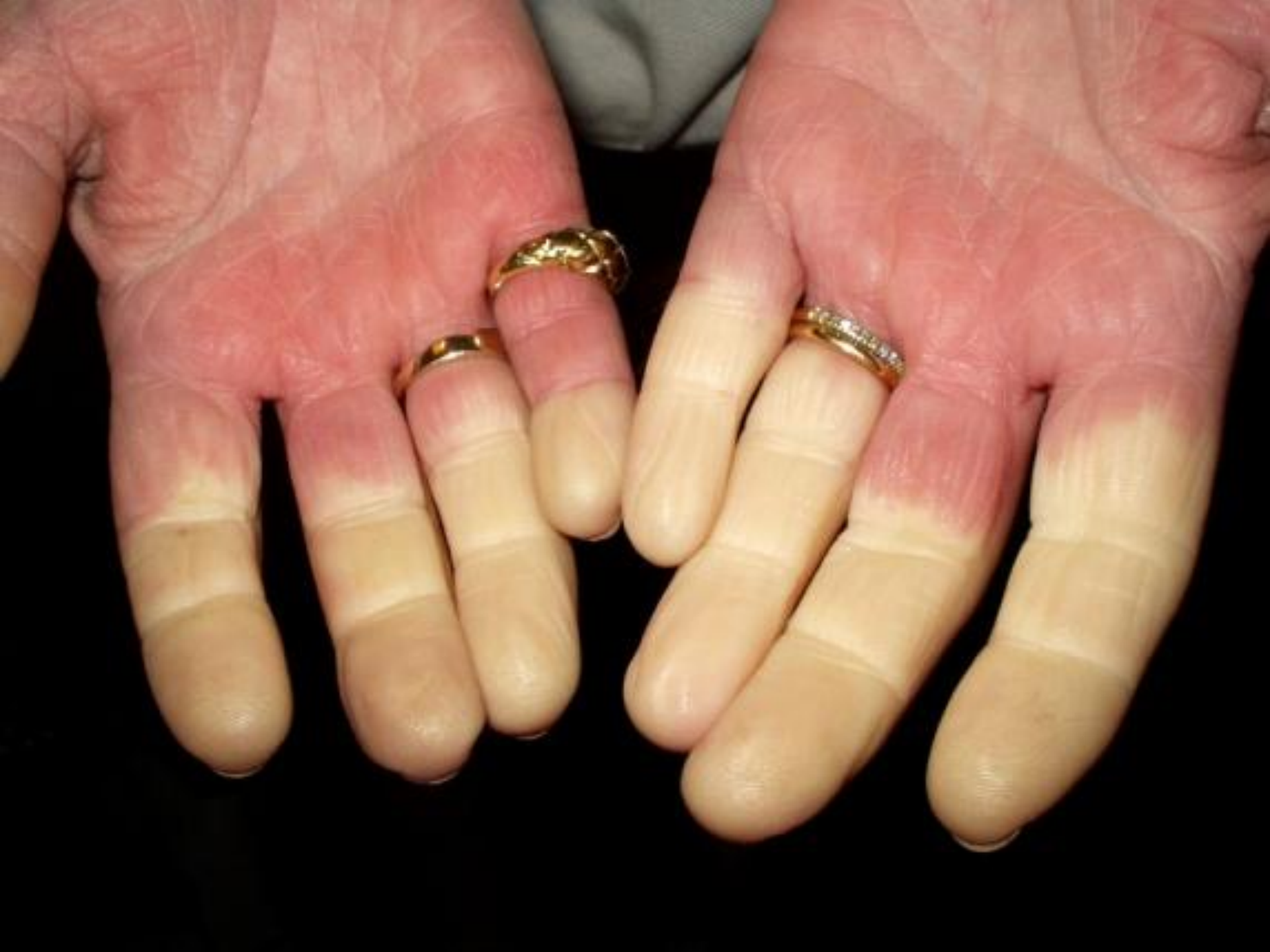
Kettaneh J Rheumatol 2007;34:97

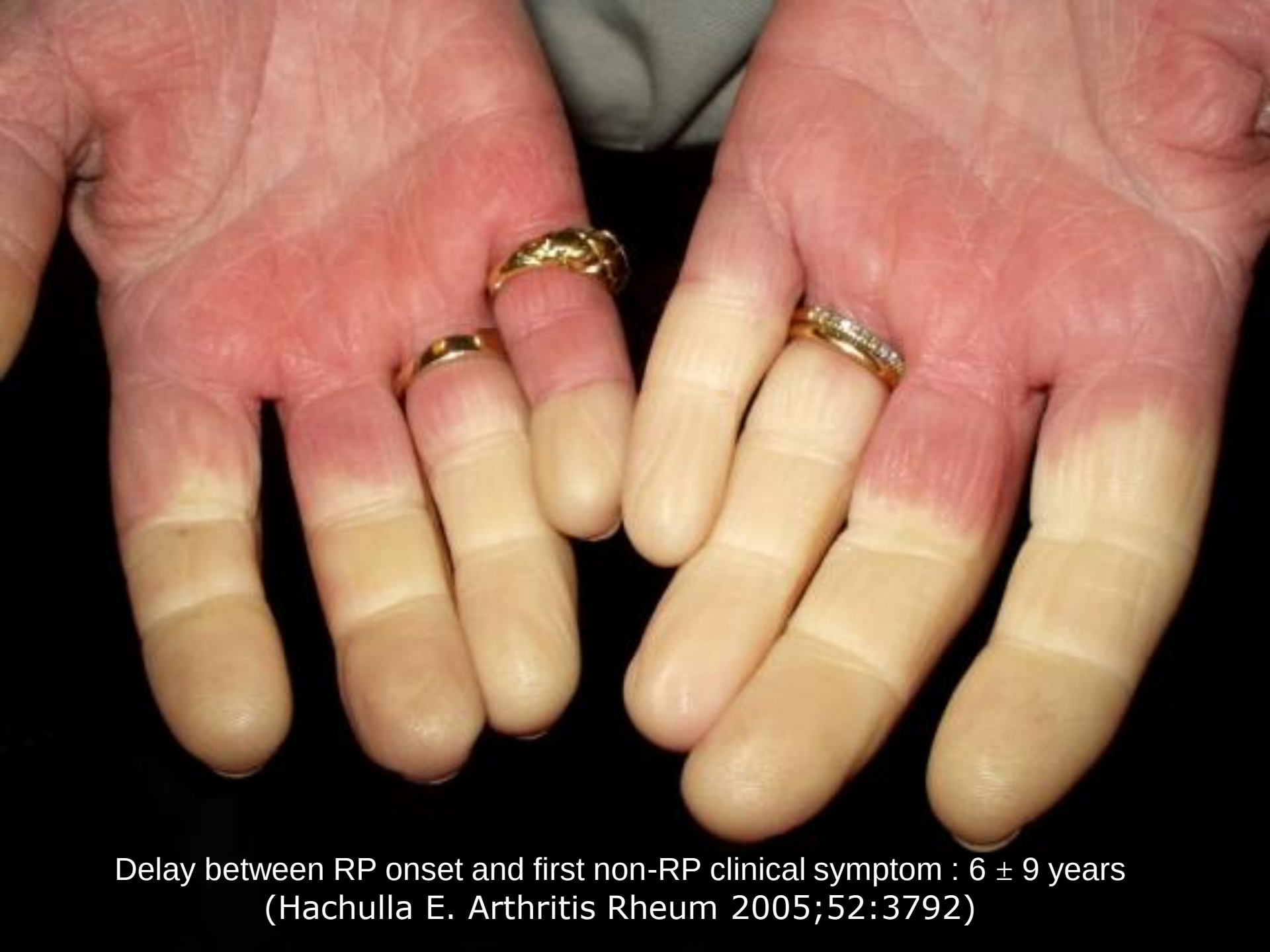
Scleroderma physiopathology



Courtesy Pr Alan Tyndall

Adapted from Varga J and Abraham D. J Clin Invest 2007;117:557



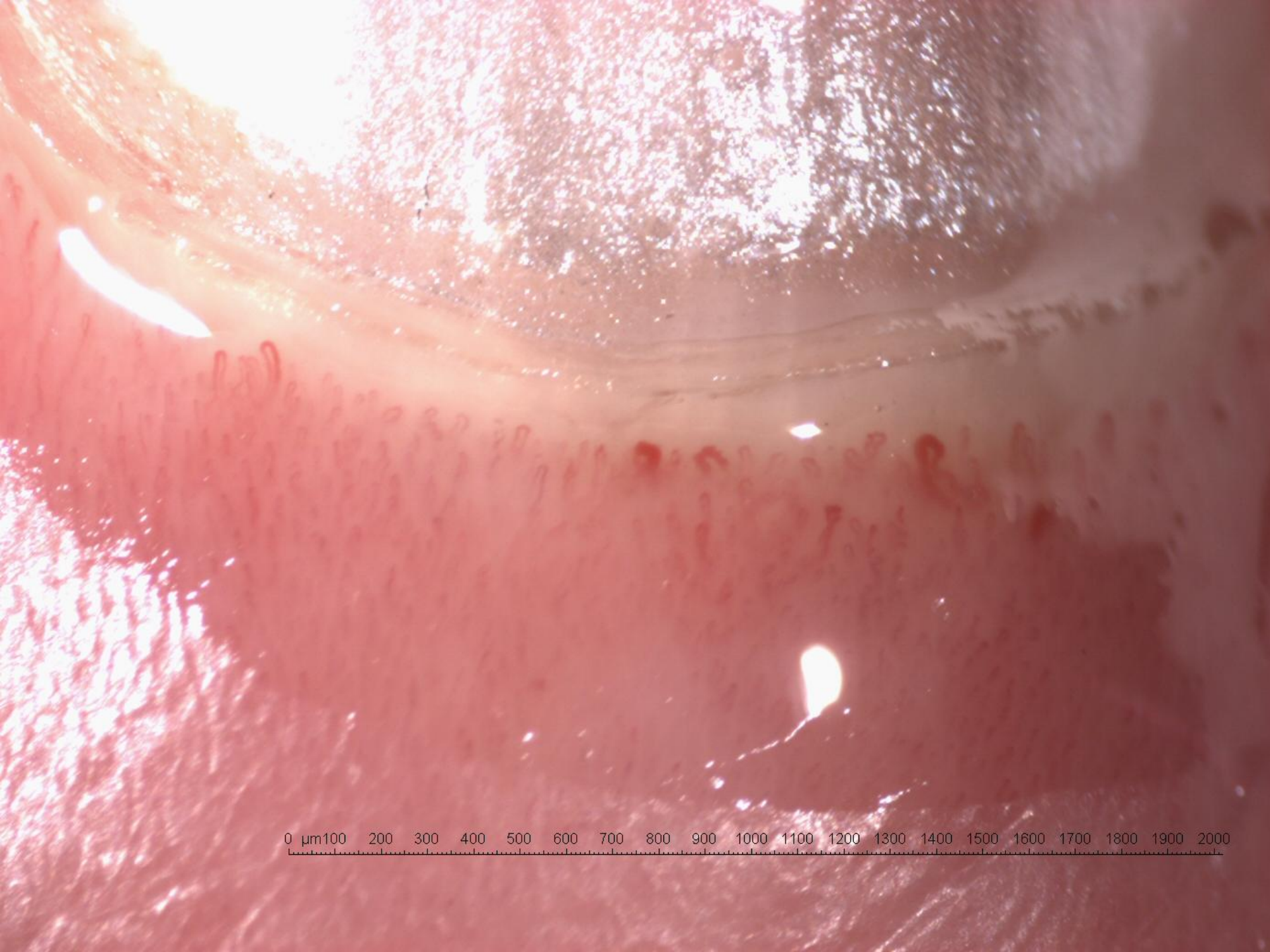


Delay between RP onset and first non-RP clinical symptom : 6 ± 9 years
(Hachulla E. Arthritis Rheum 2005;52:3792)

Raynaud's phenomenon: first sign of SSc?

	All	dcSSc	lcSSc	p
Patients	599	165	434	
Male	16%	22%	14%	0.01
Age (years)	55 ± 13	53 ± 13	55 ± 13	0.10
Occupational risks	11%	13%	10%	0.23
Delay between RP onset and first non-RP clinical symptom (years)	6 ± 9	3 ± 6	7 ± 10	<0.0001
Time since first non-RP symptom onset (years)	7 ± 7	8 ± 7	7 ± 7	0.09
Age at first non-RP symptom onset	46 ± 14	44 ± 14	47 ± 14	0.008

Hachulla E. Arthritis Rheum 2005;52:3792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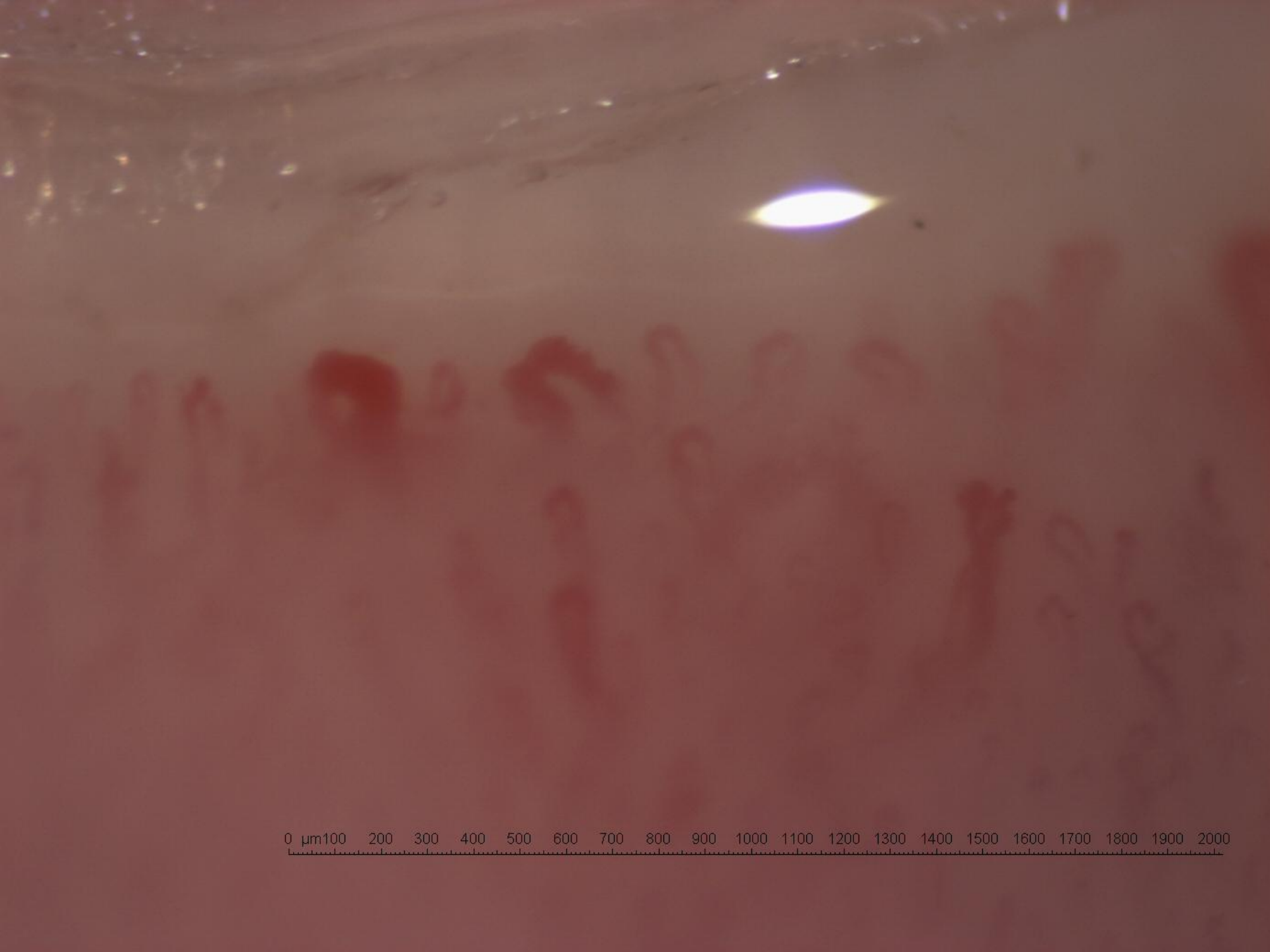
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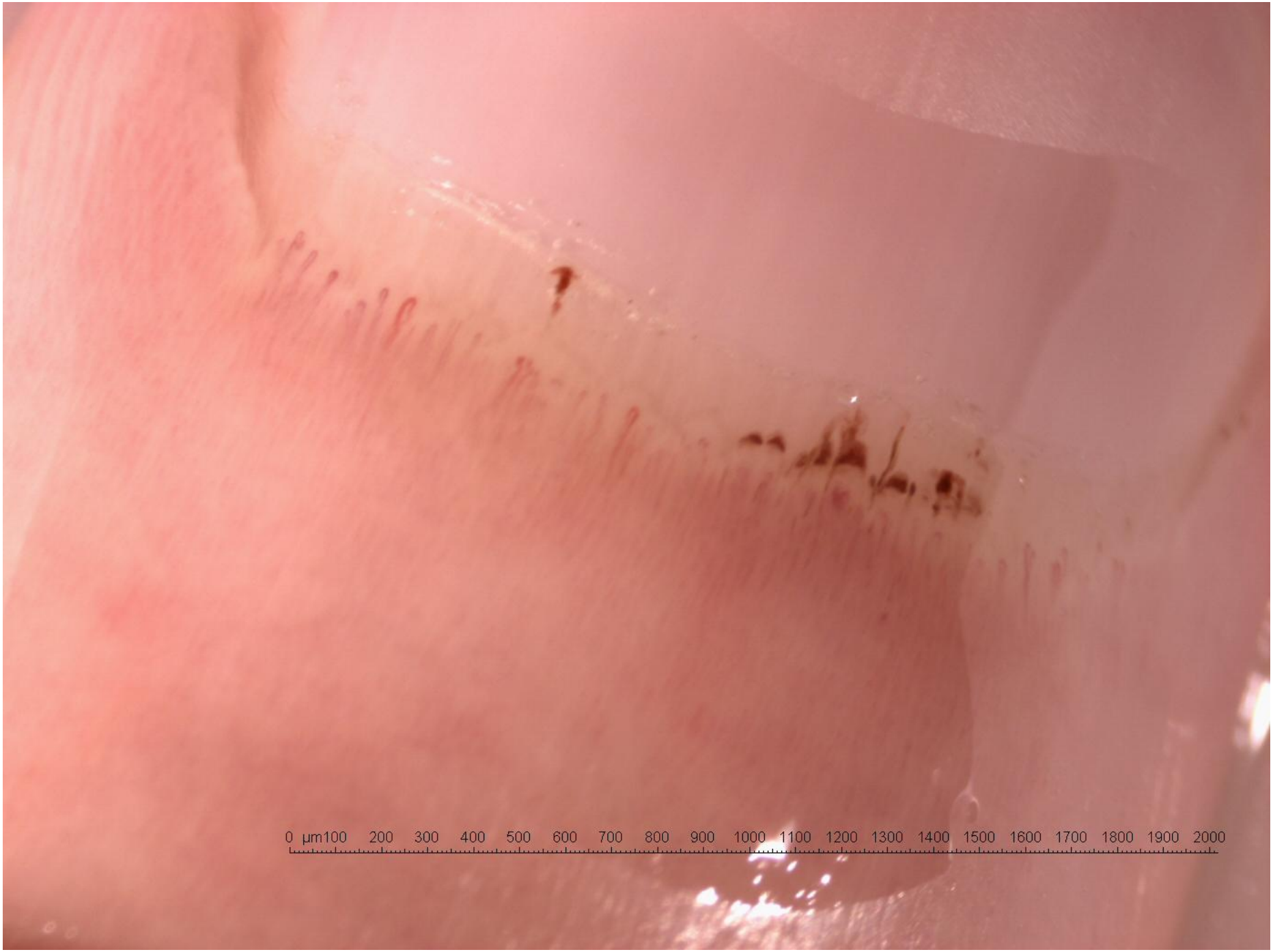
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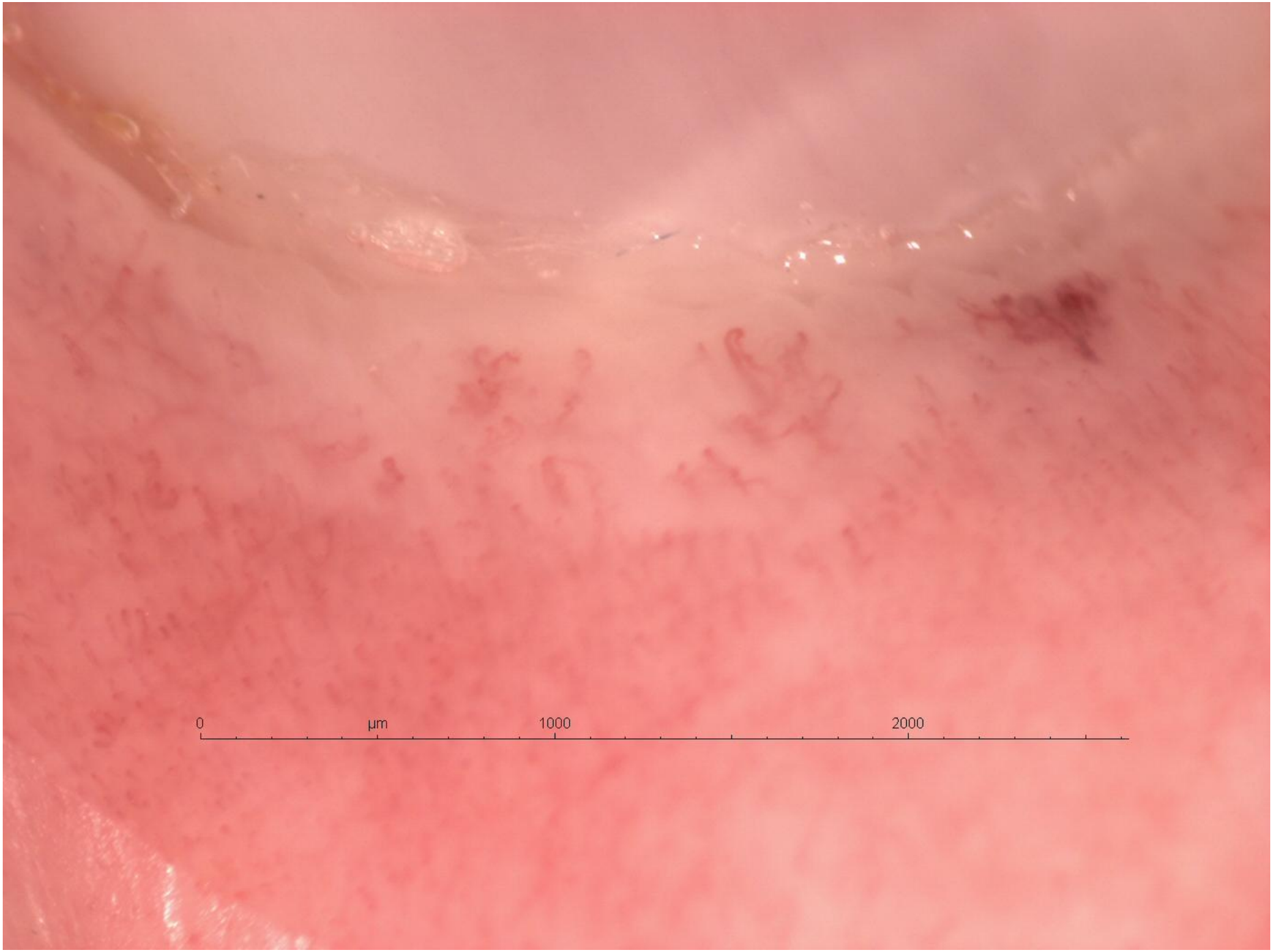
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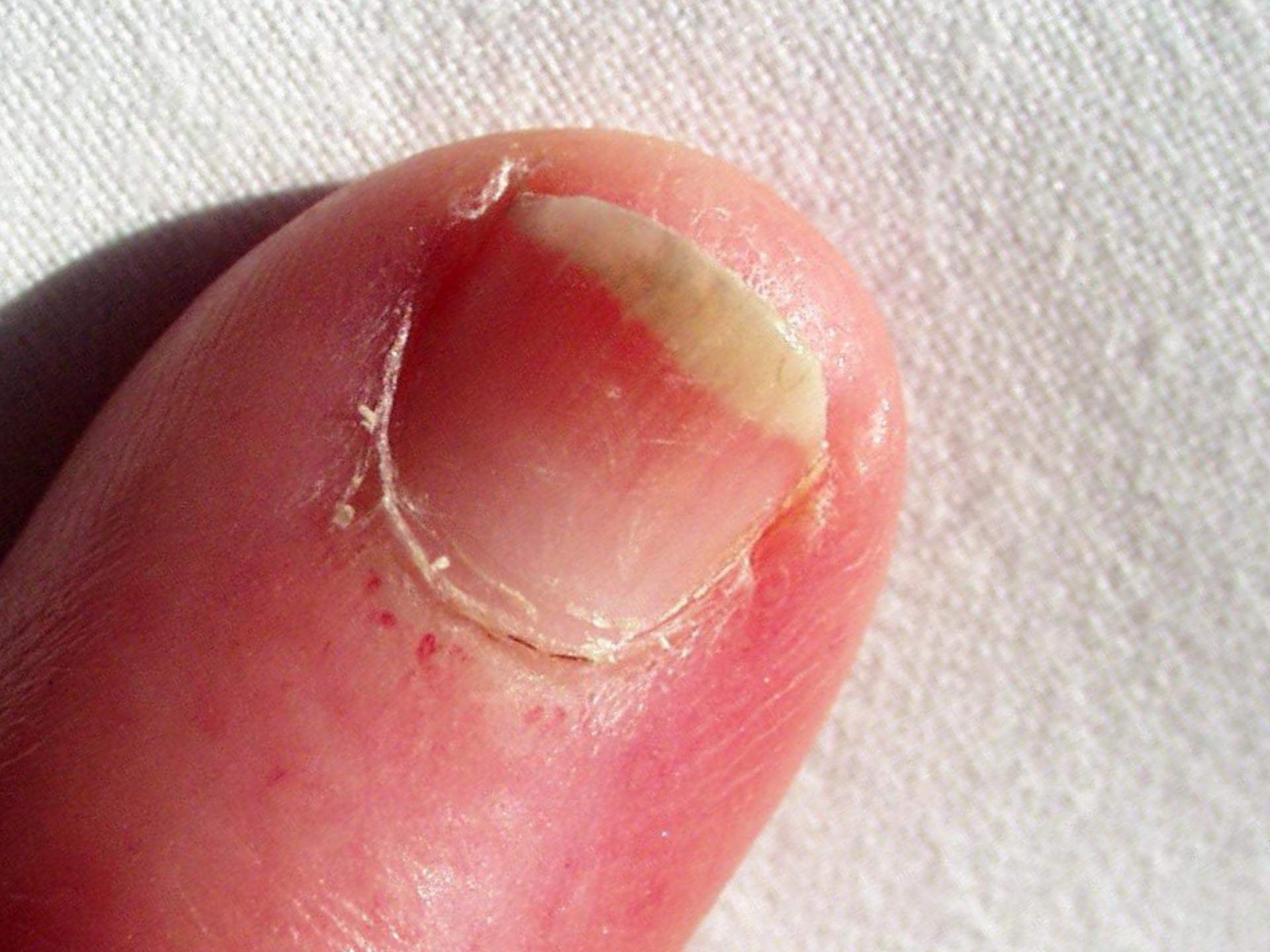
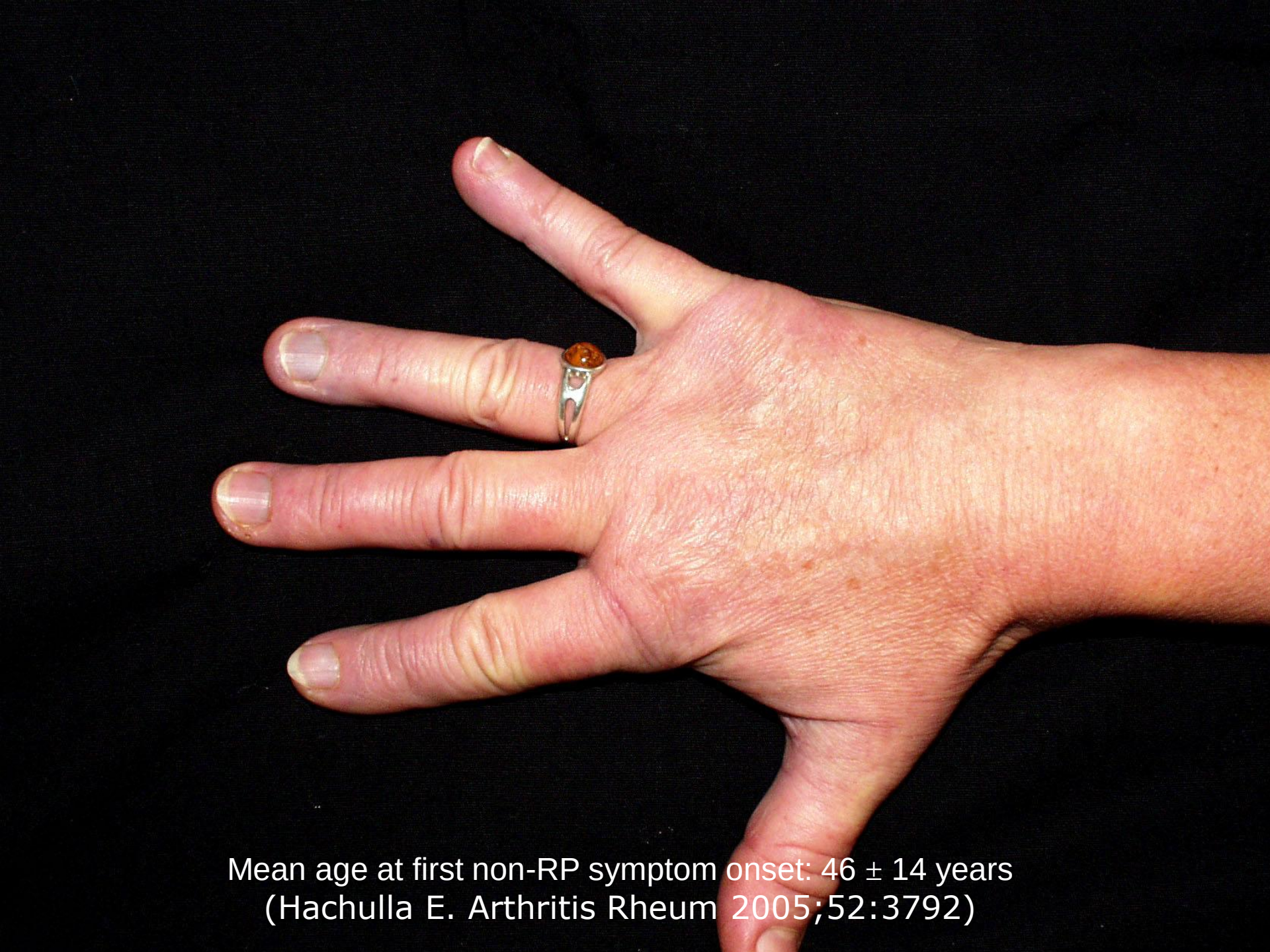
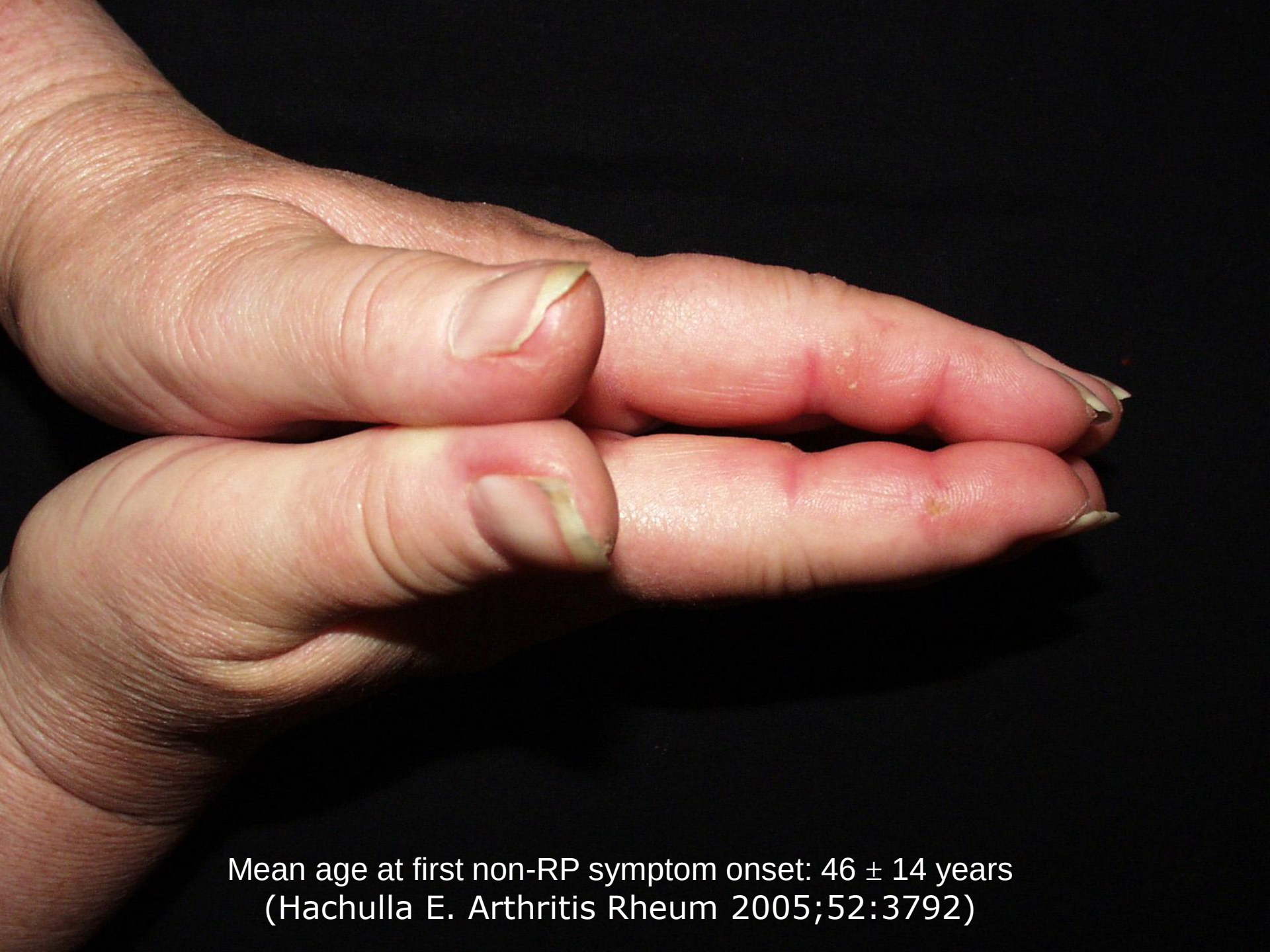




