# Cutaneous T-cell lymphoma – combination modalities in treatment

Vašků V.

I$^{st}$ Dept. of Dermatology and Venereology,

Medical Faculty Masaryk University and St. Ann´s Faculty Hospital, Brno, Czech Republic

# Cutaneous T-cell lymphoma (CTCL)

- **Larger spectrum of diseases with two characteristic features:**
- **1. Malignant expansion of T- cells clones stopped on the way from bone marrow precursor cells to helper cells**
- **2. Forming and location of lymphoma in the skin**

# CTCL[1]: EORTC[2] Classification

- Indolent
  - Mycosis fungoides (MF)
  - Mycosis fungoides plus follicular mucinosis
  - Pagetoid reticulosis
  - Large-cell CTCL, CD30+
  - Lymphomatoid papulosis
- Aggressive
  - Sézary syndrome (SS)
  - Large-cell CTCL, CD30-
  - Immunoblastic T-cell lymphoma
  - Pleomorphic T-cell lymphoma
- Provisional
  - Granulomatous slack skin
  - CTCL, pleomorphic small/medium-sized T-cell lymphoma
  - Subcutaneous panniculitis-like T-cell lymphoma

[1] CTCL Cuteanous T-Cell Lymphoma, [2] EORTC European Organisation for Research and Treatment of Cancer

# Cutaneous T-cell lymphoma

- **Three stages of CTCL with epidermotrophism:**
  - **I. Eczematoid stage (premycotic, patch stage)**
  - **II. Infiltrative stage (plaque stage)**
  - **III. Tumor stage**
- **The disease usually proceeds from stage to stage, various alterations of more stages can be present simultaneously as well.**

# CTCL: Stage and Prognosis

| | IA | IB | IIA | IIB | III | IVA | IVB |
|---|---|---|---|---|---|---|---|
| 5-year DSS (%) * | 100 | 96 | 68 | 80 | 40 | 0 | |
| 10-year DSS (%) | 98 | 83 | 68 | 42 | 20 | 0 | |
| Median survival (yr) | >32 | 12.1 | 10.0 | 2.9 | 3.6-4.6 | 1.1 | 1.1 |
| ODP (%) † | 9 | 20 | 34 | | | | |
| 5-year RFS** (%) | 50 | 36 | 9 | | | | |
| 10-year RFS (%) | 31 | 3 | | | | | |

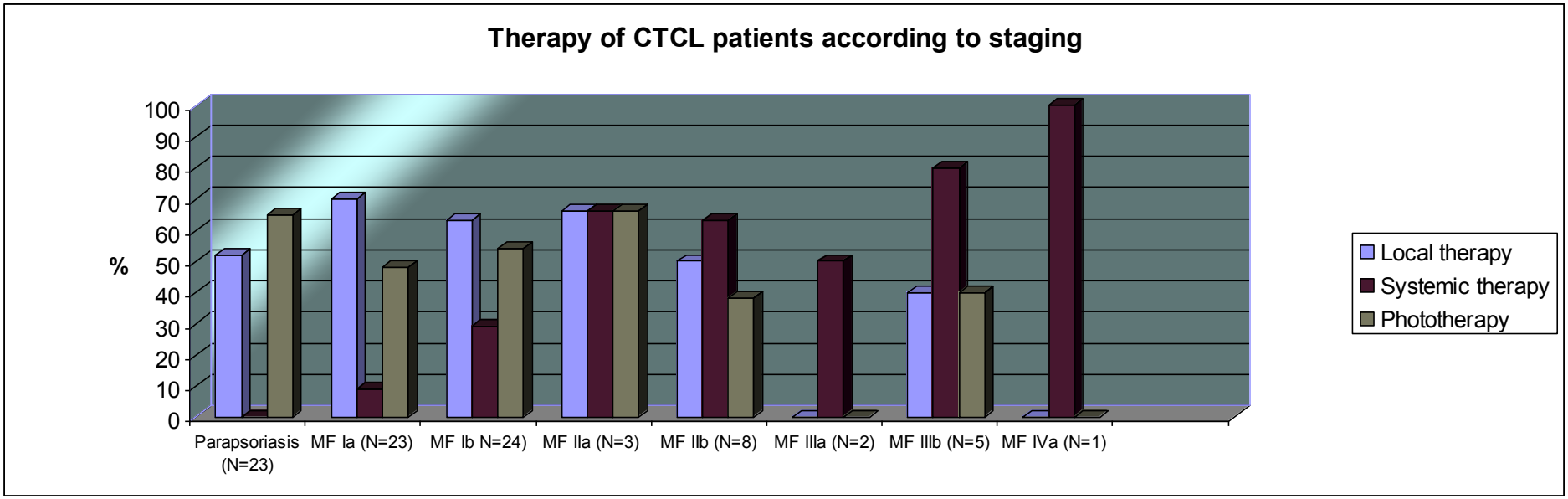
[1] DSS, disease-specific survival; [2] ODP, overall disease progression; [3] RFS, relapse-free survival

# Methods used for CTCL treatment in the I$^{st}$ Dept. of Derm. in Brno

- **Topically**: steroids
  tar
- **Phototherapy**: UVB 311 nm
  SUP
  CUP
  PUVA
- **Photodynamic therapy**
- **Systemic treatment**: acitretin
  Interferon $\alpha$2a
  Interferon $\alpha$2b
  (steroids)
  bexarotene
- **Radiotherapy** in co-operation with Dept. of Oncology

# Our experience with combination of therapeutical modalities for advanced CTCL

- PUVA / UVB 311nm + retinoids
- PUVA + interferons
- PUVA + retinoids + interferons
- PUVA + retionoids + interferons + radiotherapy
- PUVA + bexarotene
- Other combinations


Therapy of CTCL patients according to staging
%
100
90
80
70
60
50
40
30
20
10
0
Parapsoriasis (N=23)
MF Ia (N=23)
MF Ib N=24)
MF IIa (N=3)
MF IIb (N=8)
MF IIIa (N=2)
MF IIIb (N=5)
MF IVa (N=1)
Local therapy
Systemic therapy
Phototherapy

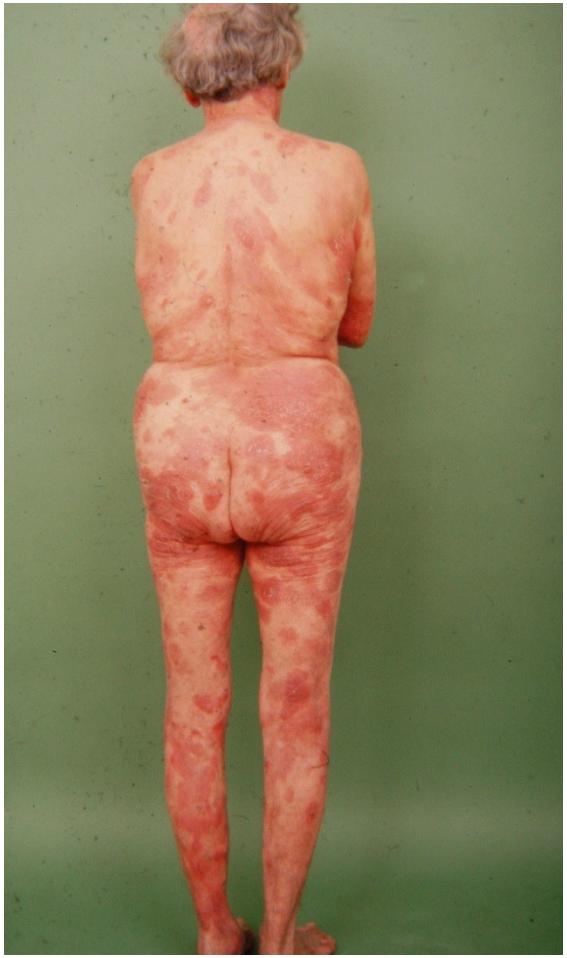
# Bexarotene Properties

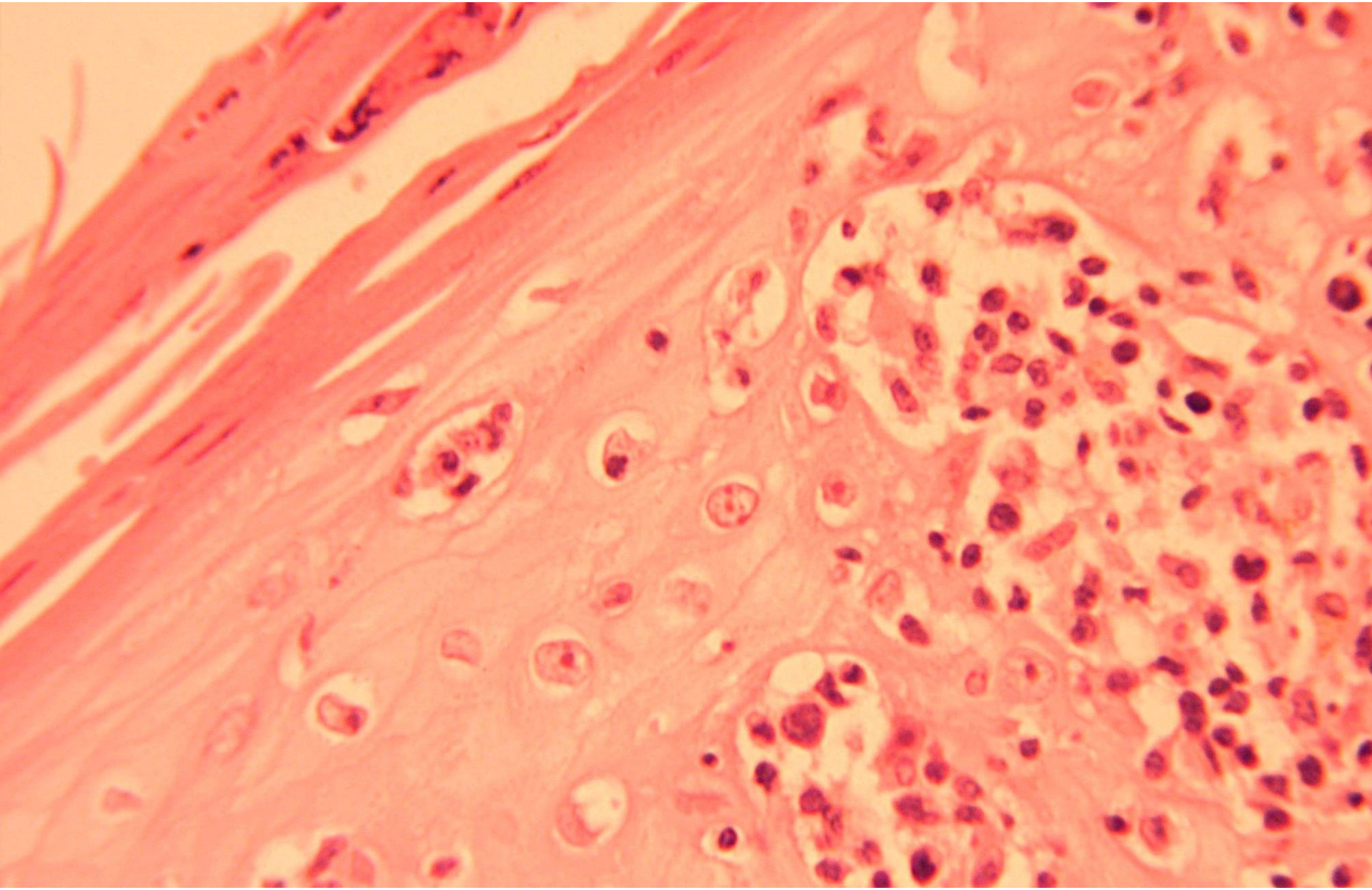


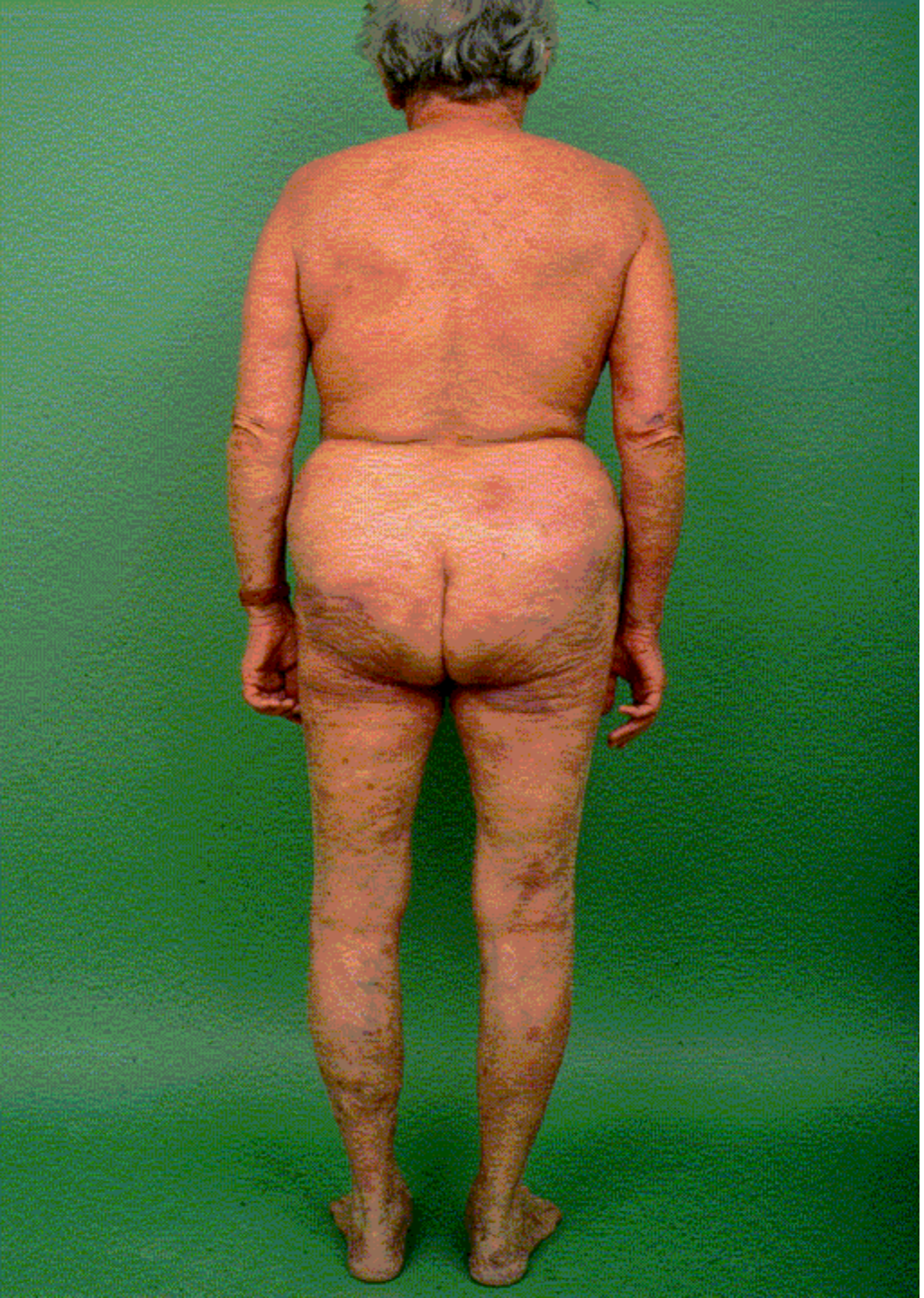

- Novel retinoid  rexinoid
- Selective retinoid X receptor (RXR) antagonist
- Modulates expression of genes regulated by retinoid response elements
- Available as topical or systemic treatment
- Mono- or combination therapy

# Bexarotene: Adverse Events

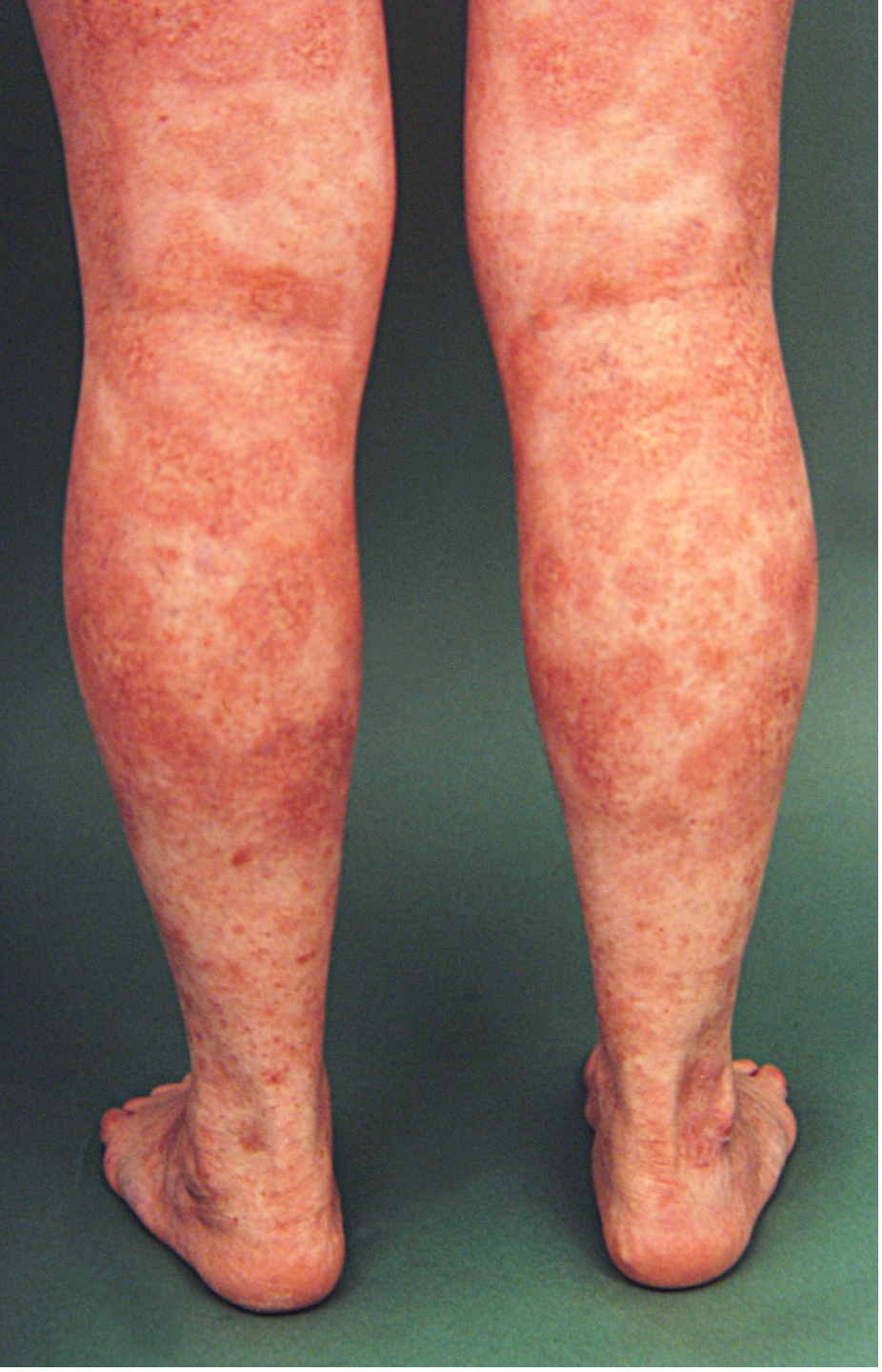
| | Incidence by initial dose (mg/m$^2$/day) | |
|---|---|---|
| Adverse event | 300 (n=84) | > 300 (n=53) |
| Hyperlididaemia | 79% | 79% |
| Hypercholestolaemia | 32% | 62% |
| Headache | 30% | 42% |
| Hypothyroidism | 29% | 53% |
| Pruritus | 25% | 15% |
| Asthaenia | 20% | 45% |
| Leukopenia | 17% | 47% |
| Rash | 17% | 23% |
| Infection | 13% | 23% |
| Exfoliative dermatitis | 10% | 28% |
| Diarrhoea | 7% | 42% |
| Anaemia | 6% | 25% |
| Anorexia | 2% | 23% |



