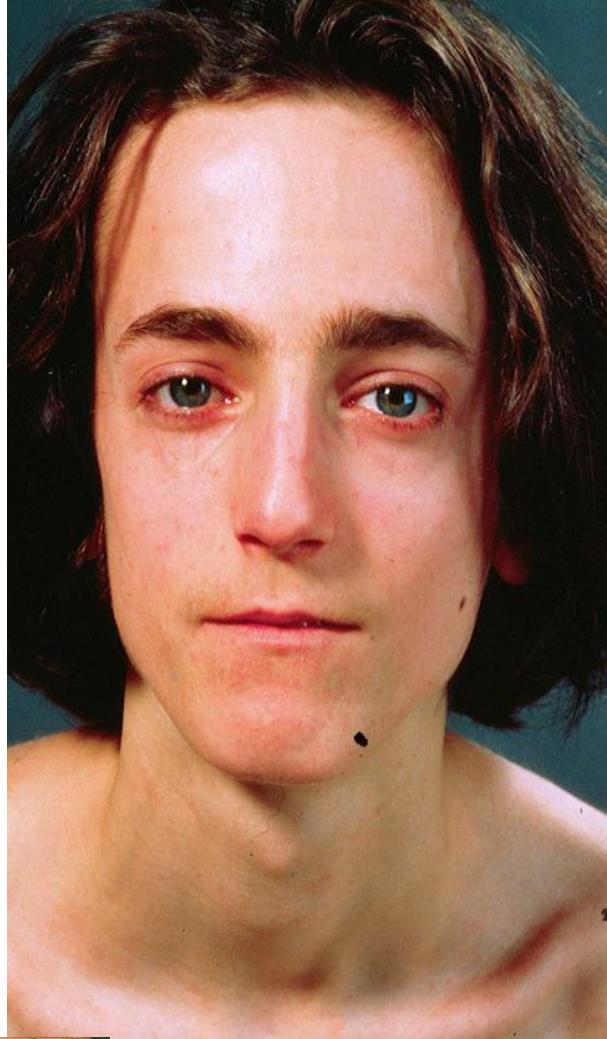


Apherenen in der Dermatologie

Michael Jünger
**Klinik und Poliklinik für Hautkrankheiten
Universitätsmedizin
Greifswald**

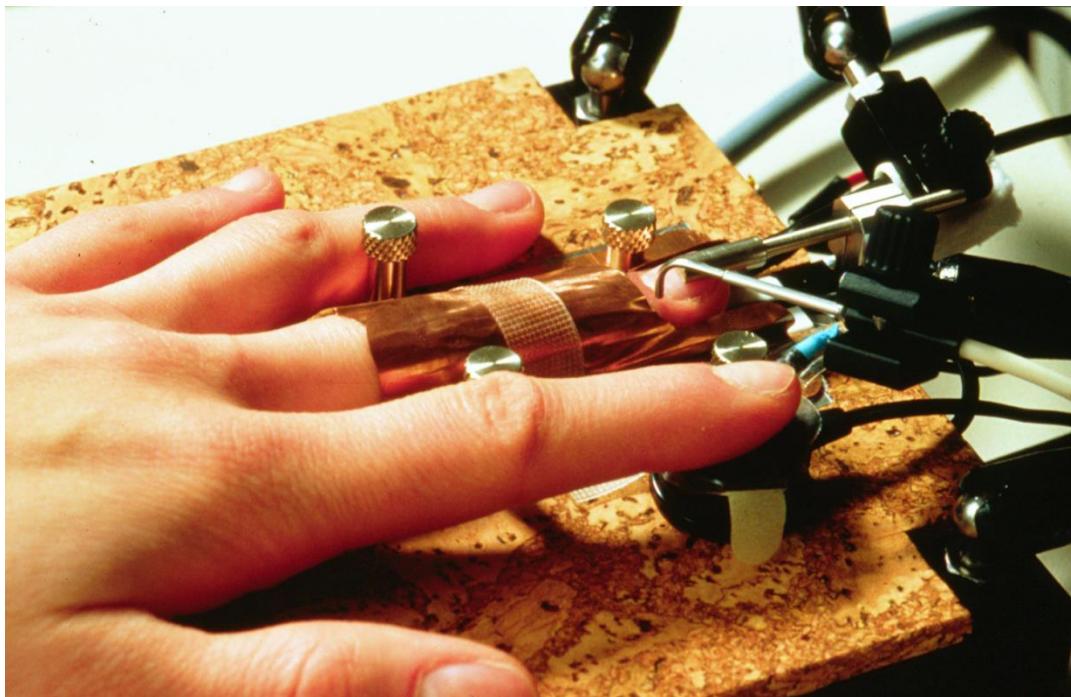
Agenda

- > Systemic Sclerosis: Raynaud Phenomenon
Acral Necrosis
- > Hard to Heal Leg Ulcers
- > Atopic Eczema
- > Pemphigus vulgaris
- > Systemic lupus erythematoses