Mean age at first non-RP symptom onset: 46 ± 14 years
(Hachulla E. Arthritis Rheum 2005;52:3792)



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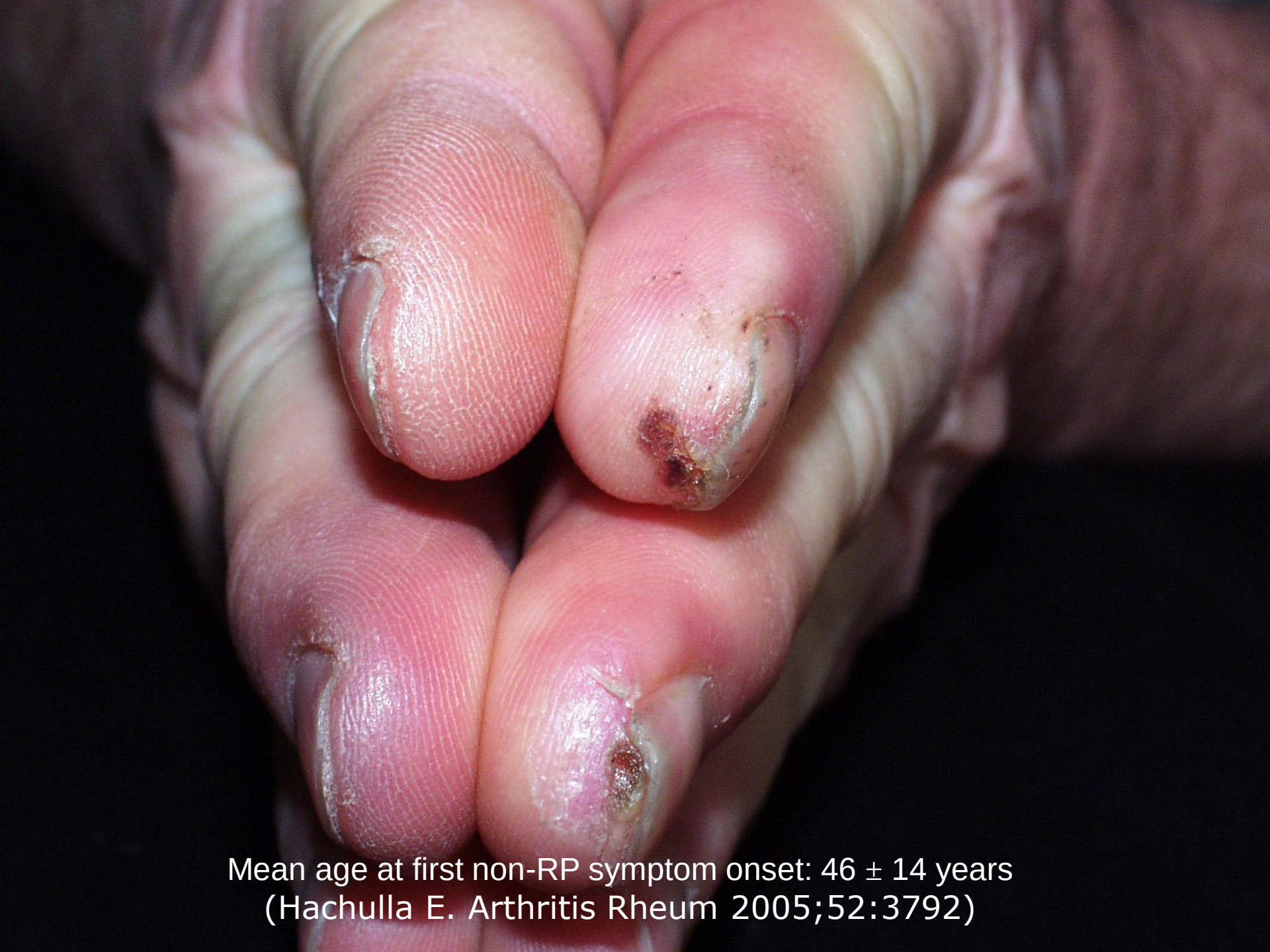

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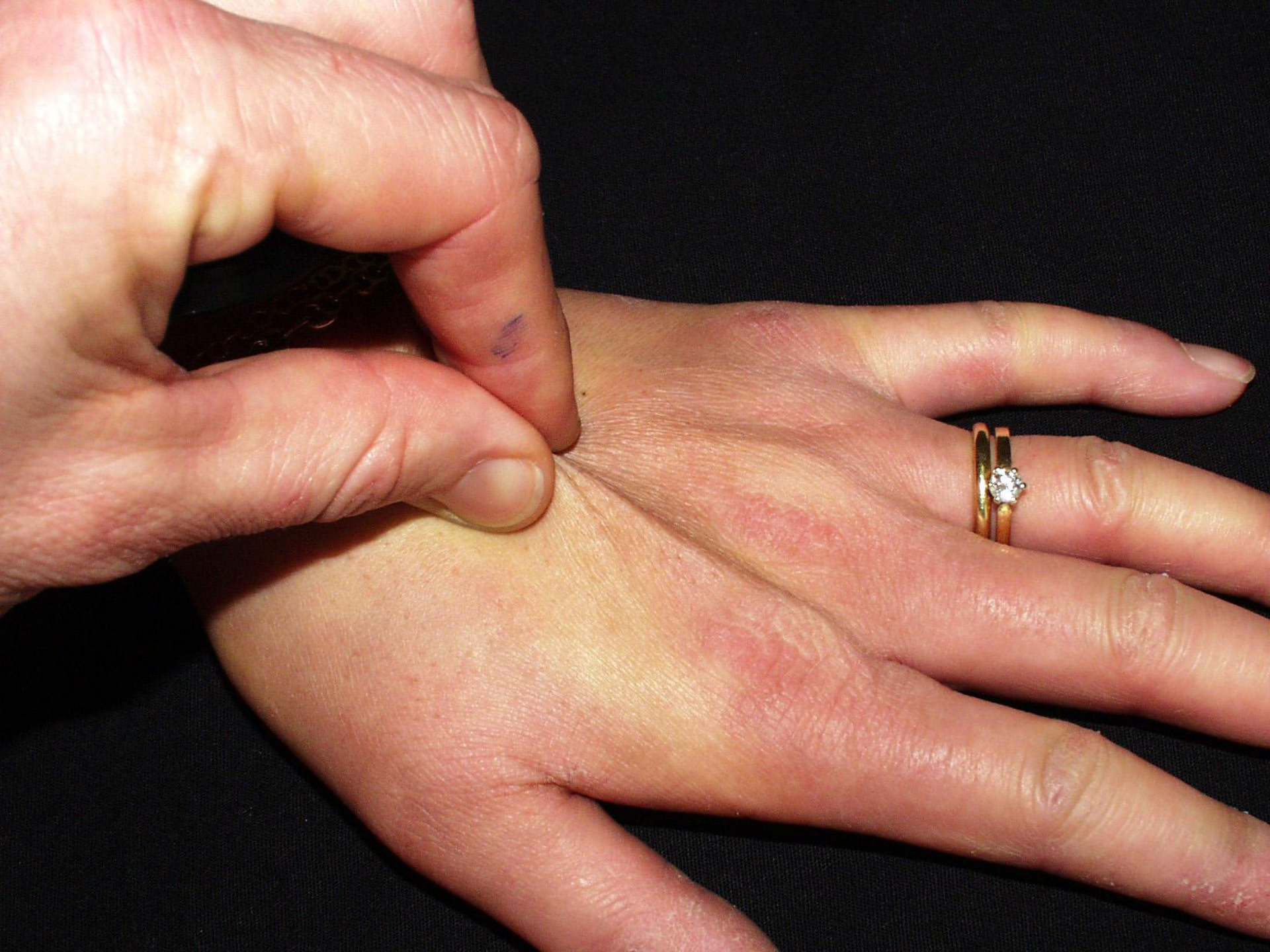


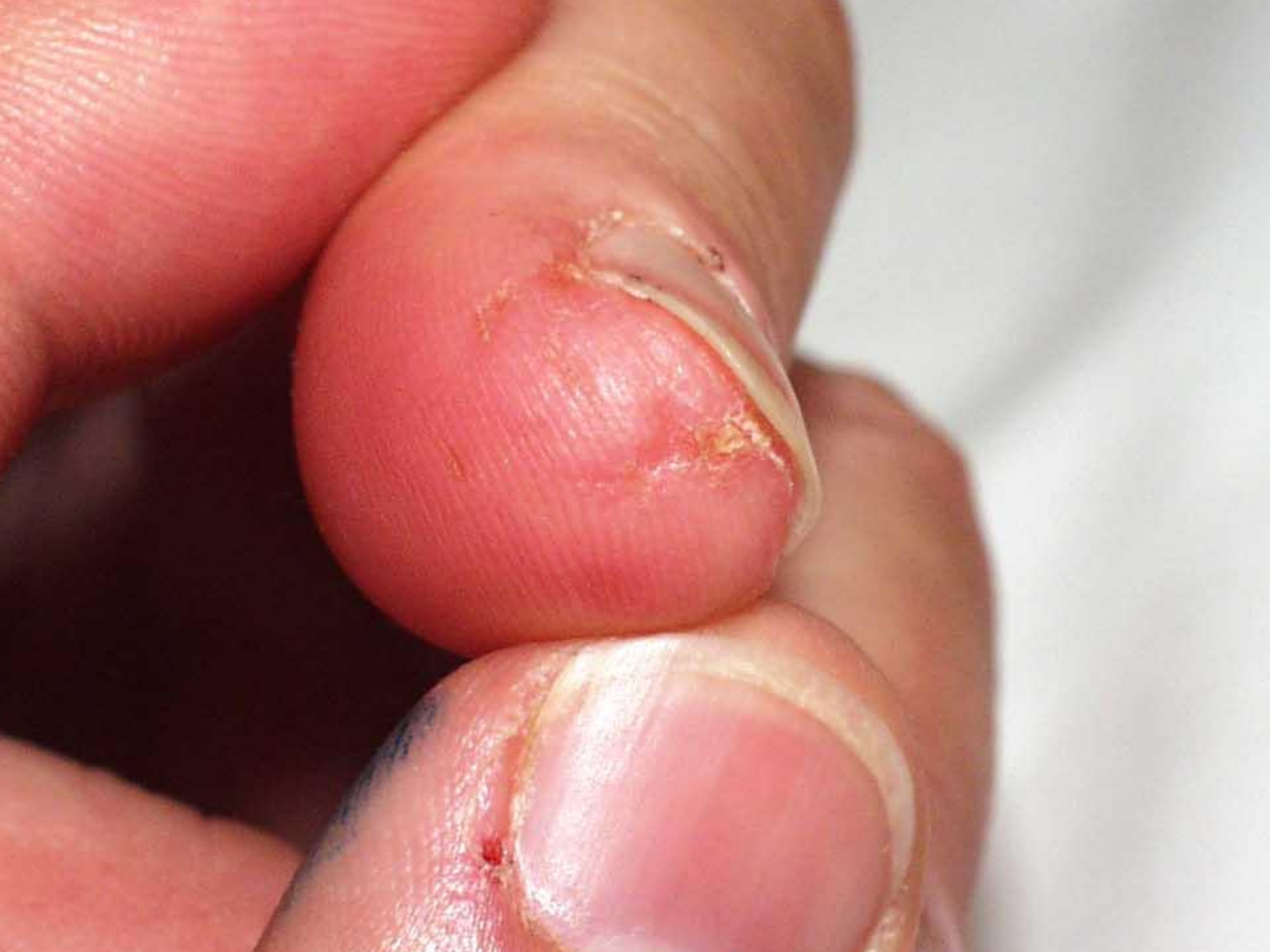
Classification criteria

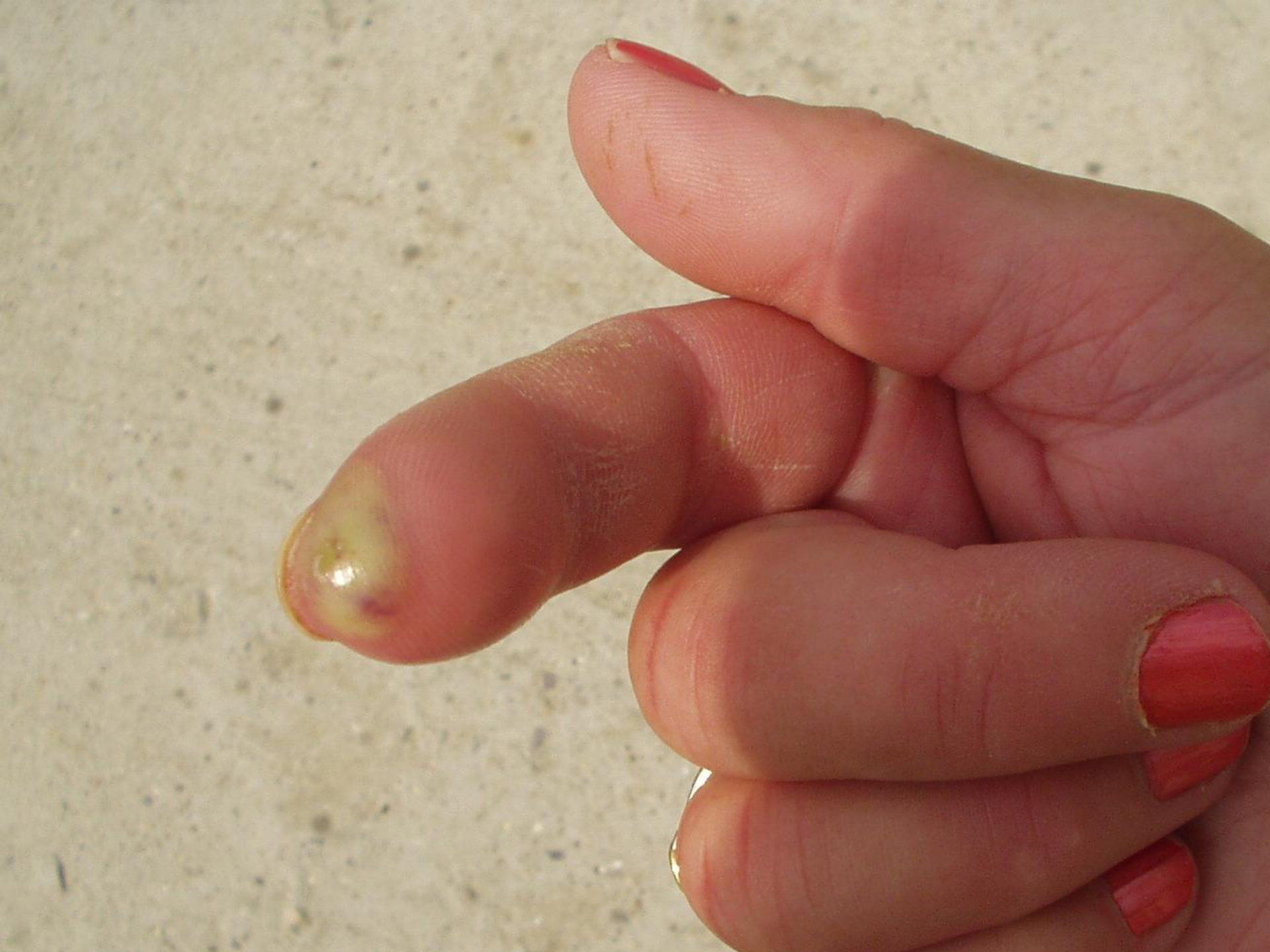
Table 1 Preliminary criteria for the classification of systemic sclerosis [9]