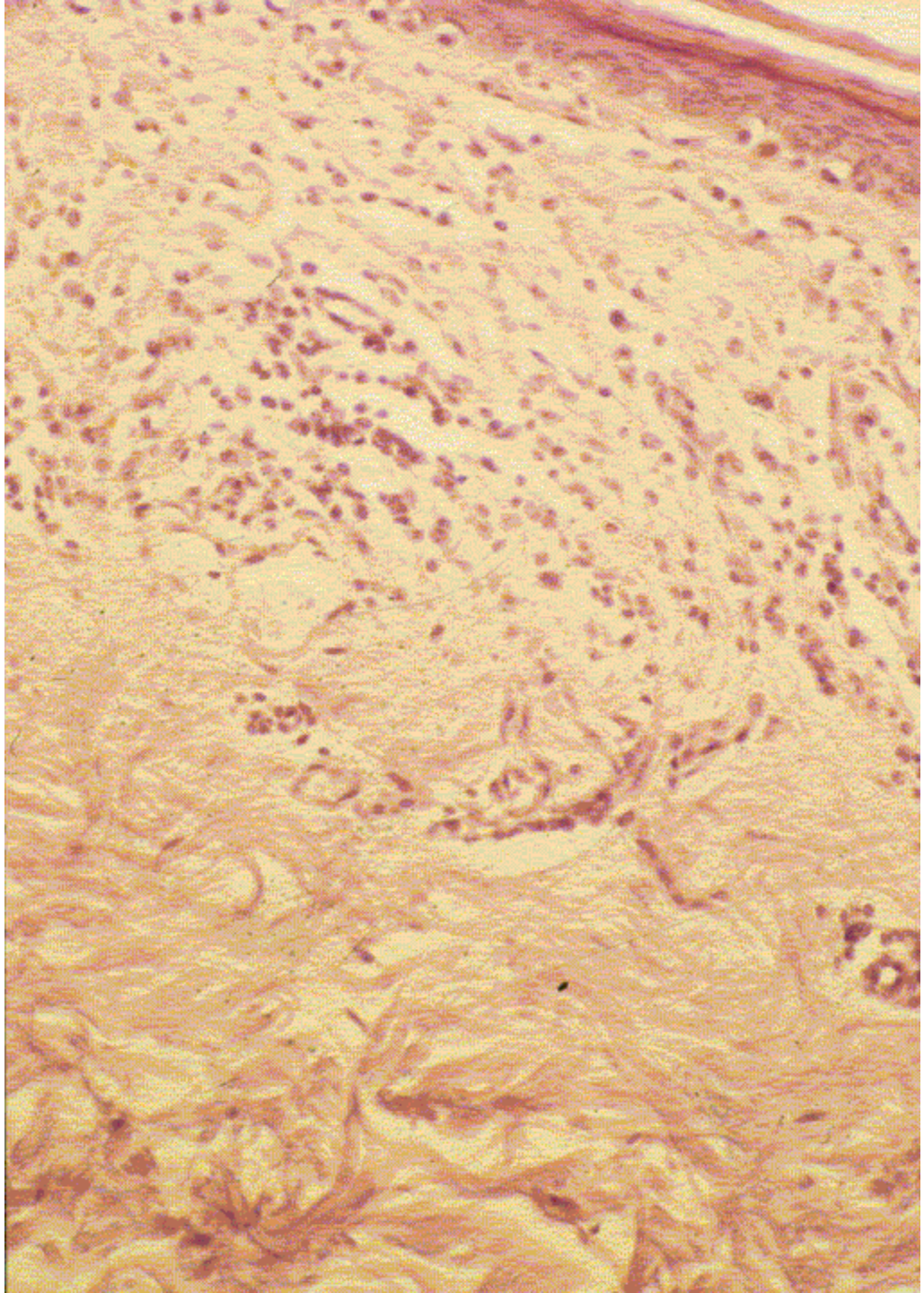


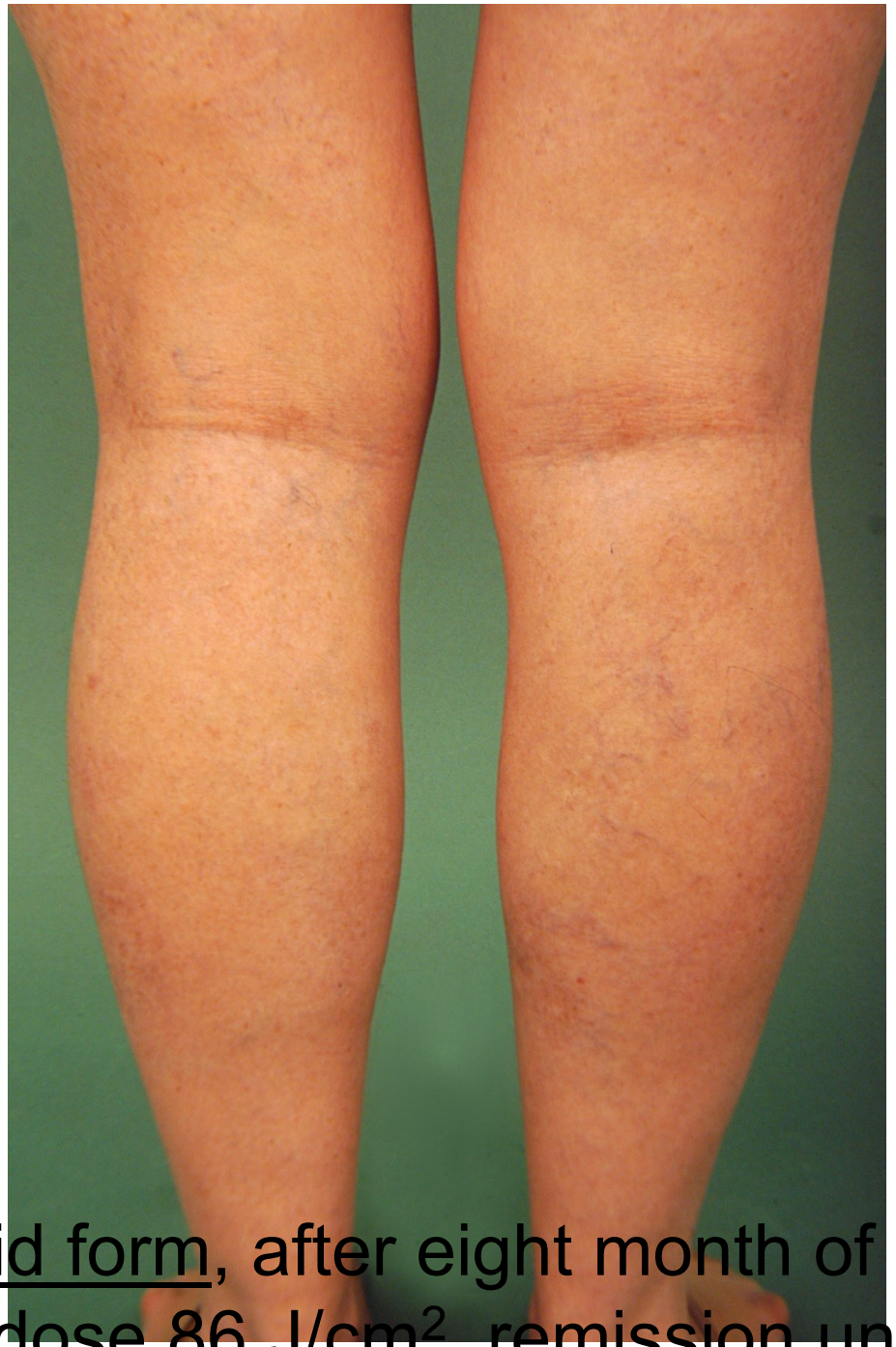


MF, after six month of PUVA

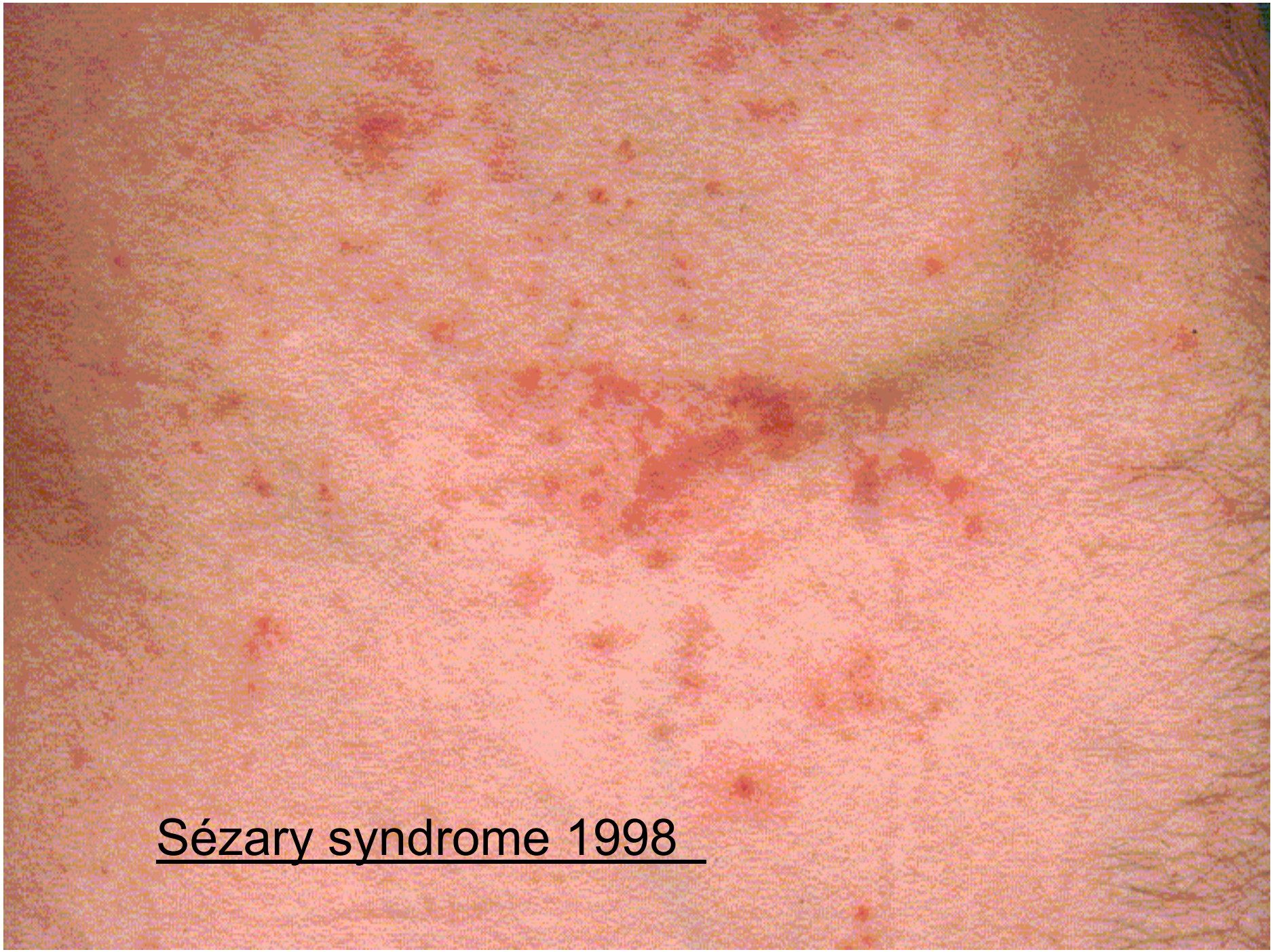


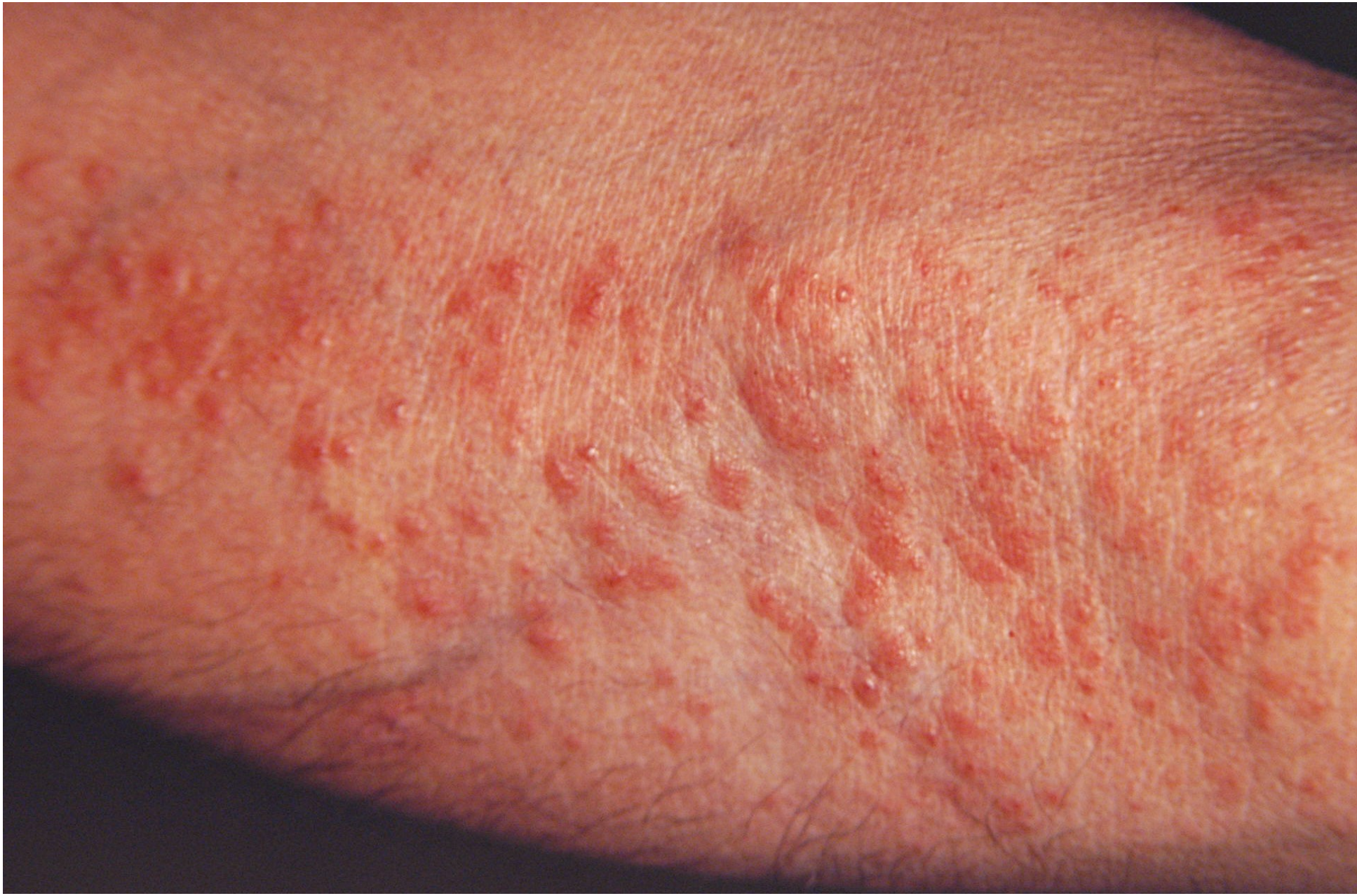
MF, lichenoid form, 1999

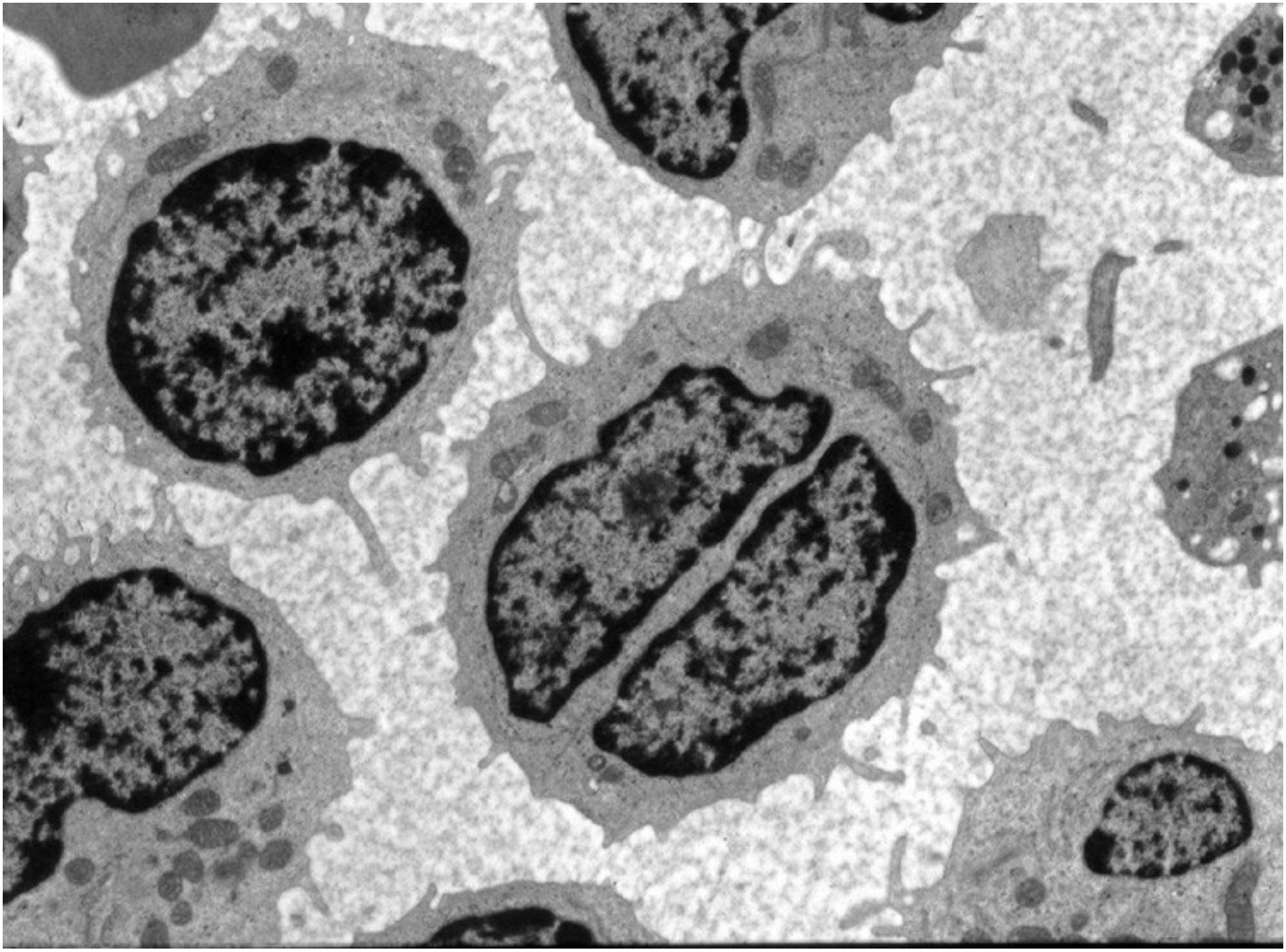


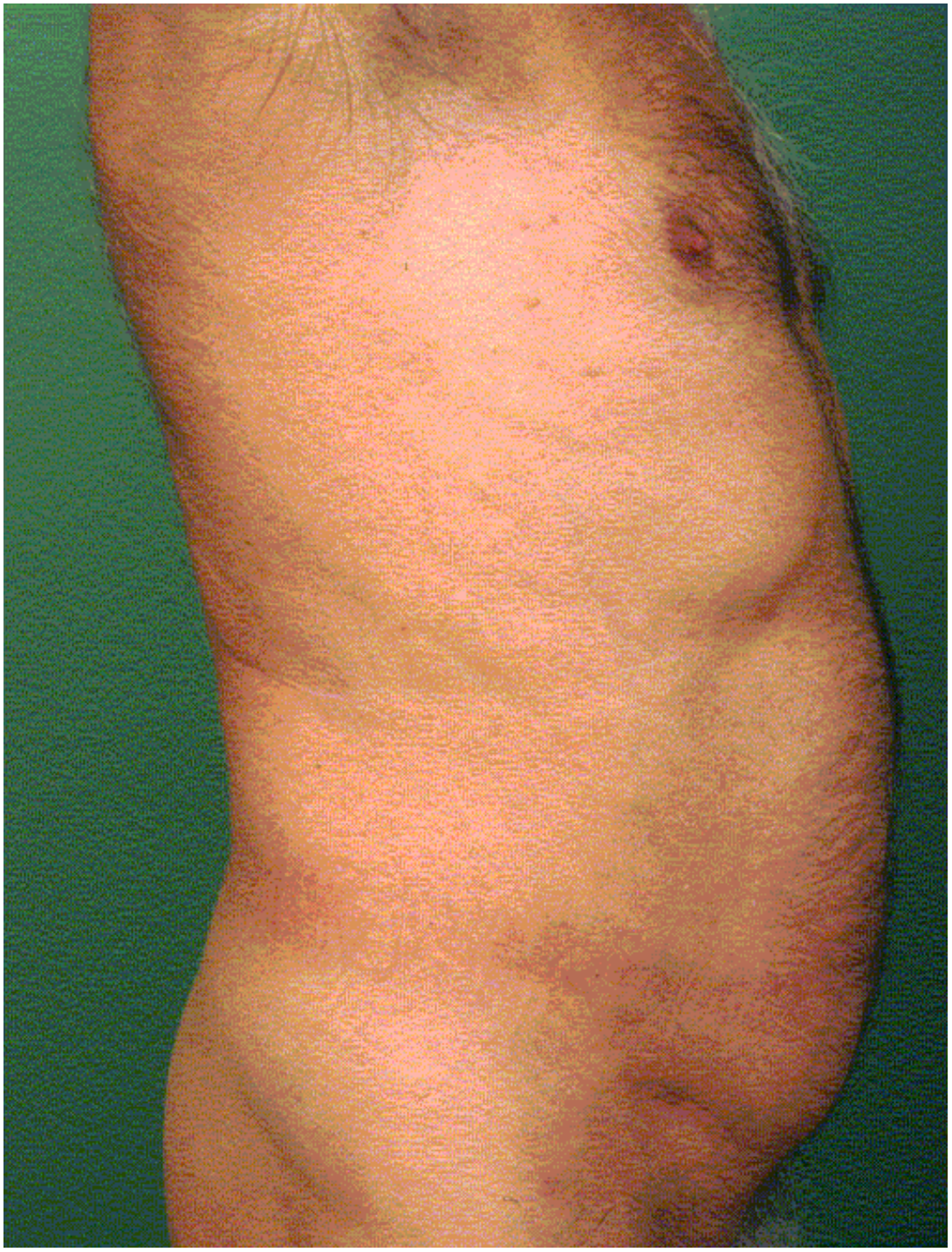


MF, lichenoid form, after eight month of PUVA, cumulative dose 86 J/cm$^2$, remission until now