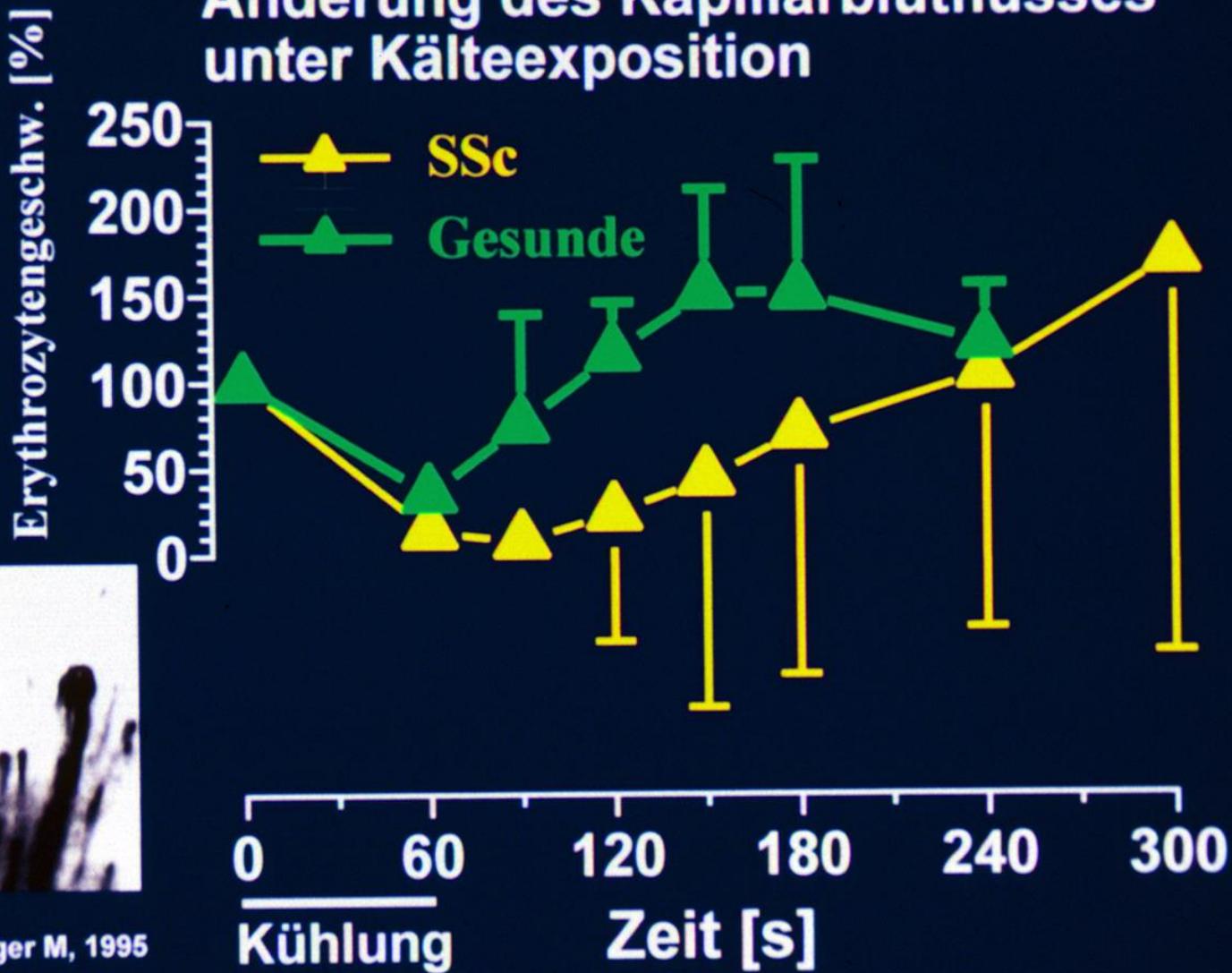








Änderung des Kapillarblutflusses unter Kälteexposition



Hahn M, Klyszcz T, Jünger M, 1995

Capillary Hemodynamics

- Vasomotion ↓
- Bloodflow ↓
- Capillary Pressure ↓

 Nutrition of the skin ↓

EL, ♂, 60 y

- since adolescence Raynaud's Syndrom
- 44 y acrosclerosis, livid colour of fingers and toes, impaired mobility of fingers
- 47 y clenching the fist not possible
- 49 y SSC diagnosed
- 56 y microstomy, dysphagy, acral necrosis, weight loss
- 60 y ANA 1:10.240; Scl 70 +; ACA -

History of Therapy

47y

Nifedipin

48y-60y

Triamcinolon p.o. (16mg/d-4mg/day)

48-49y

Azathioprin

56y-57y

Extracorporeal Photopheresis

12 cycles

57y-60y

Pentoxifyllin (200mg/d)

59y-60y

Prostacyclin-infusions

11 cycles

Rheopheresis

E.L. 61 J.

once per week for four weeks



Severe Pain at D3 right hand
Acral necrosis

Plasmaviskosität

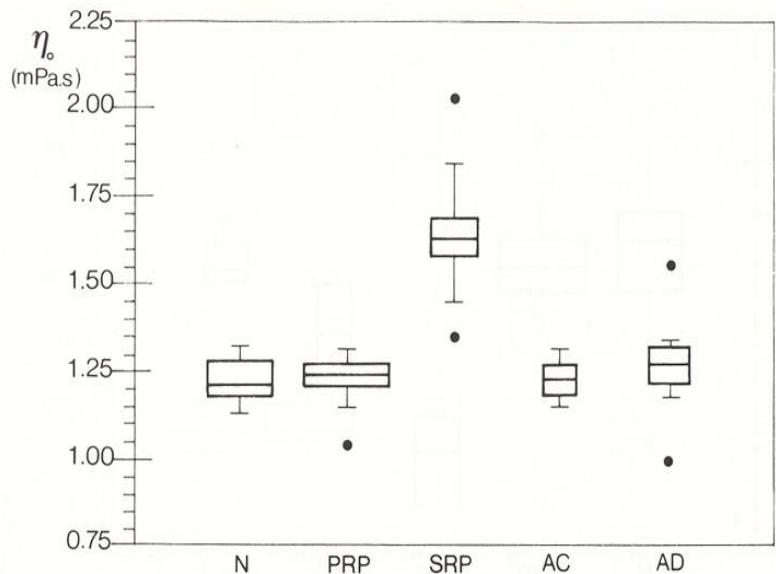


Figure 4.3 Plasma viscosity (η_0) in normal subjects (N) and patients with primary Raynaud's phenomenon (PRP), secondary Raynaud's phenomenon (SRP), acrocyanosis (AC) and asphyxia manus et digitorum (AD), presented in box plots.