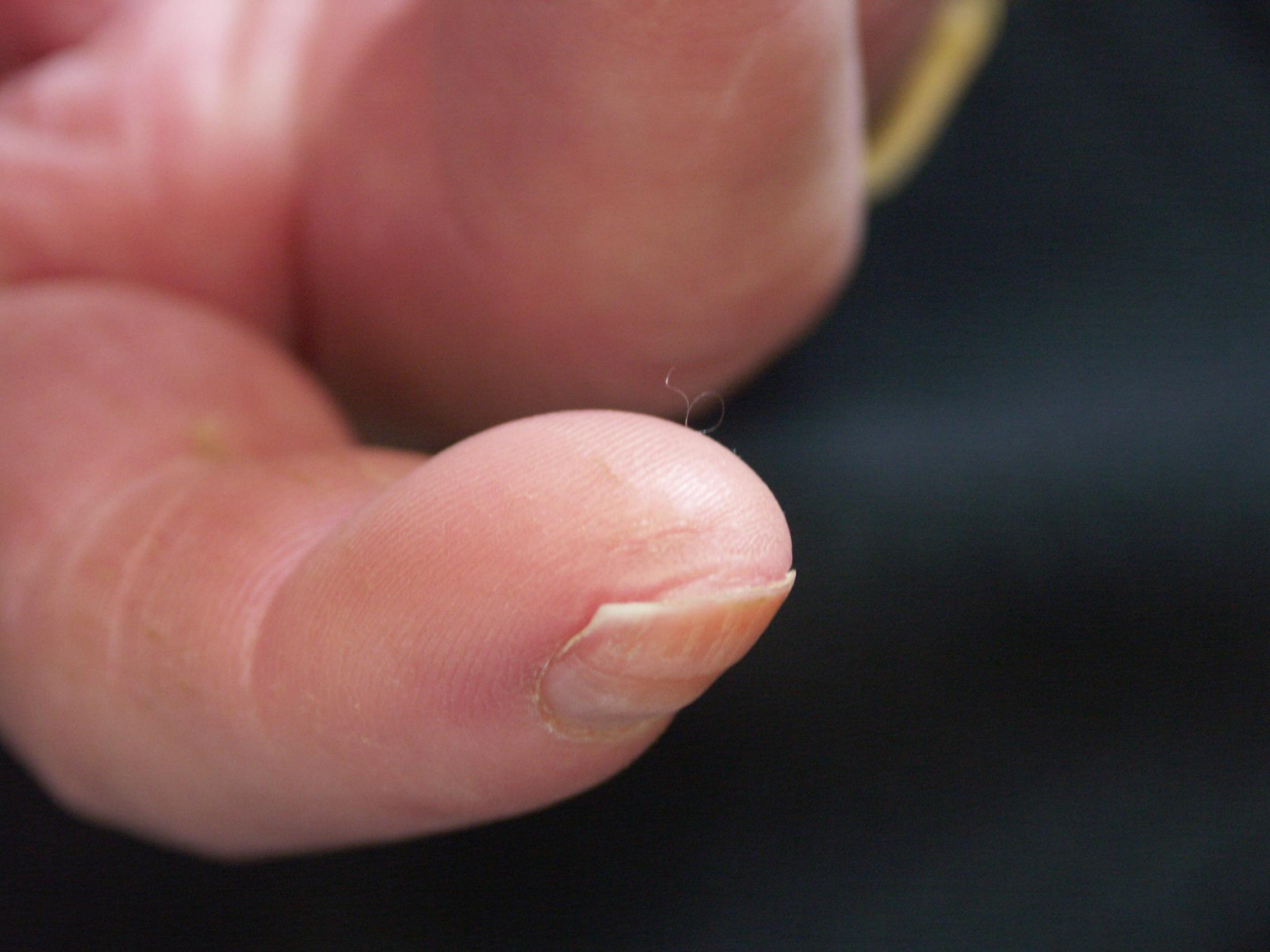
Major criterion: proximal cutaneous sclerosis (tightness, thickening, and non-pitting induration of the skin proximal to the metacarpophalangeal or metatarsophalangeal joints, affecting other parts of the extremities, face, neck, or trunk; usually bilateral, symmetrical, and almost always including sclerodactyly)
Minor criteria: sclerodactyly, digital pitting scars of fingertips or loss of substance of the distal finger pad, and bibasal pulmonary fibrosis (in the absence of proximal scleroderma)

One major criterion or two or more minor criteria were found in 97% of definite systemic sclerosis cases (sensitivity 97%) but in only 2% of the comparison patients (specificity 98%)

Arthritis Rheum 1980;23:581







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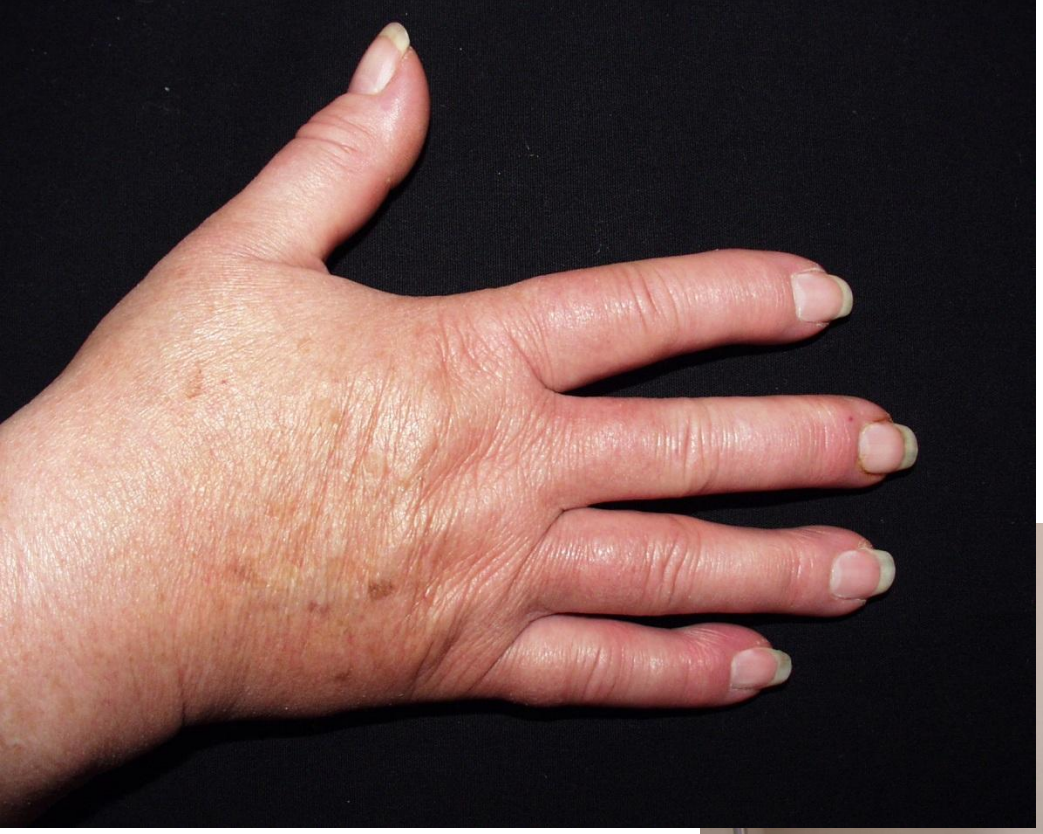
One major criterion or two or more minor criteria were found in 97% of definite systemic sclerosis cases (sensitivity 97%) but in only 2% of the comparison patients (specificity 98%)

➡ 10 to 30% of SSc patients do not fulfill the 1980 preliminary criteria!

Arthritis Rheum 1980;23:581



LeRoy EC. J Rheumatol 1988 ;15 :202

Classification criteria

Table 2 Criteria of classification of diffuse and limited cutaneous systemic sclerosis according to LeRoy et al. [13]

Diffuse cutaneous SSc (dcSSc)
Onset of Raynaud's phenomenon within 1 year of onset skin changes (puffy or hidebound)
Truncal and acral skin involvement
Presence of tendon friction rubs
Early and significant incidence of an interstitial lung disease, oliguric renal failure, diffuse gastrointestinal disease, and myocardial involvement
Absence of ACA
Nail fold capillary dilatation and capillary destruction
Antitopoisomerase antibodies (30% of patients)

LeRoy EC. J Rheumatol 1988 ;15 :202

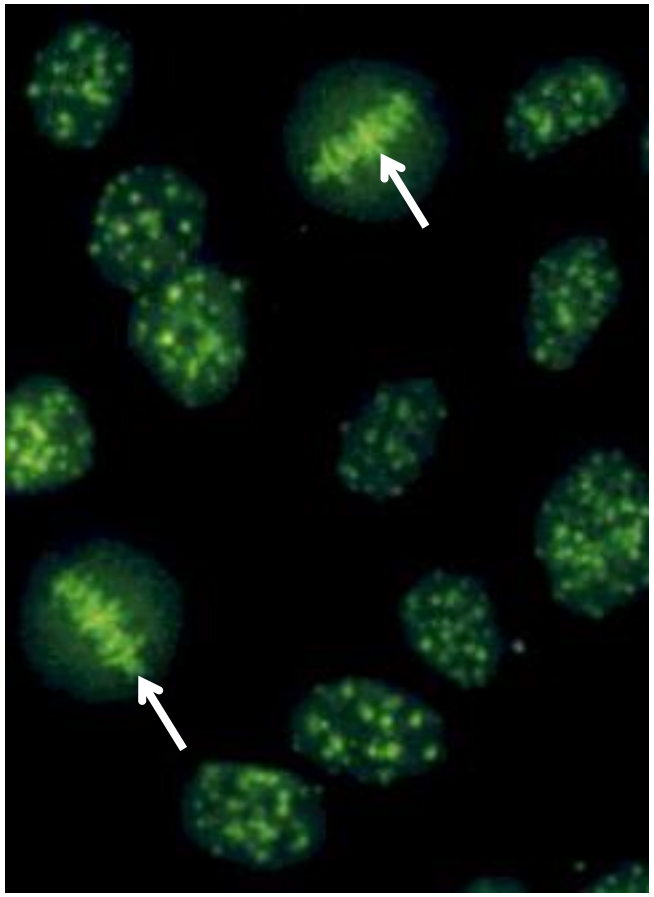
Classification criteria

Table 2 Criteria of classification of diffuse and limited cutaneous systemic sclerosis according to LeRoy et al. [13]

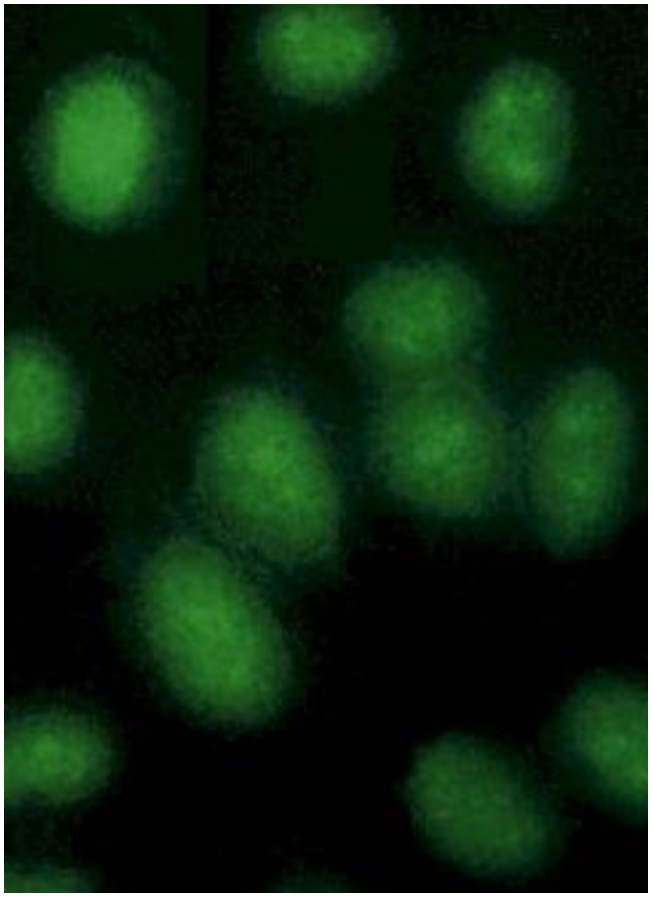
Limited cutaneous SSc (lcSSc)
Raynaud's phenomenon for years (occasionally decades)
Skin involvement limited to hands, face, feet, and forearms (acral) or absent
A significant late incidence of pulmonary hypertension, with or without interstitial lung disease, trigeminal neuralgia, skin calcifications, and telangiectasia
A high incidence of ACA (70–80%)

LeRoy EC. J Rheumatol 1988 ;15 :202

A



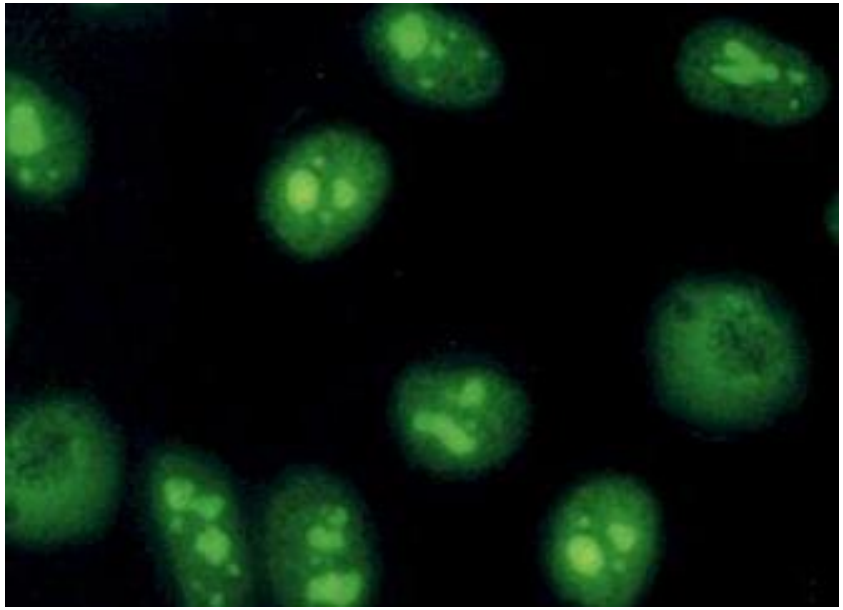
B



A] Ac anticentromères : L'aspect en IFI est très évocateur avec une fluorescence d'une trentaine de grains, réguliers, sur les noyaux de toutes les cellules à l'interphase. Ces grains s'alignent le long du fuseau de mitose en phase mitotique (plaque équatoriale, flèches). Cet examen suffit à l'identification de cette spécificité d'auto-anticorps.

B] Ac antiScl 70 : La fluorescence est homogène dite en « verre dépoli » pour l'ensemble du noyau. Un marquage du nucléole peut être observé. Les cellules en mitose sont plus fluorescentes.

C



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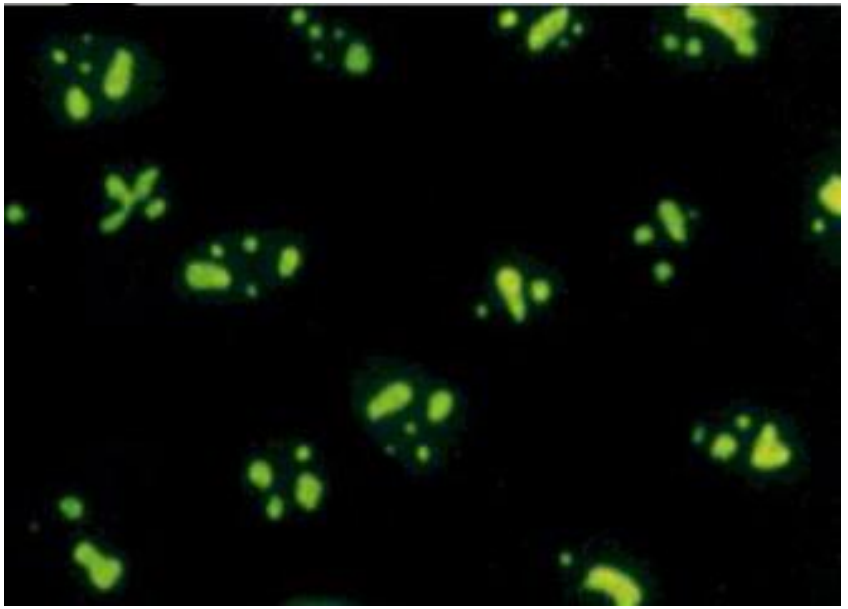
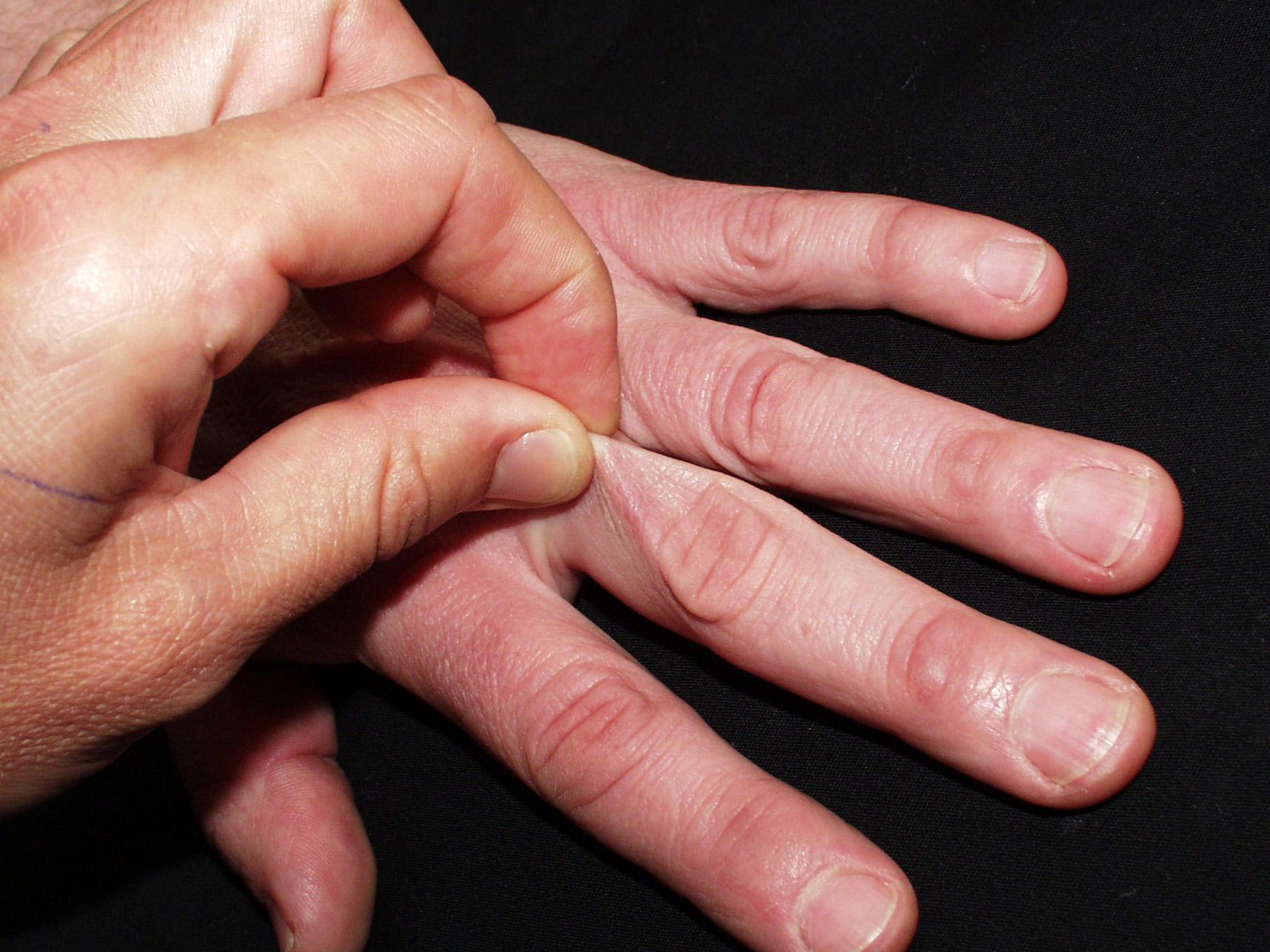
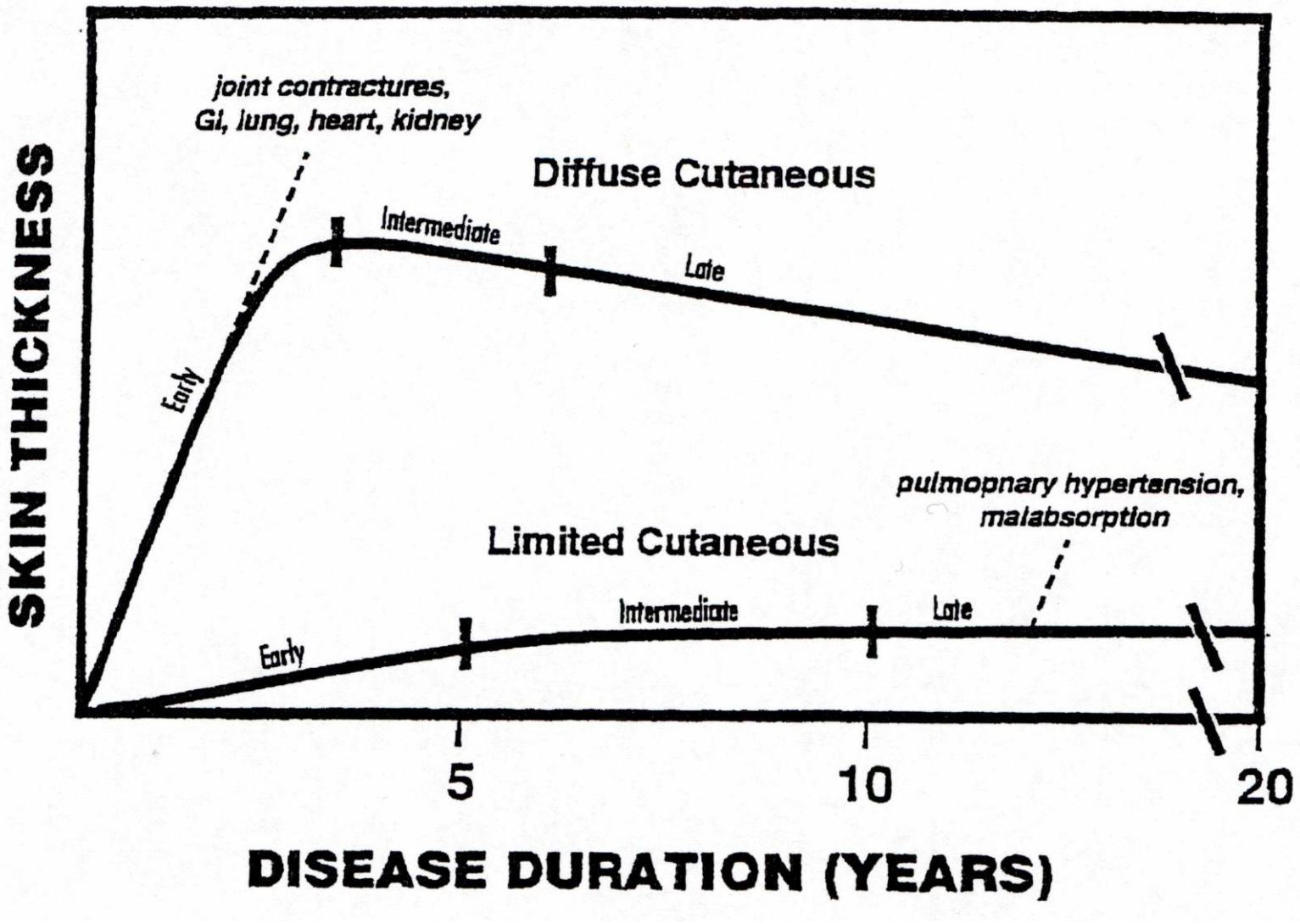


C et D] Ac antiPmScl et antiU3 RNP (antifibrillarine) : l'IFI montre un marquage nucléolaire.