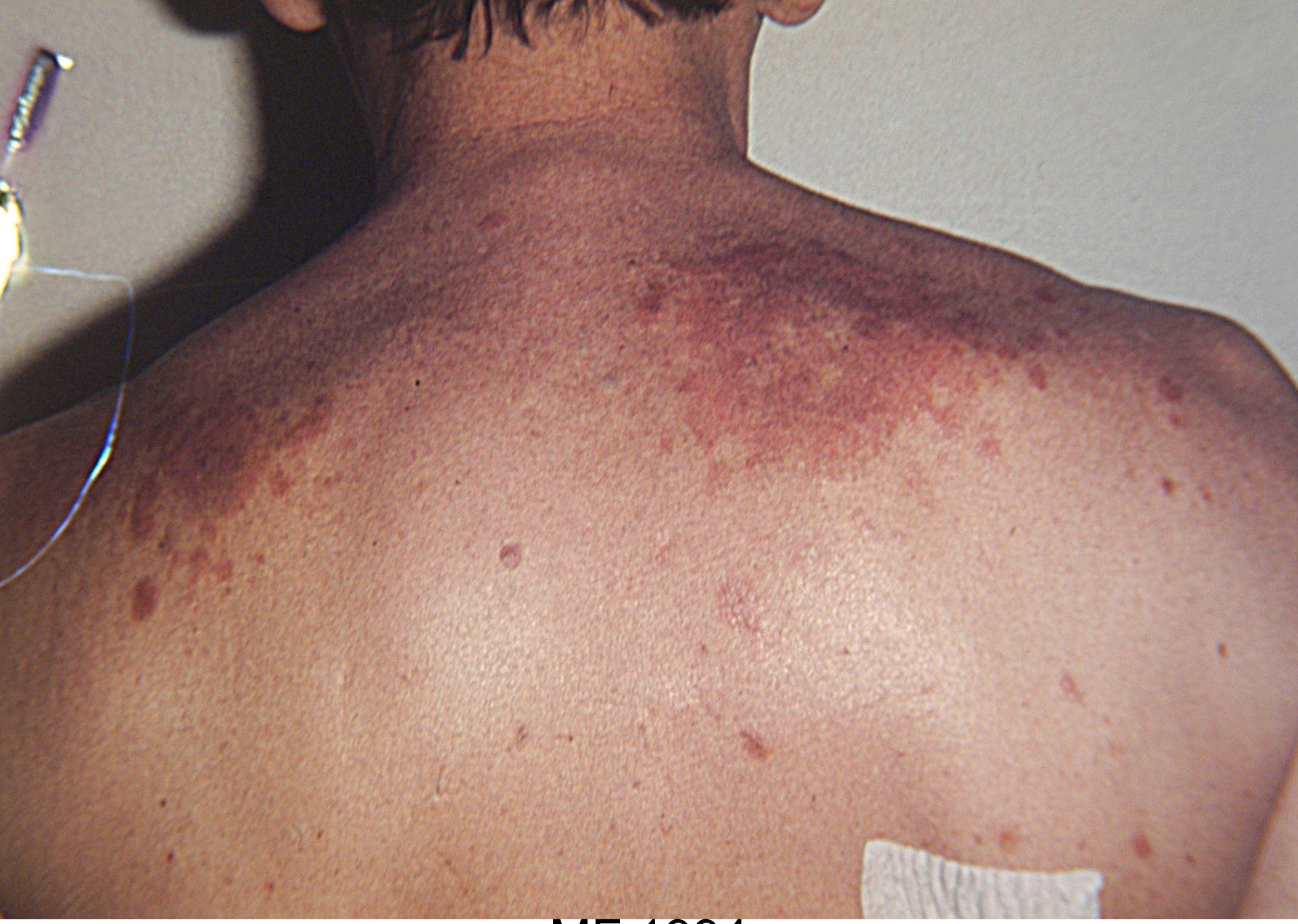

Sézary syndrome 1998



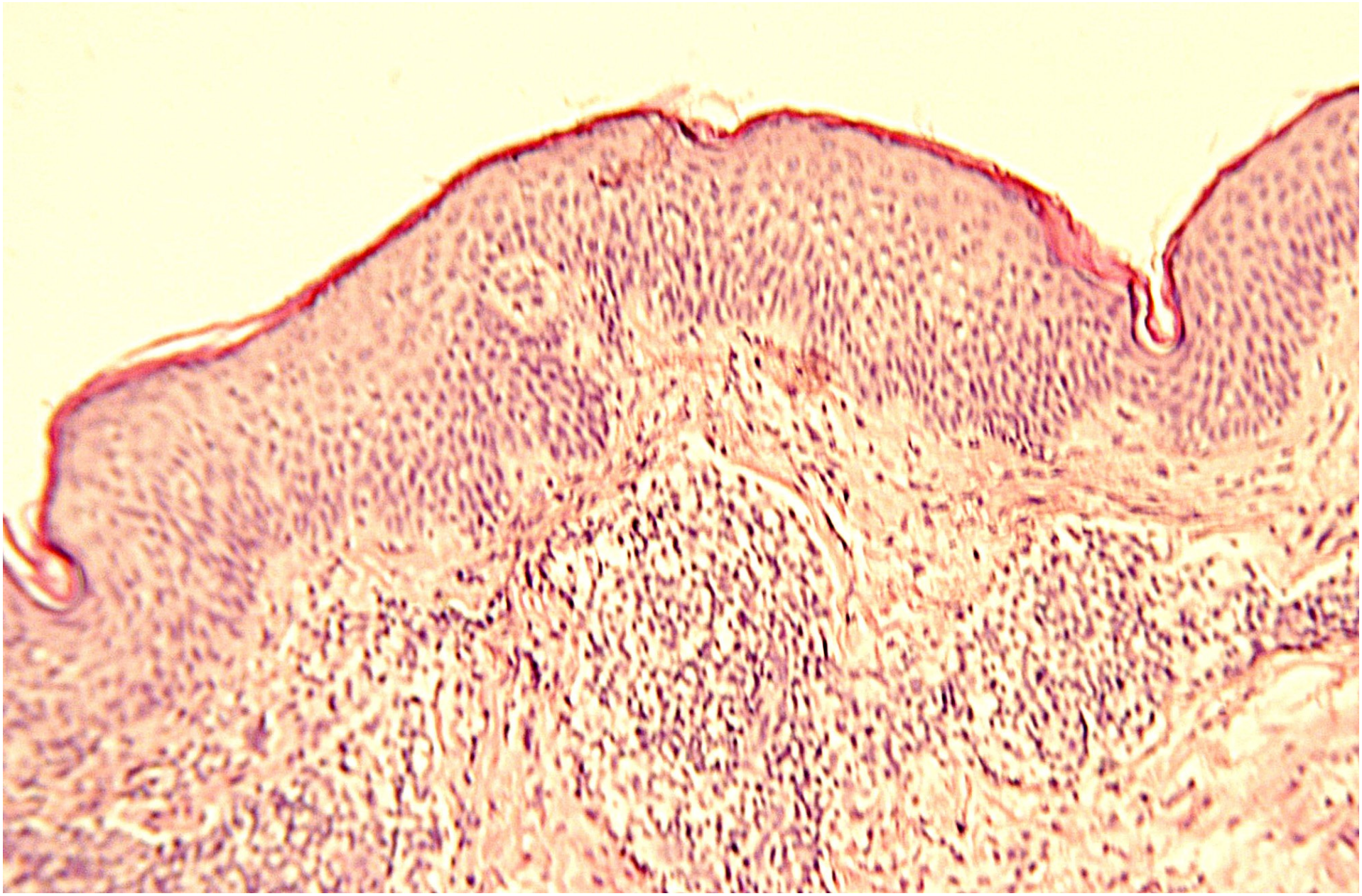


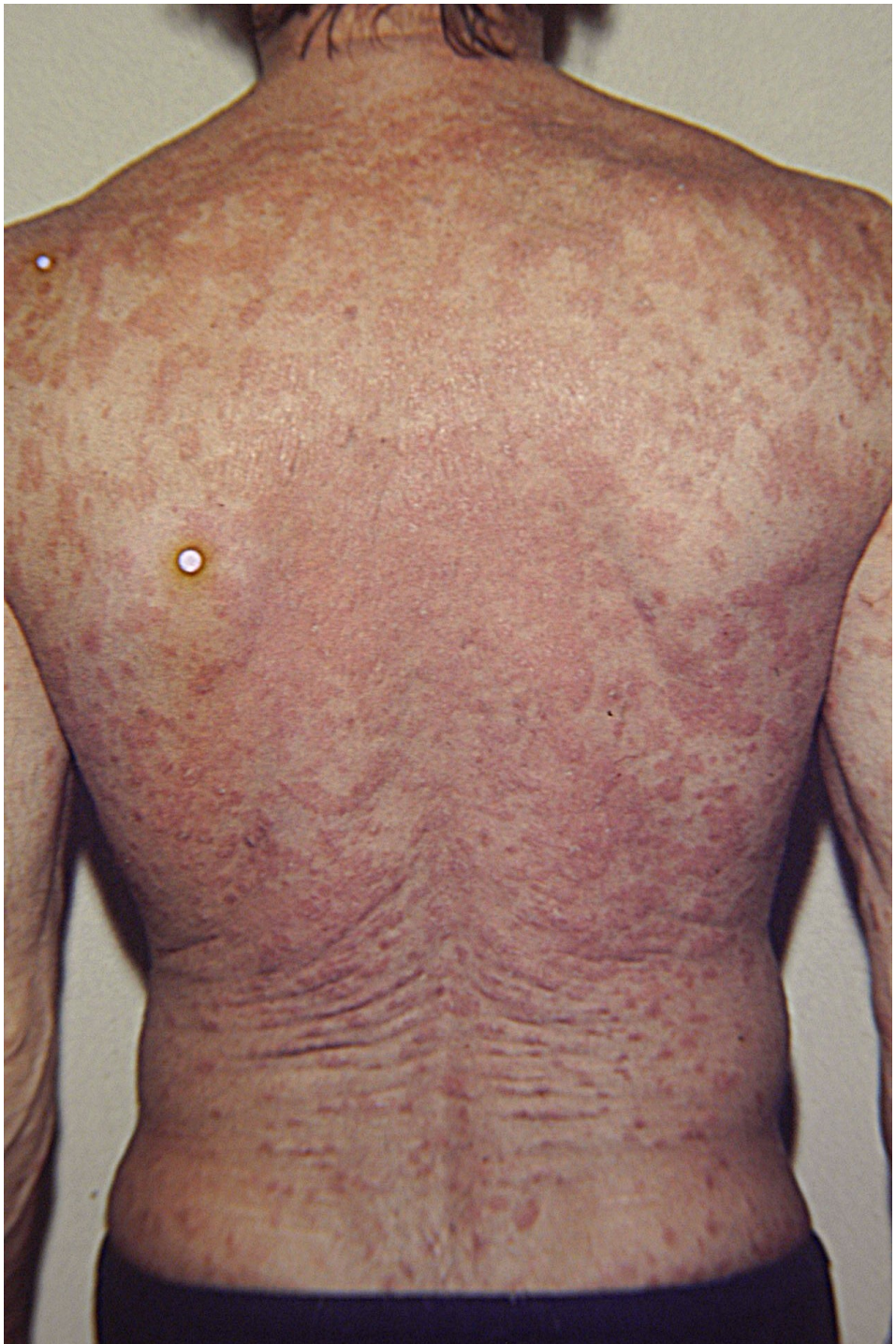


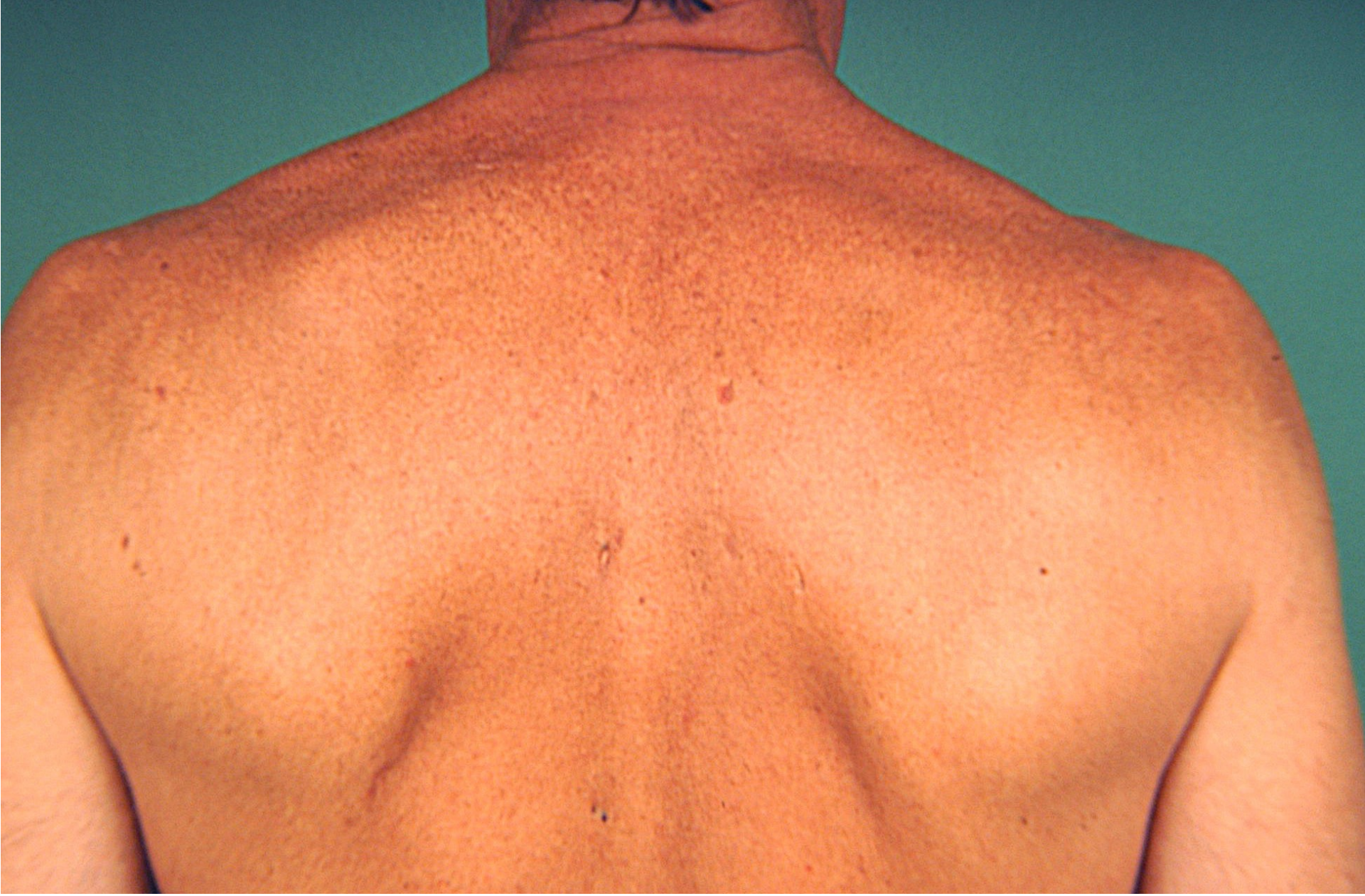
Sézary syndrome,
after rePUVA
1054 J/cm$^2$



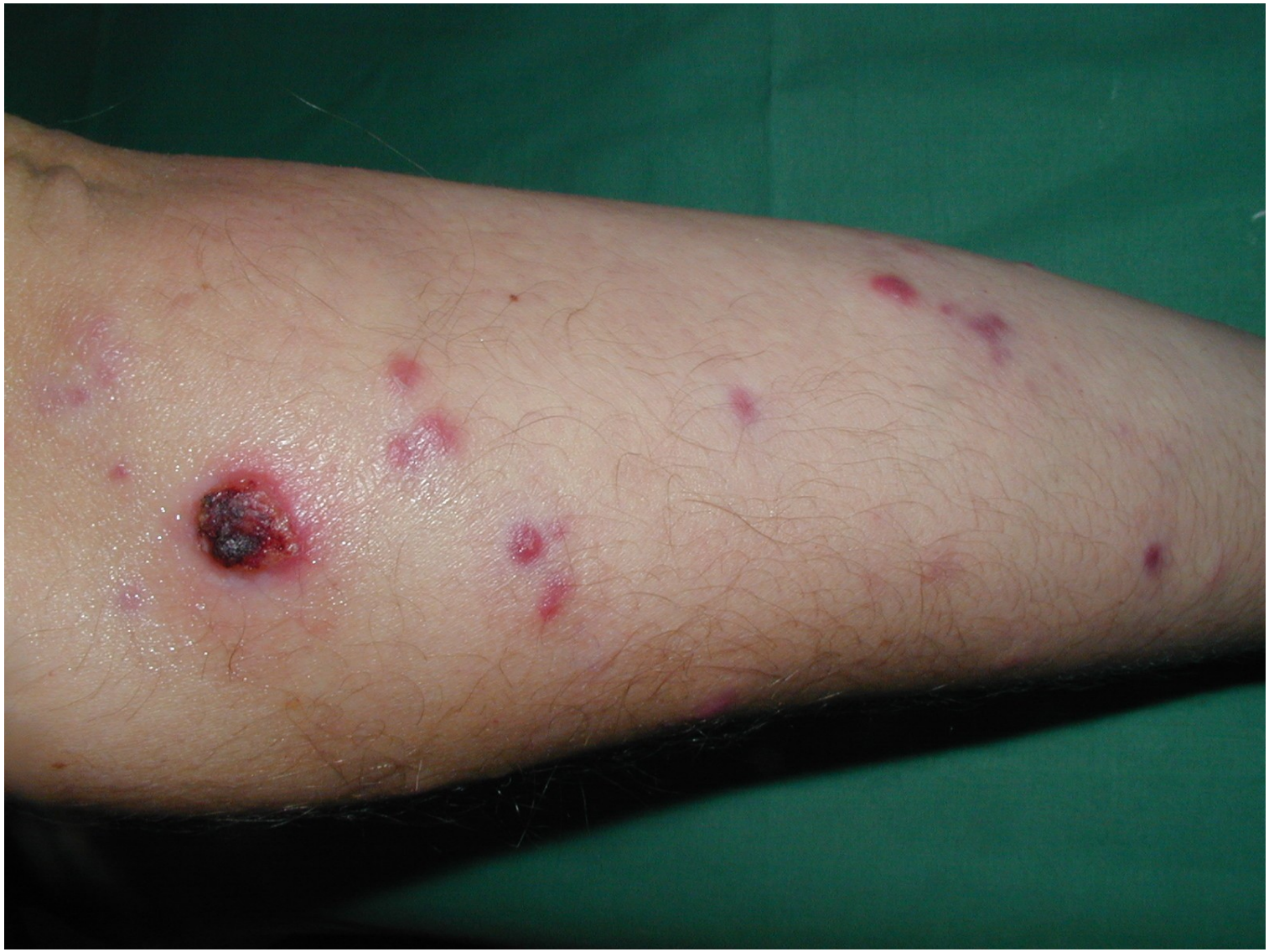
MF 1994





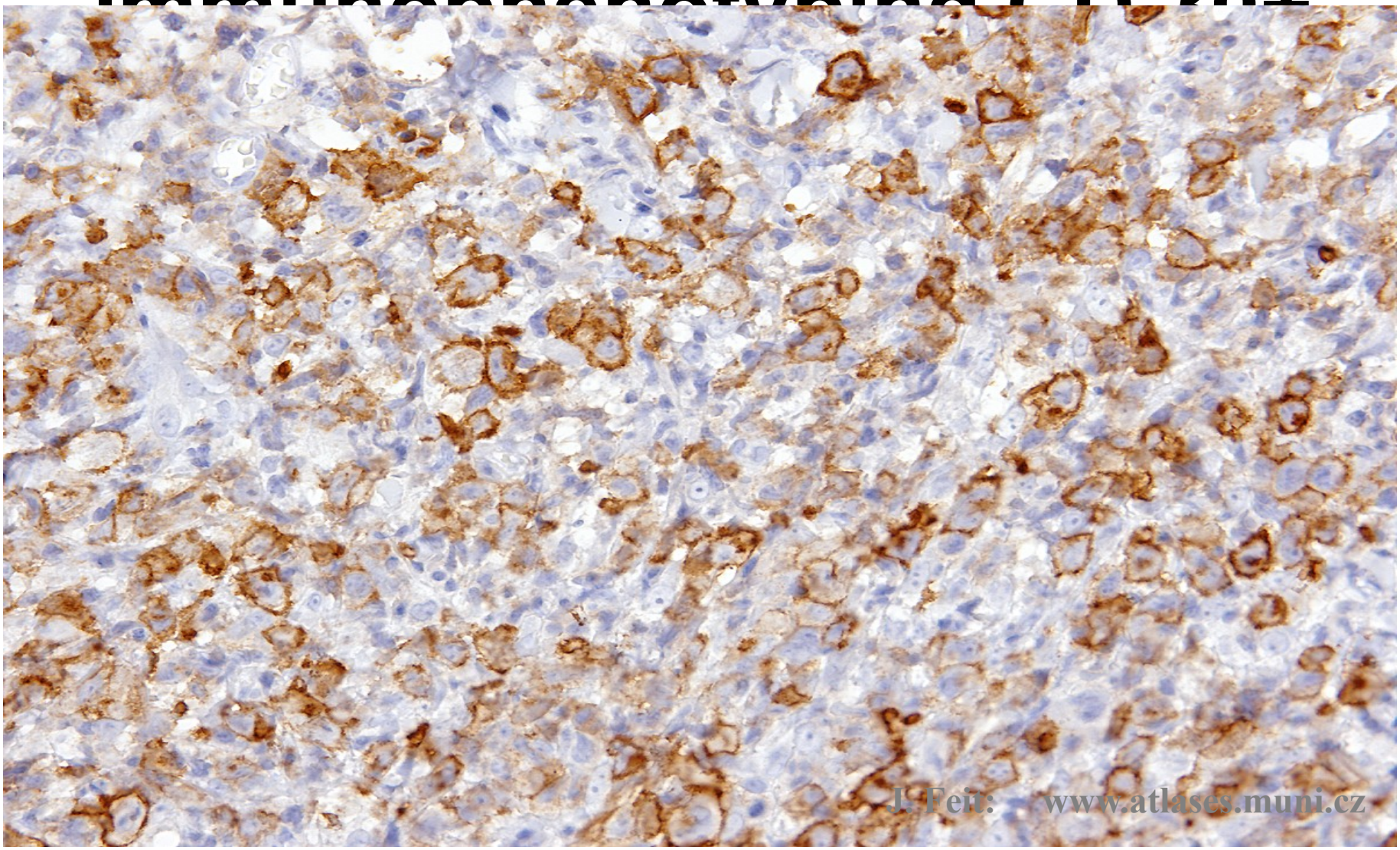


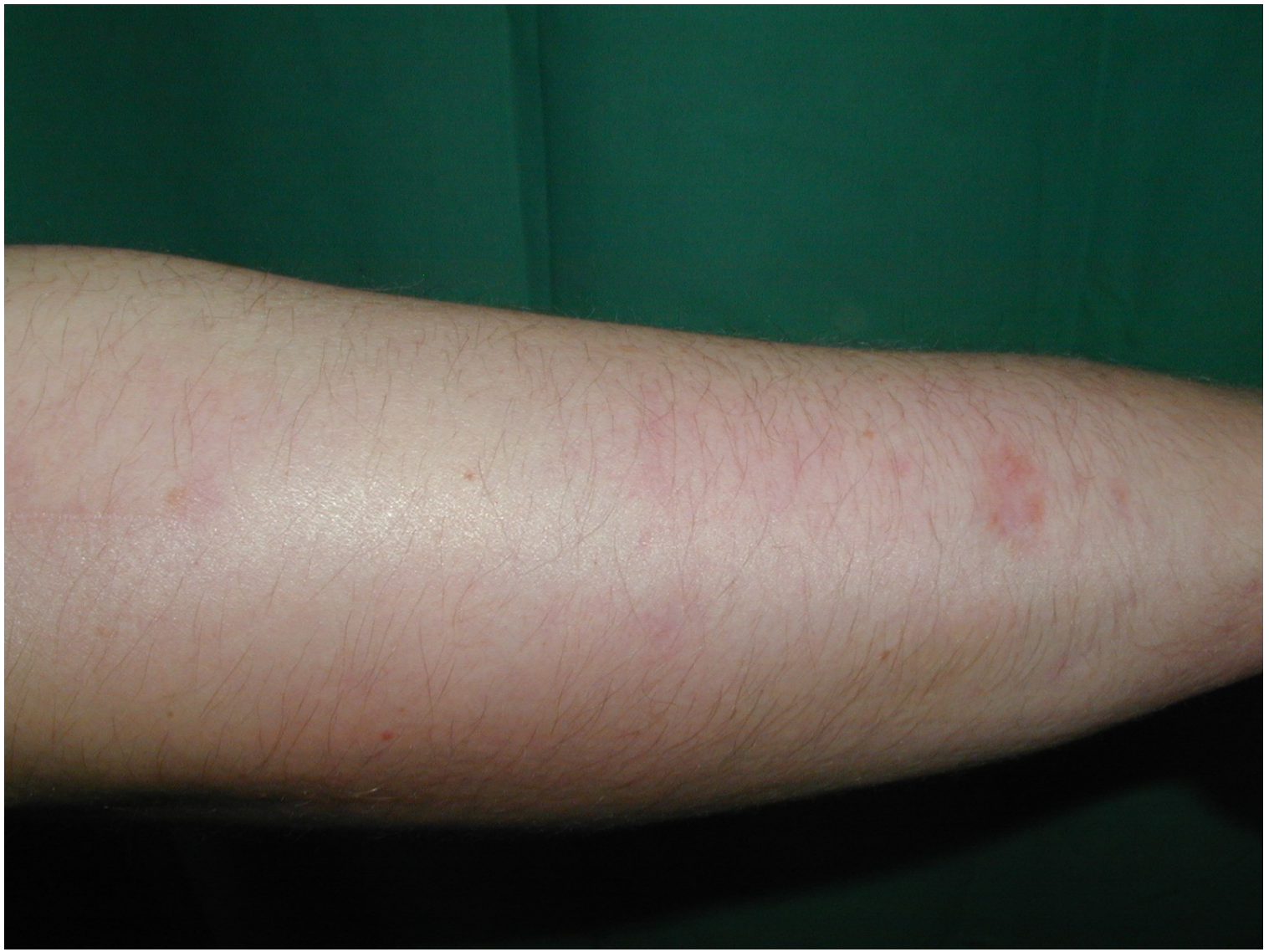
In remission after IFNα + acitretin until 2009