Erythrozytenaggregation

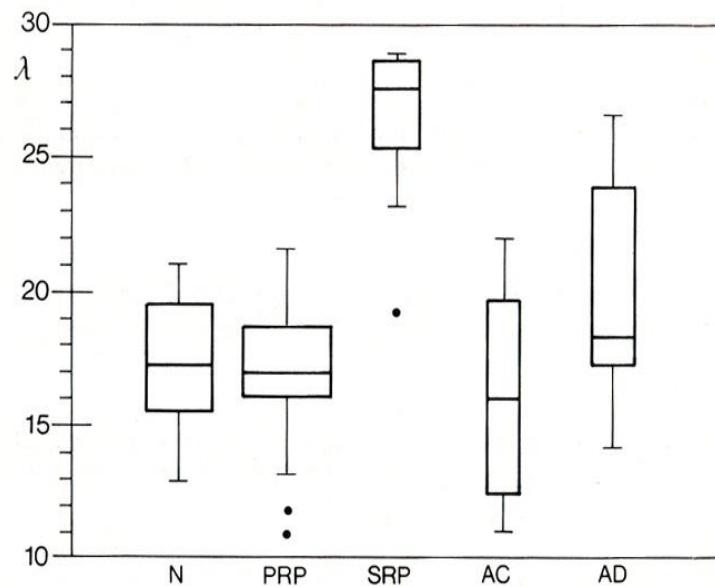
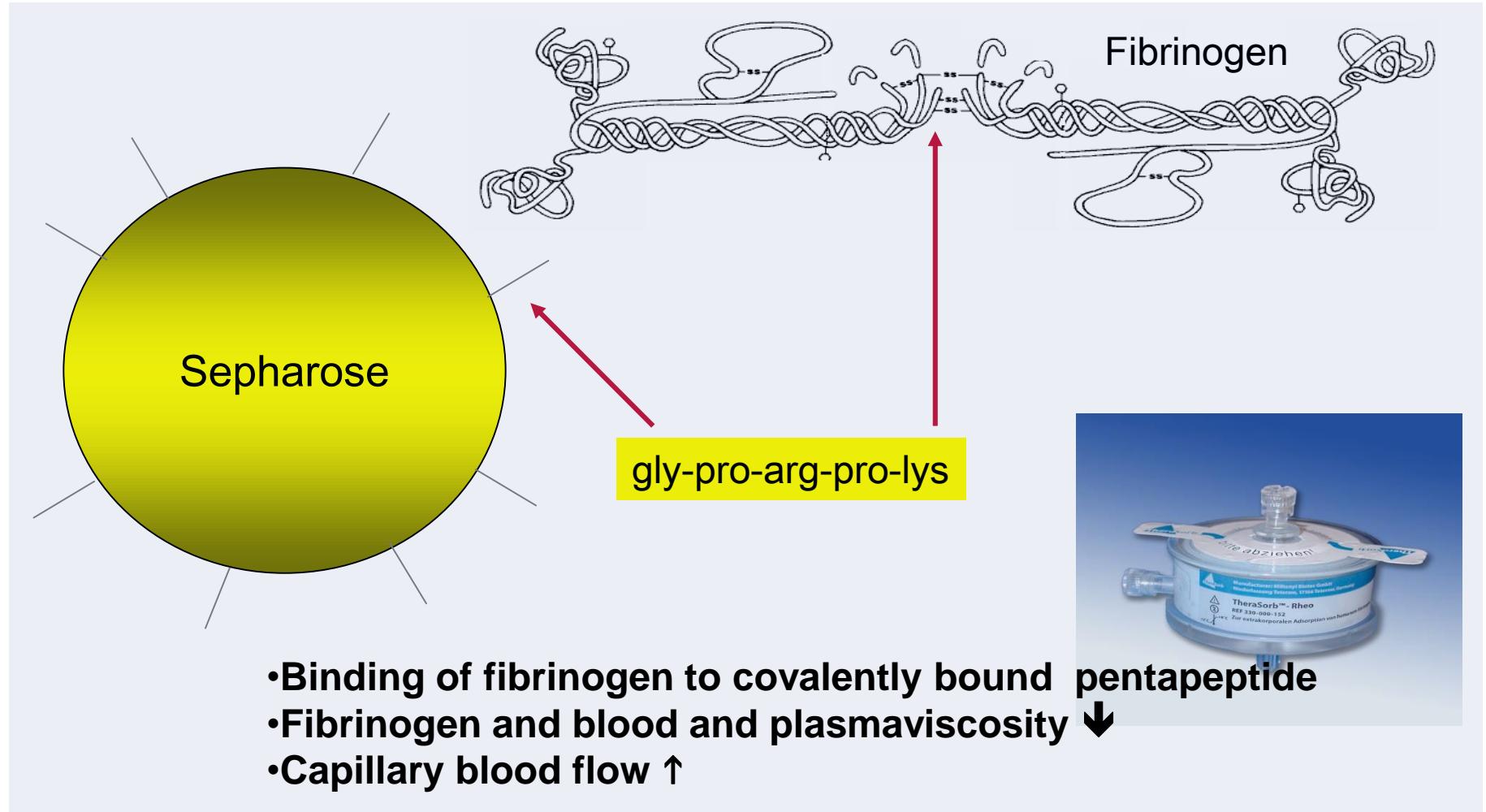


Figure 4.2 RBC aggregation (λ) in normal subjects (N) and patients with primary Raynaud's phenomenon (PRP), secondary Raynaud's phenomenon (SRP), acrocyanosis (AC) and asphyxia manus et digitorum (AD), presented in box plots.