Diffuse versus limited scleroderma

natural history



Diffuse versus limited scleroderma

	All	dcSSc	lcSSc	p
Patients	599	165 (27.5%)	434 (72.5%)	
Male	16%	22%	14%	0.01
Age (years)	55 ± 13	53 ± 13	55 ± 13	0.10
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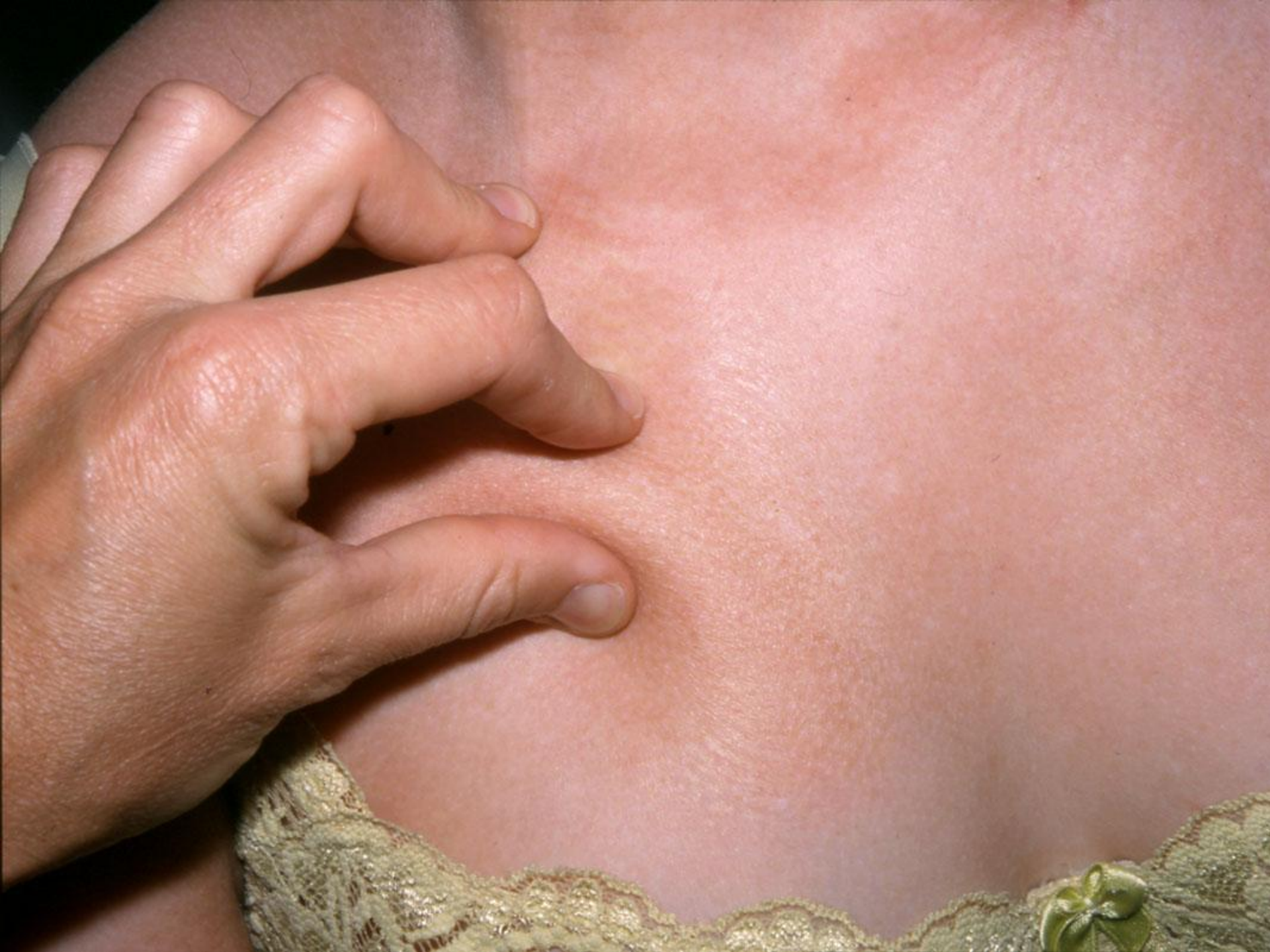
Hachulla E. Arthritis Rheum 2005;52:3792

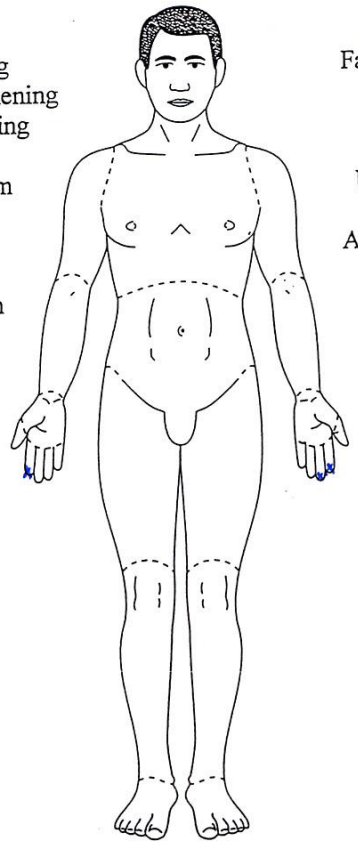


Annexe E - No 1203 Karin D.

Name: **Datum:**

MODIFIED RODNAN SKIN SCORE

0 Uninvolved
1 Mild thickening
2 Moderate thickening
3 Severe thickening



Face [2]

Upper arm [0]

Anterior chest [0]

Forearm [2]

Hand [2]

Fingers [3]

Thigh [0]

Leg [0]

Foot [0]

Upper arm [0]

Abdomen [0]

Forearm [2]

Hand [2]

Fingers [3]

Thigh [0]

Leg [0]

Foot [0]

Total Skin Score 16

Diffuse versus limited scleroderma
survival

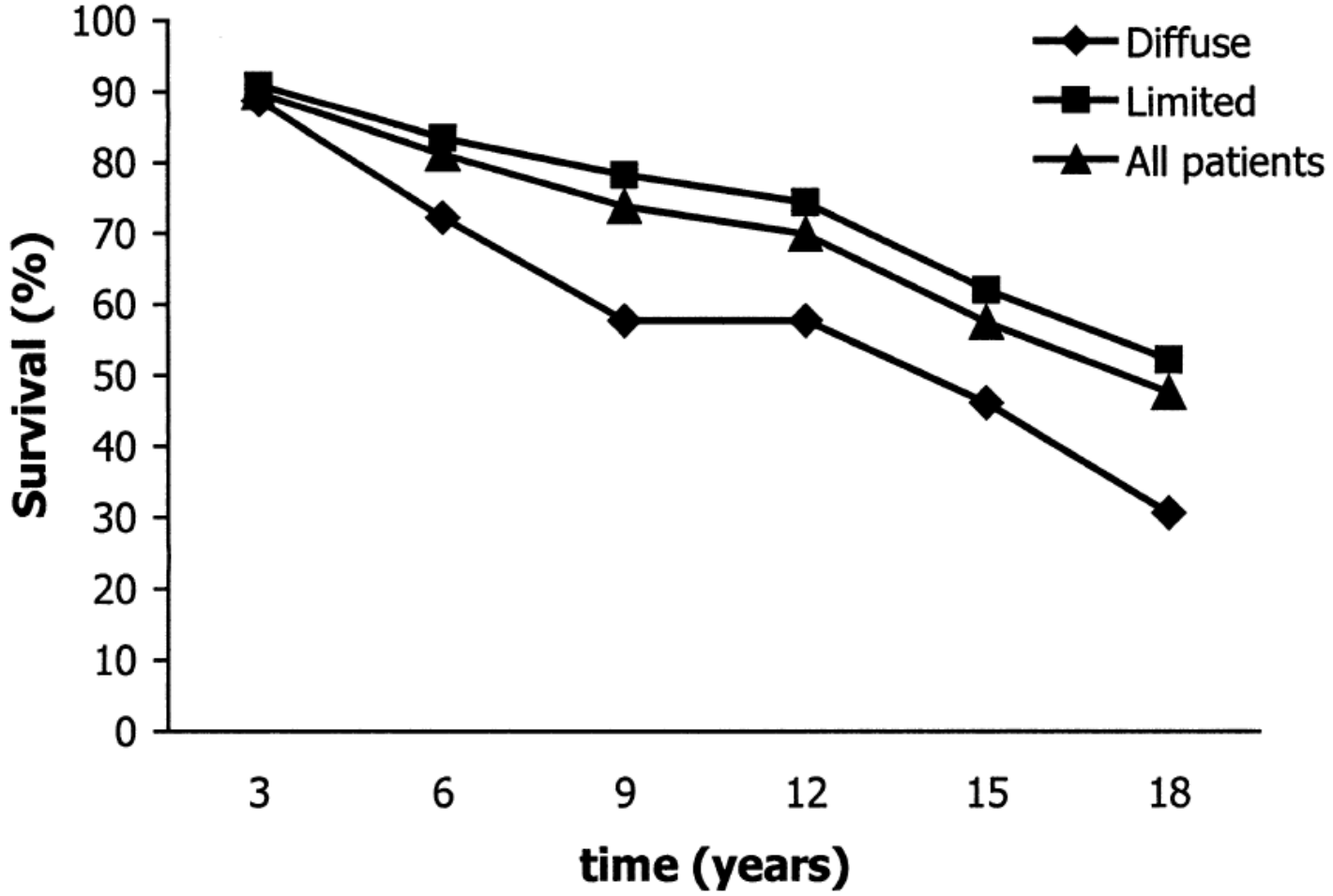
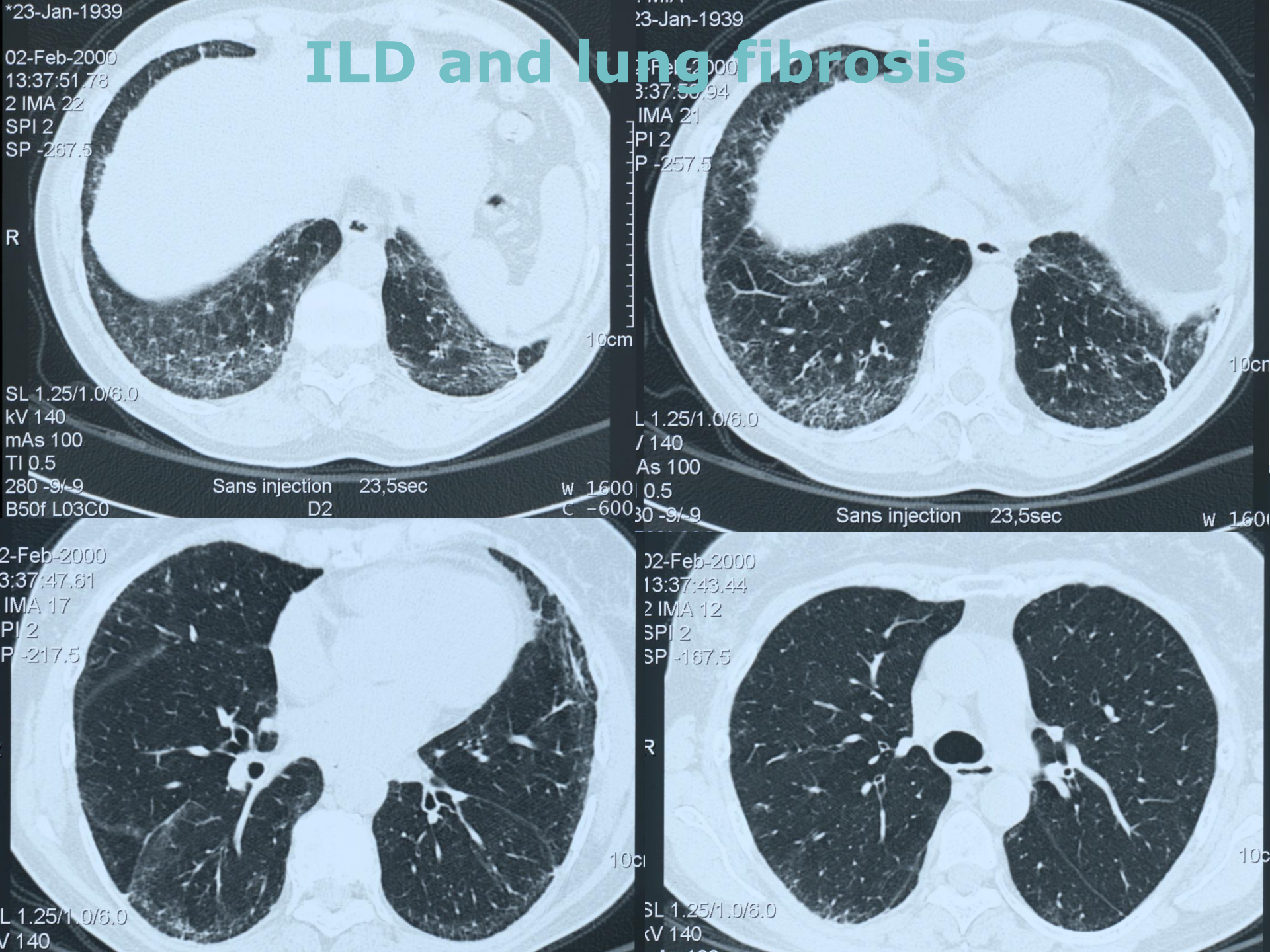


Figure 4 Survival in years among SSc patients, for total cases, as well as for diffuse and limited subtypes.

Alamanos Y. Semin Arthritis Rheum 2005; 34: 714

ILD and lung fibrosis



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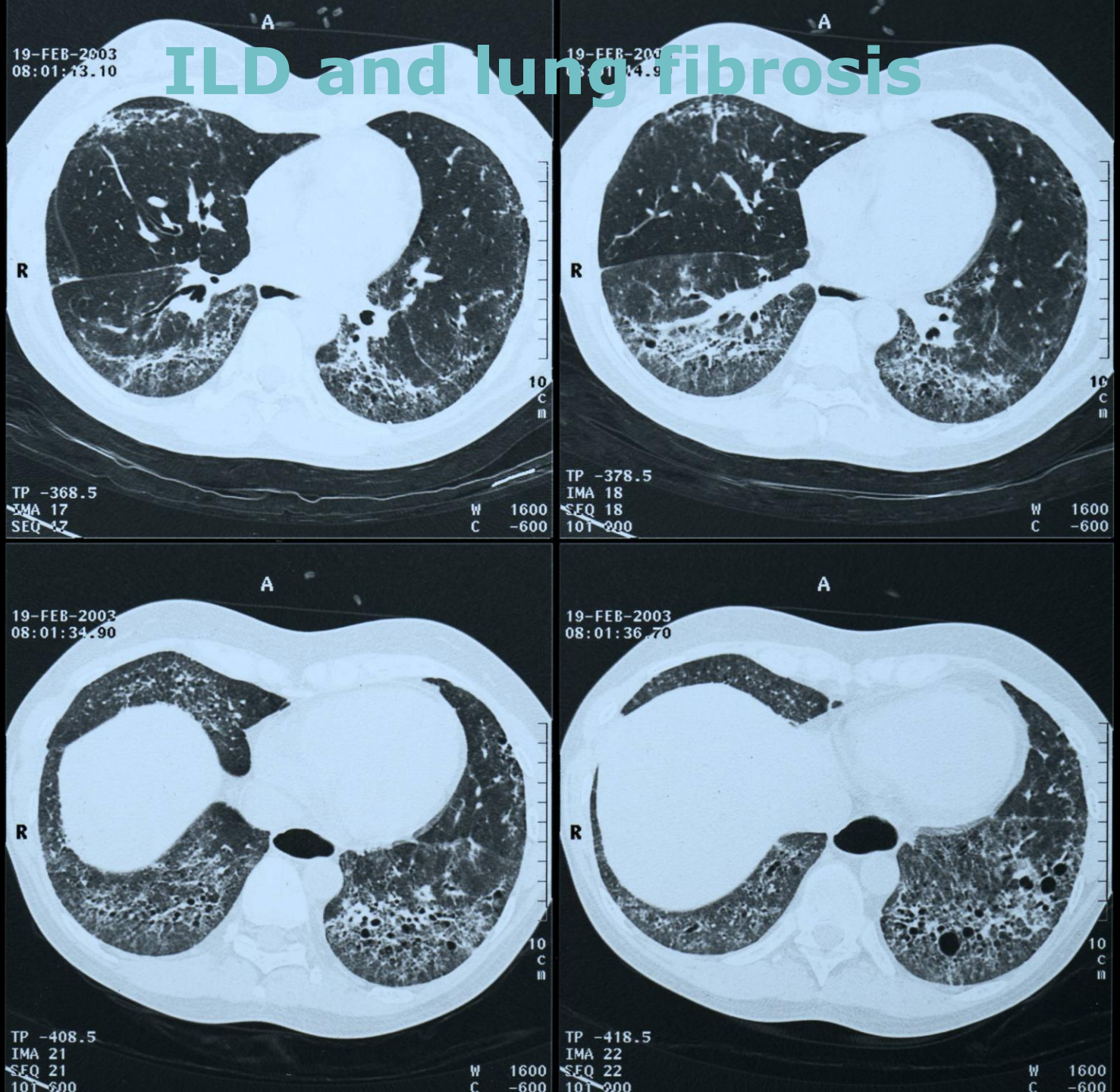
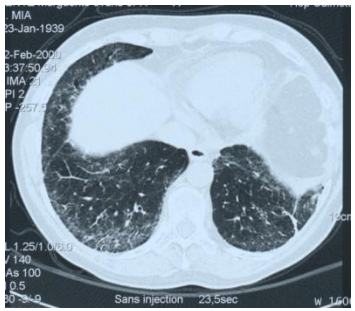
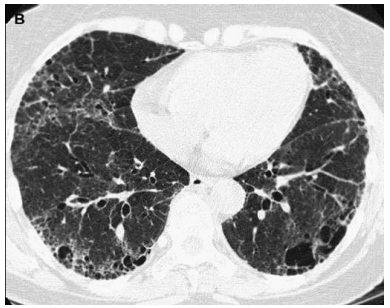


ILD extent on HRCT scan
Interest in clinical practice





B

HRCT extent

< 20%

Indeterminate

> 20%

FVC ≥ 70%

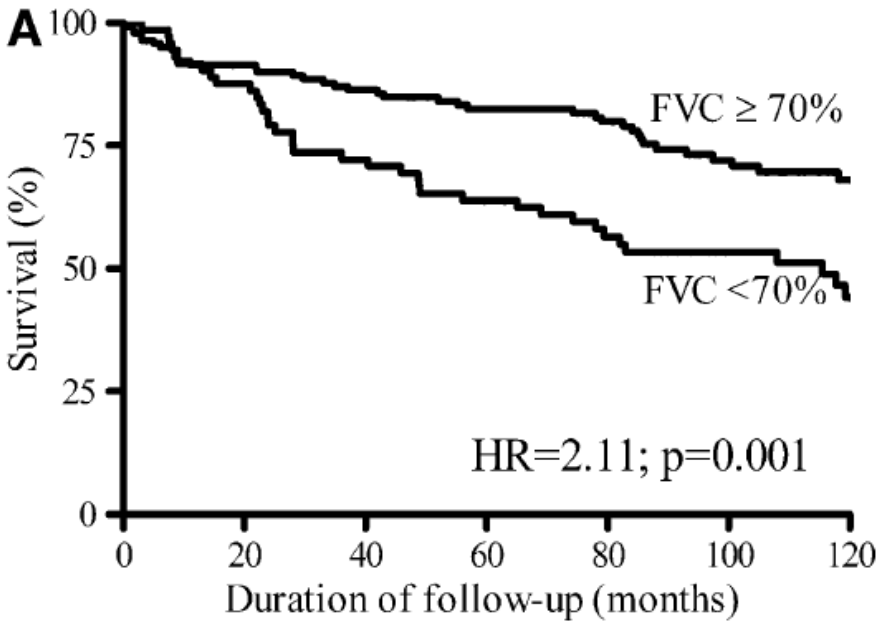
FVC < 70%

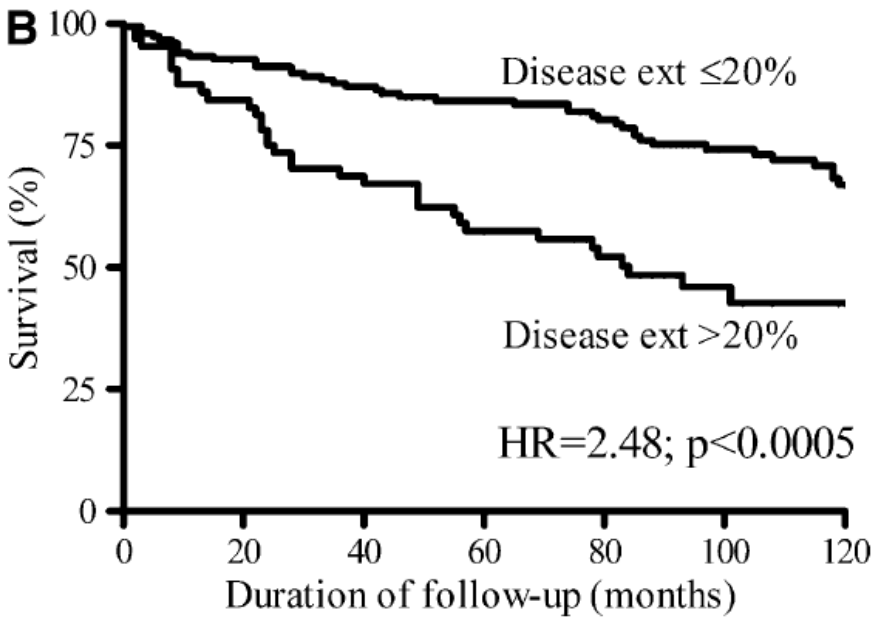
Limited Disease

Extensive Disease

Goh NS. Am J Respir Crit Care Med 2008; 177: 1248

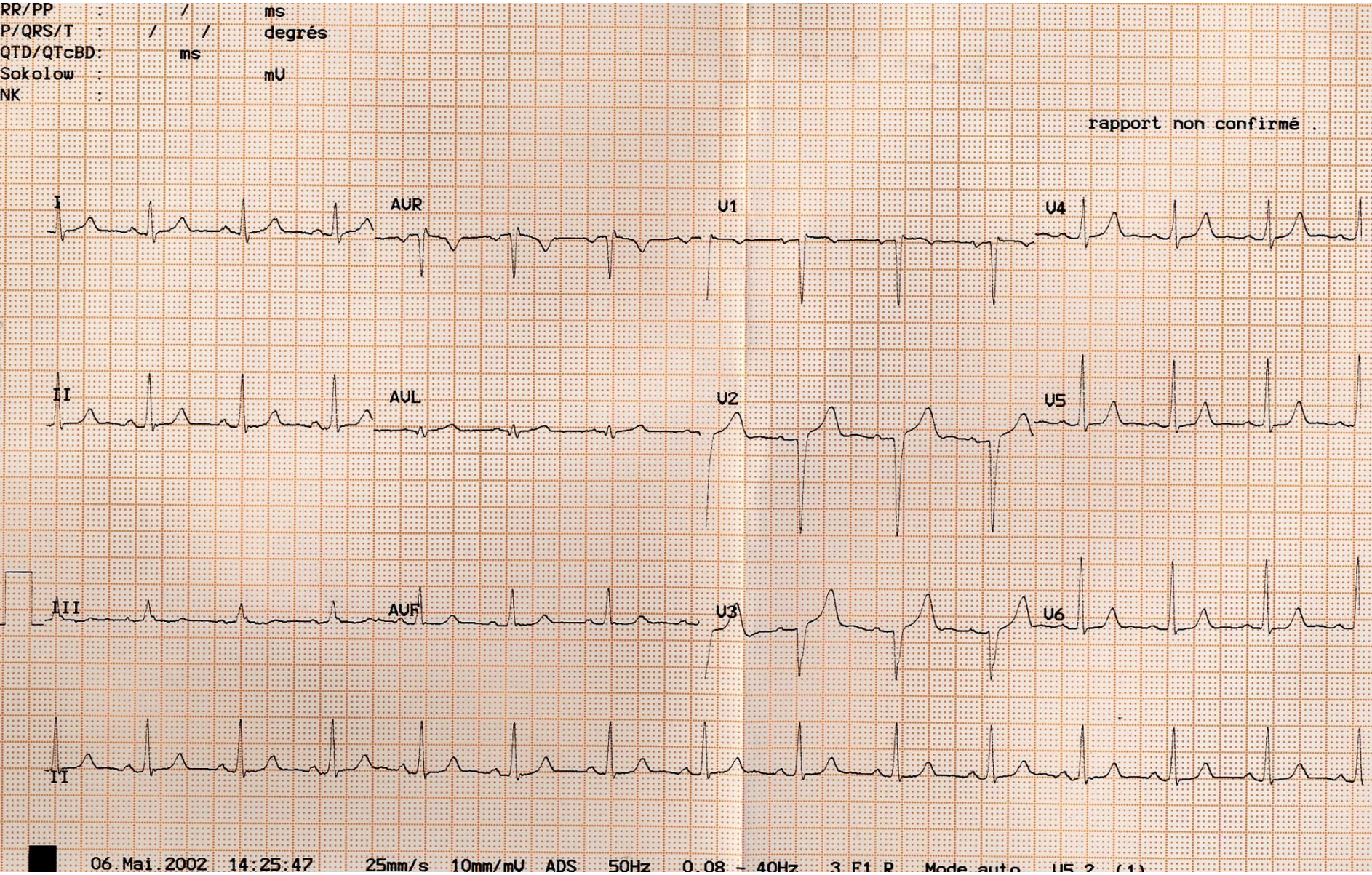
ILD extent on HRCT scan
Interest in clinical practice