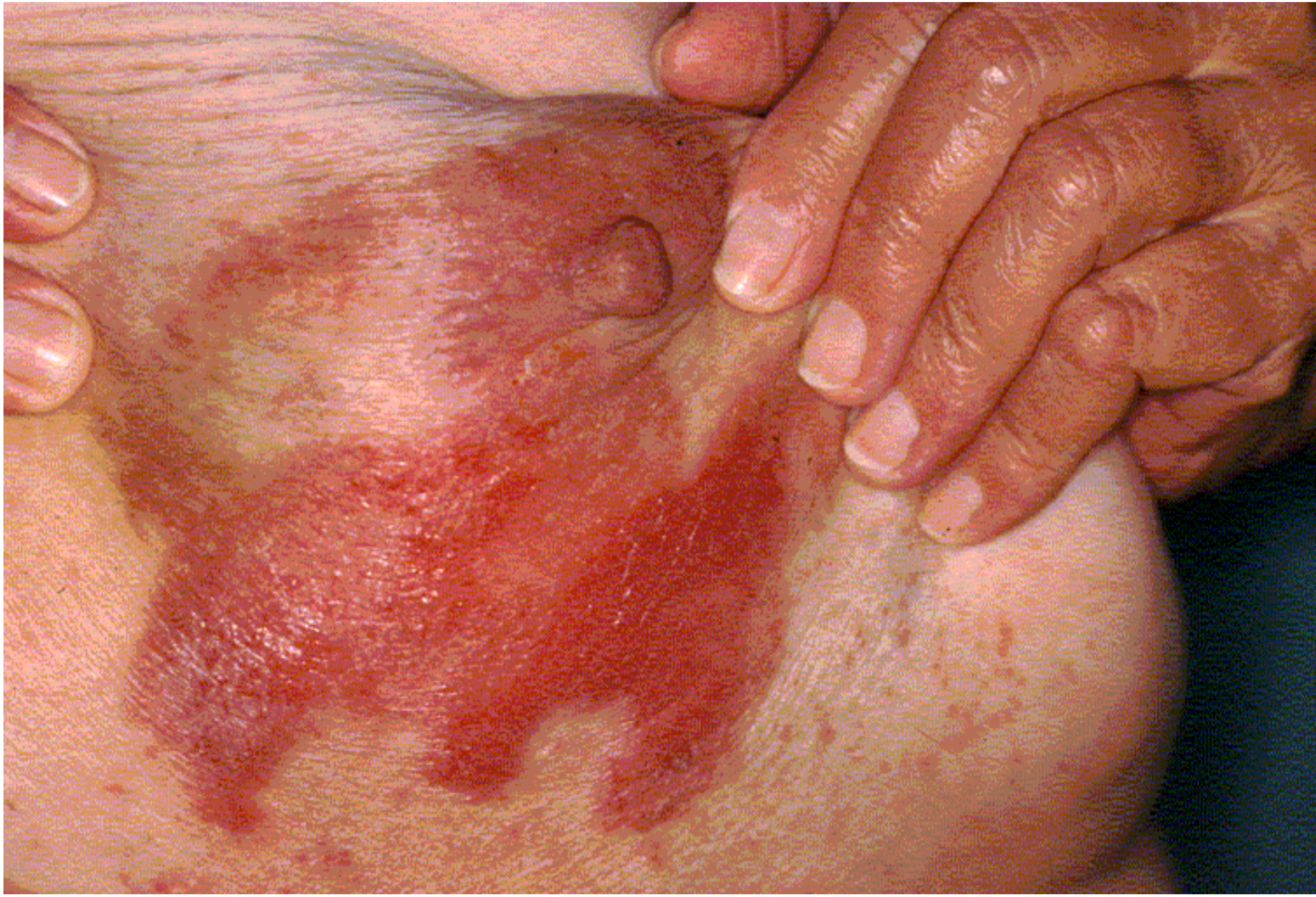
LyP

# Immunophenotyping CD 30+

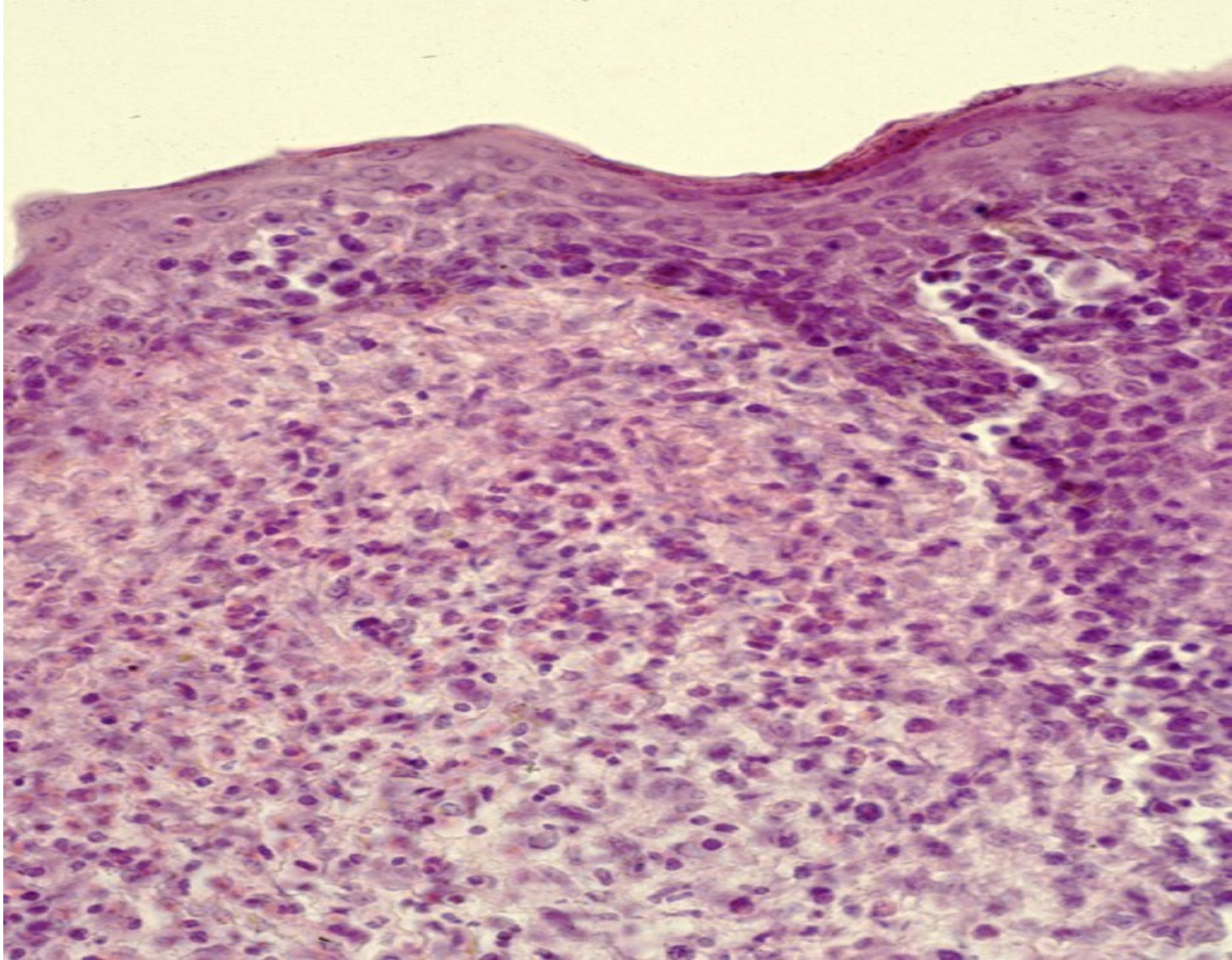


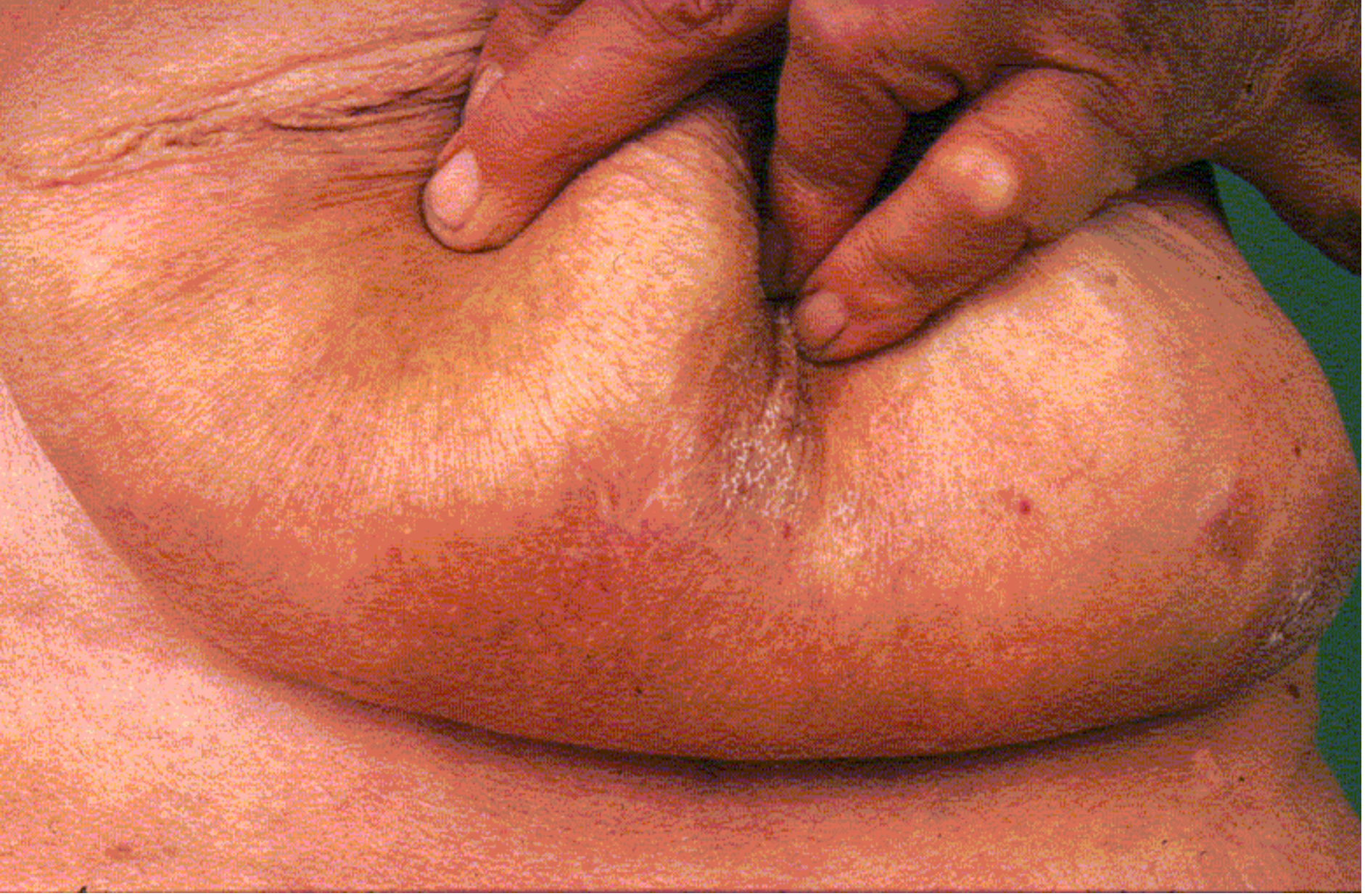


Remission after rePUVA treatment

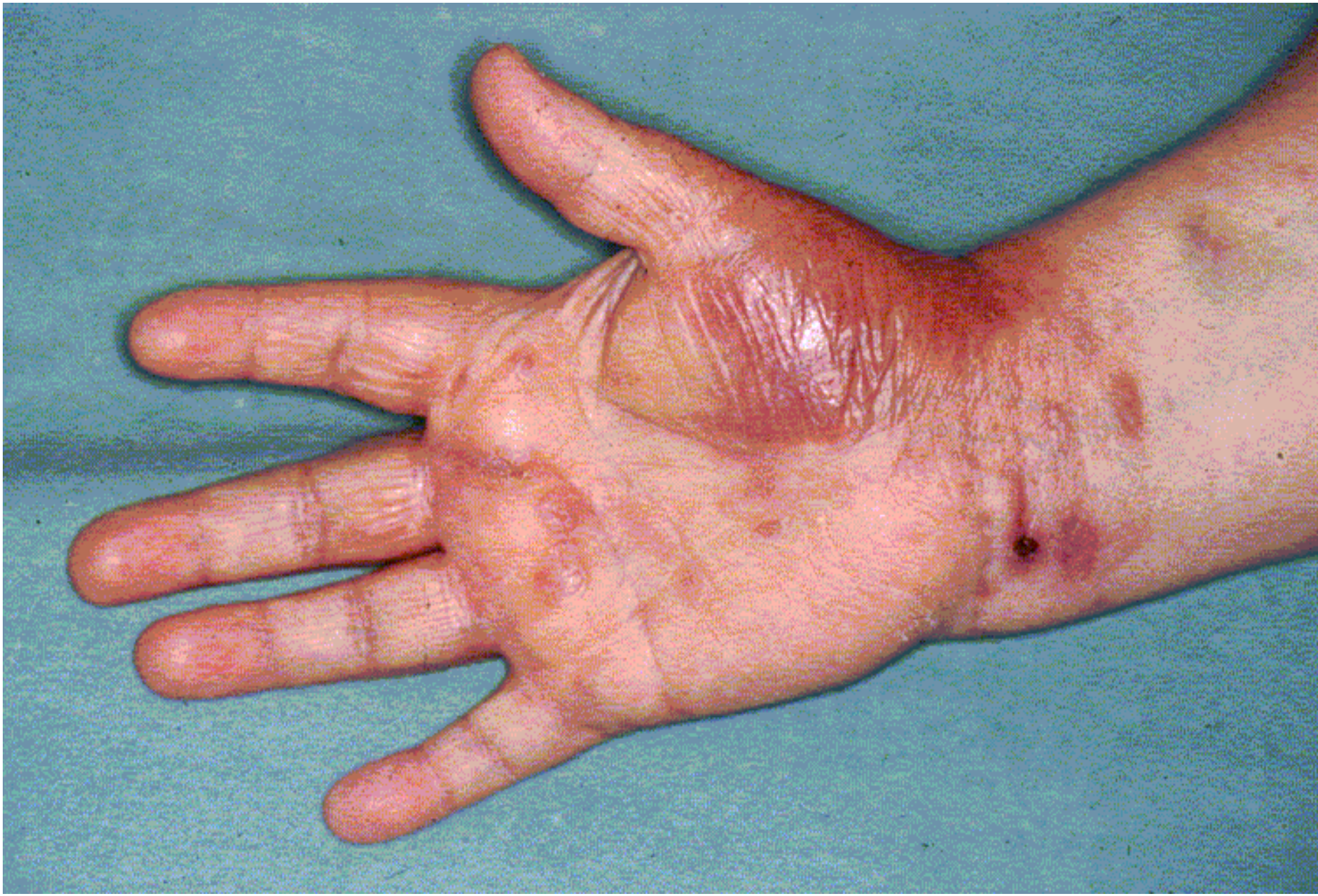


MF 1998

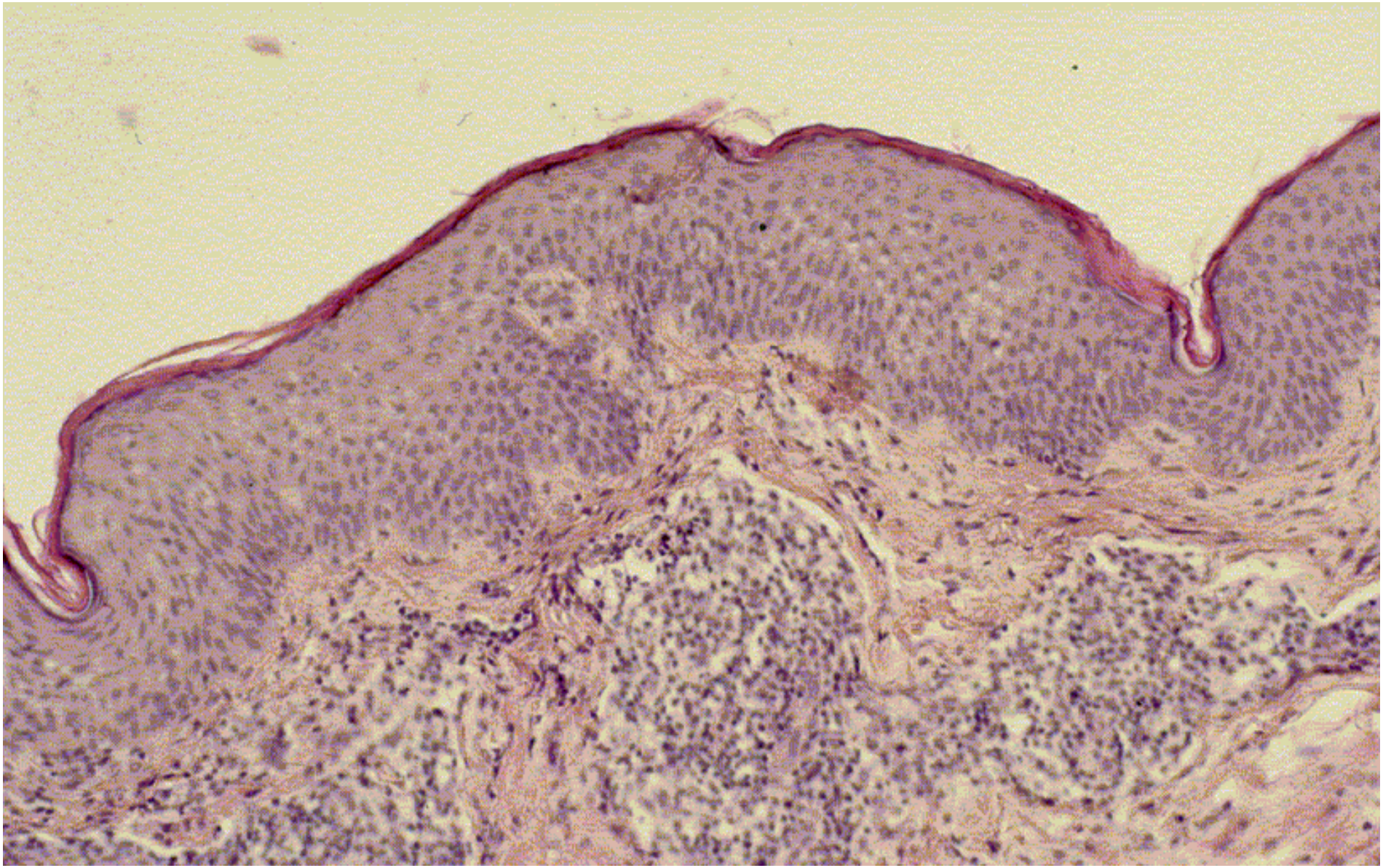


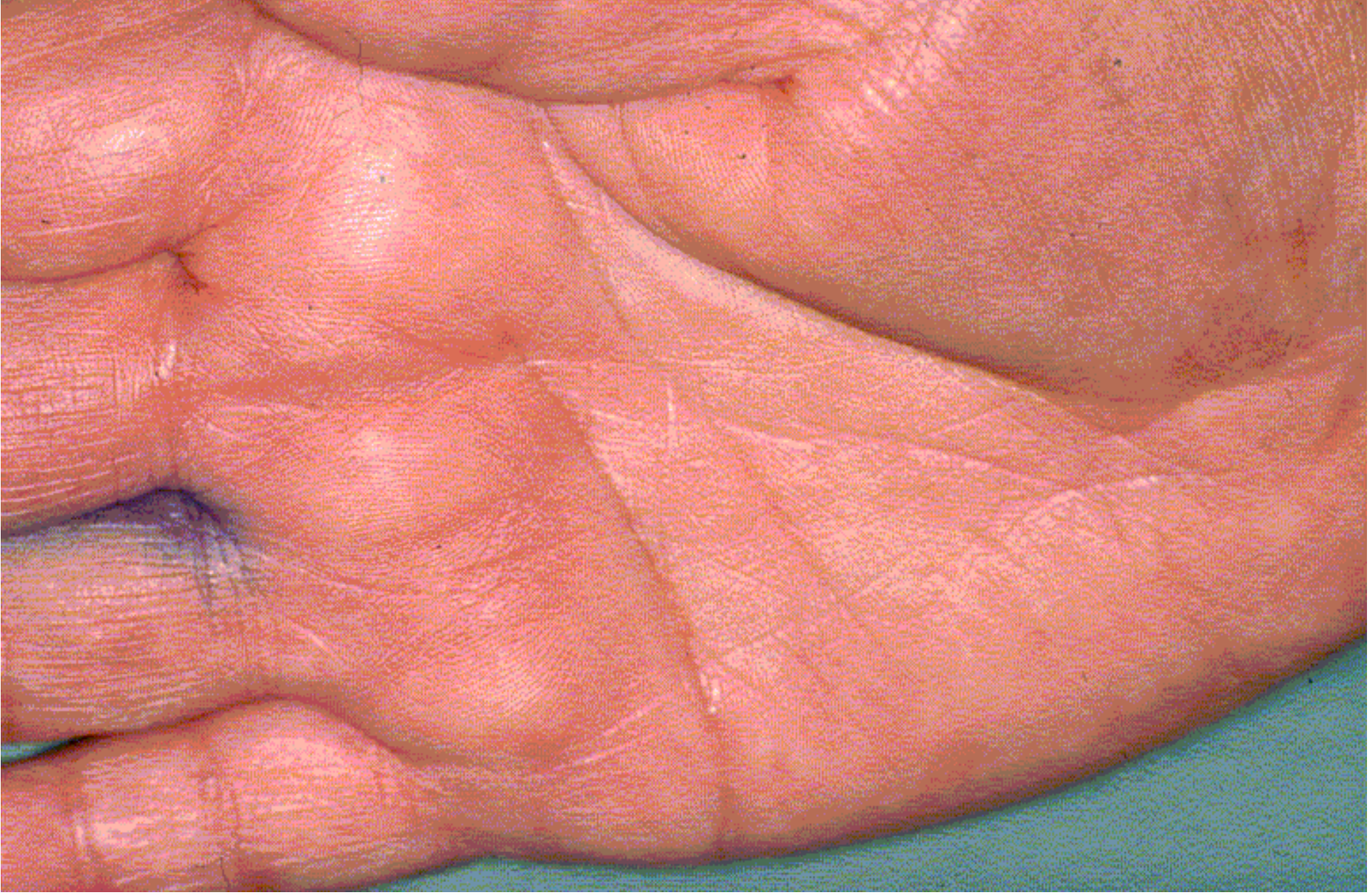


MF after 12 month of PUVA and Intron-A cumulative dose 210 J/cm$^2$, in remission with low dose of acitretin until now

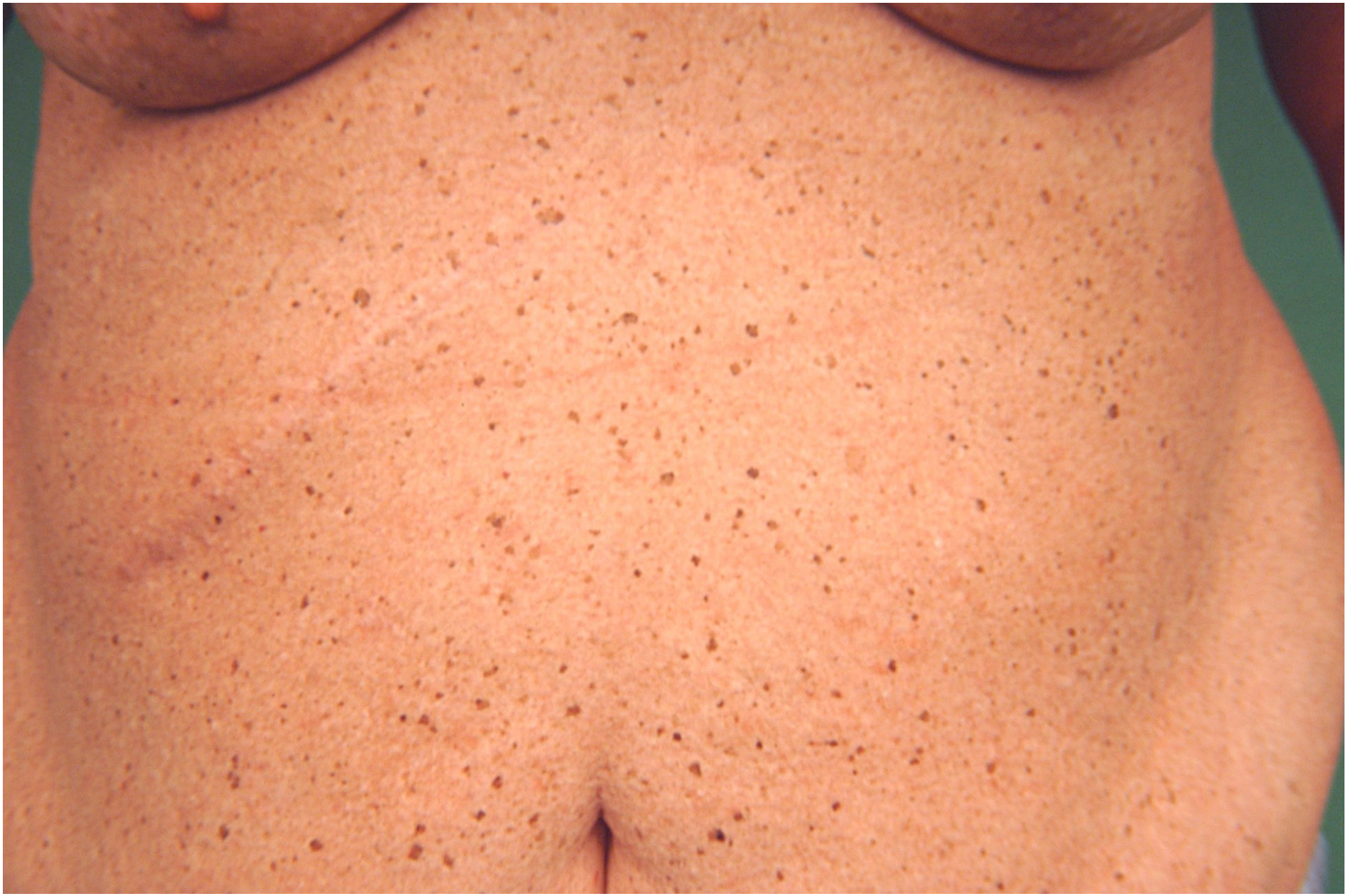


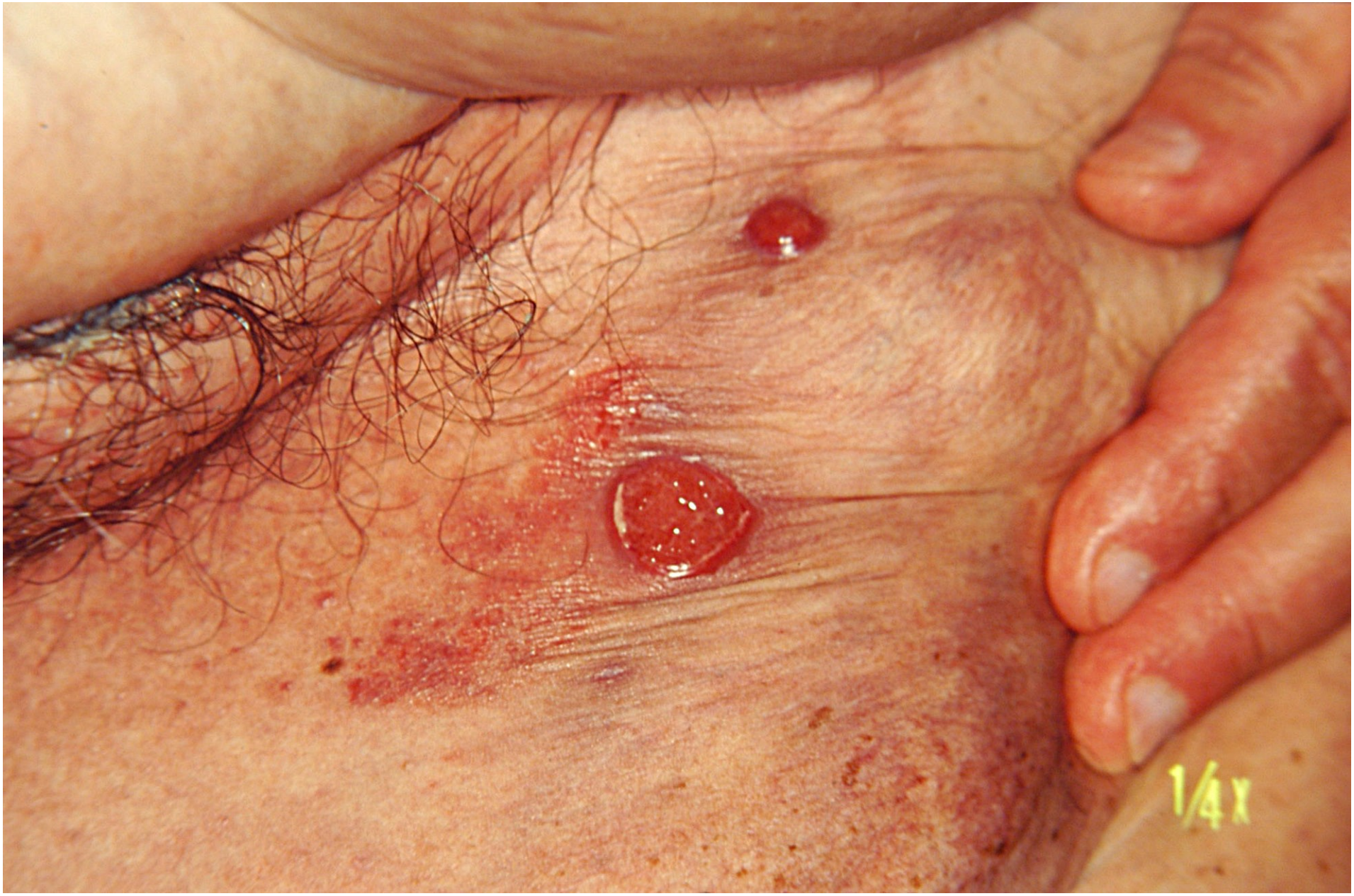
MF 1995

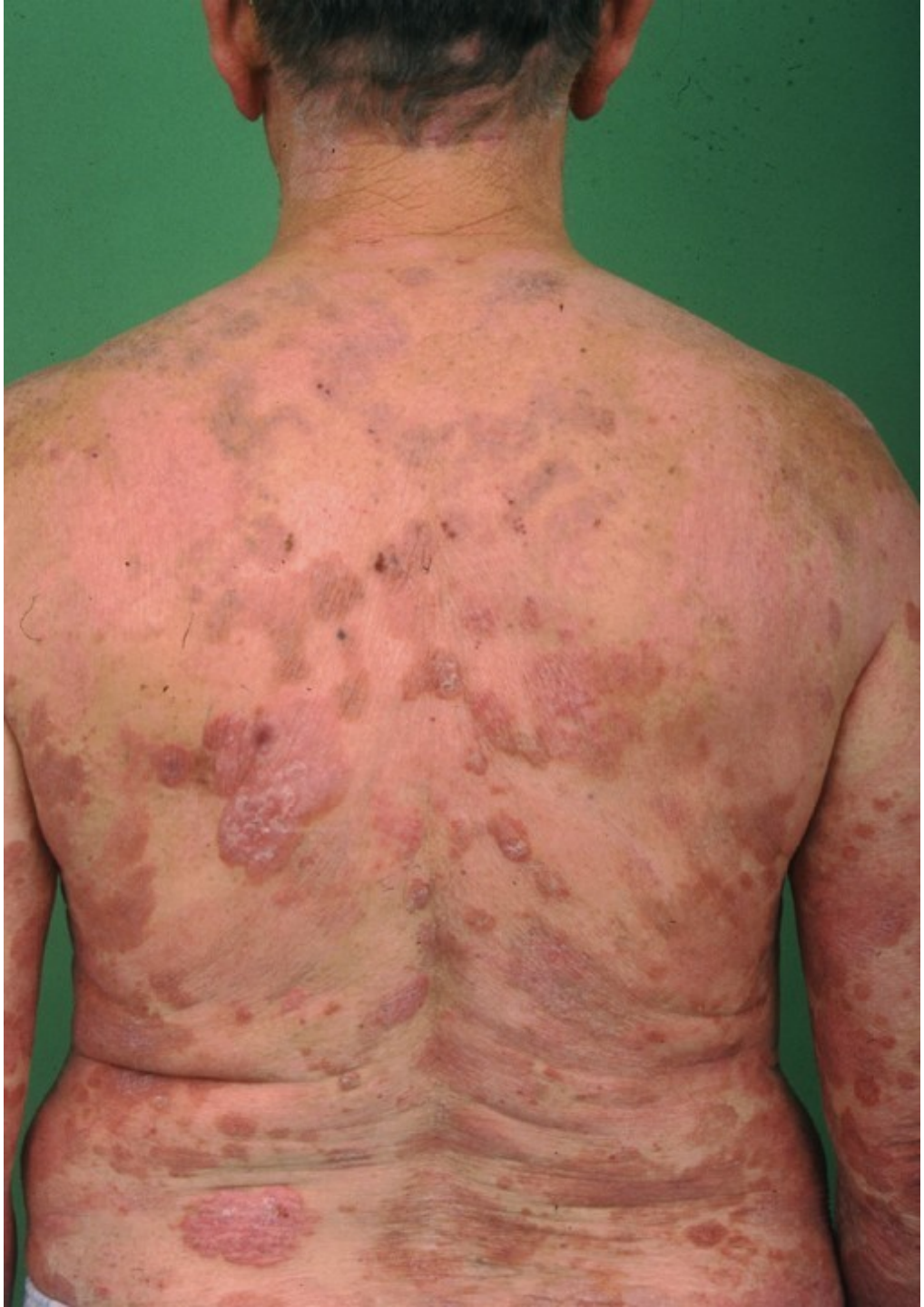




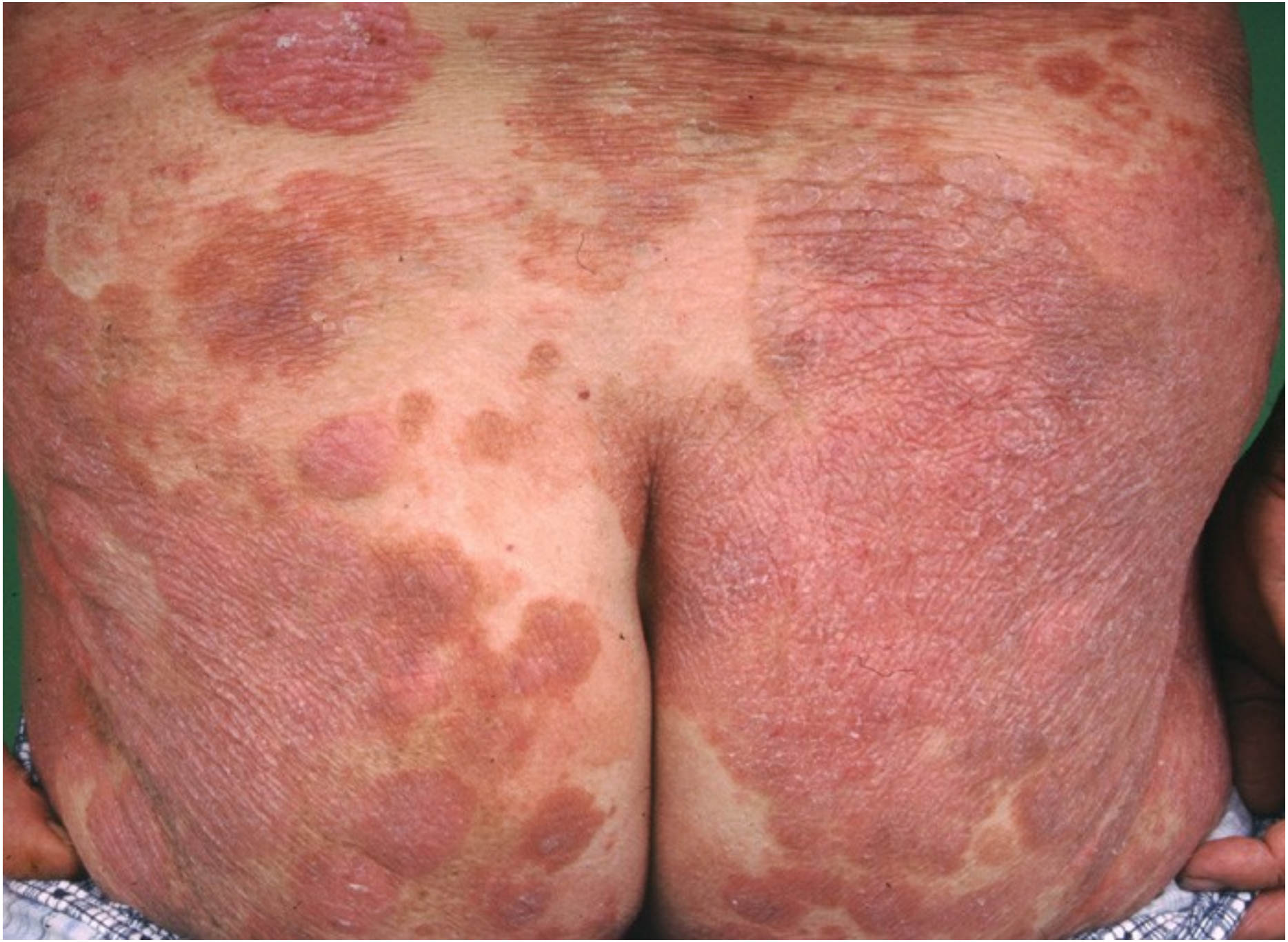
MF 1998, after rePUVA, cumulative dose 500 J/cm$^2$