TheraSorb™-Rheo







Clinical course:

After 4 weeks healed necrosis at the tip of D3

After 5 weeks Raynaud's attacks
 shorter and less painful



**After 6 weeks,
4th plasmapheresis**

**No analgetics
No pain**

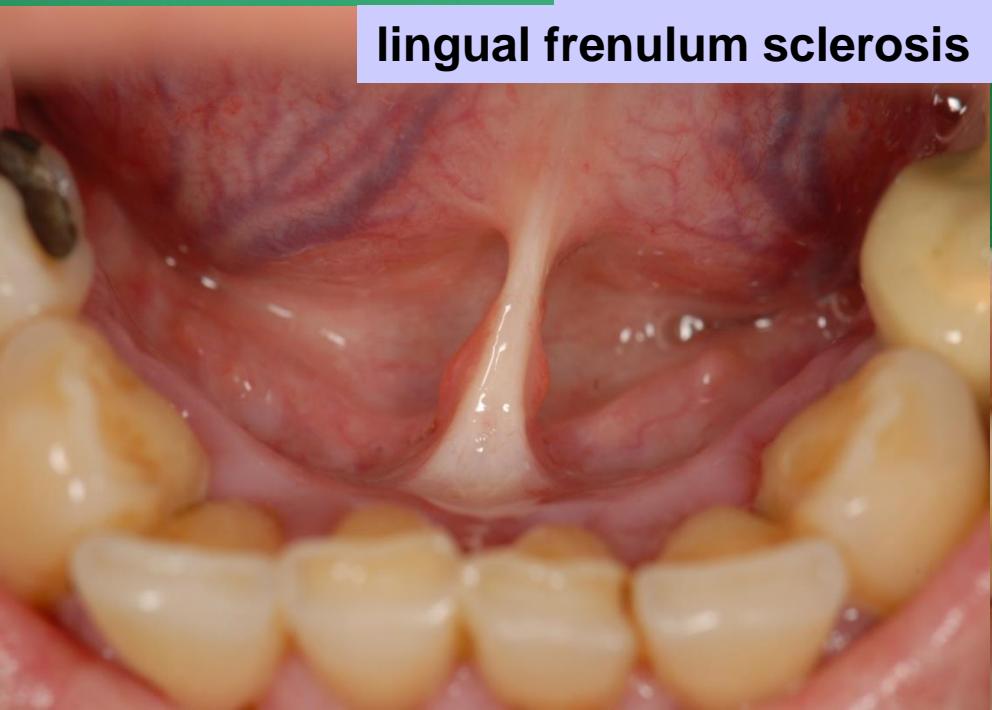
36 year old patient

- Since 1993 systemic sklerosis, Scl 70 pos., (cutaneous, pulmonary, cardiovascular and gastrointestinal manifestation)
- Systemic immunsuppressive treatment: azathioprine und prednisolone
- additional: vasodilators, bronchospasmolytic agents
- Status post allogene stem cell transpantation in 1999
- 09/2007 start of fibrinogen apheresis: multiple acral ulcerations

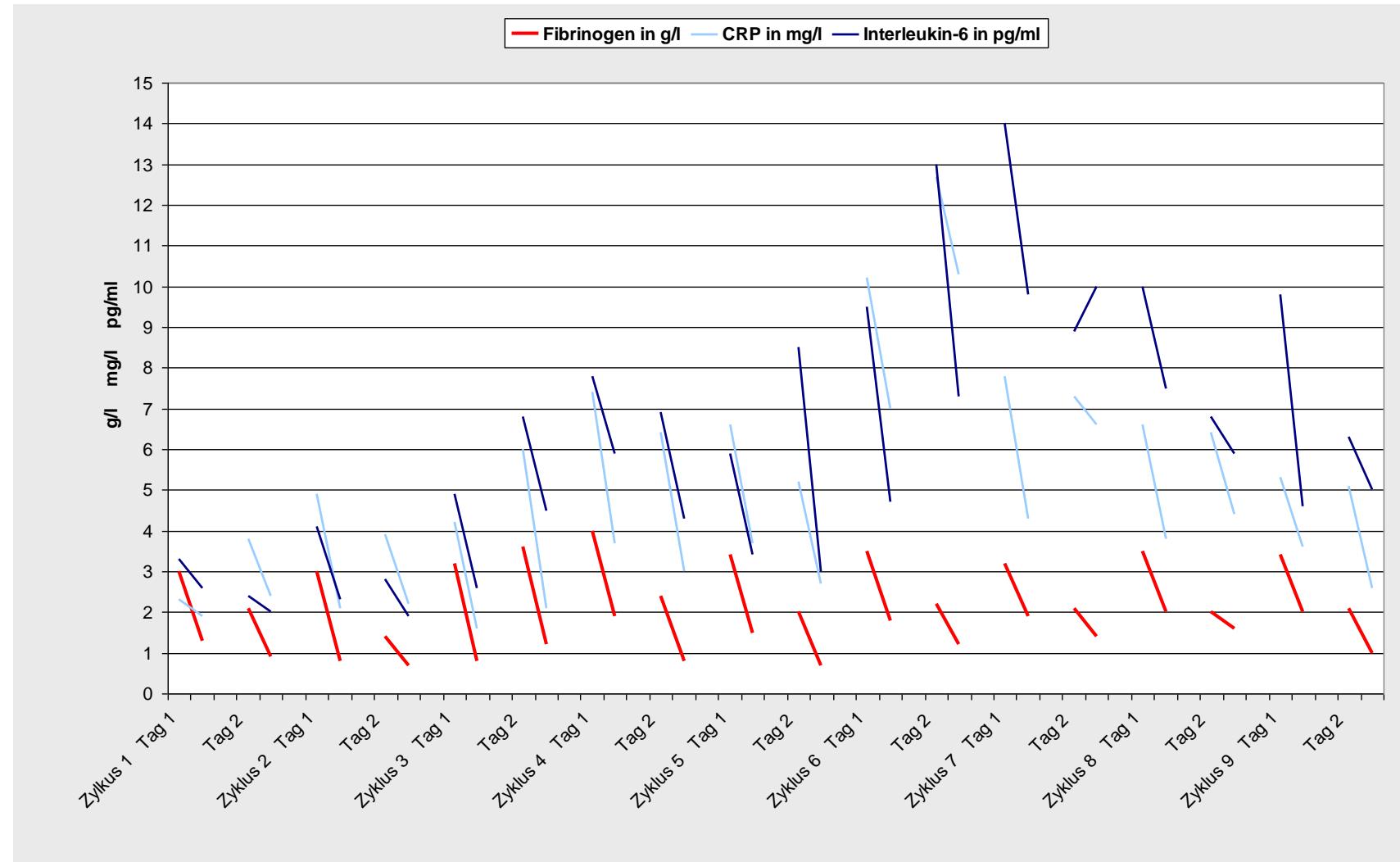


dermosclerosis teleangiectasia

lingual frenulum sclerosis fingertip necrosis



Fibrinogen, CRP and IL-6 during therapy (9 cycles)