Goh NS. Am J Respir Crit Care Med 2008; 177: 1248

Heart involvement



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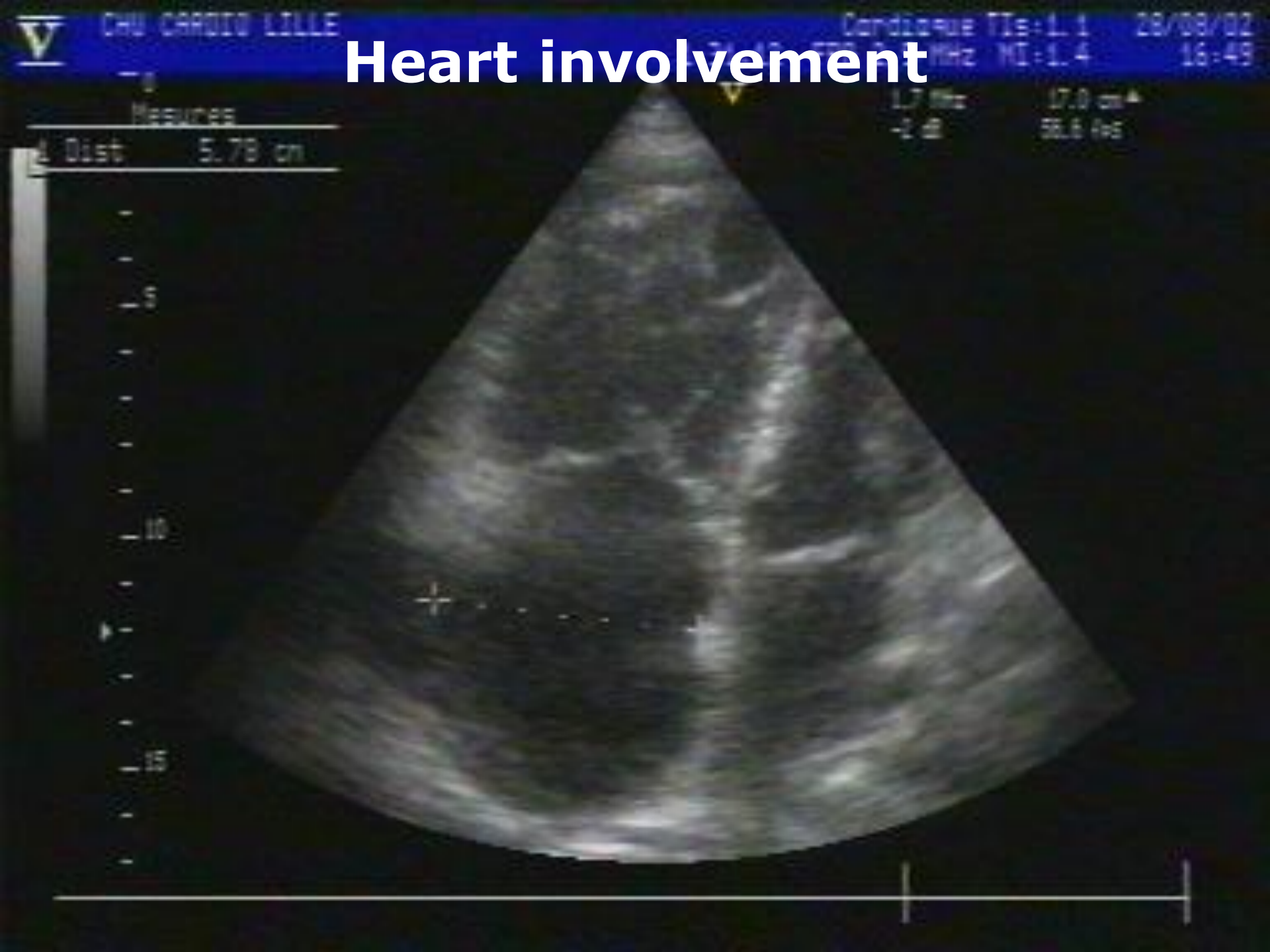

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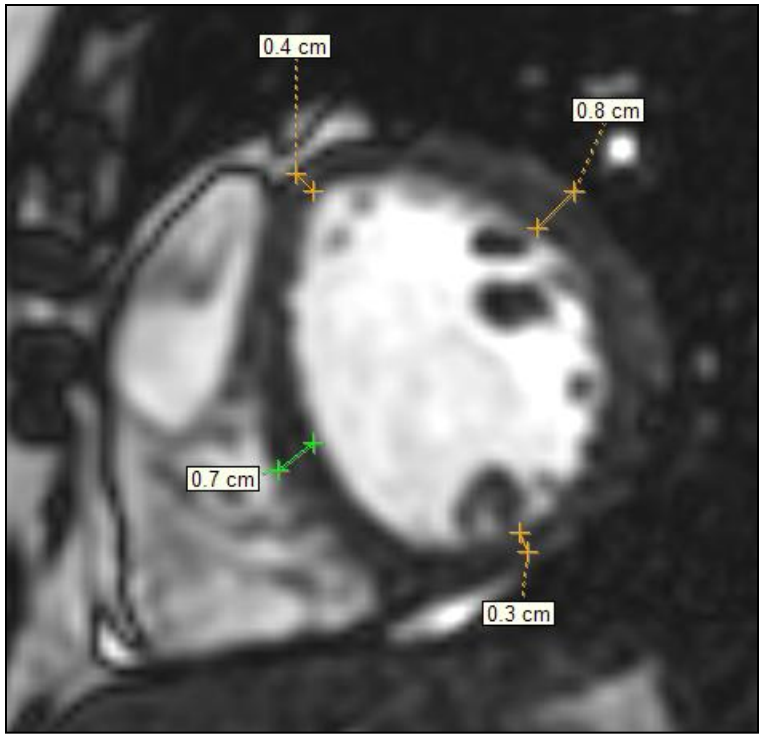
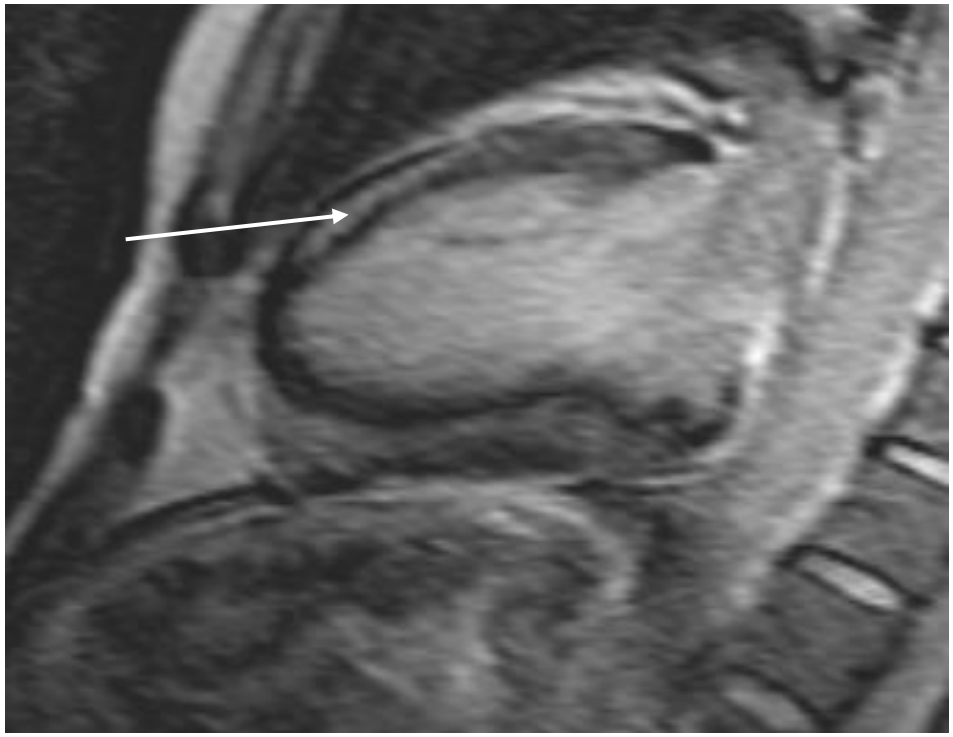


Localized thinning of LV in 29%

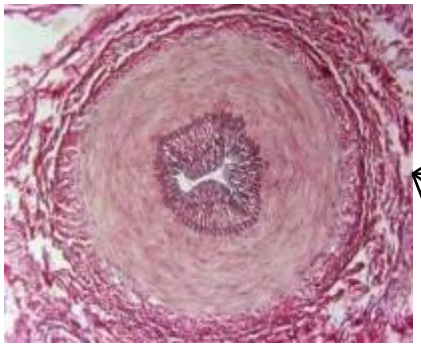


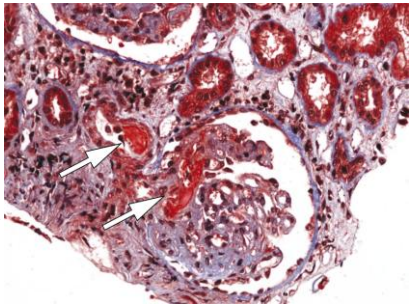
T2 delayed contrast enhancement in 12%

Hachulla AL. Ann Rheum Dis 2009; 68: 1878

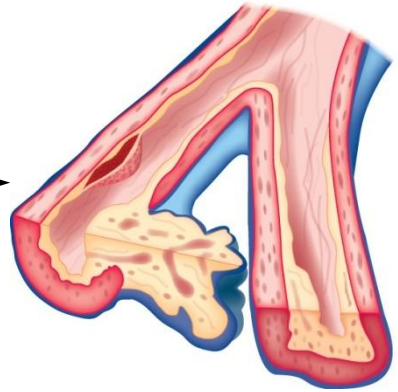
Microangiopathy

- **Intimal and medial hyperplasia & proliferation**
- **Adventitial fibrosis**
- **Compromised lumen**

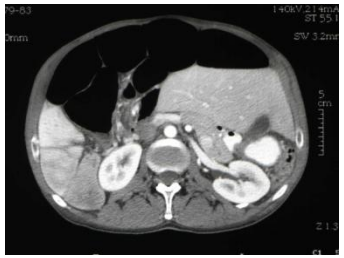




Scleroderma renal crisis[1]



Pulmonary arterial hypertension



Gut involvement

Digital arteriopathy

1. Image courtesy of Luc Mouthon

Scleroderma renal crisis

Table 1 Renal crisis classification

In the presence of limited or diffuse cutaneous systemic sclerosis:

1. A new onset of blood pressure >150/85 mmHg obtained at least twice over a 24-h period. This blood pressure is chosen because it is that defined by the New York Heart Association as significant hypertension.
2. A documented decrease in the renal function as defined by a decrement of at least 30% in the calculated glomerular filtration rate (eGFR). When possible, a repeat serum creatinine concentration and recalculation of the eGFR should be obtained to corroborate the initial results.

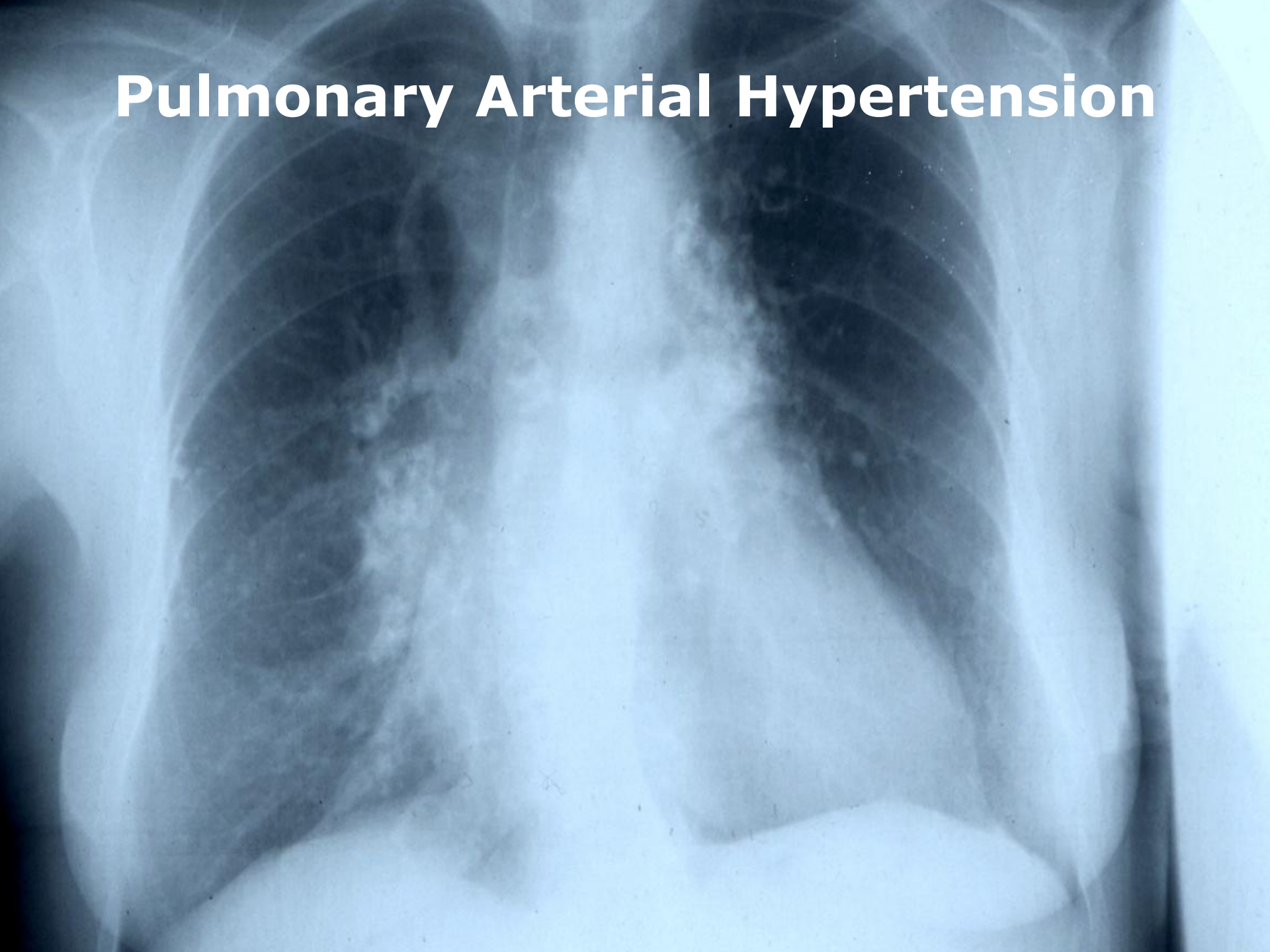
To corroborate further the occurrence of acute renal crisis, it would be desirable to have any of the following, if available:

- Microangiopathic haemolytic anaemia on blood smear
- Retinopathy typical of acute hypertensive crisis
- New onset of urinary RBCs (excluding other causes)
- Flash pulmonary oedema
- Oliguria or anuria
- Renal biopsy showing characteristic changes

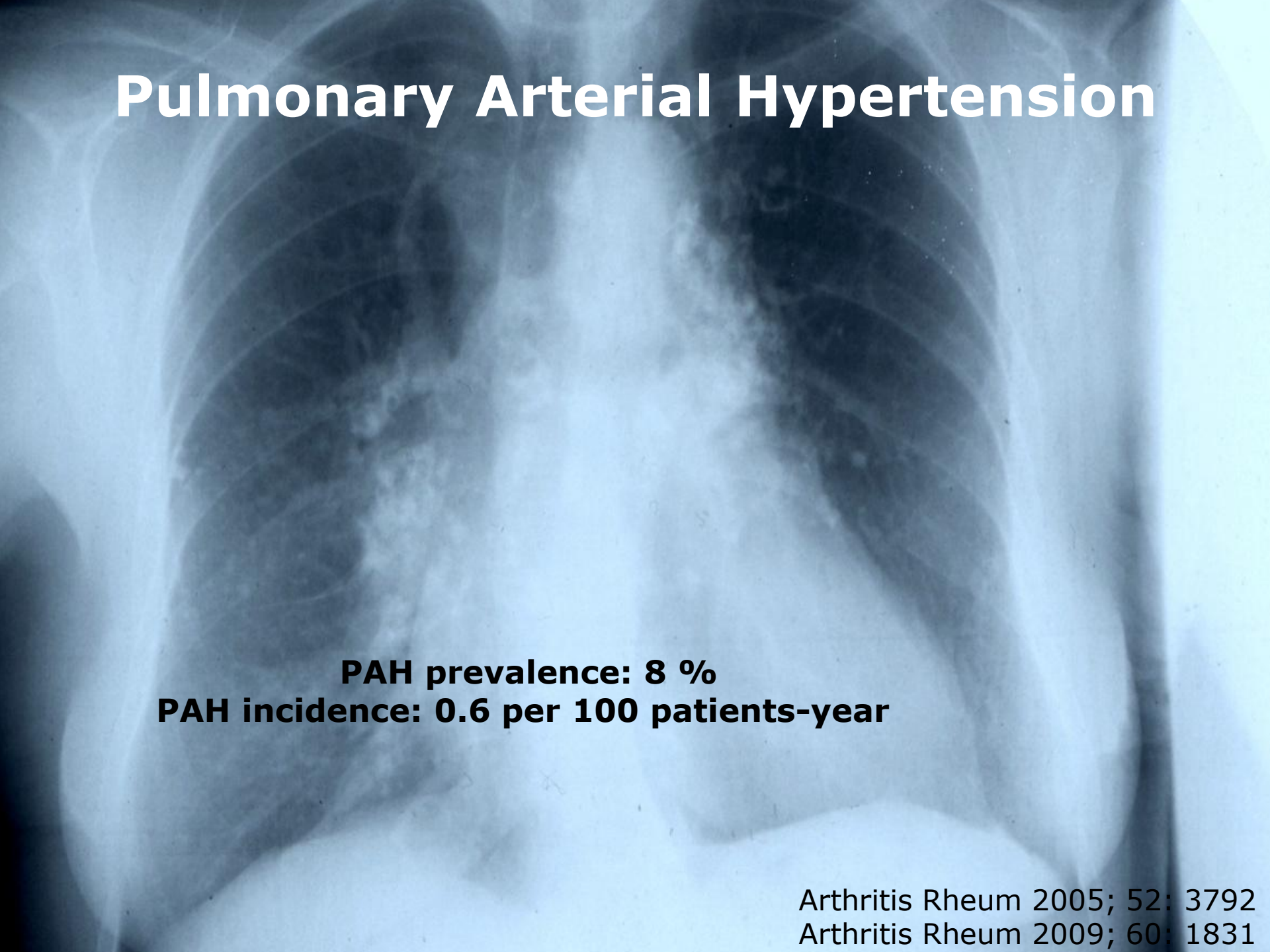
Renal biopsy showing an alternative cause excludes the case from classification as SRC

Penn H Q J Med 2007; 100: 485

Pulmonary Arterial Hypertension



Pulmonary Arterial Hypertension

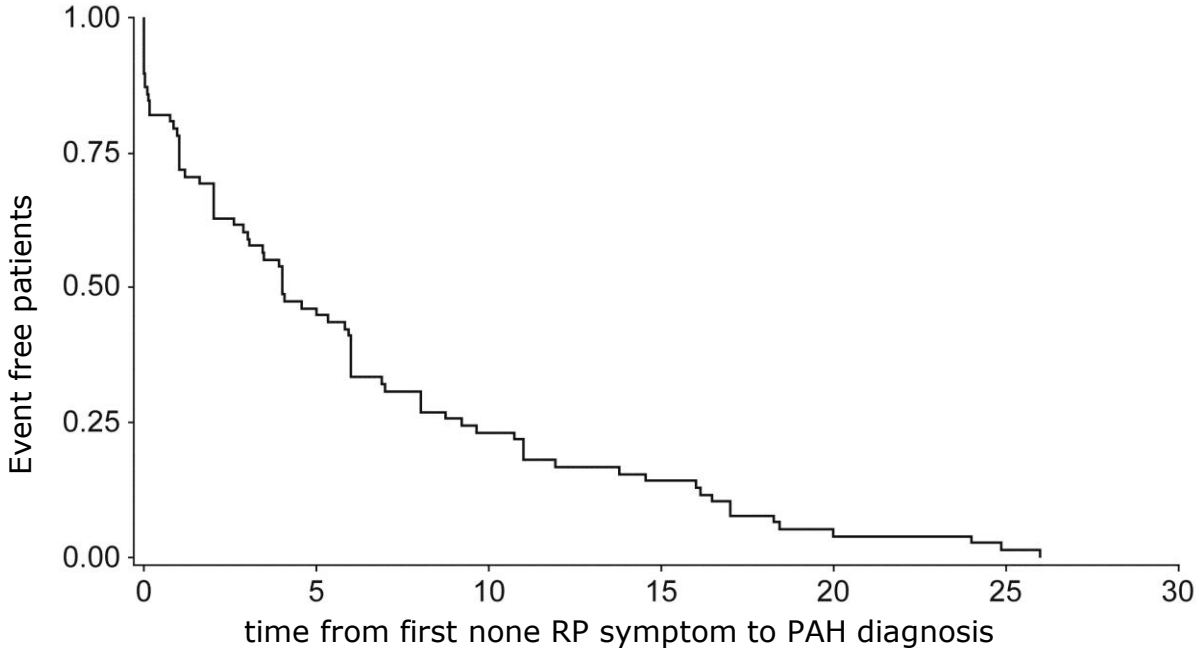


PAH prevalence: 8 %
PAH incidence: 0.6 per 100 patients-year

Arthritis Rheum 2005; 52: 3792
Arthritis Rheum 2009; 60: 1831

Time between SSc diagnosis and PAH diagnosis

n=78

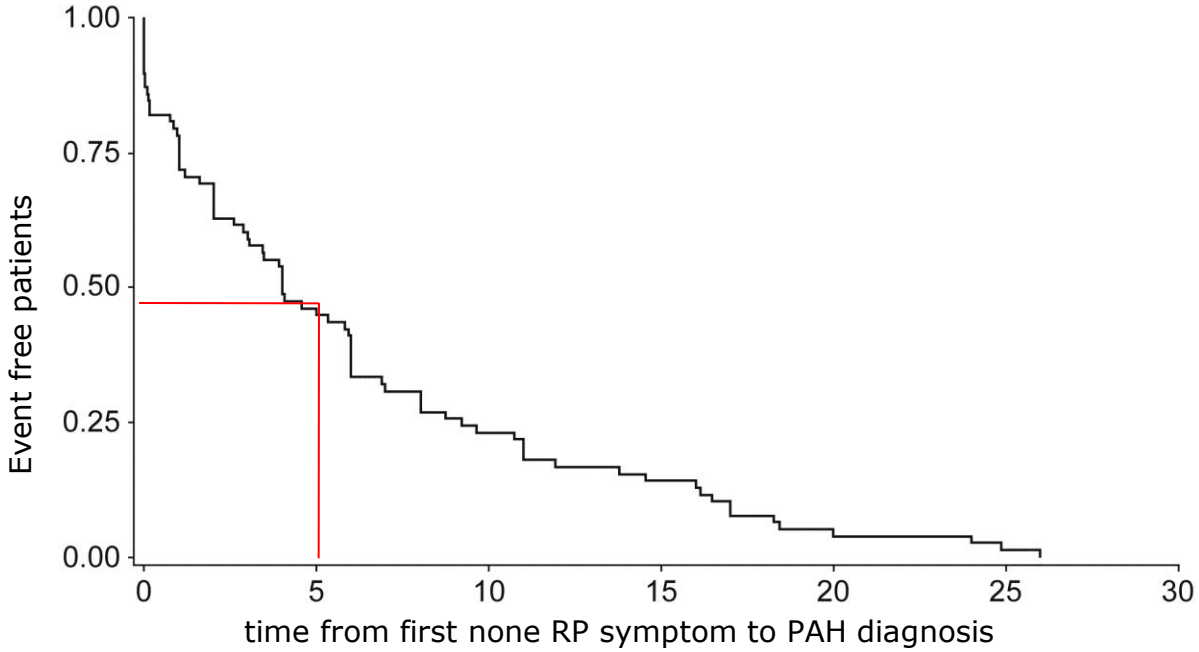


Time (years)	0	2.5	5	7.5	10	12.5	15	17.5	20	22.5	25	27.5
N at risk	78	49	36	24	18	13	11	6	4	3	1	0
Events	-	29	13	12	6	5	2	5	2	1	2	1