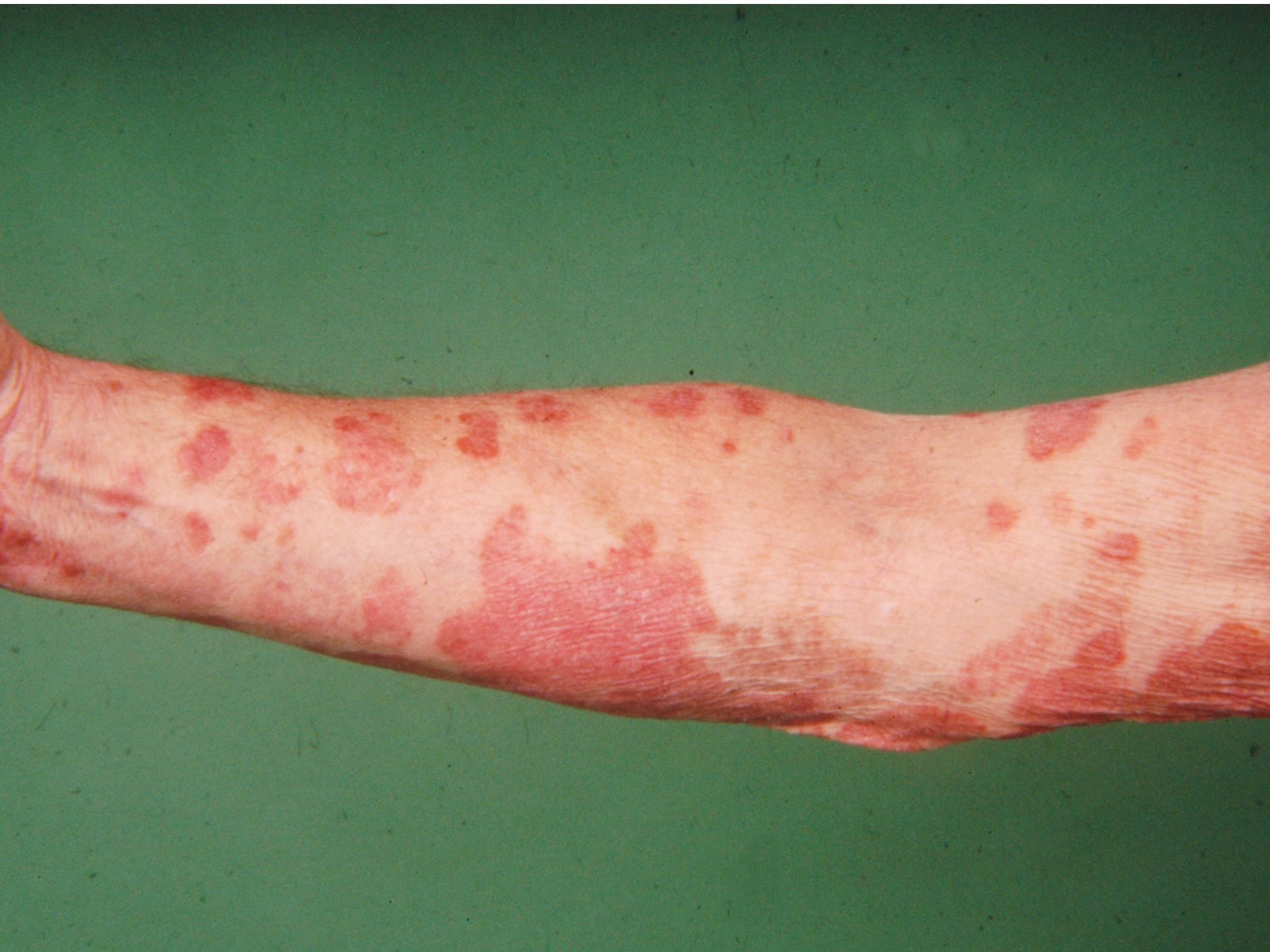


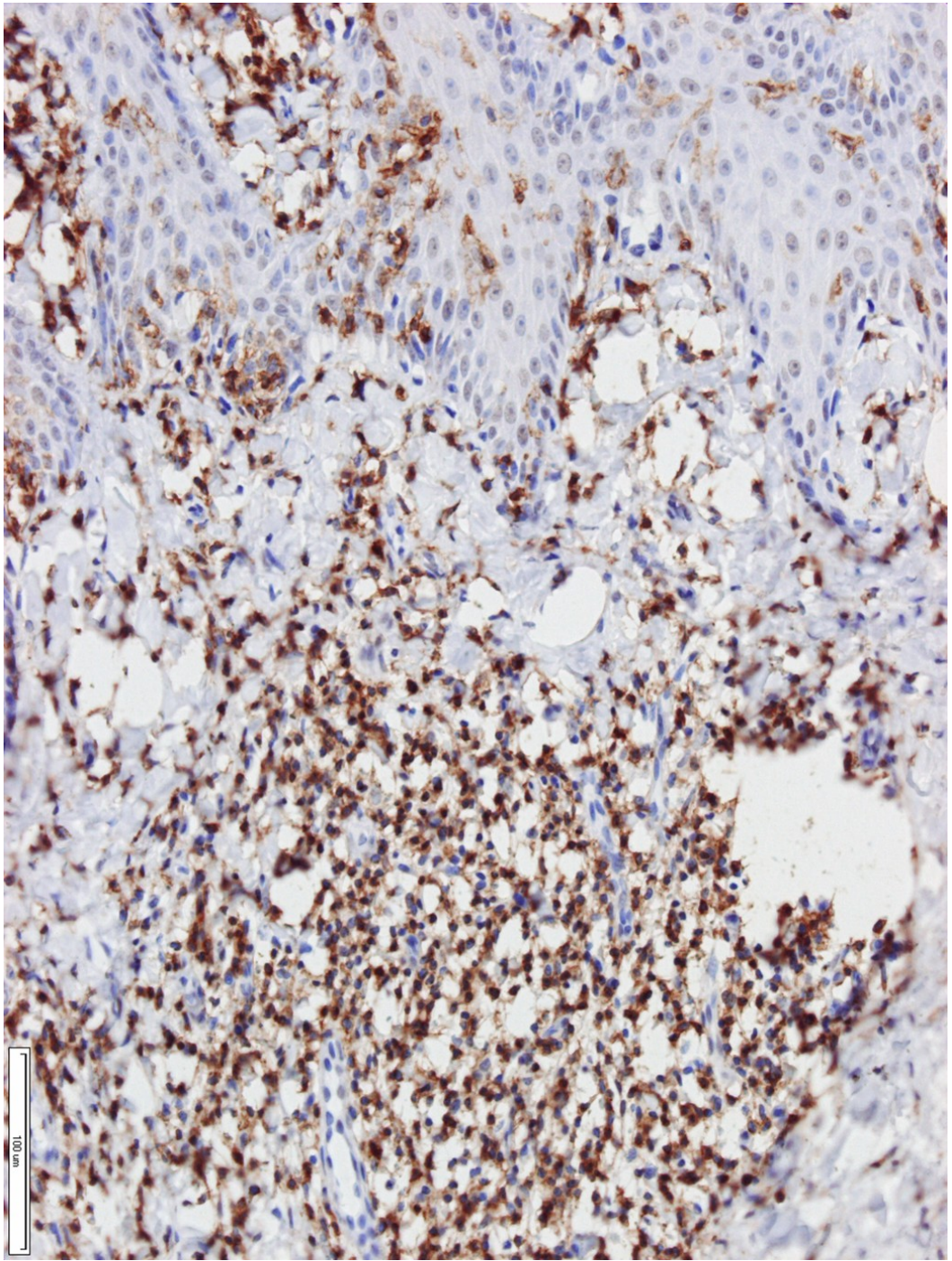

1/4x

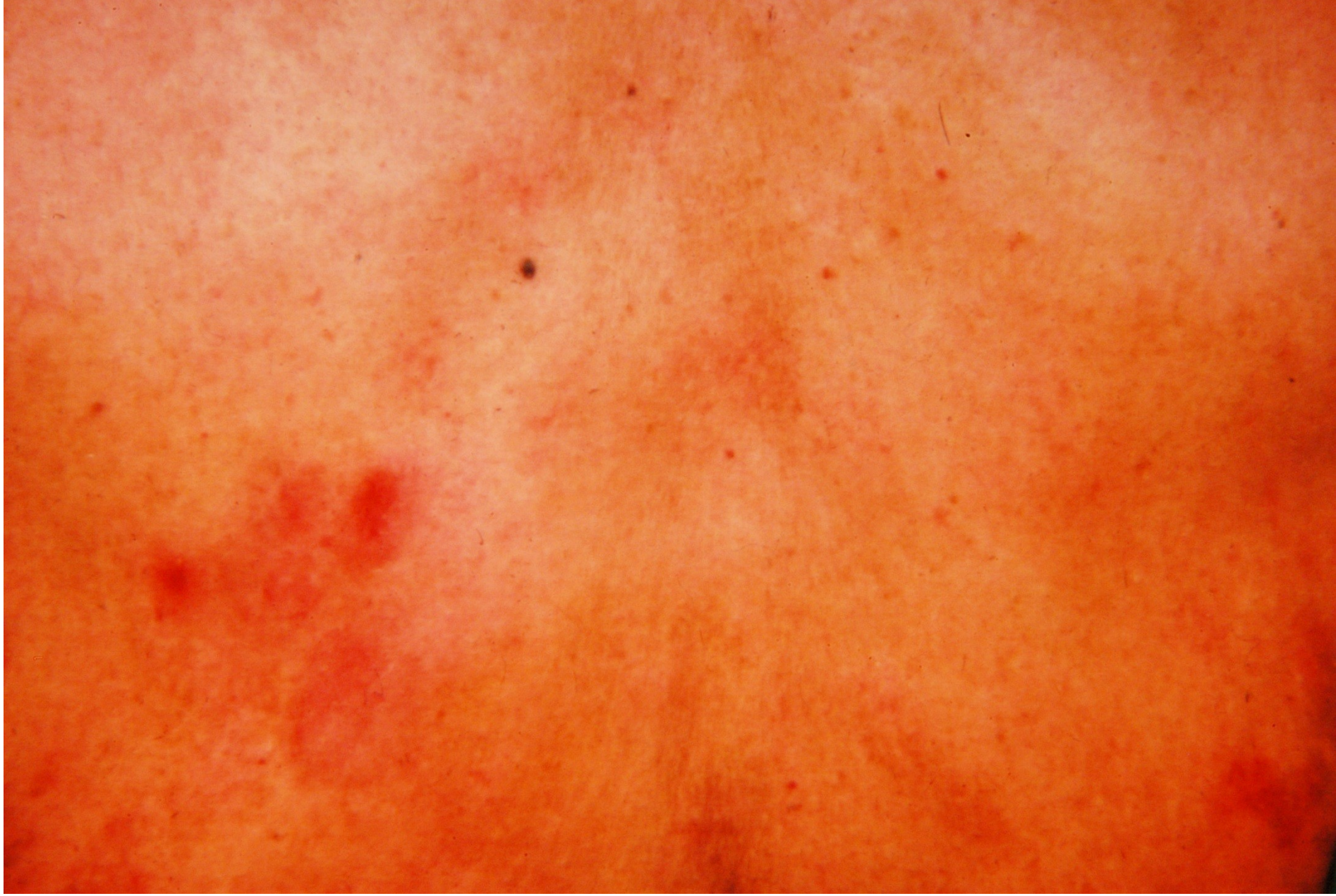


MF - before therapy

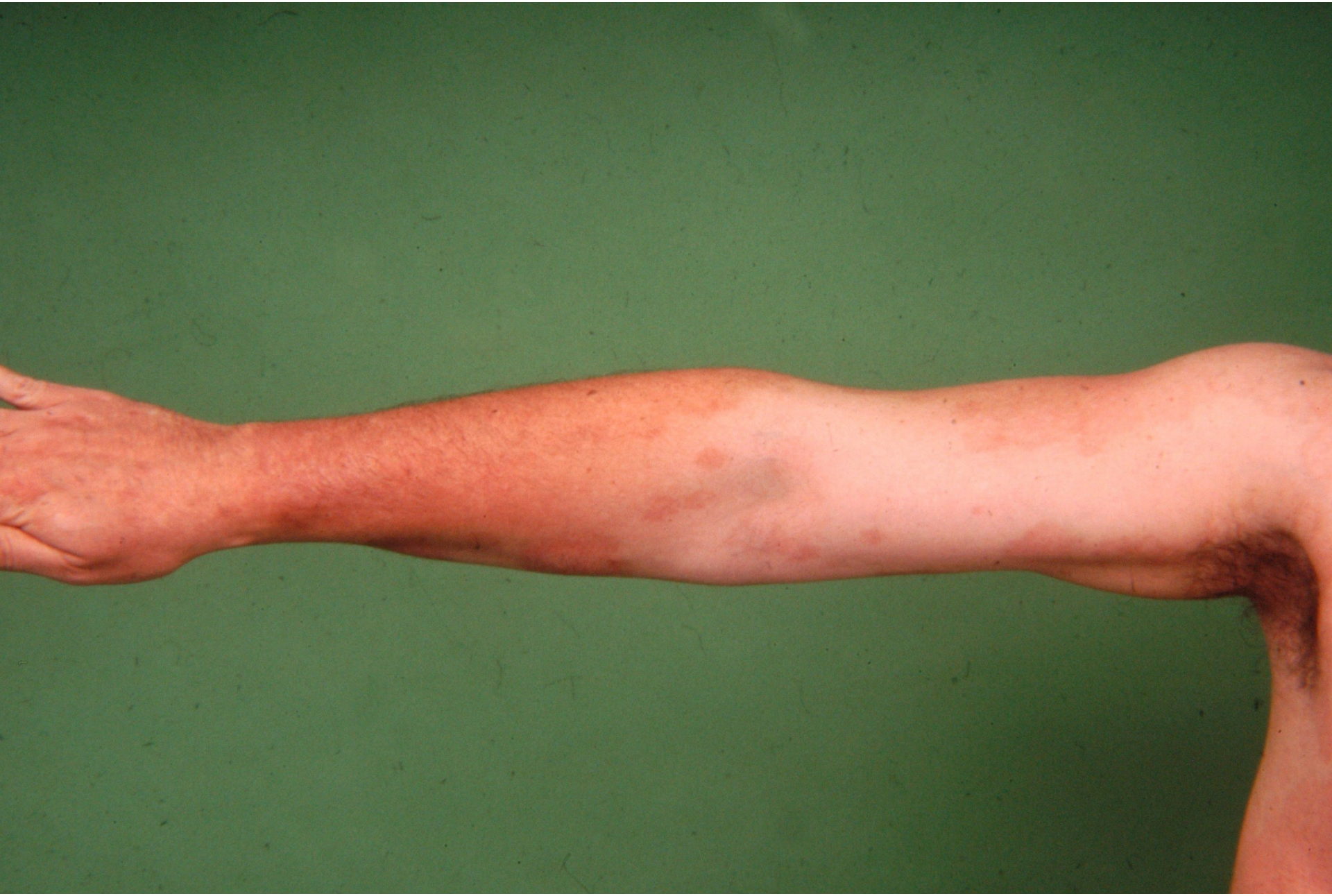


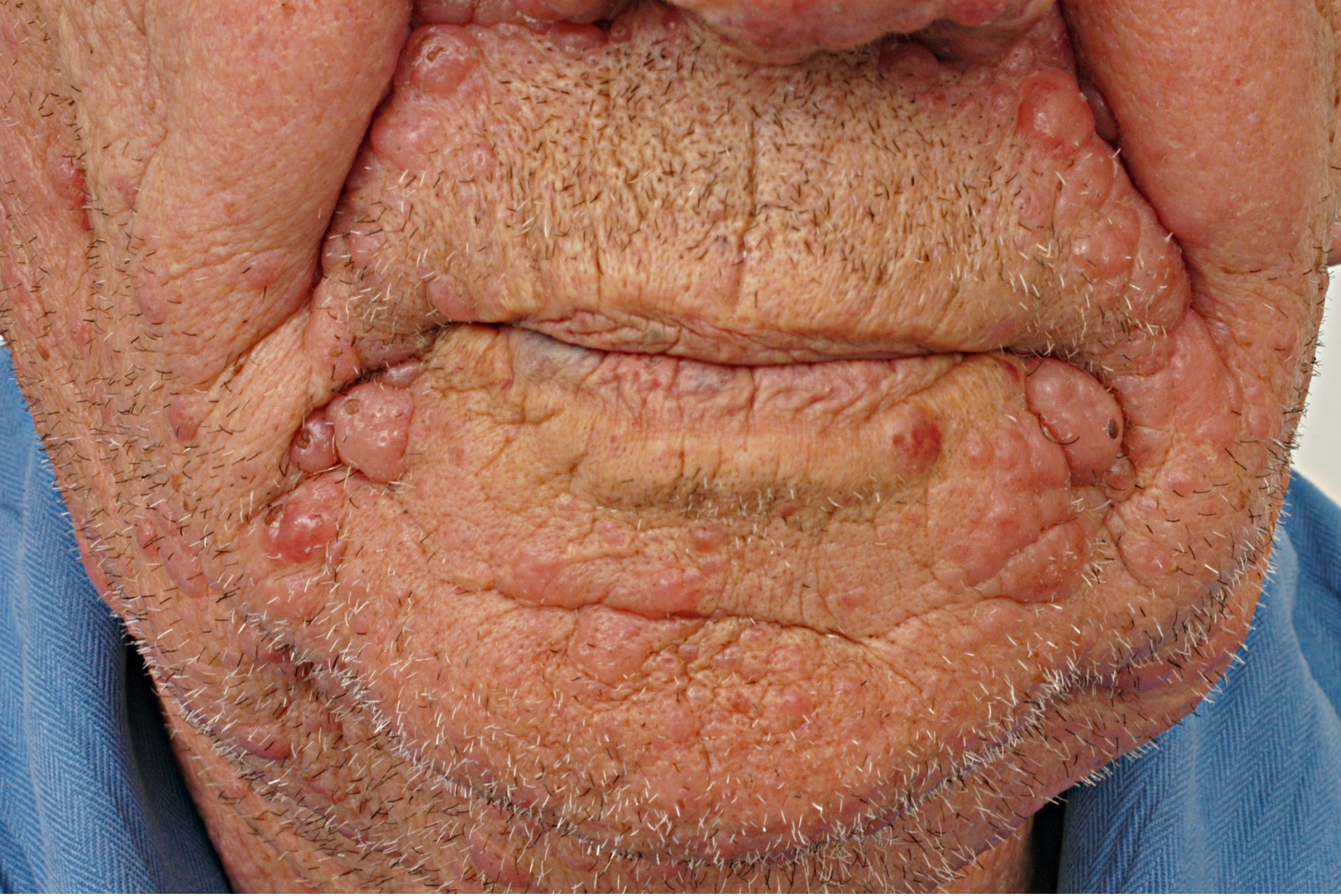



100 um

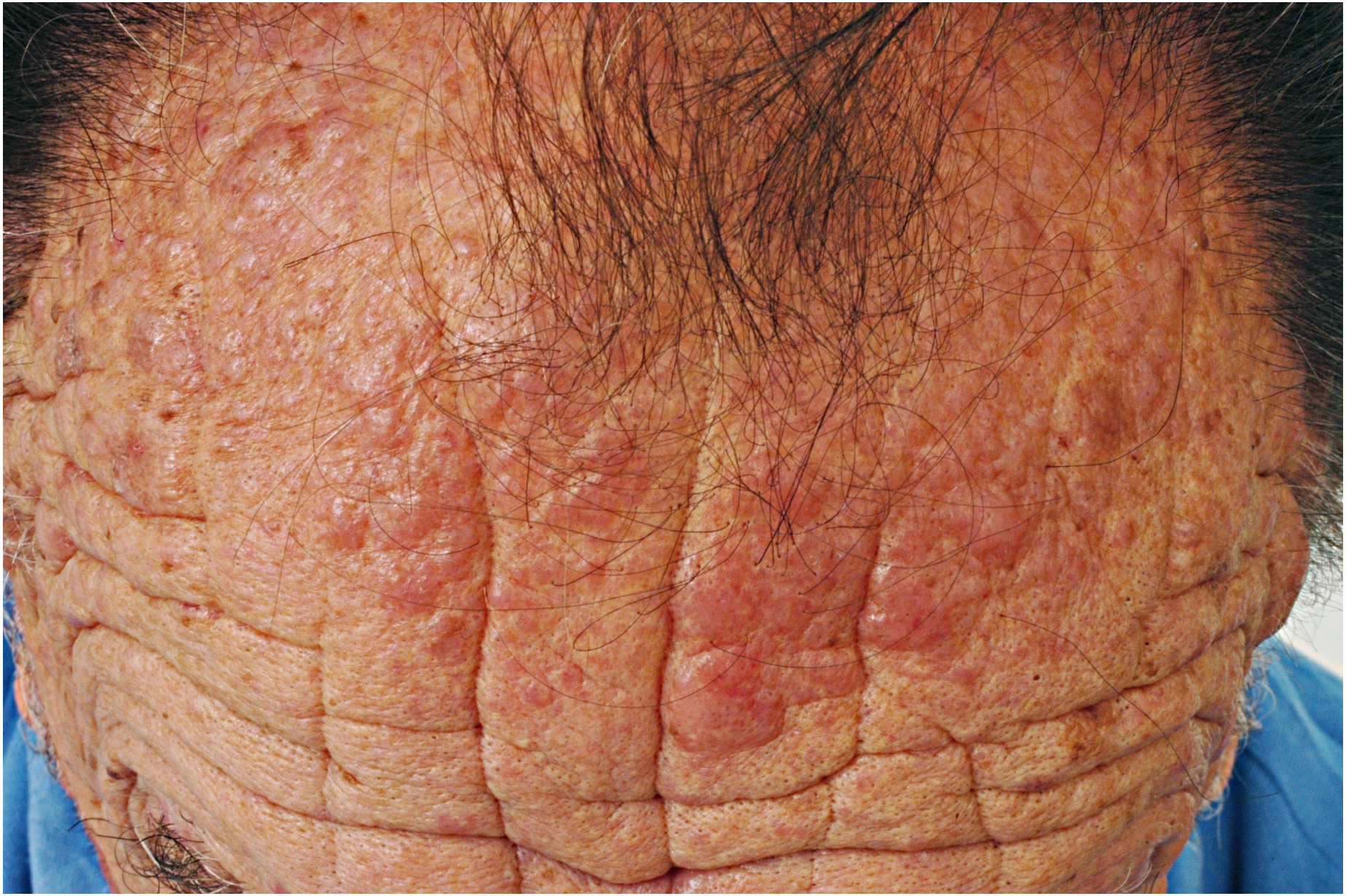


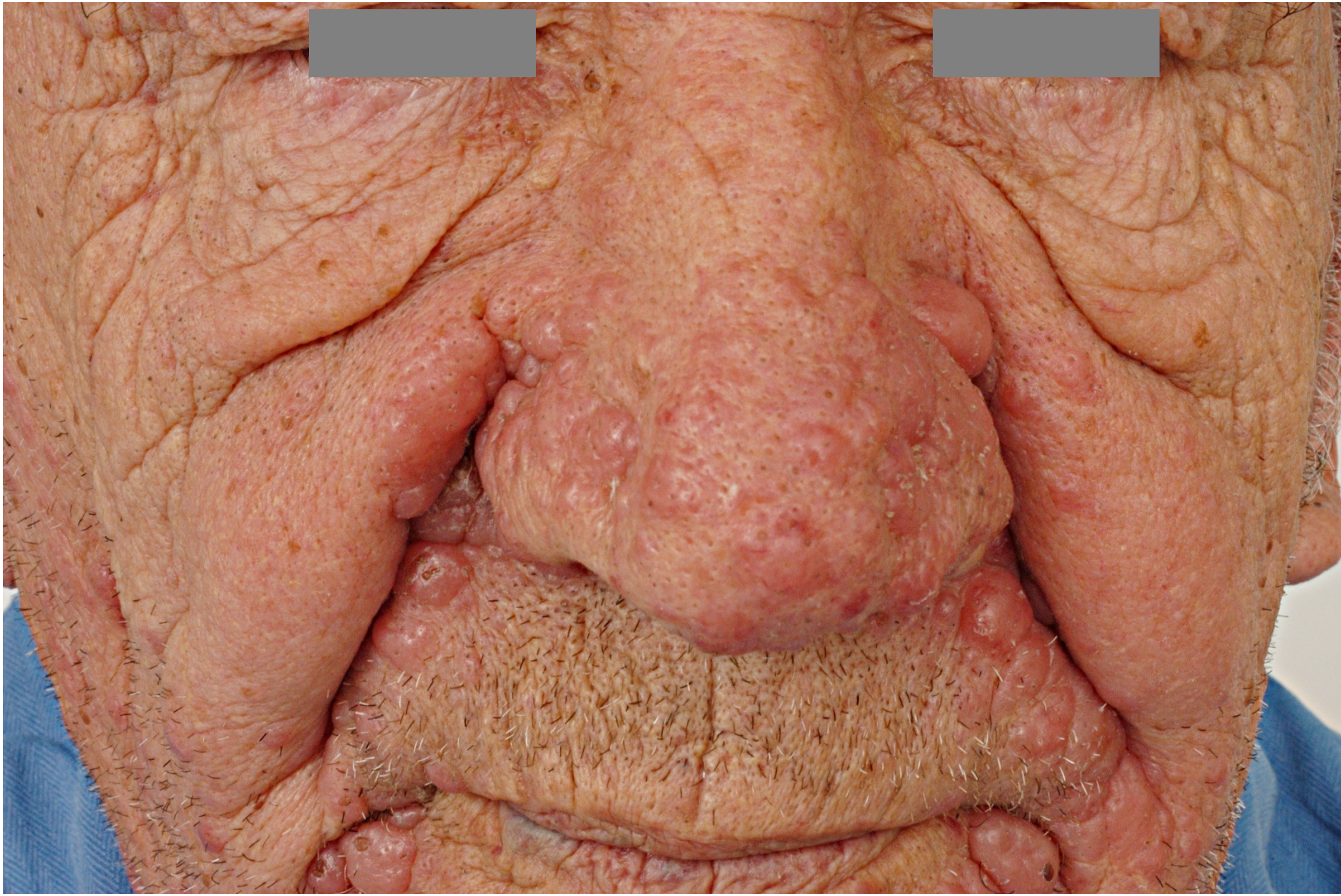
Remission after IFNα + acitretin