before



before



after



after



54 year old patient

- Since 1991 systemic sklerosis, Scl 70 pos., (cutaneous, pulmonary, gastrointestinal manifestation)
- Systemic immunosuppressive treatment: azathioprine und prednisolone
- Additional: vasodilators, bronchospasmolytic agents
- 02/2008 Fibrinogenapheresis because of a new ulceration at the dorsal foot

Phase I: reduction of ulcer size and generation of granulation tissue

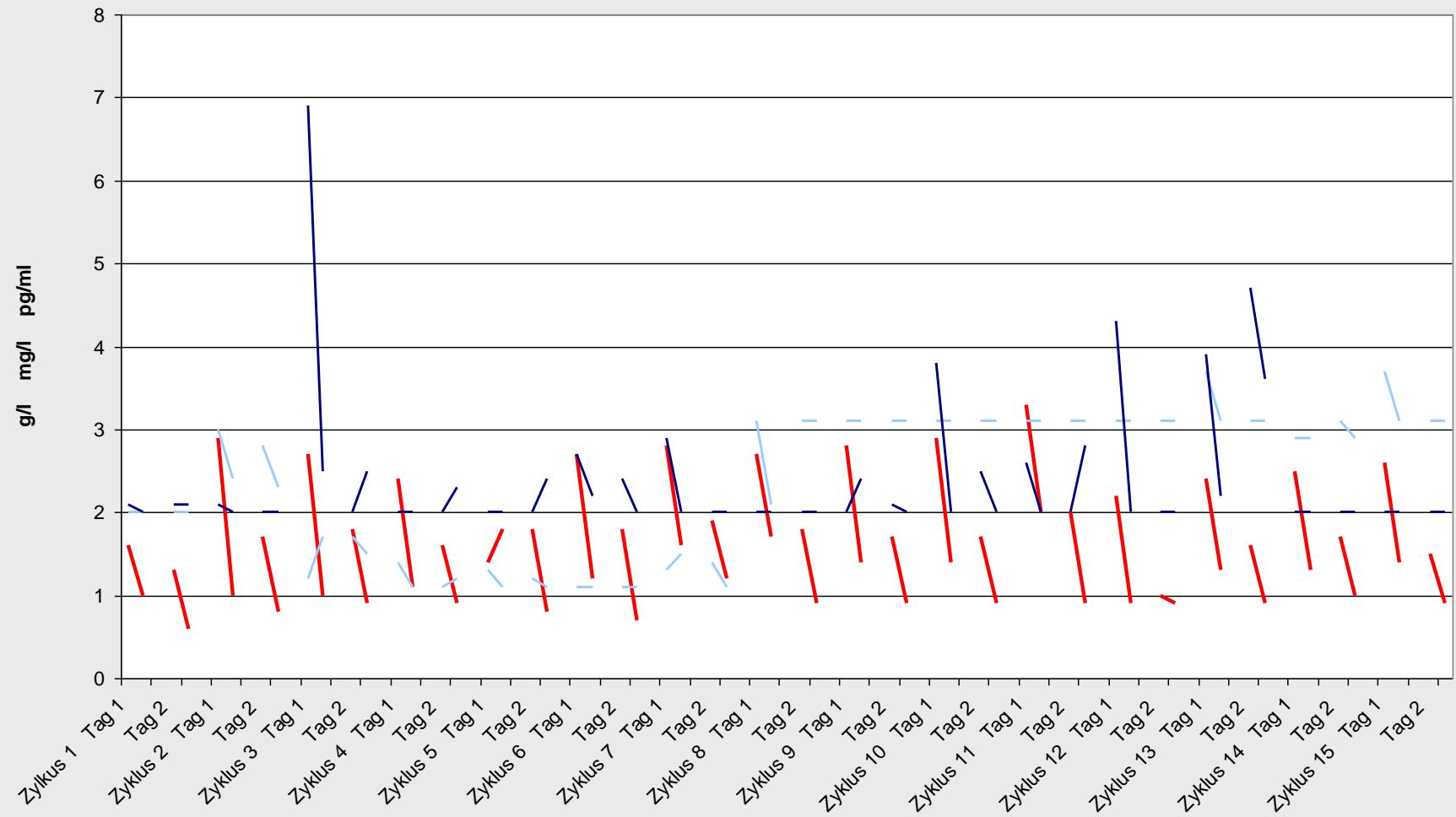


Phase II: additional application of reverdin skin grafts to accelerate wound closure