Hachulla E. Chest 2009; 136: 1211

Time between SSc diagnosis and PAH diagnosis

n=78



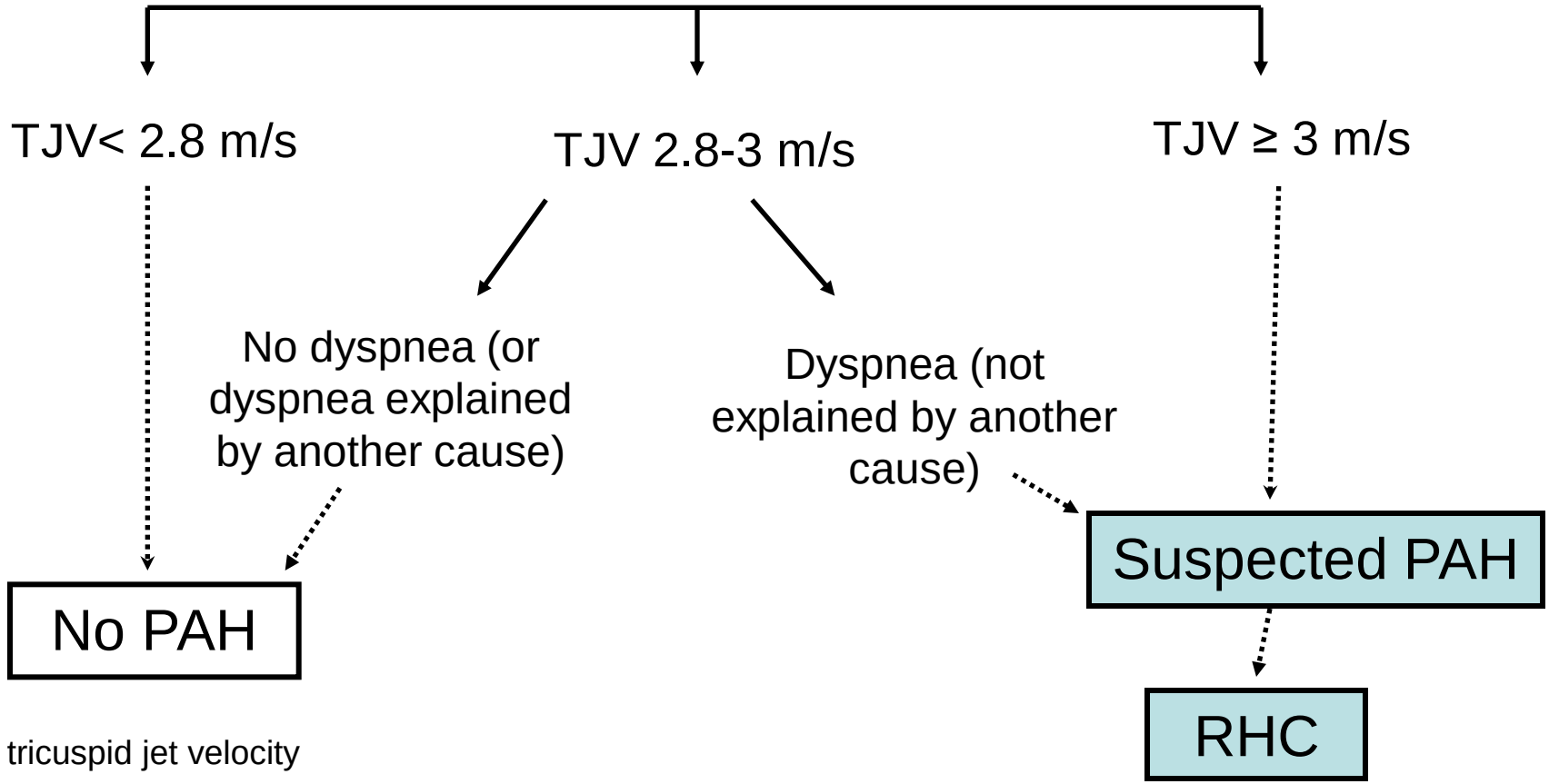
Time (years)	0	2.5	5	7.5	10	12.5	15	17.5	20	22.5	25	27.5
N at risk	78	49	36	24	18	13	11	6	4	3	1	0
Events	-	29	13	12	6	5	2	5	2	1	2	1

→ 55.1% during the 5 first years
→ 22% dSSc and 78% lSSc

Hachulla E. Chest 2009; 136: 1211

Doppler echocardiography = PAH screening tool

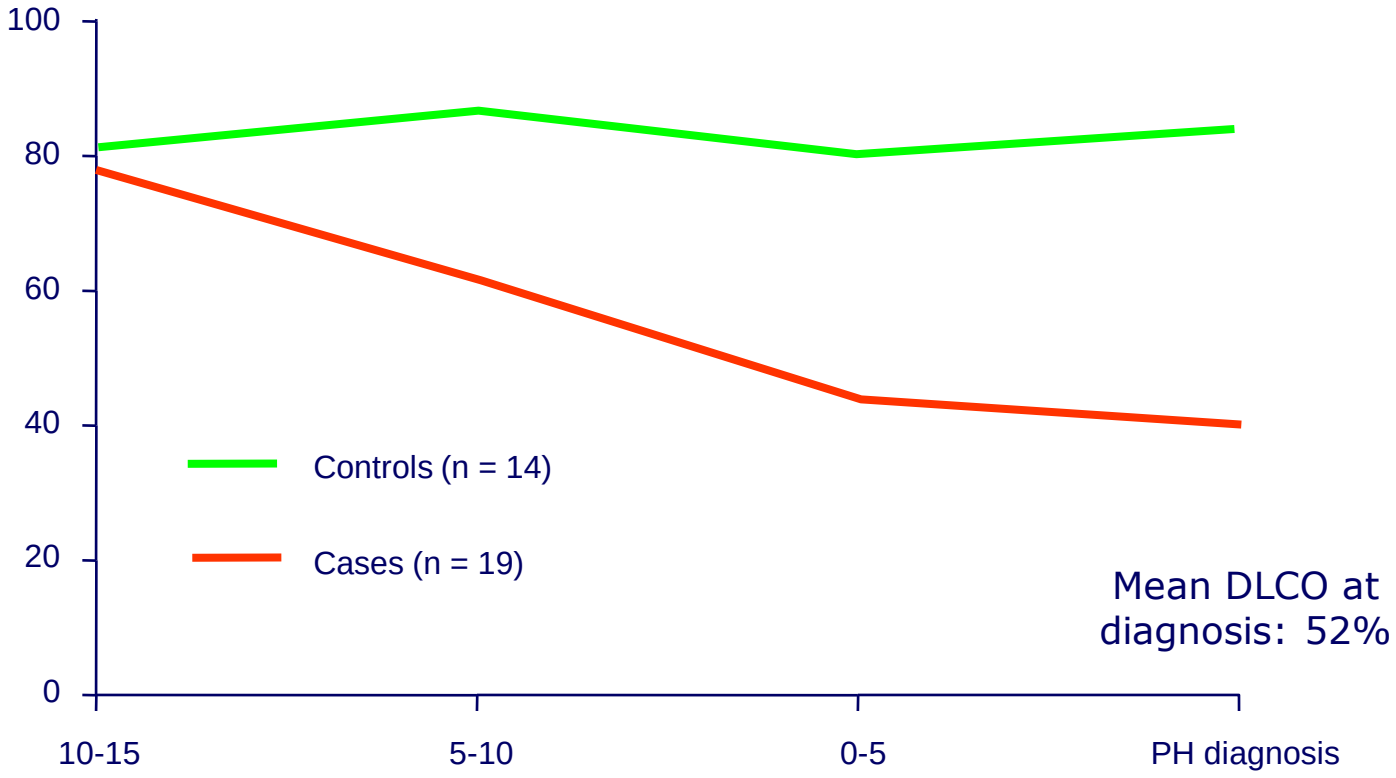
ItinerAIR study



TJV= tricuspid jet velocity

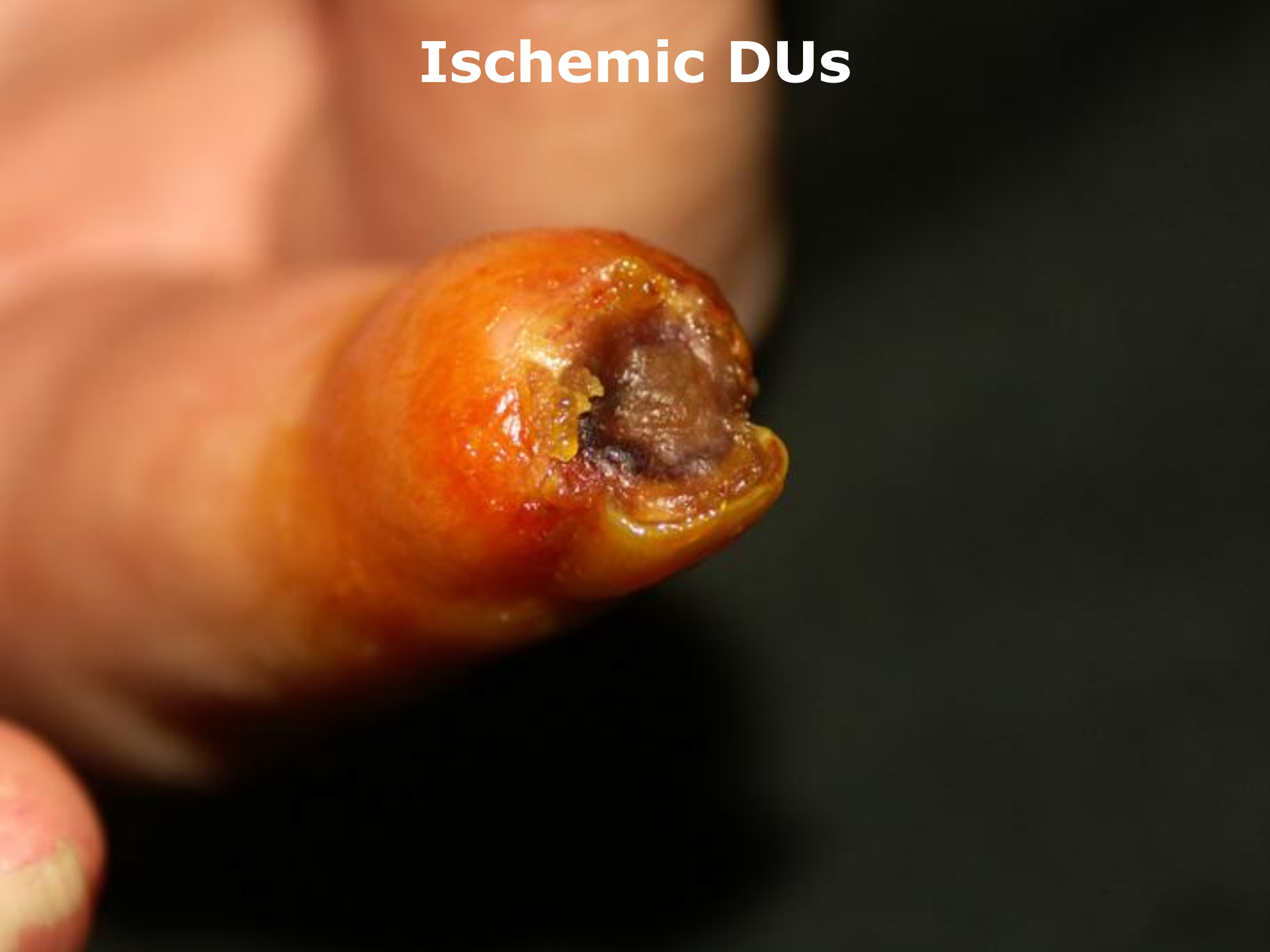
Hachulla E. Arthritis Rheum 2009; 60: 1831

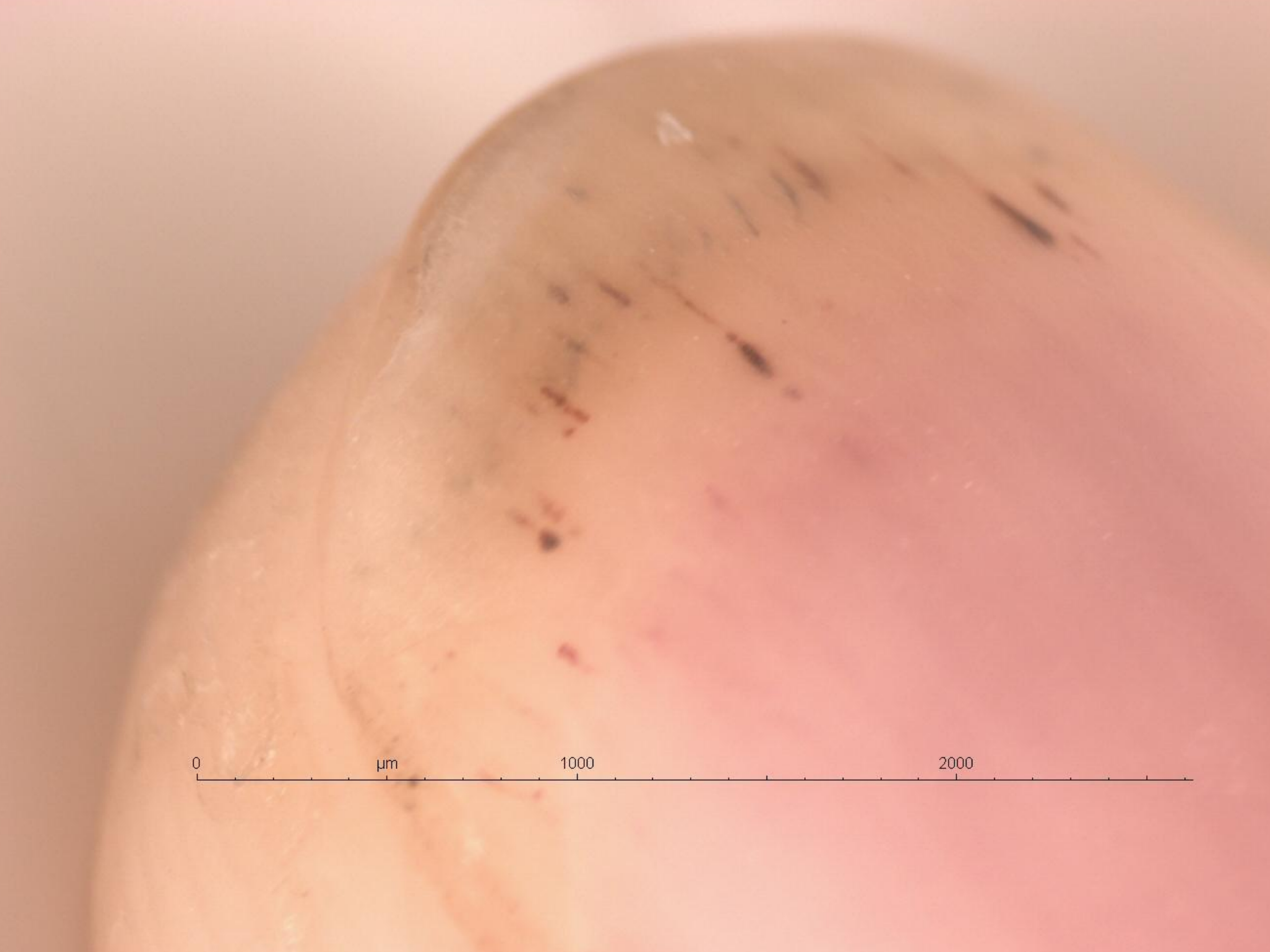
DLCO: a PAH predictive factor ?

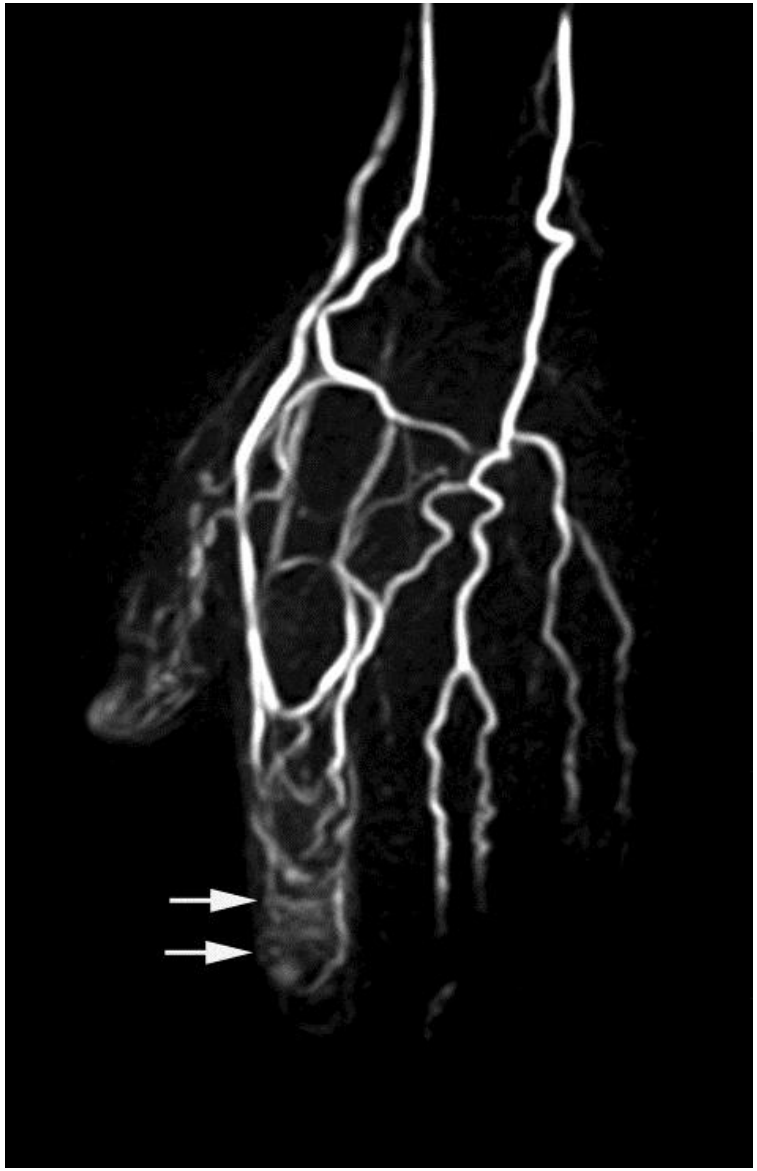


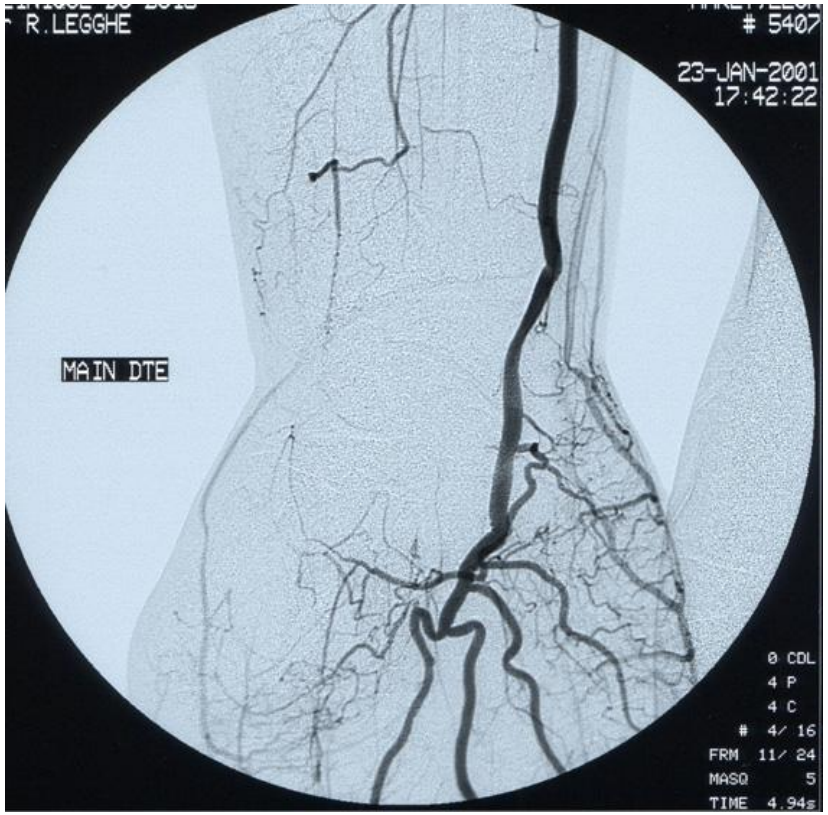
Steen V, Medsger TA Jr. Arthritis Rheum 2003 ;48 :516