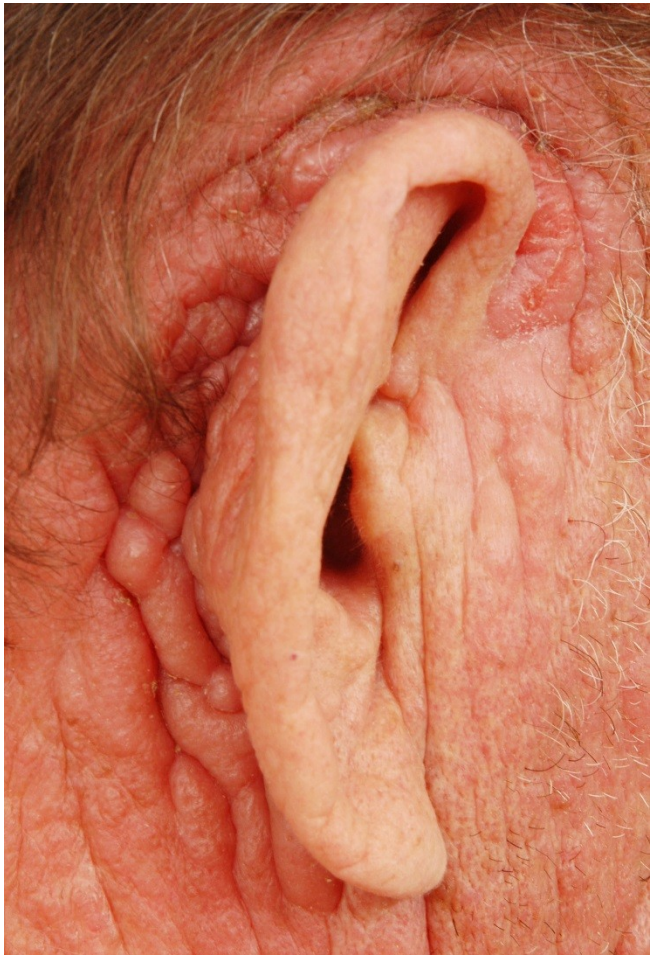


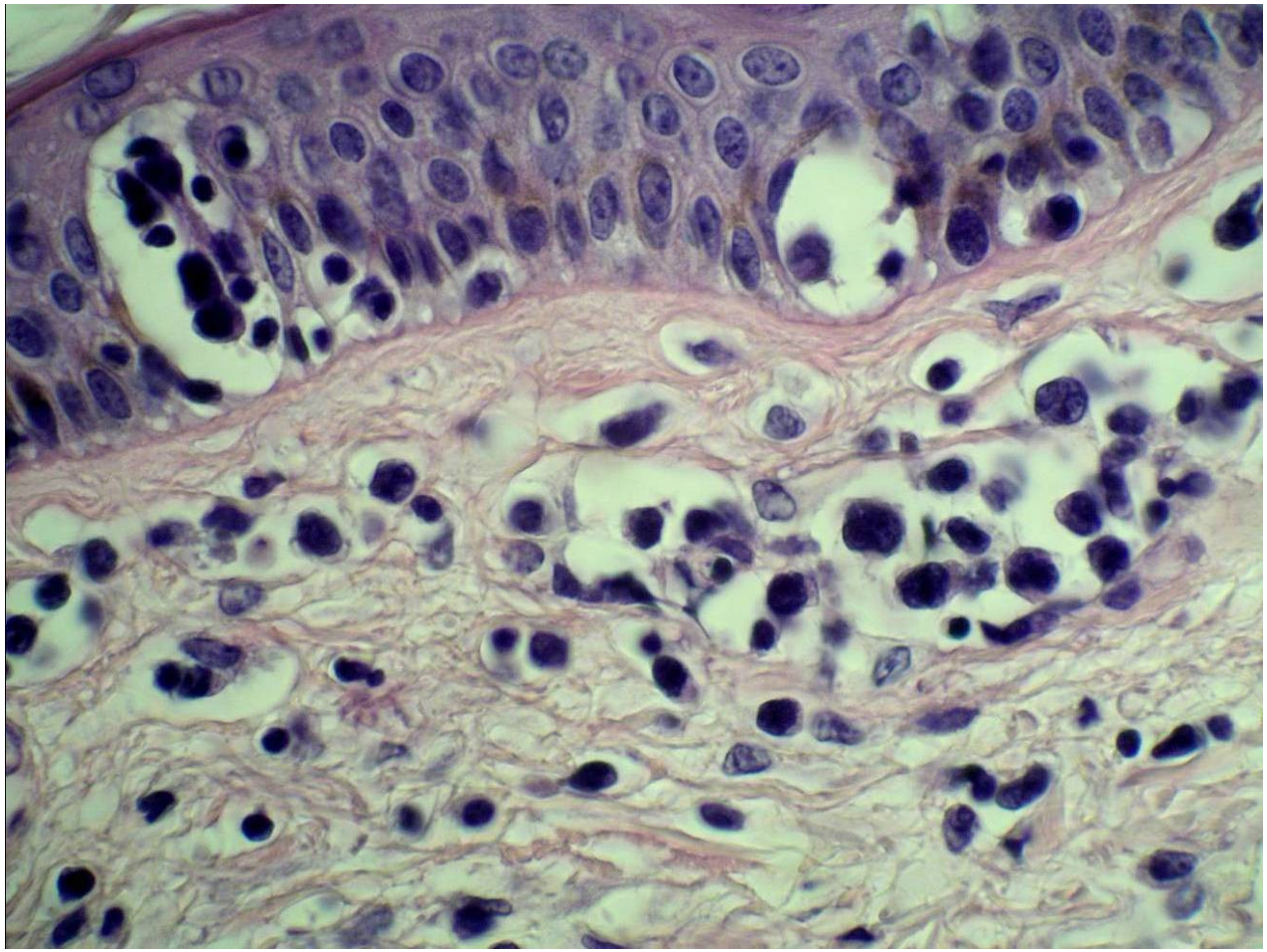


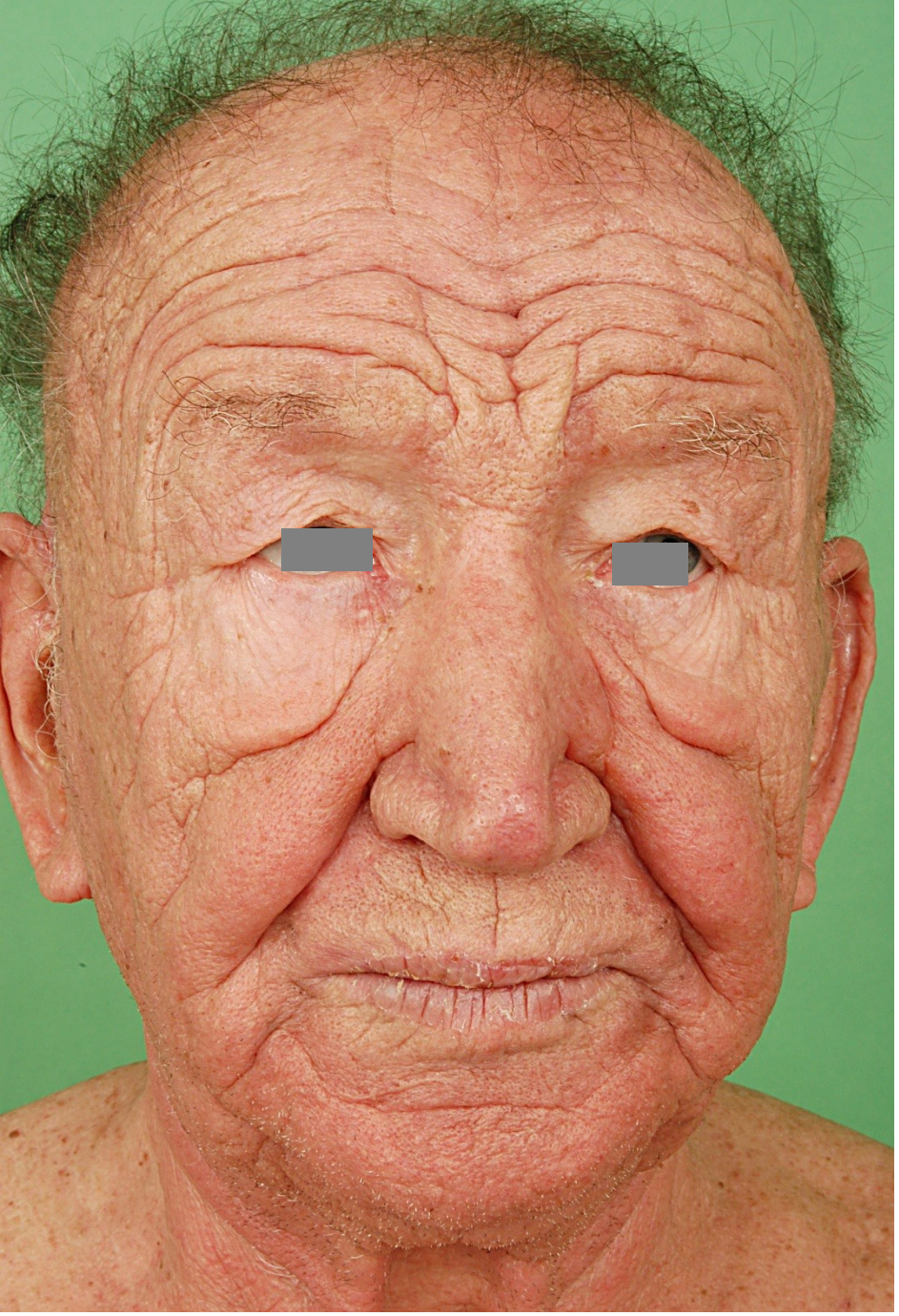
MF - before therapy, 2007



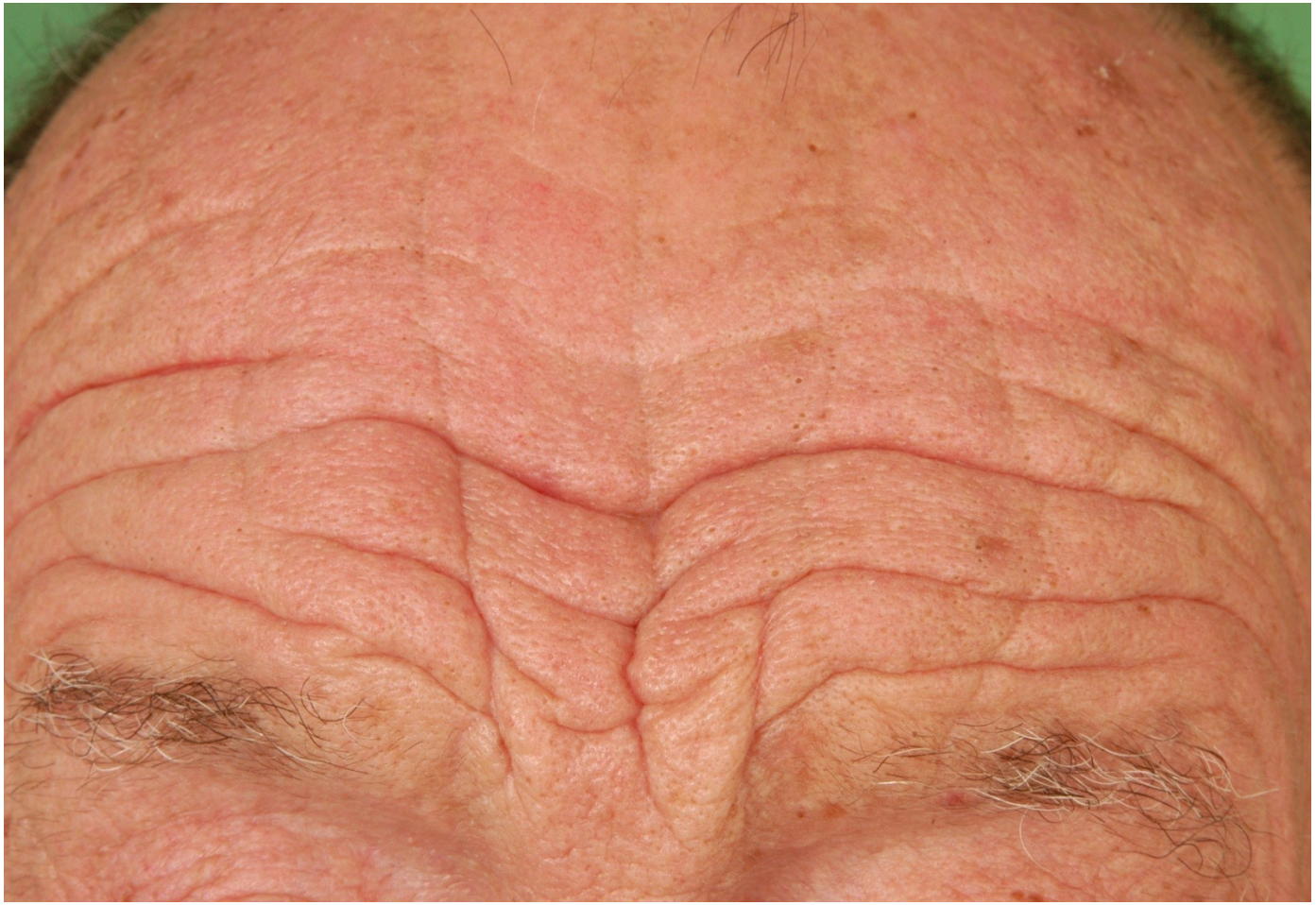


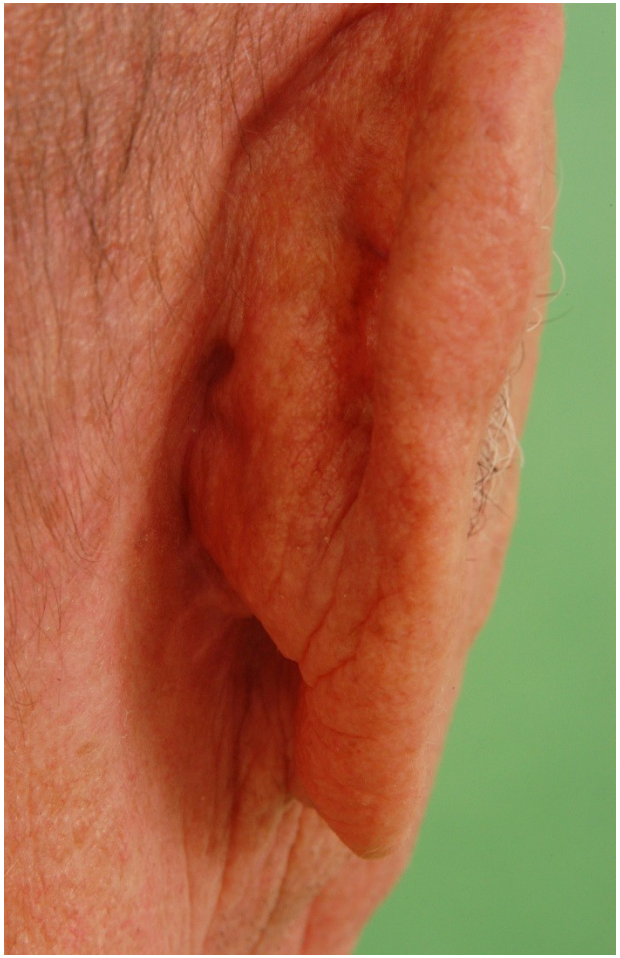




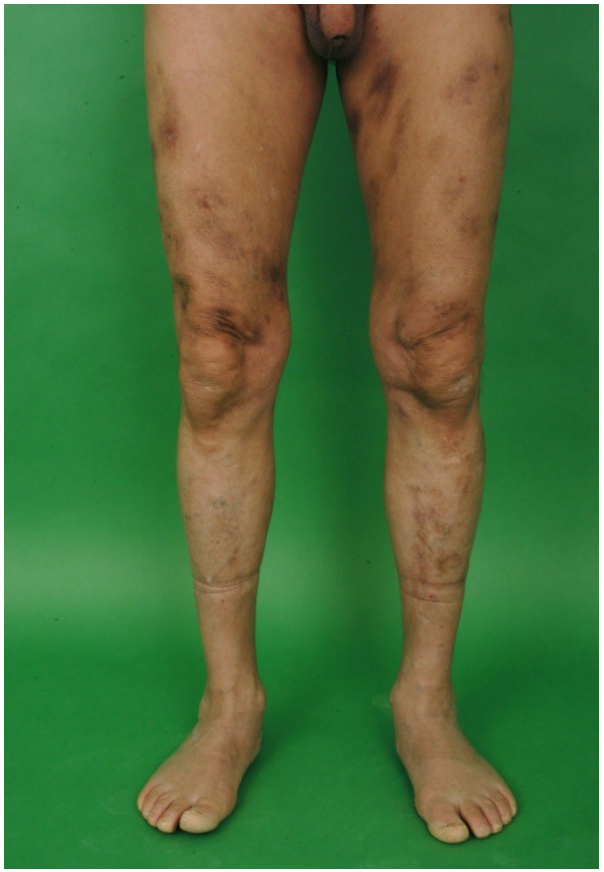


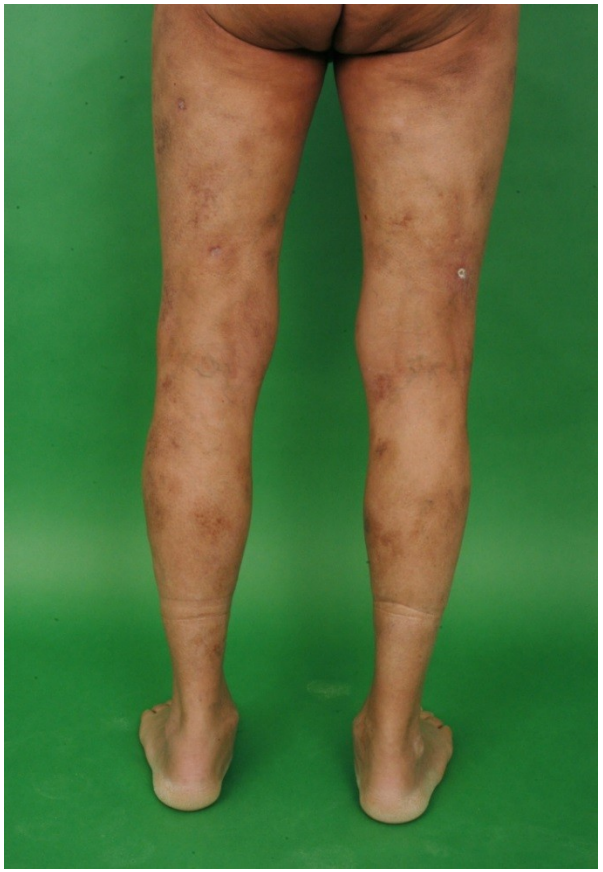
Complete remission after rePUVA + IFNα until now