Fibrinogen, CRP and IL-6 in rheopheresis

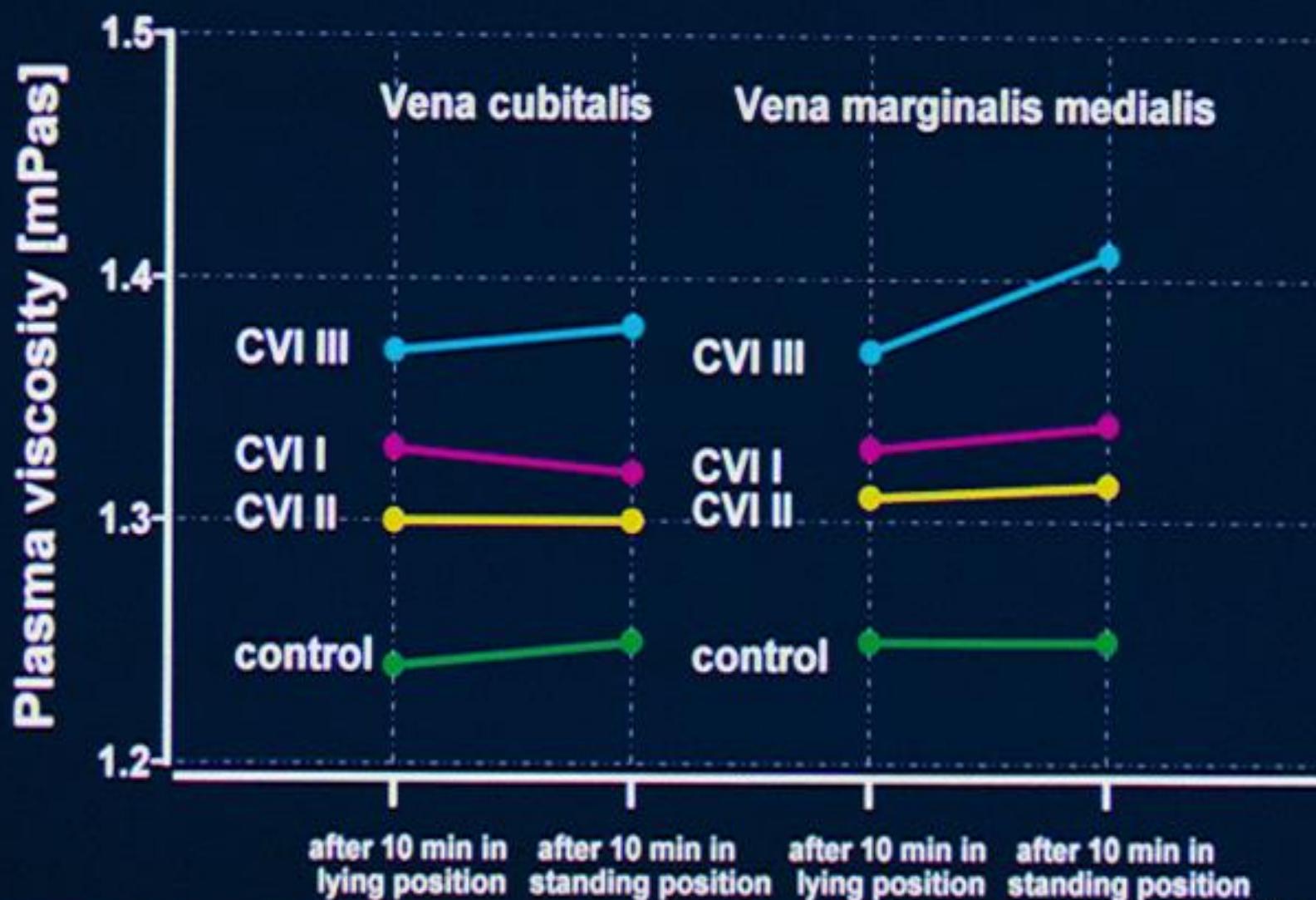
— Fibrinogen in g/l — CRP in mg/l — Interleukin-6 in pg/ml



Plasmapheresis / Rheopheresis in Systemic Sclerosis

- > IL-6 ↓
- > CRP ↓
- > Fibrinogen ↓
 - nutritive skin perfusion ↑
 - autoimmune inflammation ↓

Plasma Viscosity*) in an arm and foot vein: in supine position and standing upright



Venous ulcers – Case reports 1

62 year-old Patient

- History of ulcerations on the left lower leg and forefoot since 2002
- Postthrombotic syndrome: 1997 deep vein thrombosis (left leg)
- Occlusive arterial disease: Condition after PTA und stent implantation (a. fibularis) and ilomedine treatment, ulcer debridements
- Patient presented with pain

Comorbidities:

Overweight (BMI 31.6, „moderately obese“)

Left ventricular hypertrophy

Alcohol abuse, smoker

Venous ulcers – Case reports 1

Complex therapy:

- Pain treatment (ischiadicus nerve block)
- Local treatment:
antiseptic wound dressings, biodebridement
- Therapy of the edema:
apparative/manual lymph drainage, compression therapy
- Further Therapy:
arterial balloon angioplasty
07.2010: vain attempt to recanalize left arteria tibialis anterior and posterior.
Split skin graft and rheopheresis
- Until now, 9 cycles of 2 treatment sessions each in intervals of 4 weeks
- Good clinical response: shrinking in ulcer size and stable local condition

Change of clinical aspects from May, 2010 to August 2011 under complex treatment



Clinical improvement of ulcers after reintensified rheopheresis



May 2011



August 2011

Venous ulcers - Case reports 2

52 year-old Patient

- Since 2 years ulcer on the left lower leg
- No history of deep vein thrombosis or thrombophlebitis
- No prior therapy / operations on the veins
- Occasional use of compression bandages
- Patient presented with pain and growing ulceration.
- Family history of varicosis

Comorbidities

Hypertension

BMI 33.1 (moderately obese)

Venous ulcers - Case reports 2

Clinical findings:

Ulceration enclosing nearly the complete circumference

Duplex sonography: Chronic venous insufficiency Widmer III
(saphenous varicosis, varicosity of lateral saphenous branches)