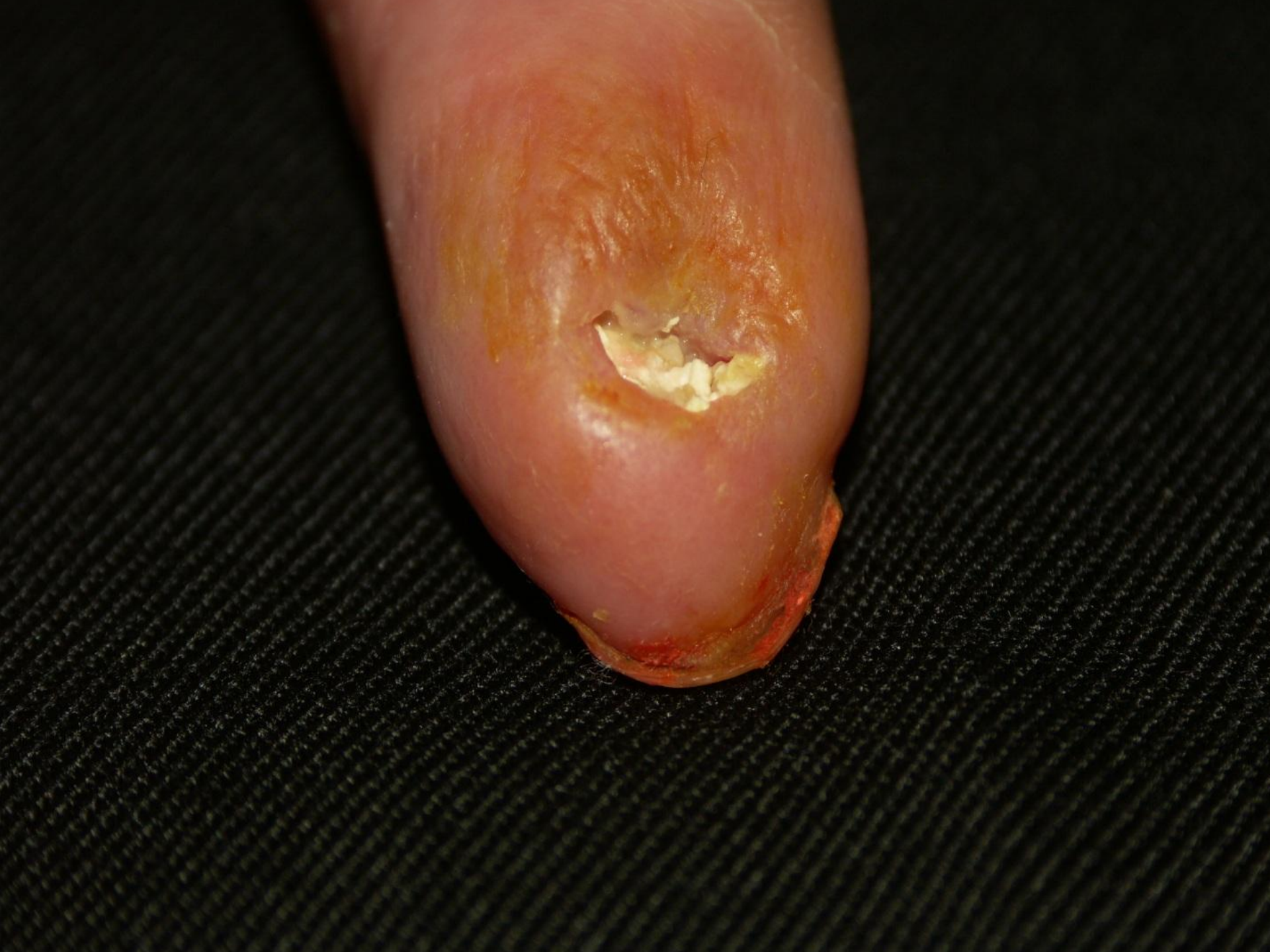
Ischemic DUs



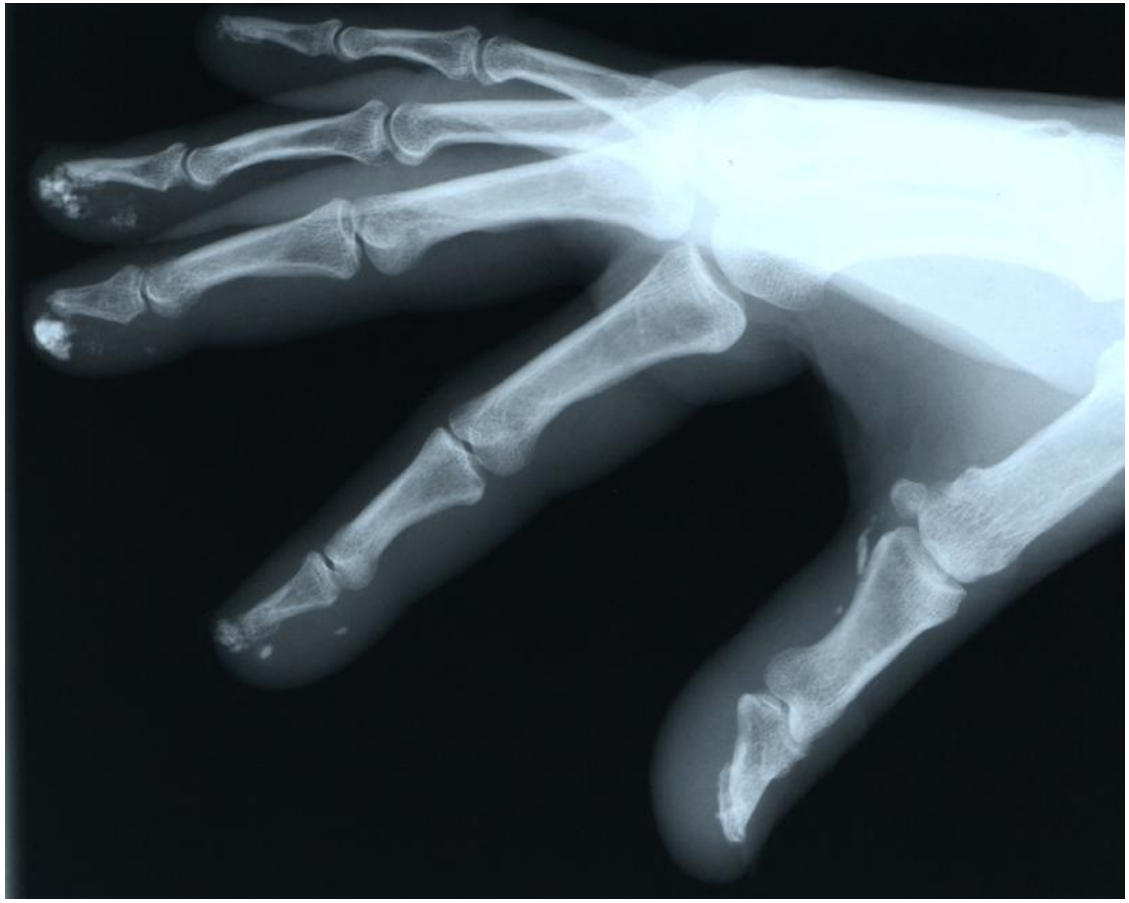

0
µm
1000
2000




R.LEGGHE
5407
23-JAN-2001
17:42:22
MAIN DTE
0 CDL
4 P
4 C
4/ 16
FRM 11/ 24
MASQ 5
TIME 4.94s



Calcifications sous-cutanées

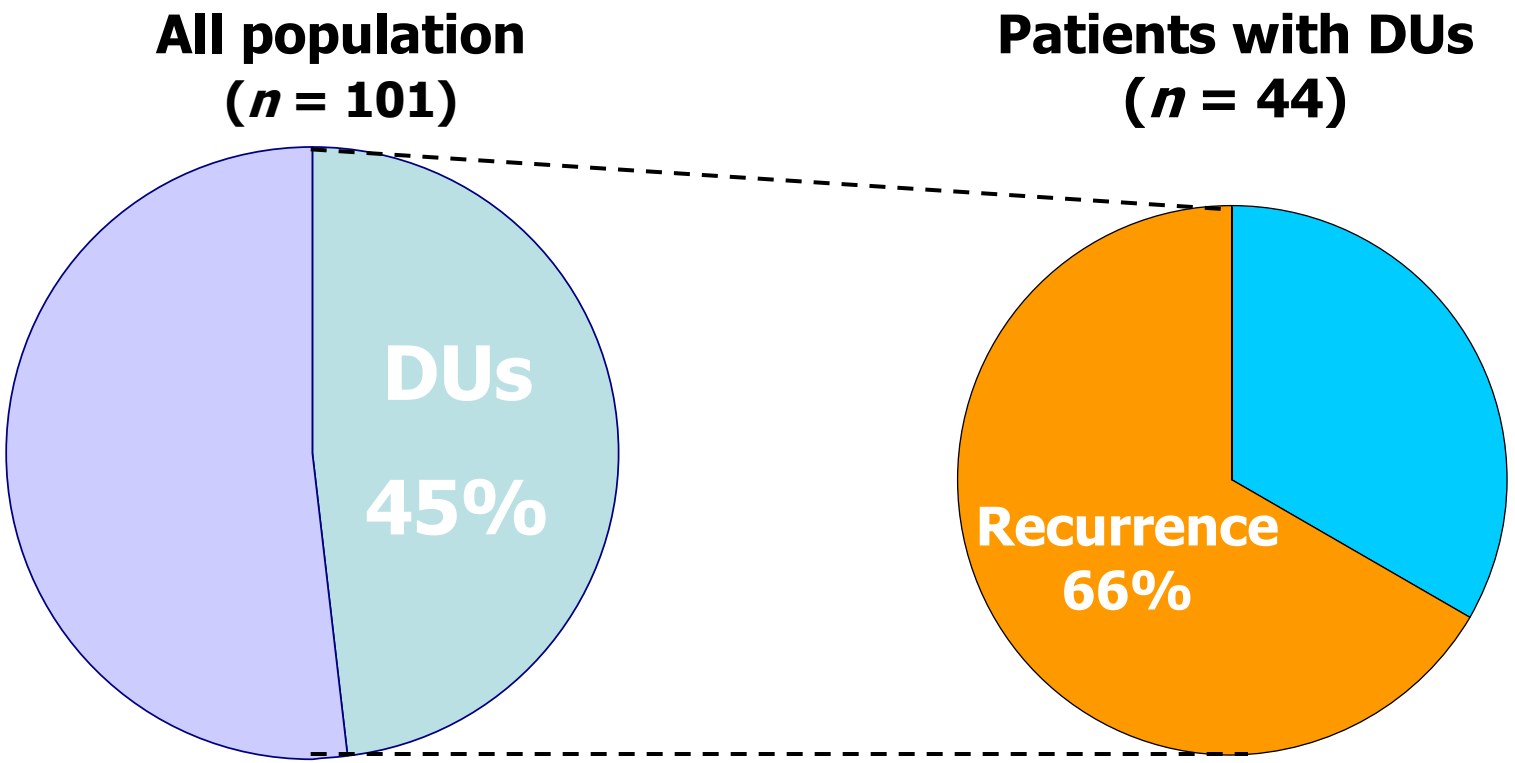


ne concernent pas que le CREST syndrome:

- 1/3 des formes limitées,
- 1/4 des formes diffuses

KOZIMOR THERESE
February 2005

Ischemic DUs: prevalence

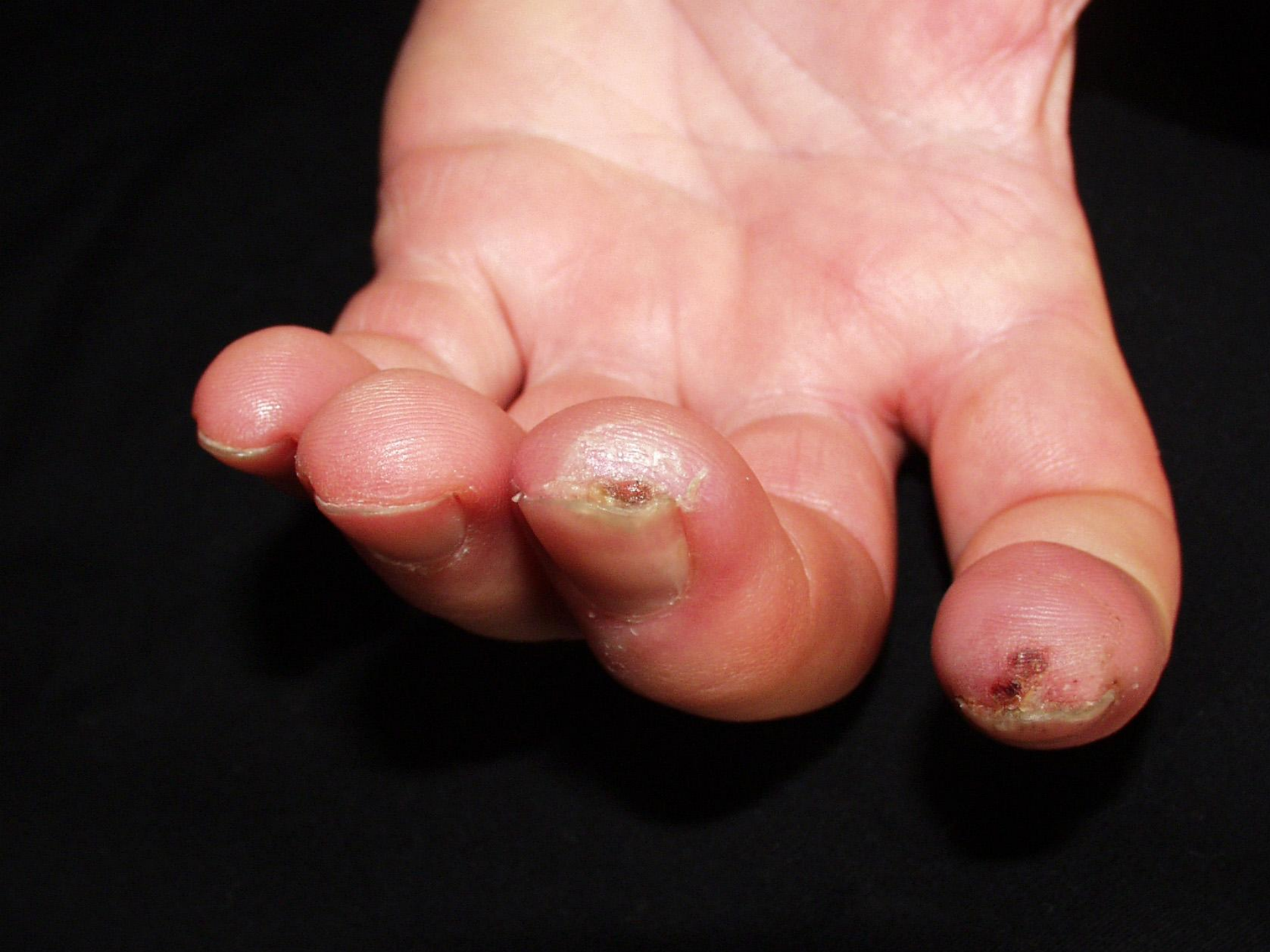


Hachulla E et al. J Rheumatol 2007; 34:2423-30

Time to first Ischemic DUs after first SSc non RP symptom

First DU
<1 year 19/44 (43%)
<5 years 32/44 (73%)

Hachulla E et al. J Rheumatol 2007; 34:2423-30.

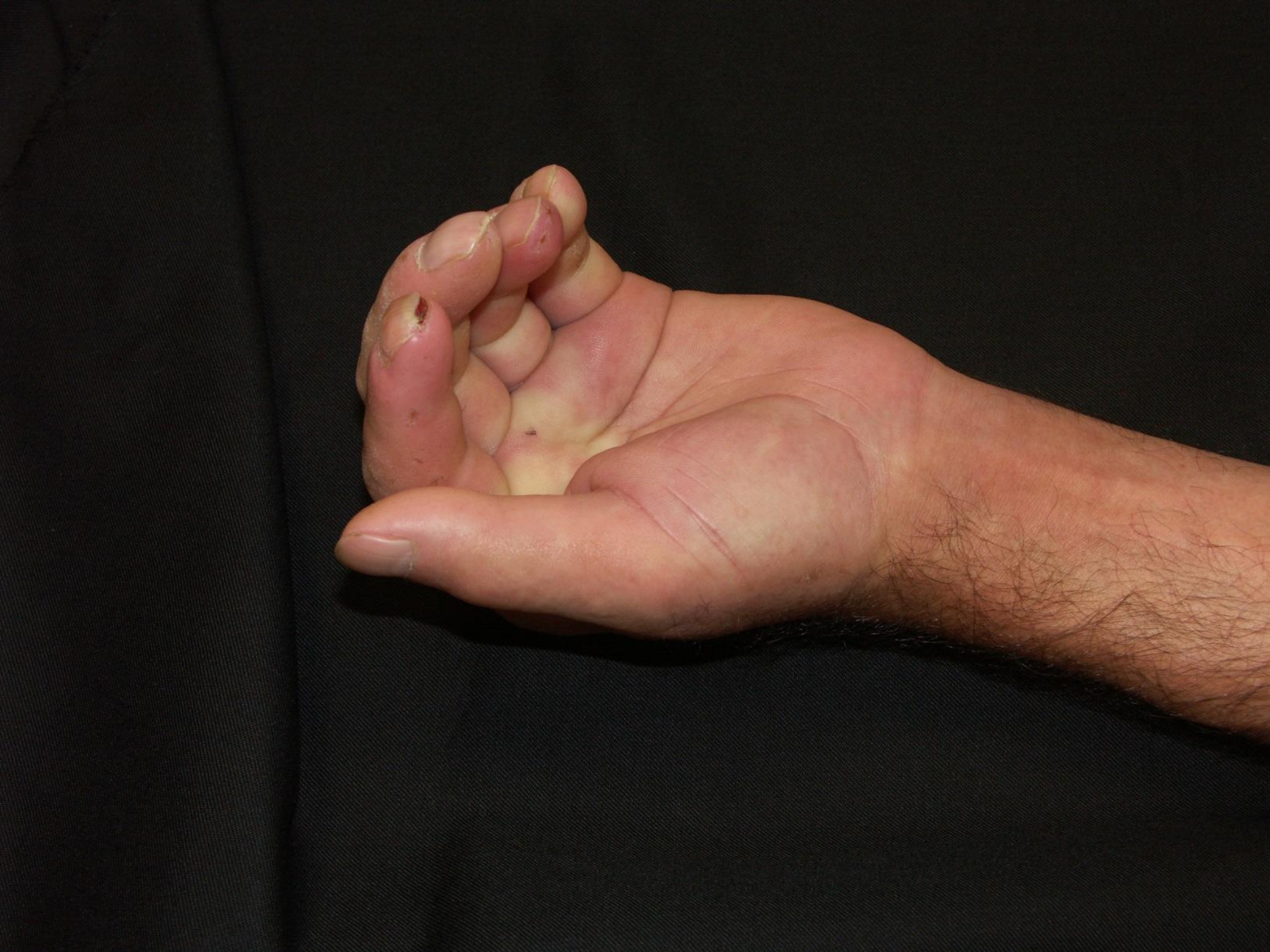


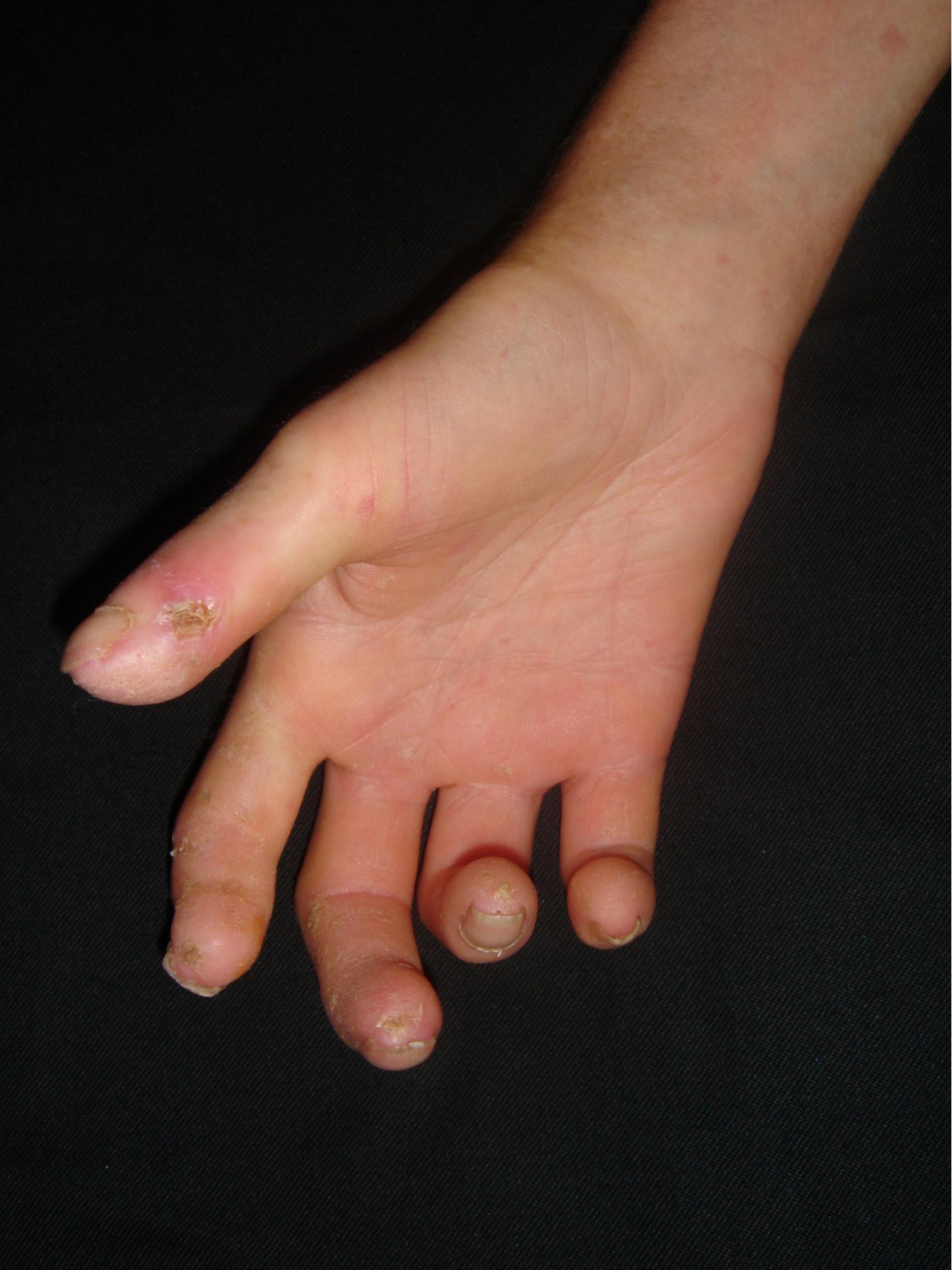
Yearly incidence of DU

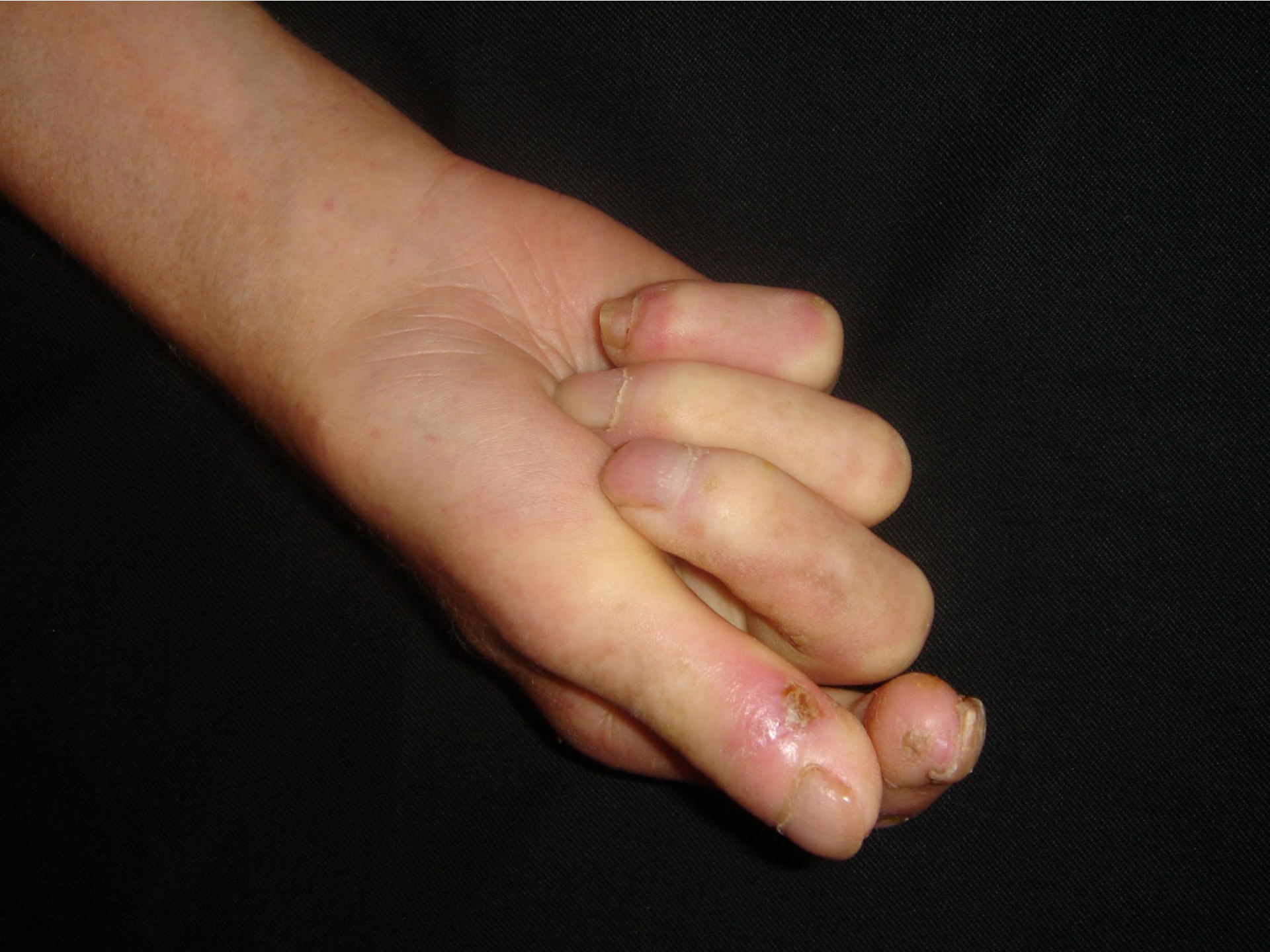
Délai entre les 2 premiers épisodes d'ulcères digitaux*	Patients n	Incidence annuelle des ulcères digitaux (moyenne ± SD)	p
< 1 an	10	0.96 ± 0.61	0.048
≥ 1 an	19	0.50 ± 0.28	
< 2 ans	14	0.85±0.57	0.04
≥ 2 ans	15	0.48±0.26	