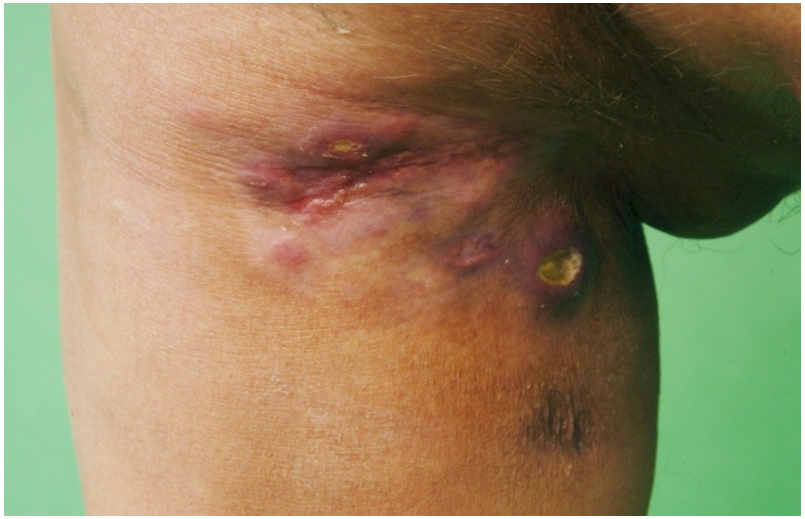


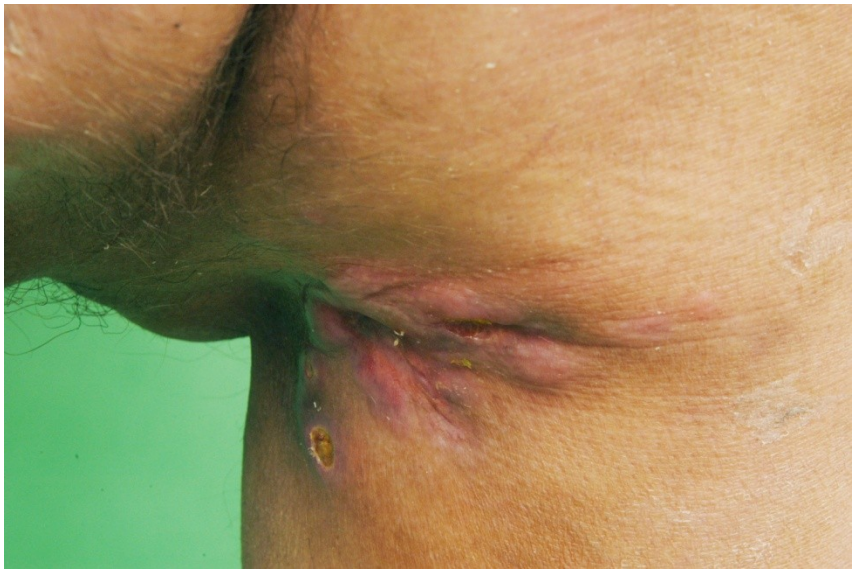


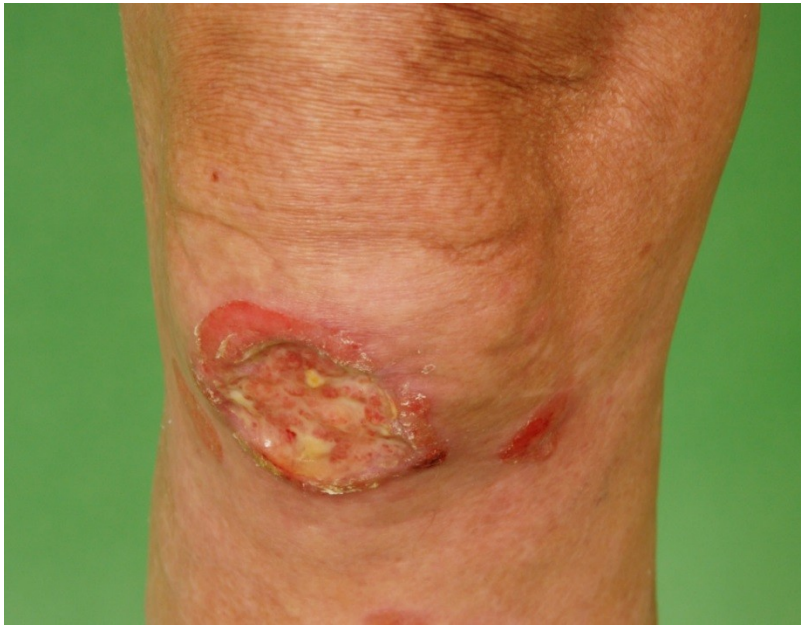
# MF – before therapy, 2007

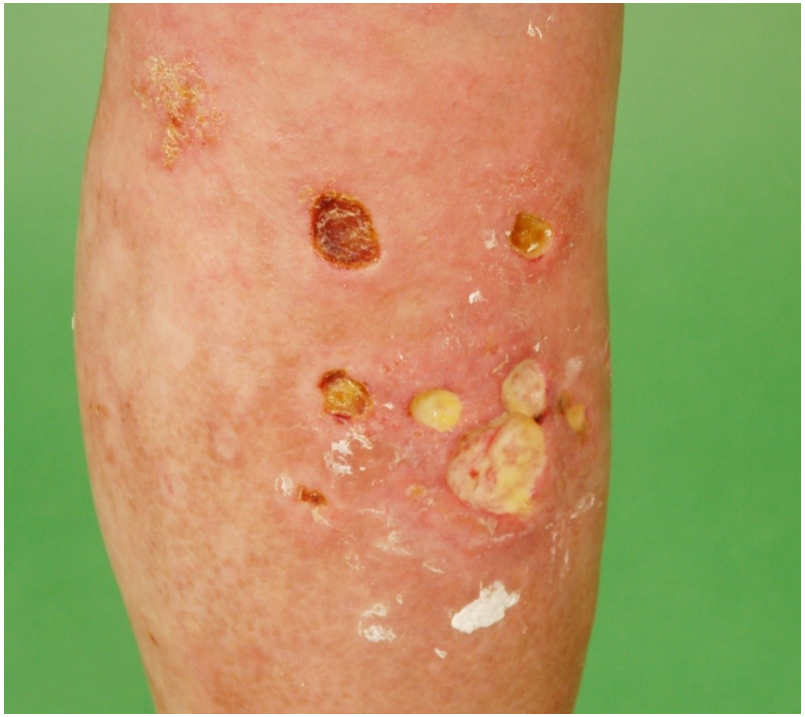


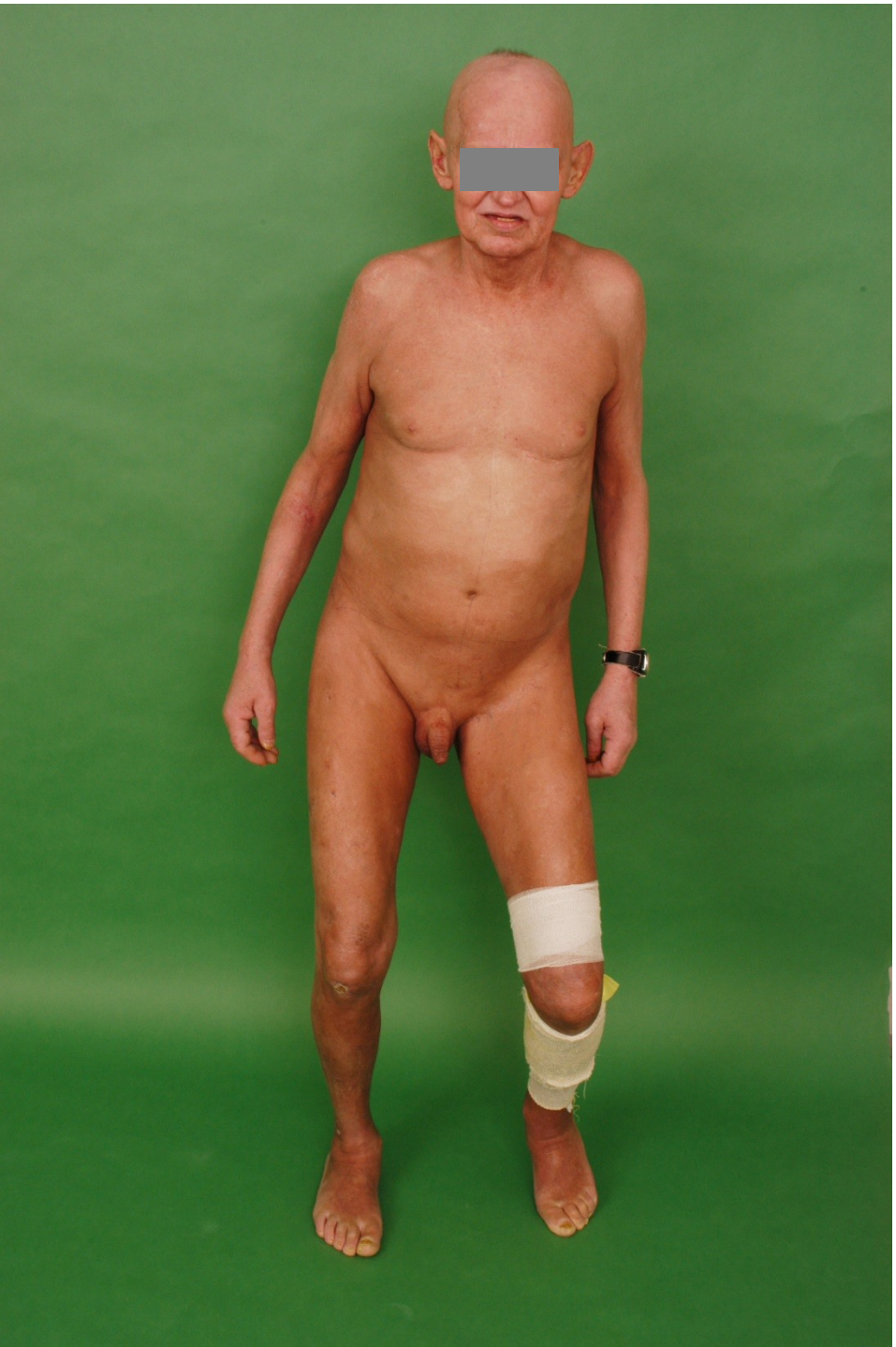




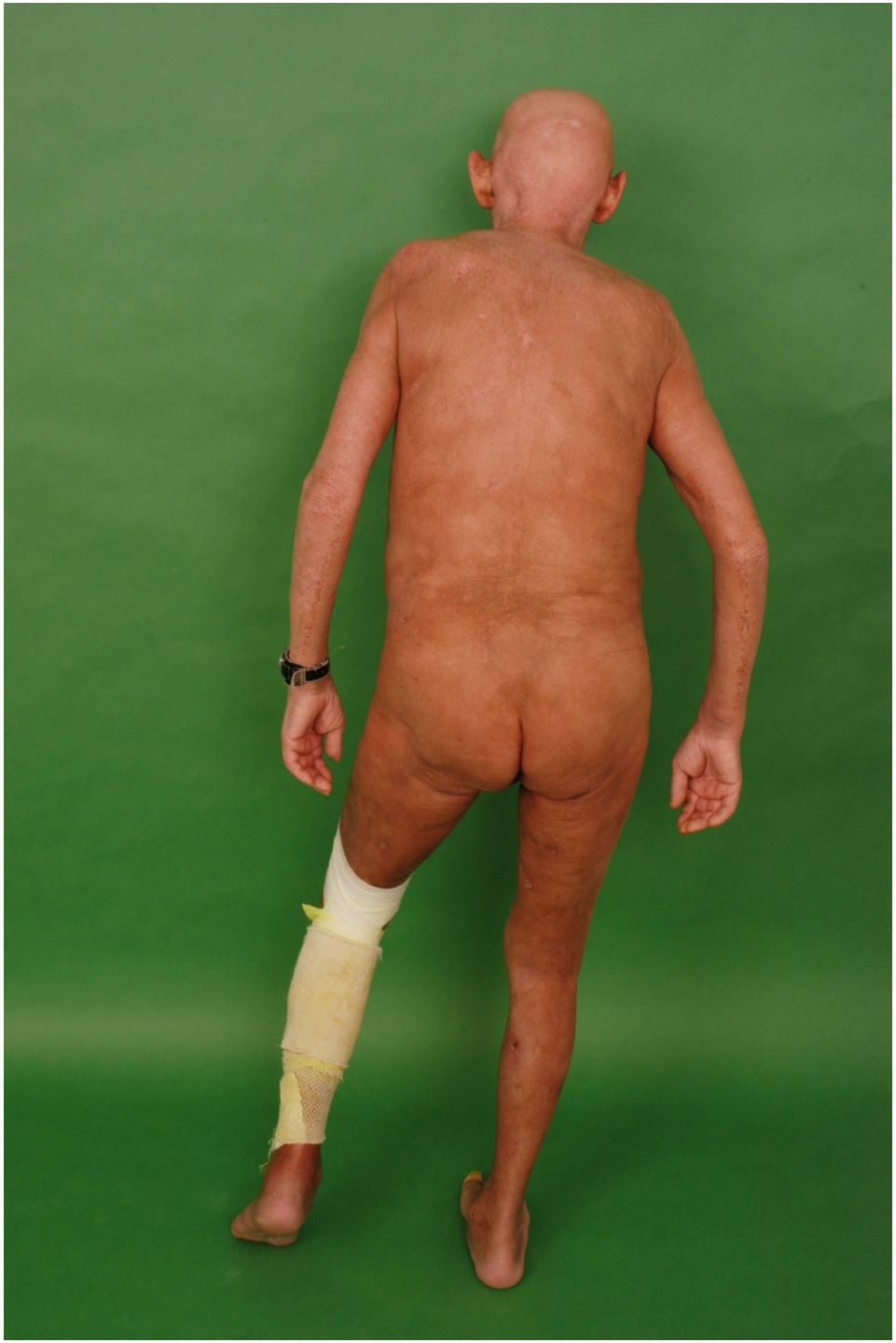




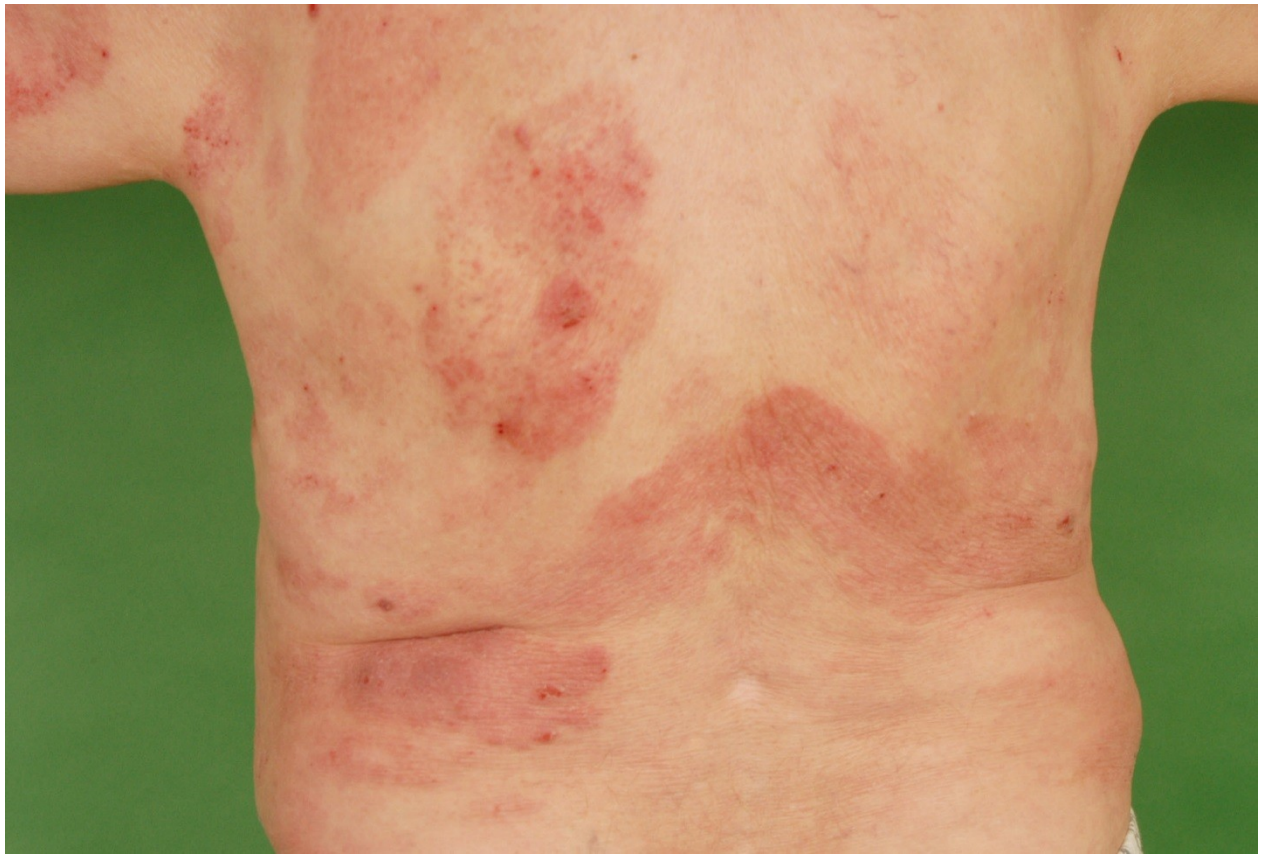




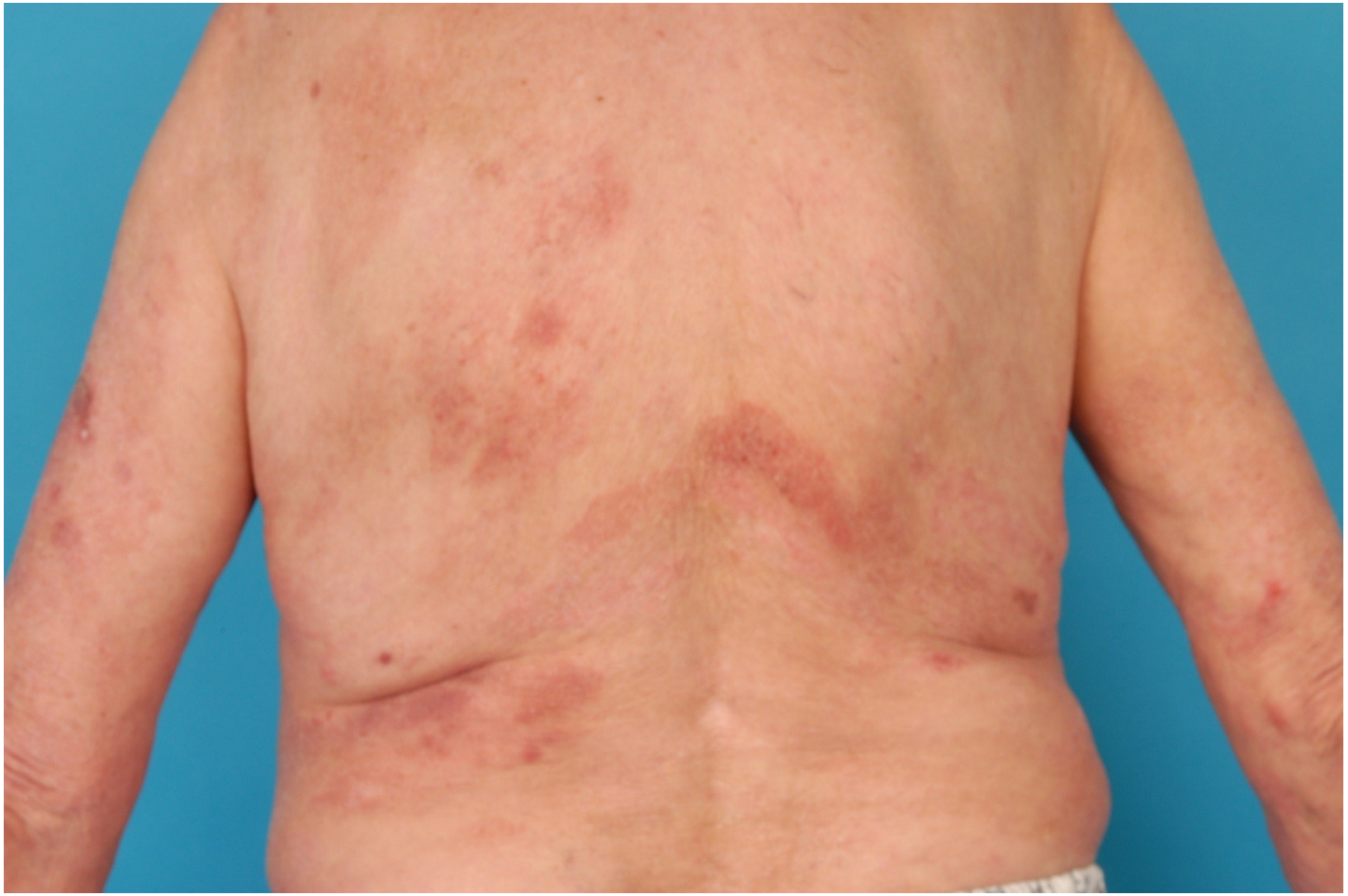
After 2 years of bexarotene therapy



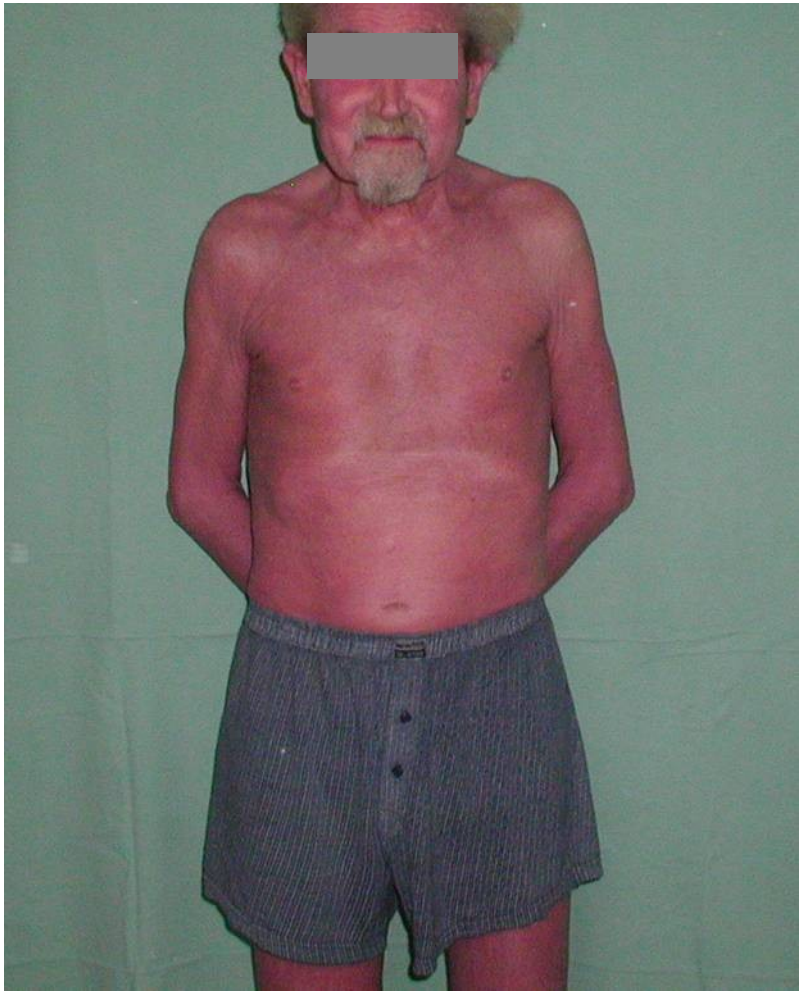
# MF – before therapy

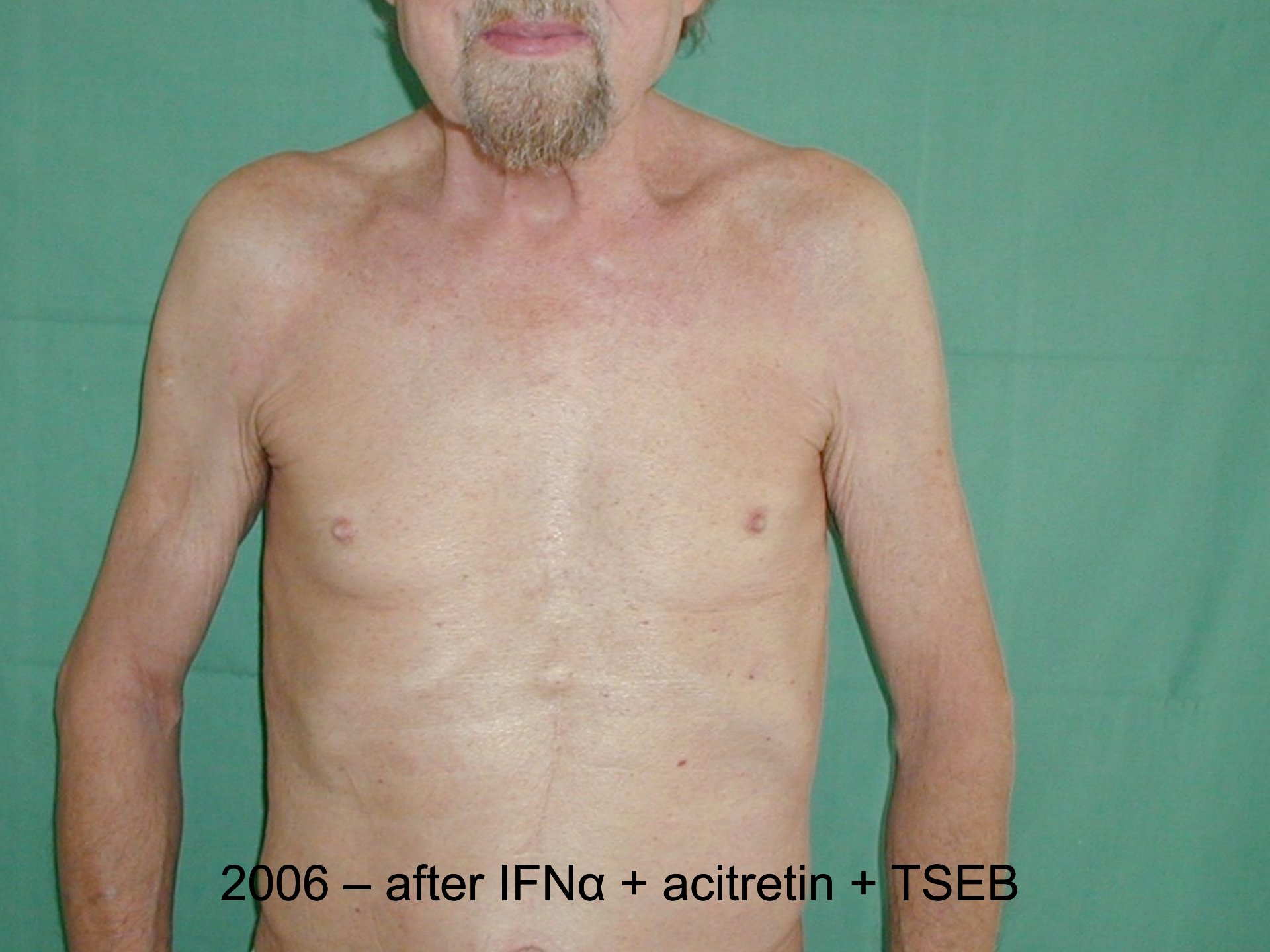


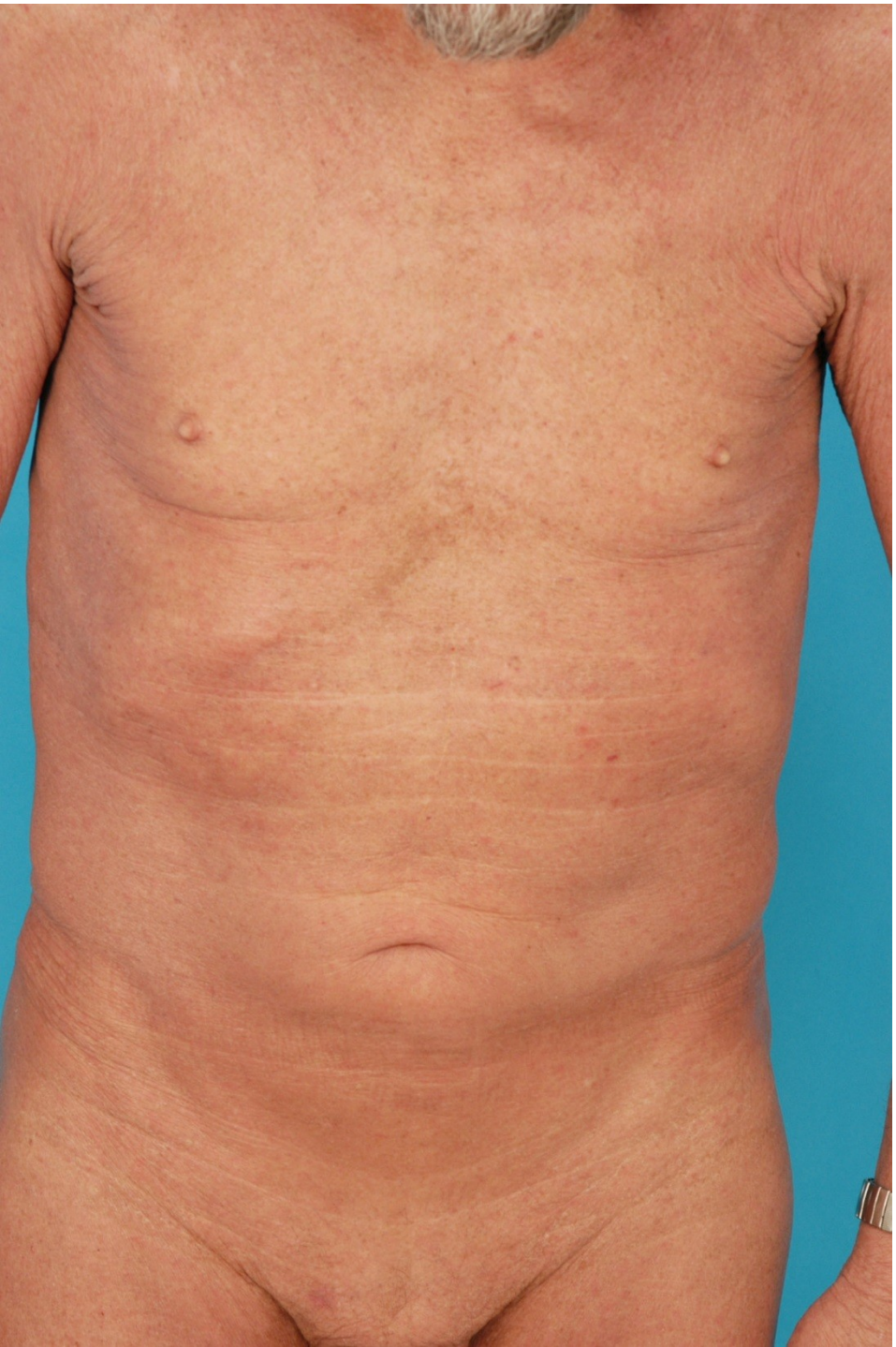
# MF – after 2 months bexarotene therapy