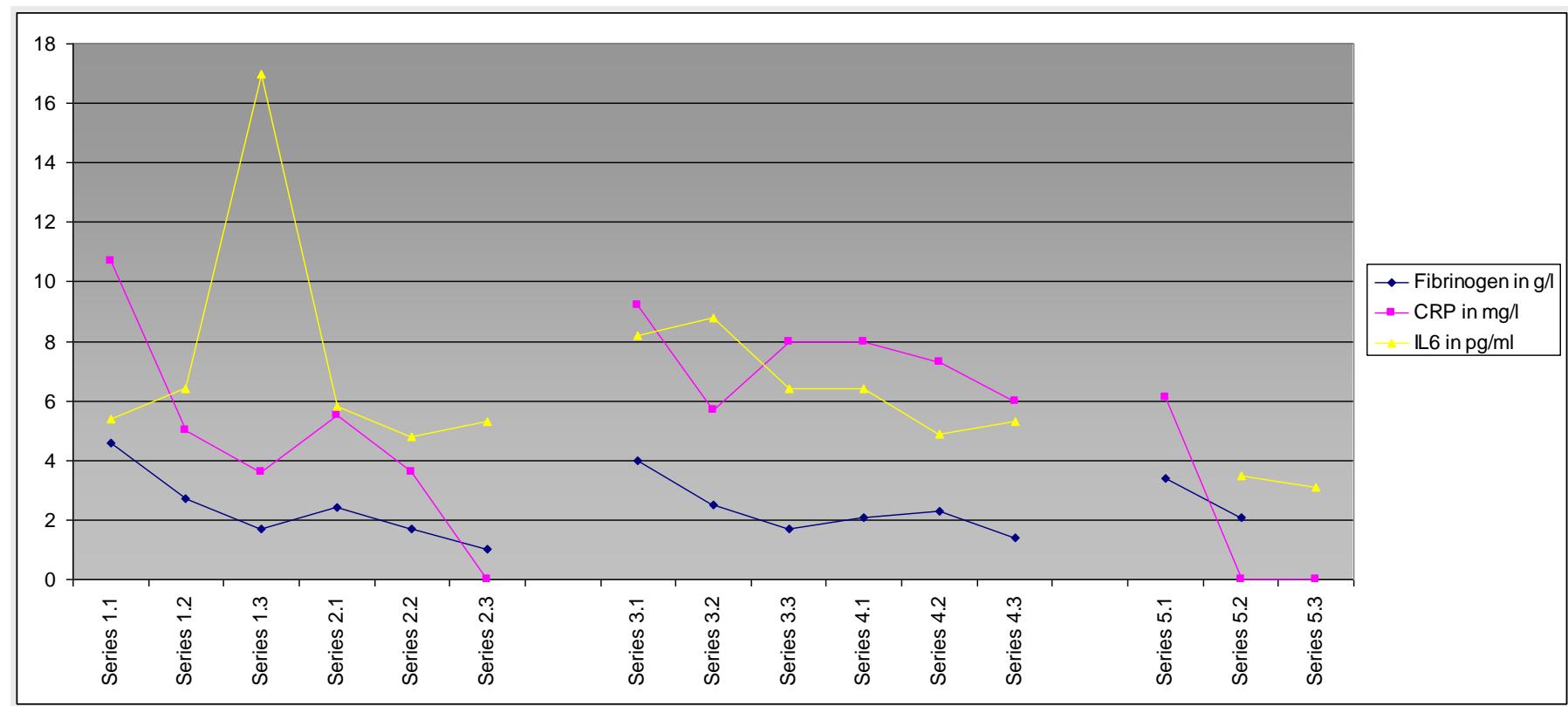
Therapy:

- 12/2009 endovenous steam vein occlusion of the greater saphenous vein
- Intense local therapy
- Compression therapy
- Rheopheresis (3 Cycles with 2 treatments)

Change of clinical aspects from May, 2010 to August 2011 under complex treatment



Venous ulcers - Case reports 2



Conclusions: Rheopheresis (FA)



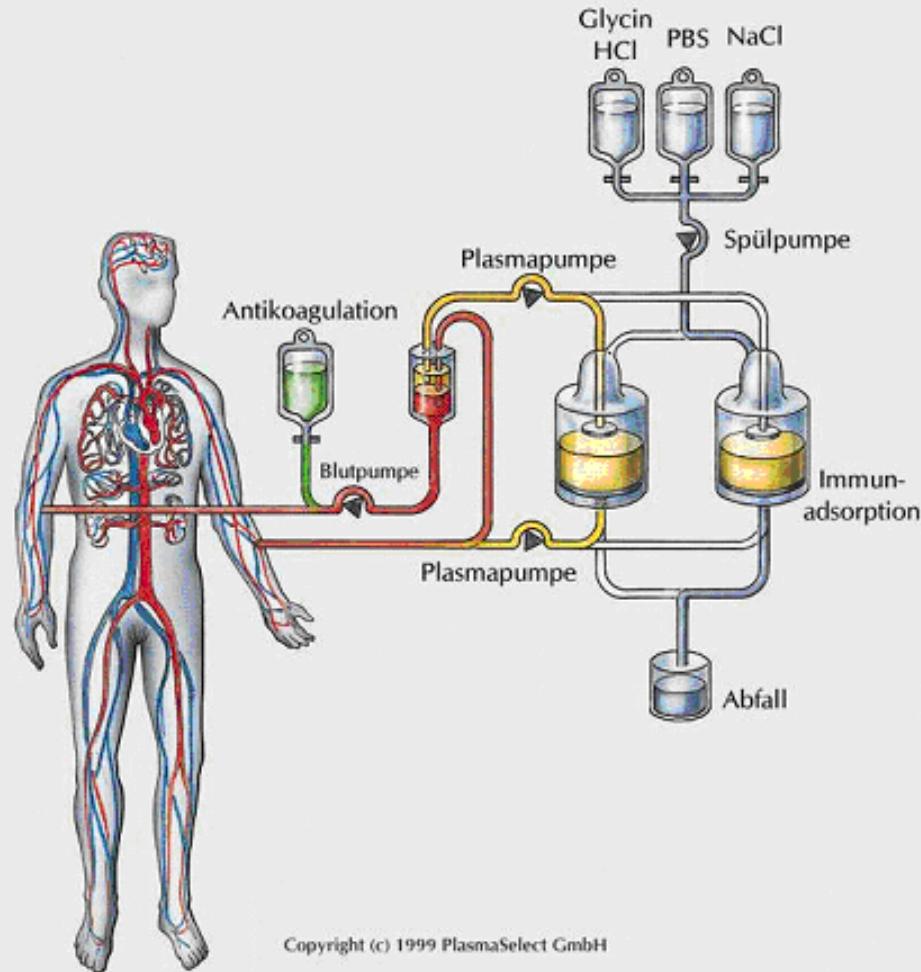
- **reduces pain**
- **accelerates epithelisation in leg ulcers (v, mixed)**
- **a cost-benefit-analysis assessment is needed**