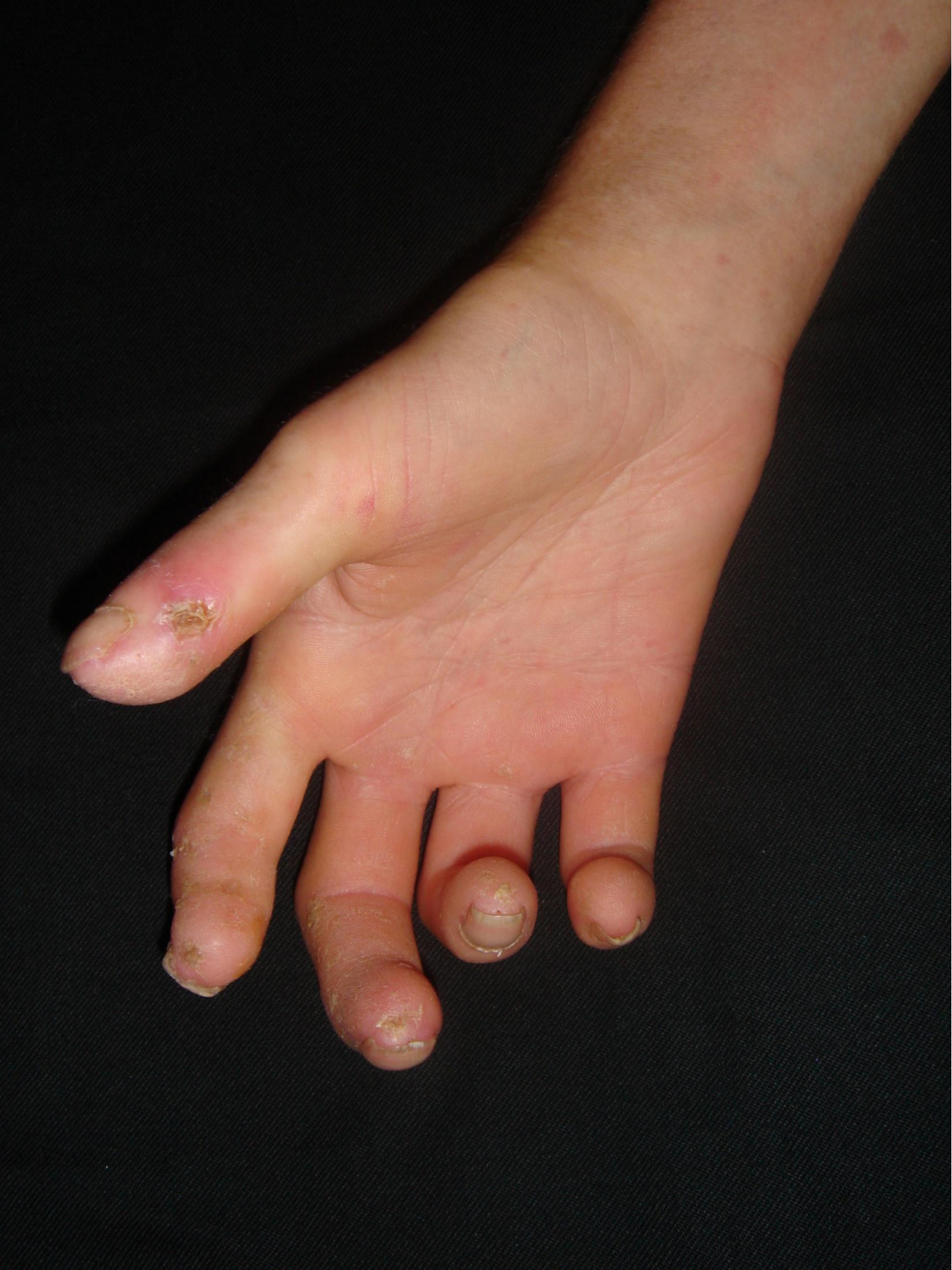
* Chez les patients ayant fait au moins 2 épisodes d'ulcères digitaux

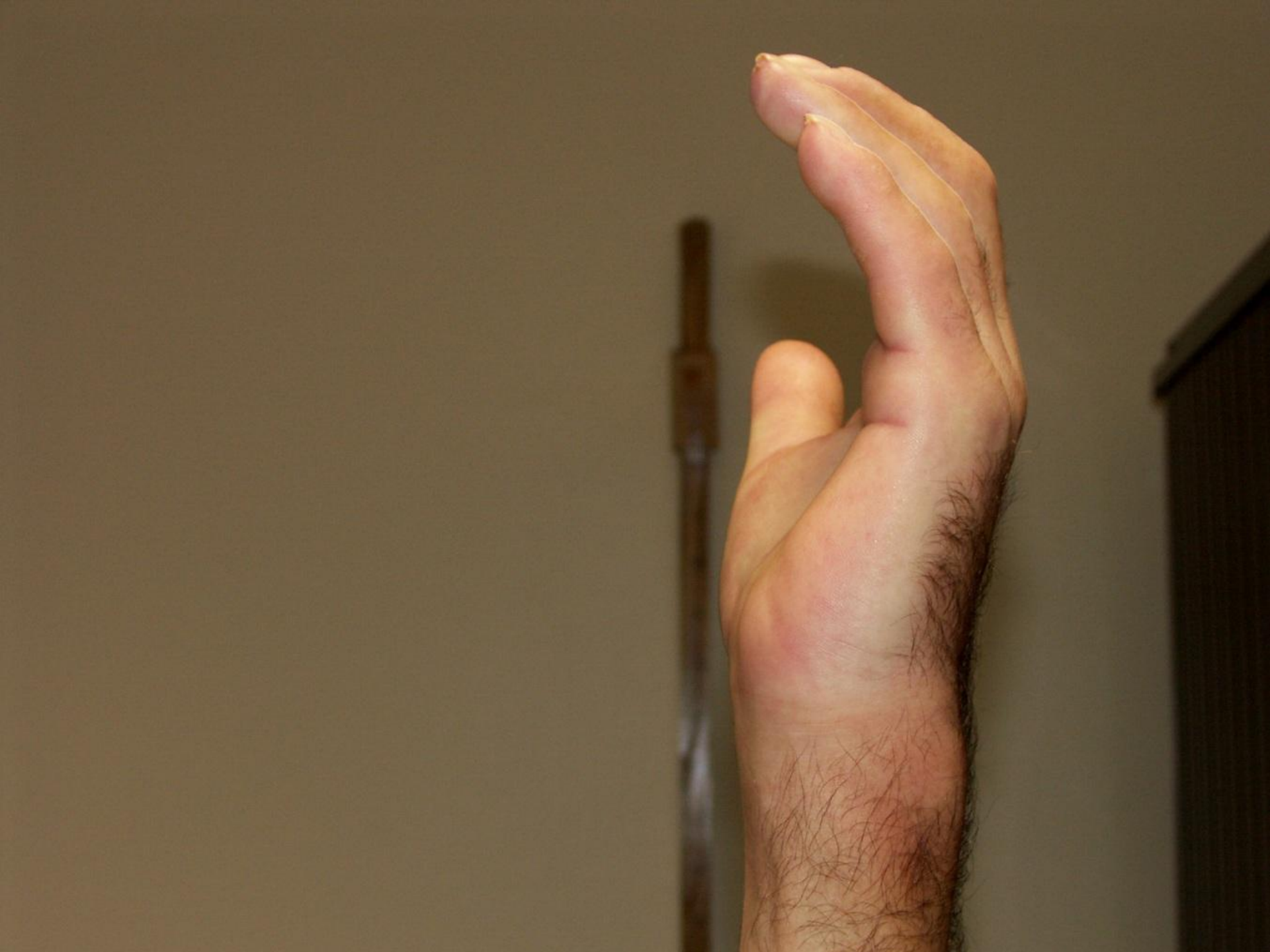
Hachulla E. J Rheumatol 2007, 34: 2423

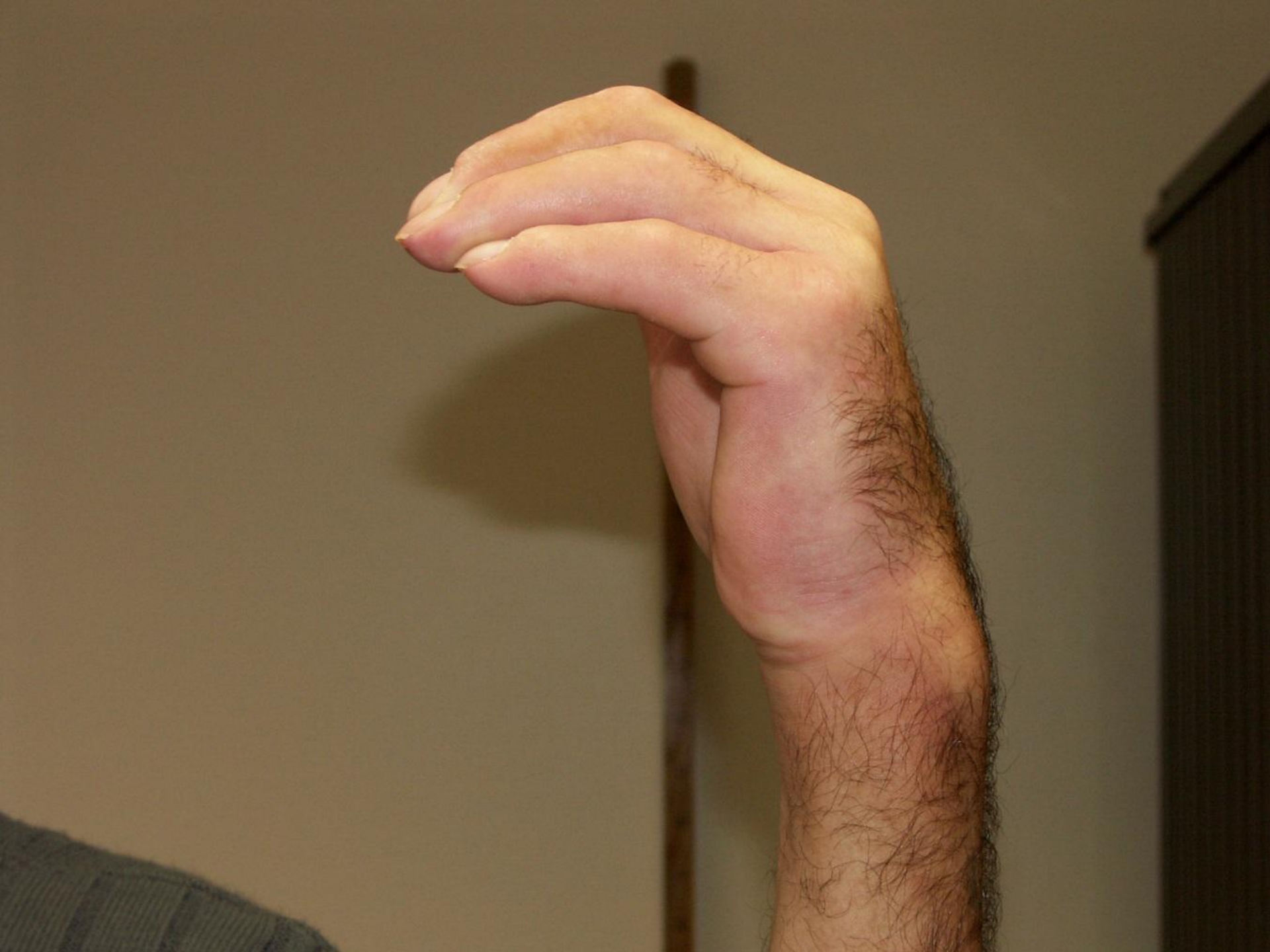












Échelle de la main de Cochin

Annexe 1. Version française de l'échelle.

Réponses aux questions : 0 = oui sans difficulté ; 1 = possible avec très peu de difficultés ; 2 = possible avec quelques difficultés ; 3 = possible avec beaucoup de difficultés ; 4 = presque impossible ; 5 = impossible.
Veuillez répondre aux questions ci-dessous, sans appareillage adapté :

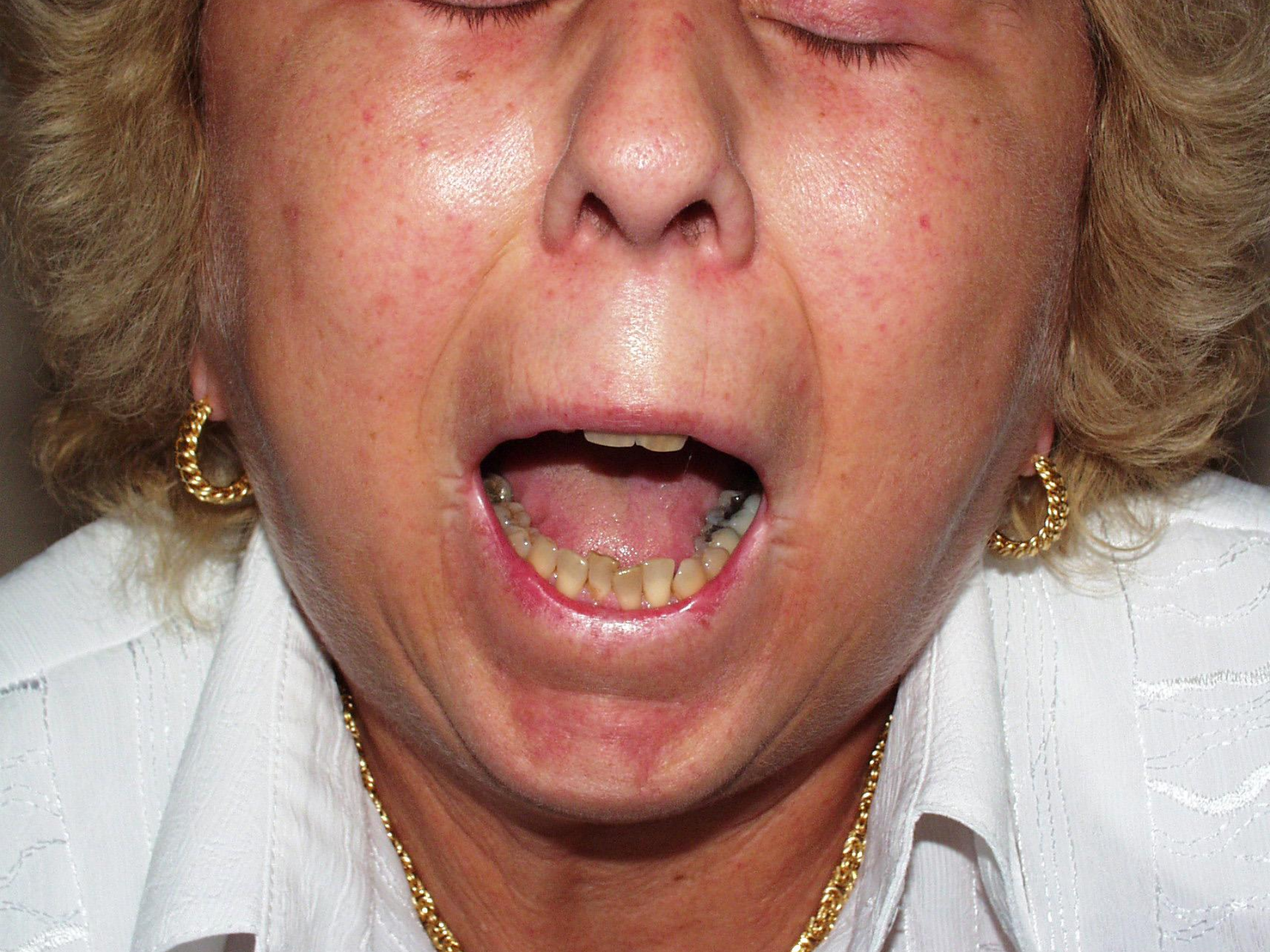
C1- *À la cuisine*
Pouvez-vous tenir un bol ?
Pouvez-vous saisir une bouteille pleine et la lever ?
Pouvez-vous tenir un plat plein ?
Pouvez-vous verser le liquide de la bouteille dans un verre ?
Pouvez-vous dévisser le couvercle d'un pot déjà ouvert une fois ?
Pouvez-vous couper de la viande avec un couteau ?
Pouvez-vous piquer efficacement avec une fourchette ?
Pouvez-vous peler des fruits ?

C2 – *Habillage*
Pouvez-vous boutonner votre chemise ?
Pouvez-vous ouvrir puis fermer les fermetures éclairs ?

C3 – *Toilette*
Pouvez-vous presser un tube de dentifrice plein ?
Pouvez-vous tenir votre brosse à dent efficacement ?

C4 – *Au bureau*
Pouvez-vous écrire une phrase courte avec un crayon ou un stylo ordinaire ?
Pouvez-vous écrire une lettre avec un crayon ou un stylo ordinaire ?

C5 – *Divers*
Pouvez-vous tourner une poignet de porte ronde ?
Pouvez-vous utiliser des ciseaux pour couper un morceaux de papier ?
Pouvez-vous saisir les pièces de monnaie sur une table ?
Pouvez-vous tourner une clé dans la serrure ?



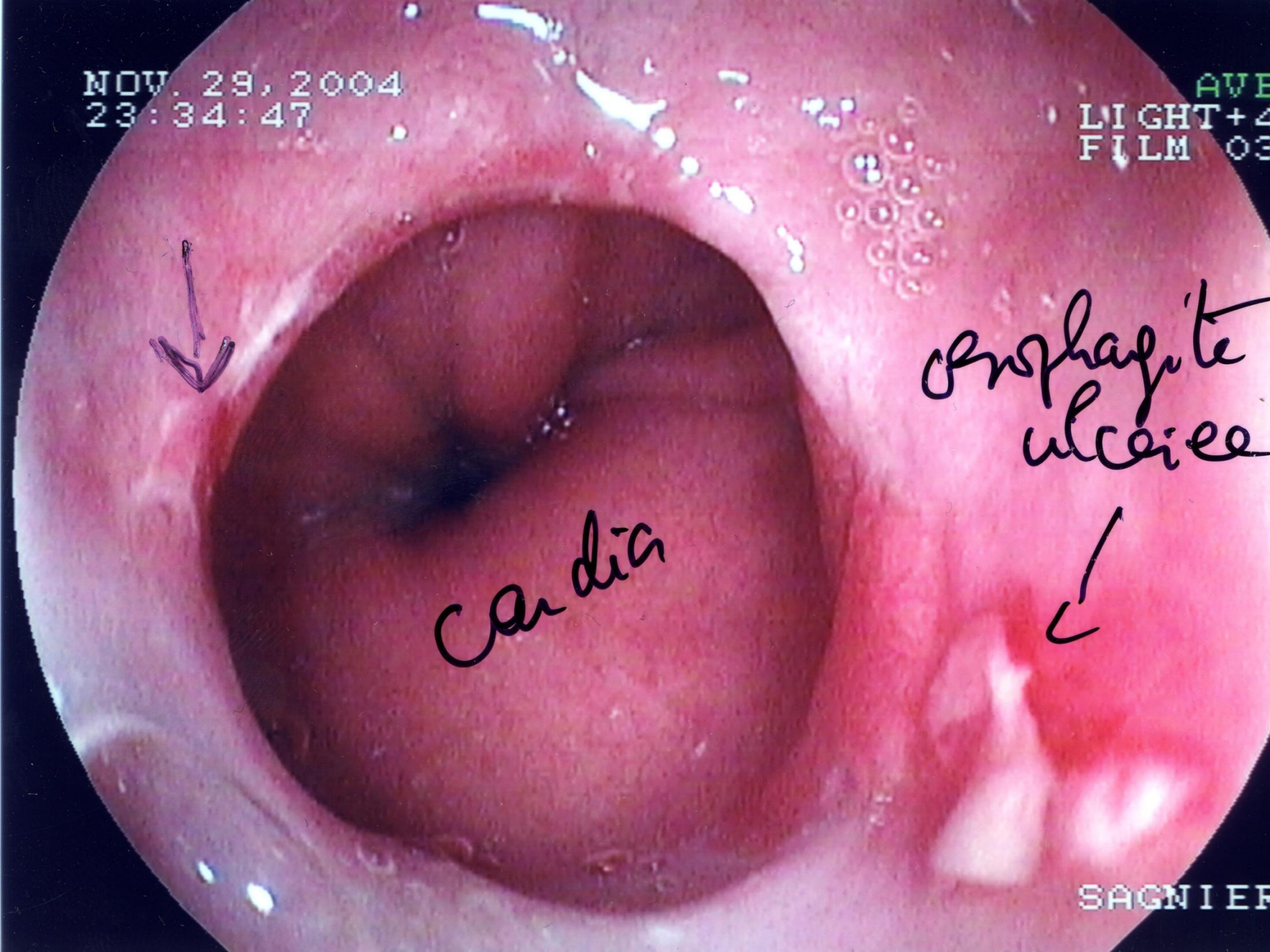
Échelle de bouche de Cochin

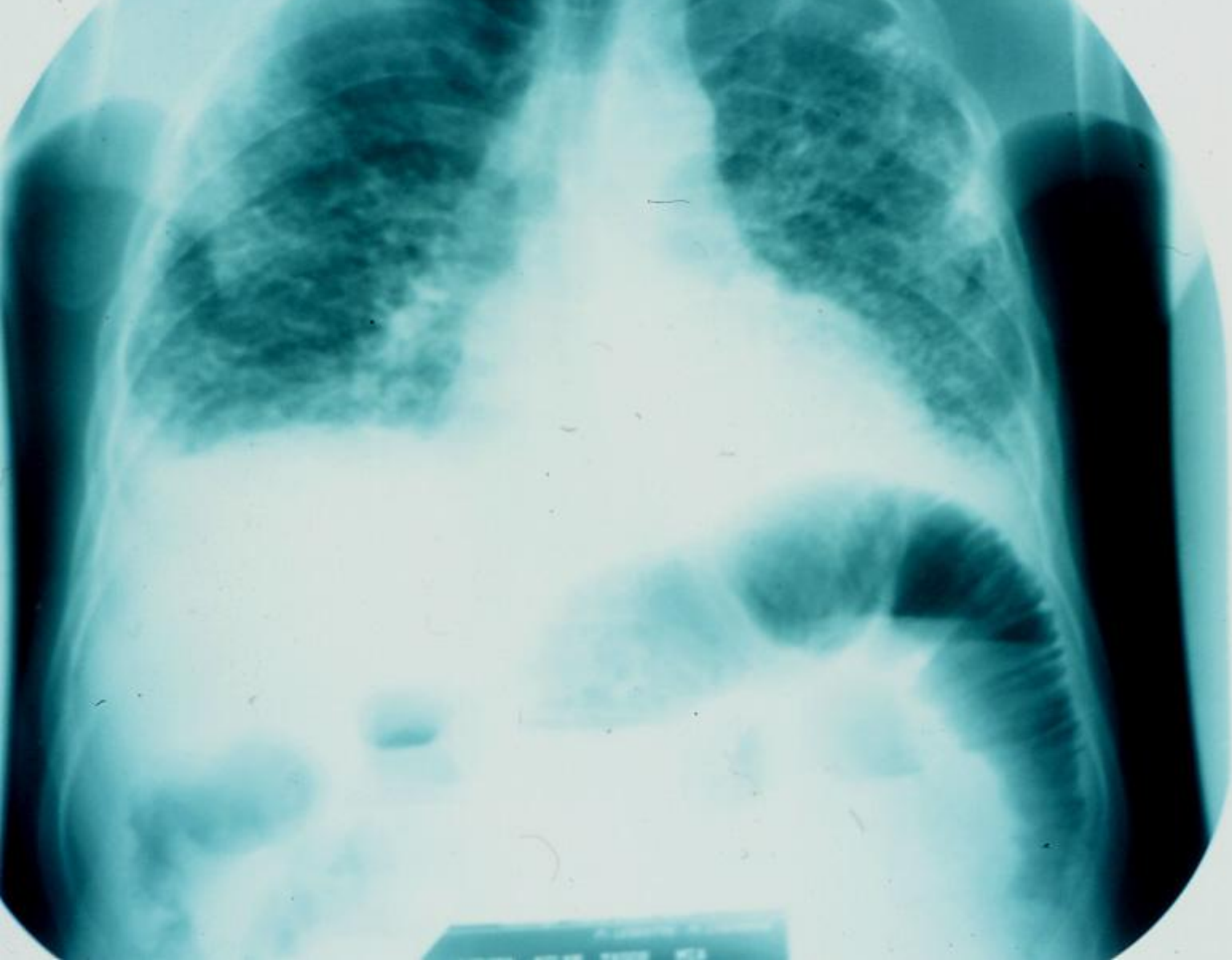
The Mouth Handicap in Systemic Sclerosis (MHISS) scale

As you probably aware, your systemic sclerosis might involve your face and your mouth. This questionnaire is aimed at assessing how much your face and mouth involvement affects your daily life.

		Never	Rarely	Occasionally	Often	Always
1	I have difficulties opening my mouth	0	1	2	3	4
2	I have to avoid certain drinks (sparkling, alcohol, acidic)	0	1	2	3	4
3	I have difficulties chewing	0	1	2	3	4
4	My dentist has difficulties taking care of my teeth	0	1	2	3	4
5	My dentition has become altered	0	1	2	3	4
6	My lips are retracted and/or my cheeks are sunken	0	1	2	3	4
7	My mouth is dry	0	1	2	3	4
8	I must drink often	0	1	2	3	4
9	My meals consist of what I can eat and not what I would like to eat	0	1	2	3	4
10	I have difficulties speaking clearly	0	1	2	3	4
11	The appearance of my face is modified	0	1	2	3	4
12	I have trouble with the way my face looks	0	1	2	3	4

Mouthon L. Ann Rhem Dis 2008; 67: 110


NOV. 29, 2004
23:34:47
AVE
LIGHT+4
FILM 03
cardia
oesophagite ulcérée
SAGNIER



Sclérodermie systémique: quelles explorations systématiques?

Initial

- Bilan clinique: peau, articulations, nécroses digitales, auscultation pulmonaire, RGO, recherche d'un syndrome de Sjögren
- 6MWT, classe de dyspnée
- Capillaroscopie
- AAN, bilan hépatique, créatinine, BU, NFS, fer ferritine, TSH FT4, CPK
- ECG, thorax
- Echocardiographie
- EFR (CPT, CVF, VEMS, DLCO)
- scanner thoracique en coupes fines
- fibroscopie haute, Manométrie œsophagienne, selon clinique

Annuel, tous les 6 mois les 3 premières années si dcSSc

- Clinique
- EFR (CPT, CVF, DLCO)
- Echocardiographie, VIT
- bilan hépatique, créatinine, BU, NFS, fer ferritine, BNP?