# Erythrodermic MF – before therapy 2003

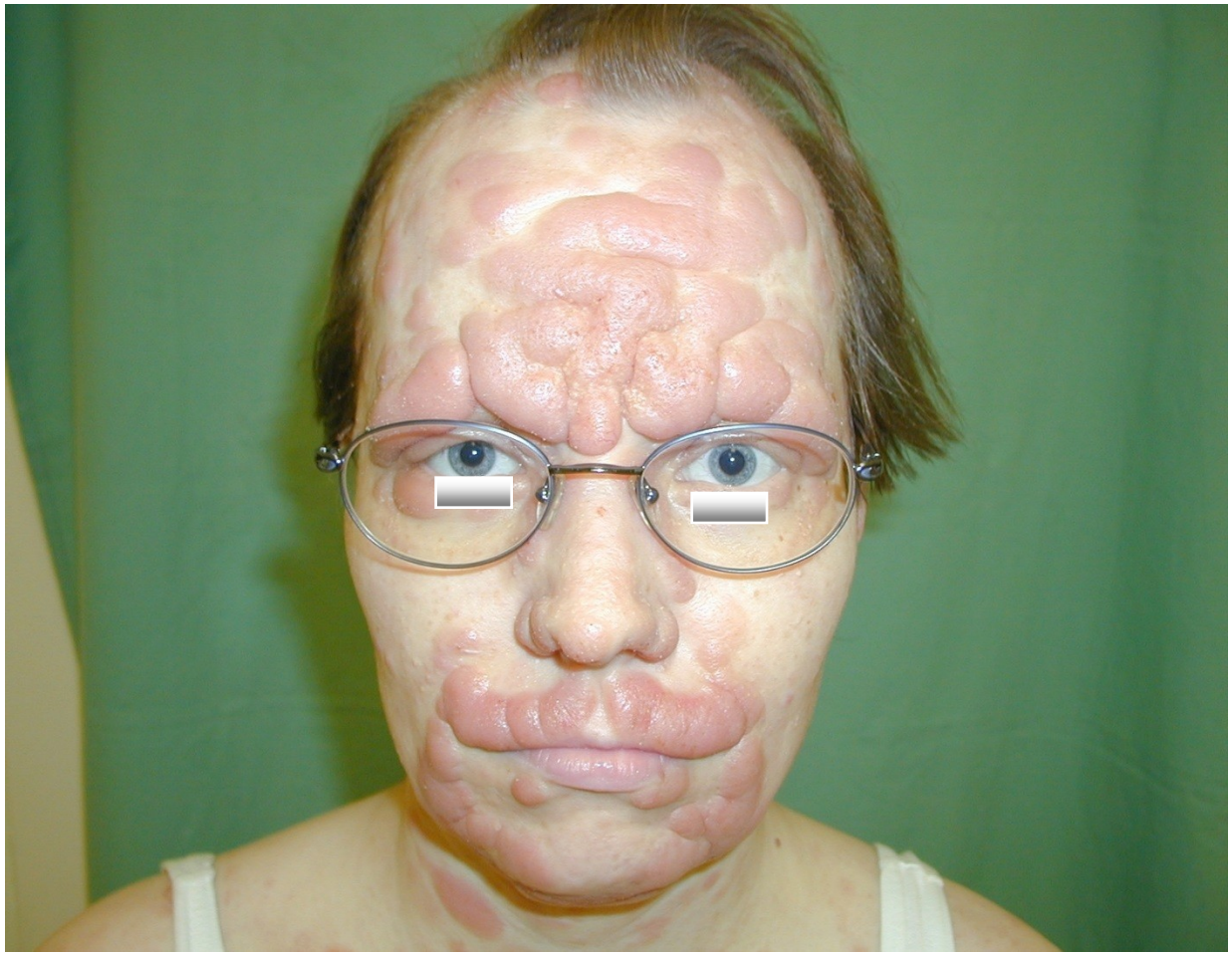



2006 – after IFNα + acitretin + TSEB

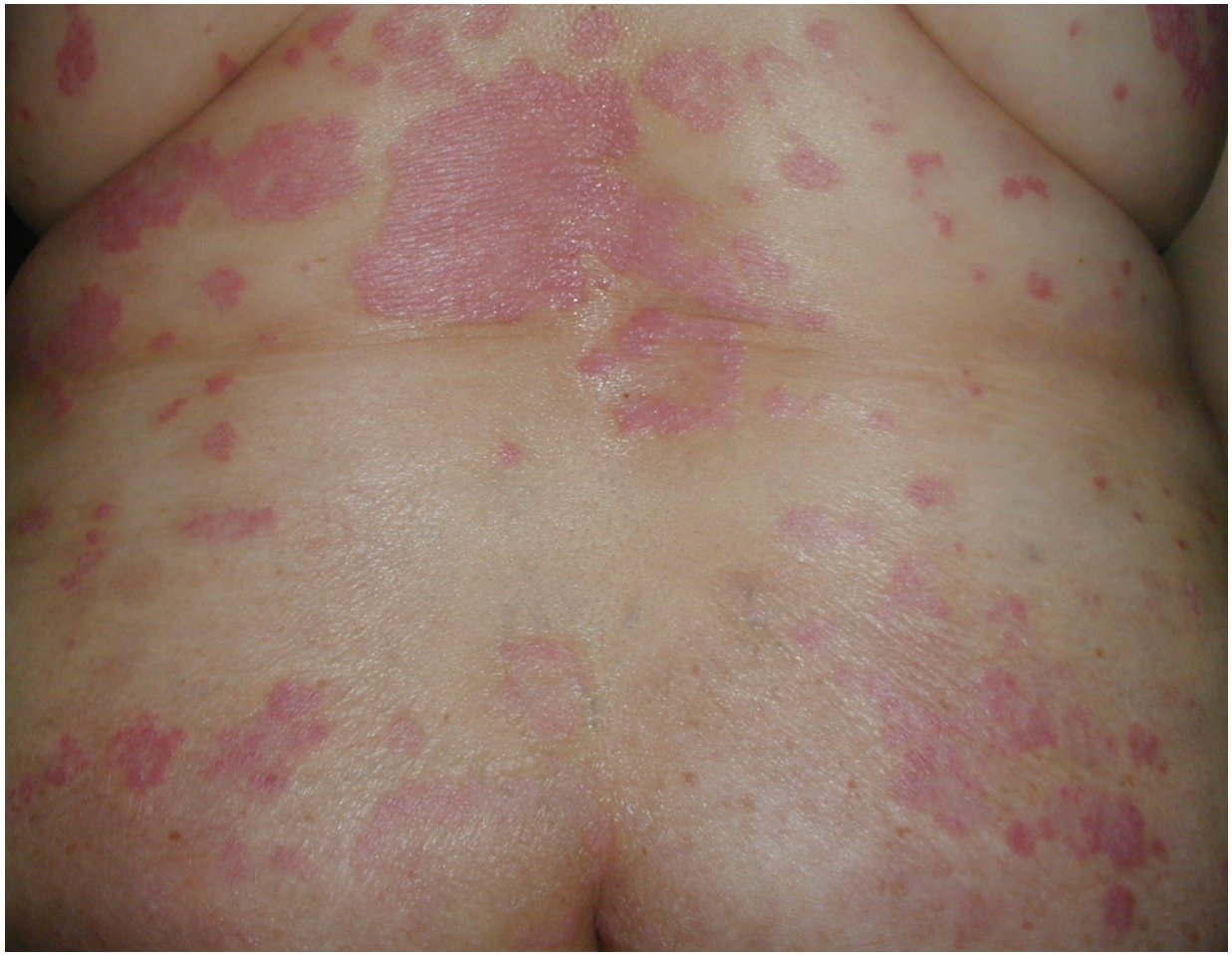


2009 – bexarotene therapy

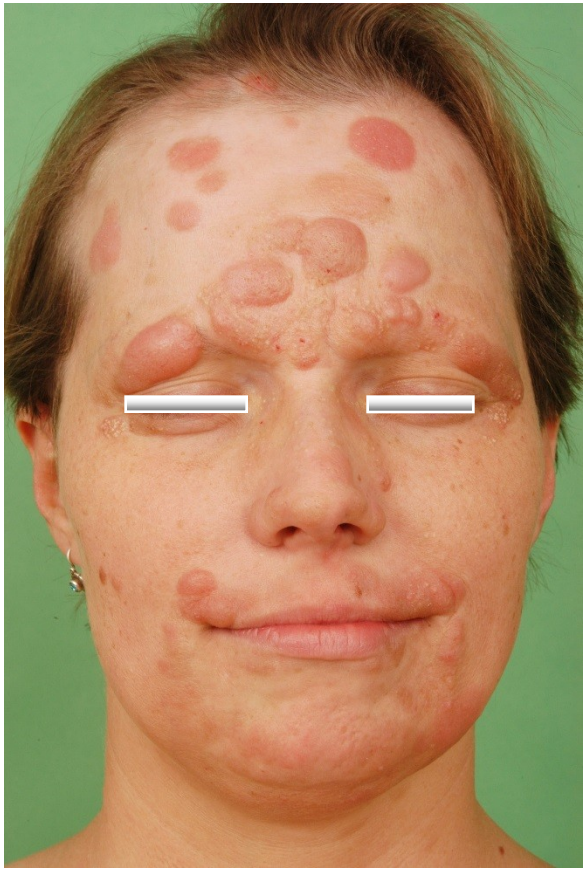
# MF – before therapy

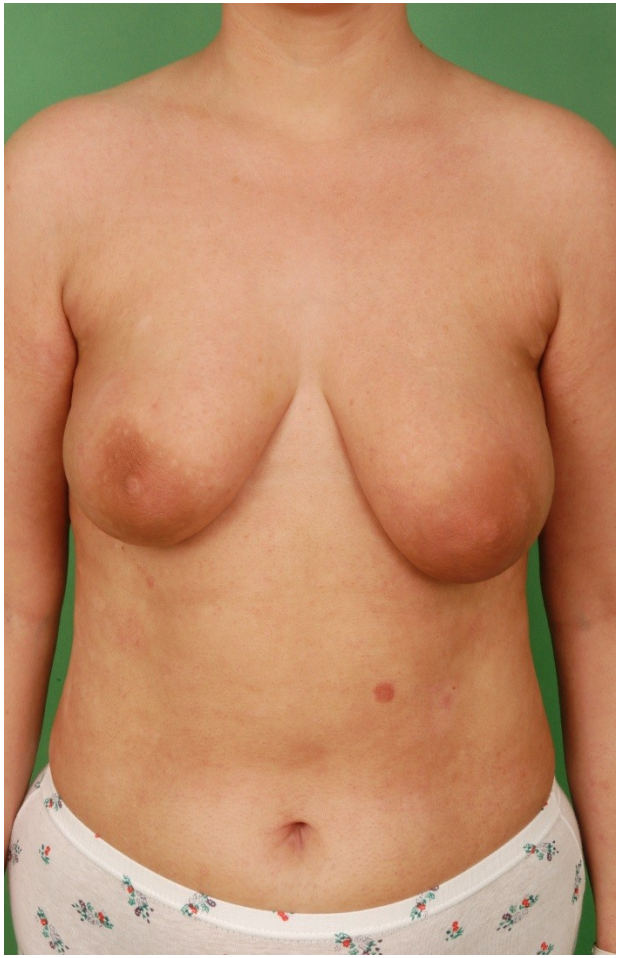


# MF – before therapy

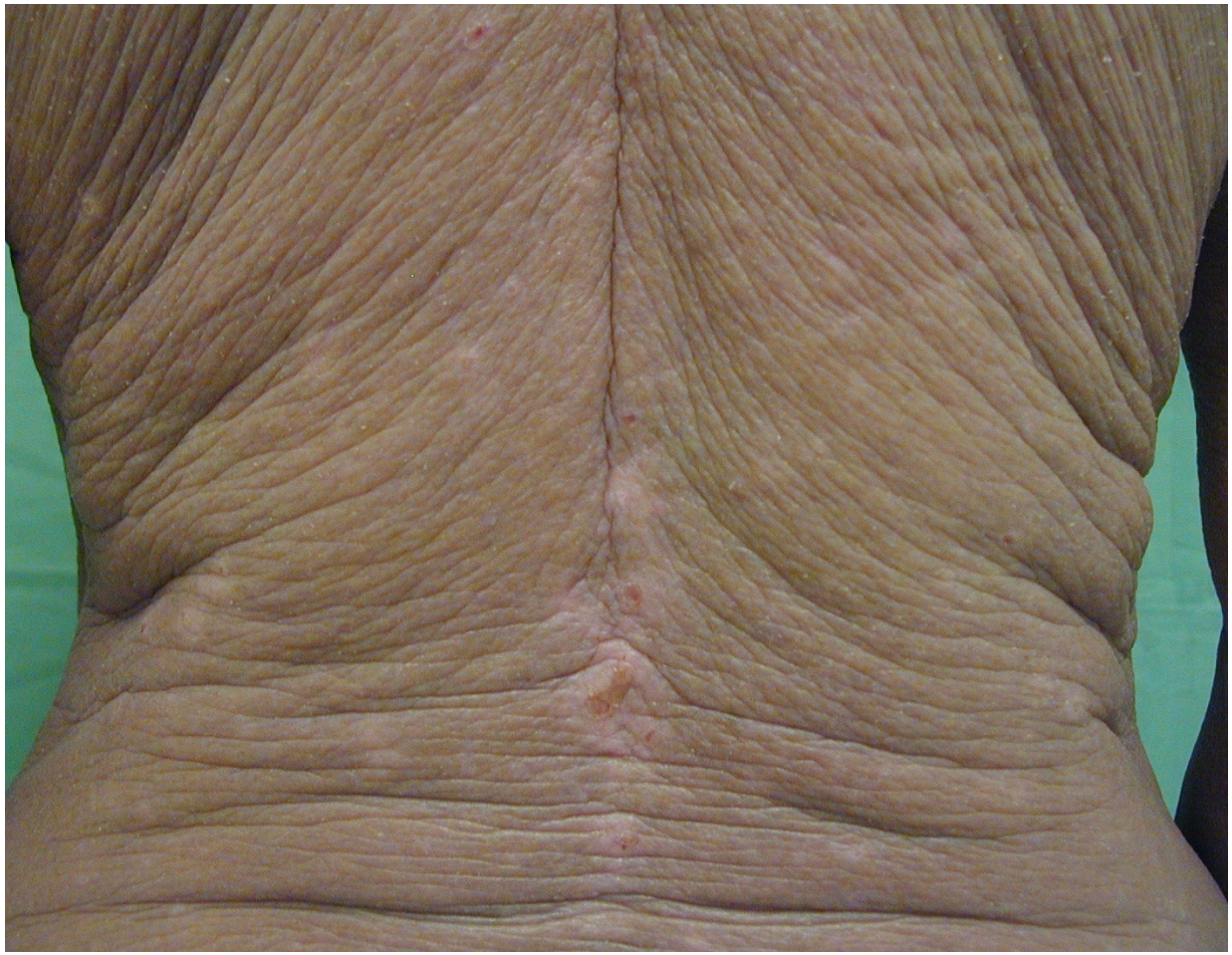


# 3 months bexarotene therapy + PUVA

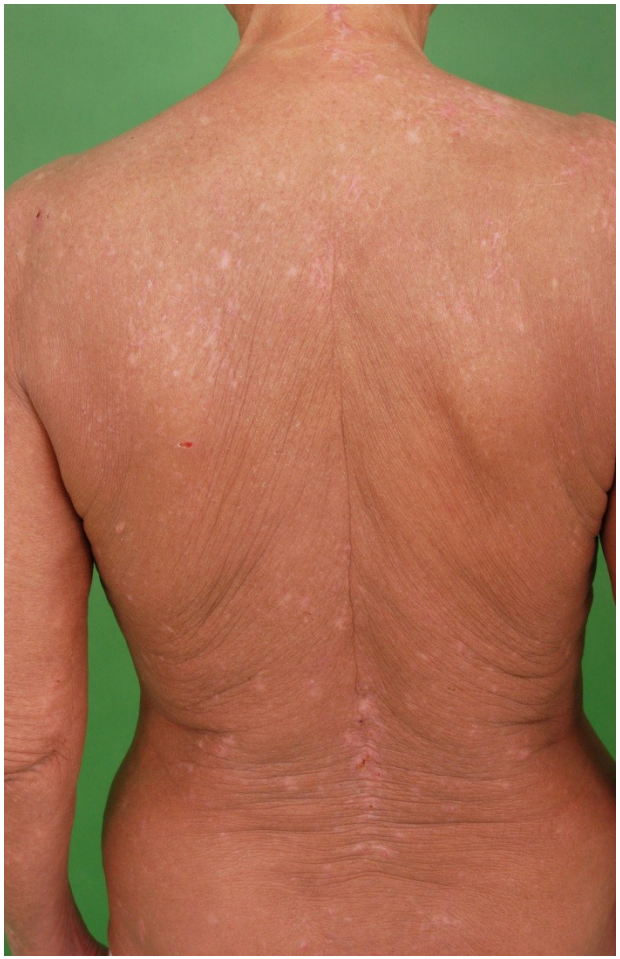


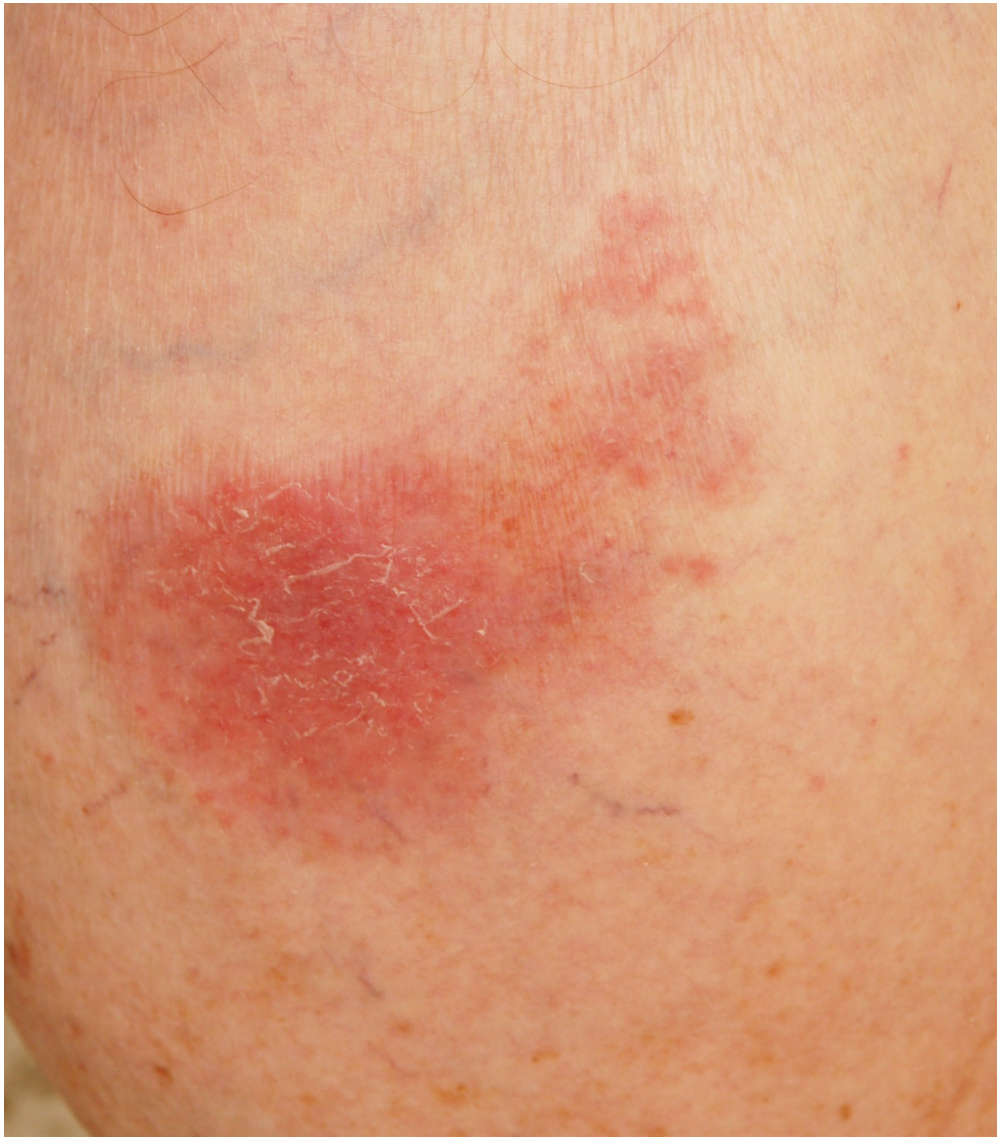


# Sézary syndrome

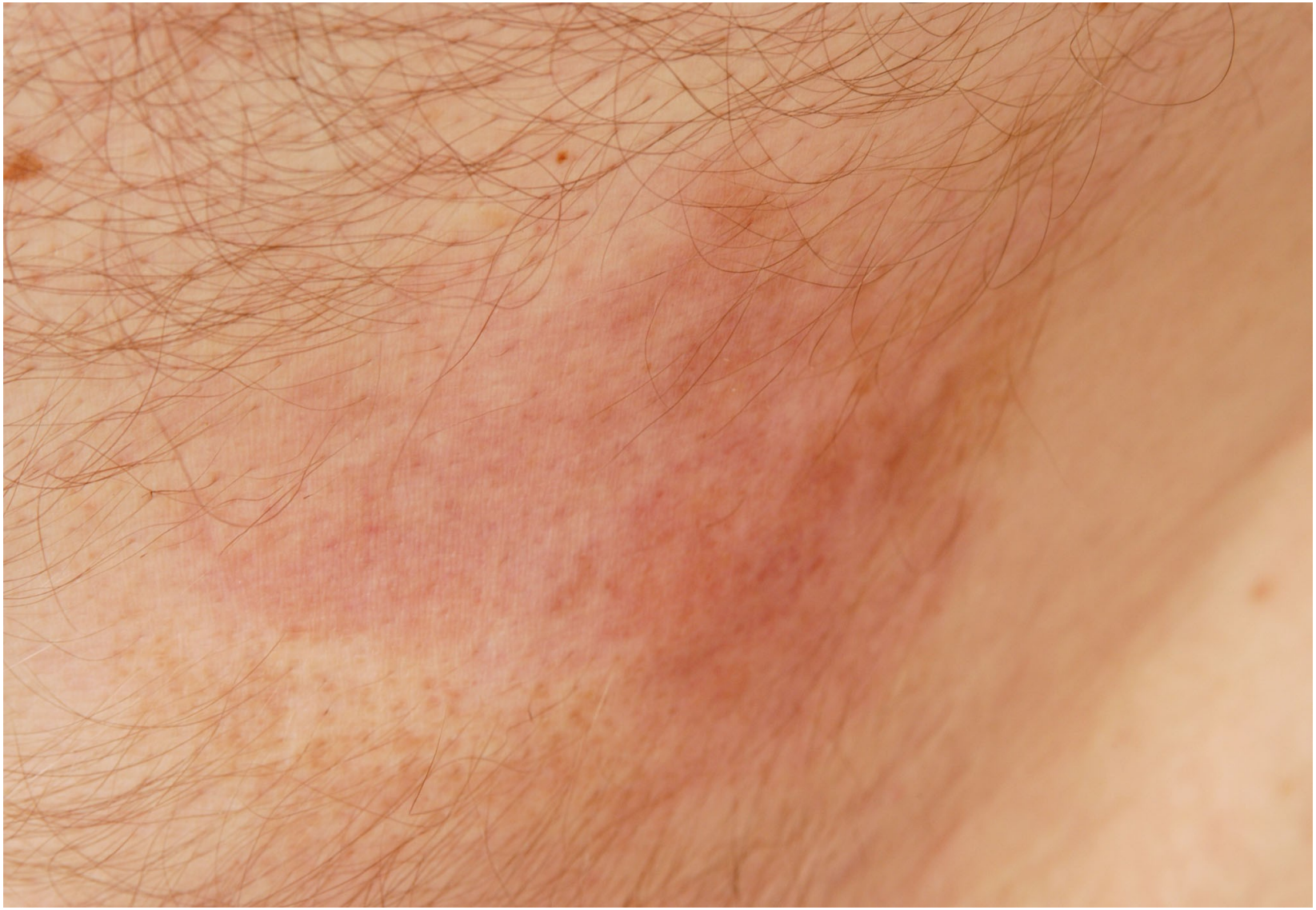


# Sézary syndrome – 3 months bexarotene + PUVA therapy





MF before PDT



After PDT

# Conclusion

- In dermatology we have possibilities to treat CTCL by many methods according to diagnose and staging.
- In initial stage of mycosis fungoides we are able to stop or to control it’s development
- In Sézary syndrome recent immunotherapy can attribute to longer remission