Atopic eczema

Syn.: Atopic Dermatitis, endogenous eczema, neurodermatitis, neurodermitis, Besnier Prurigo

Atopic eczema with increased IgE-
Production: **extrinsic atopic dermatitis**

New Approach: Decrease of IgE by Immunadsorption



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Immunapheresis (IgG ↓, IG Flex, **Miltenyi**)



Simultaneous reduction of:

IgG (Subtypes 1-4)

IgM, IgA, IgE, IgD

Circ. immunocomplexes

Rheumatoid factors (IgG)

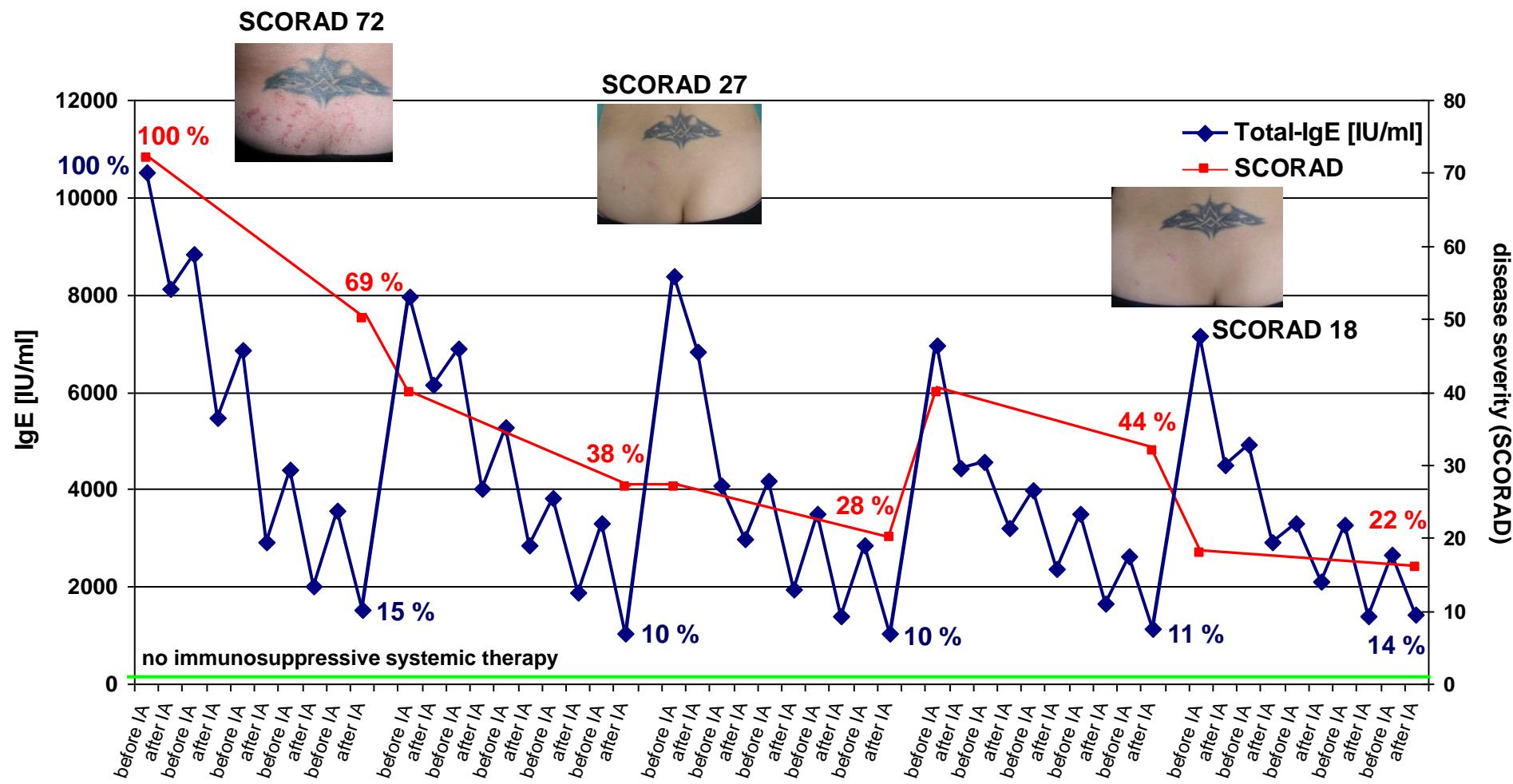
Fragments of immunglobulines

Coagulation-factors (?)

Atopic Dermatitis, 5 series, Patient-ID 02, female, 31 y



 Universitätsmedizin
GREIFSWALD



Atopic Dermatitis, 5 series, Patient-ID 02, female, 31 y

before 1st series

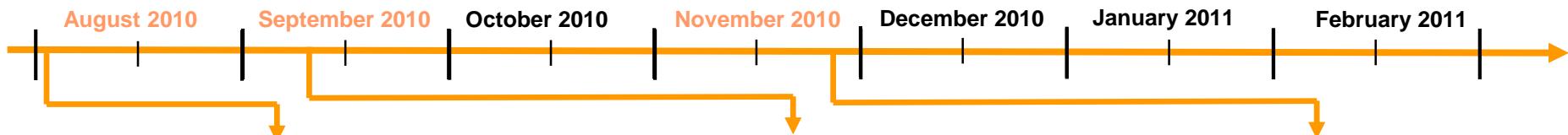
before therapy

after 2nd series

1.5 month later

after 4th series

4 month later



SCORAD 72

SCORAD 27

SCORAD 18

Atopic Dermatitis, 4 series, Patient-ID 03, male, 40 y

SCORAD 60

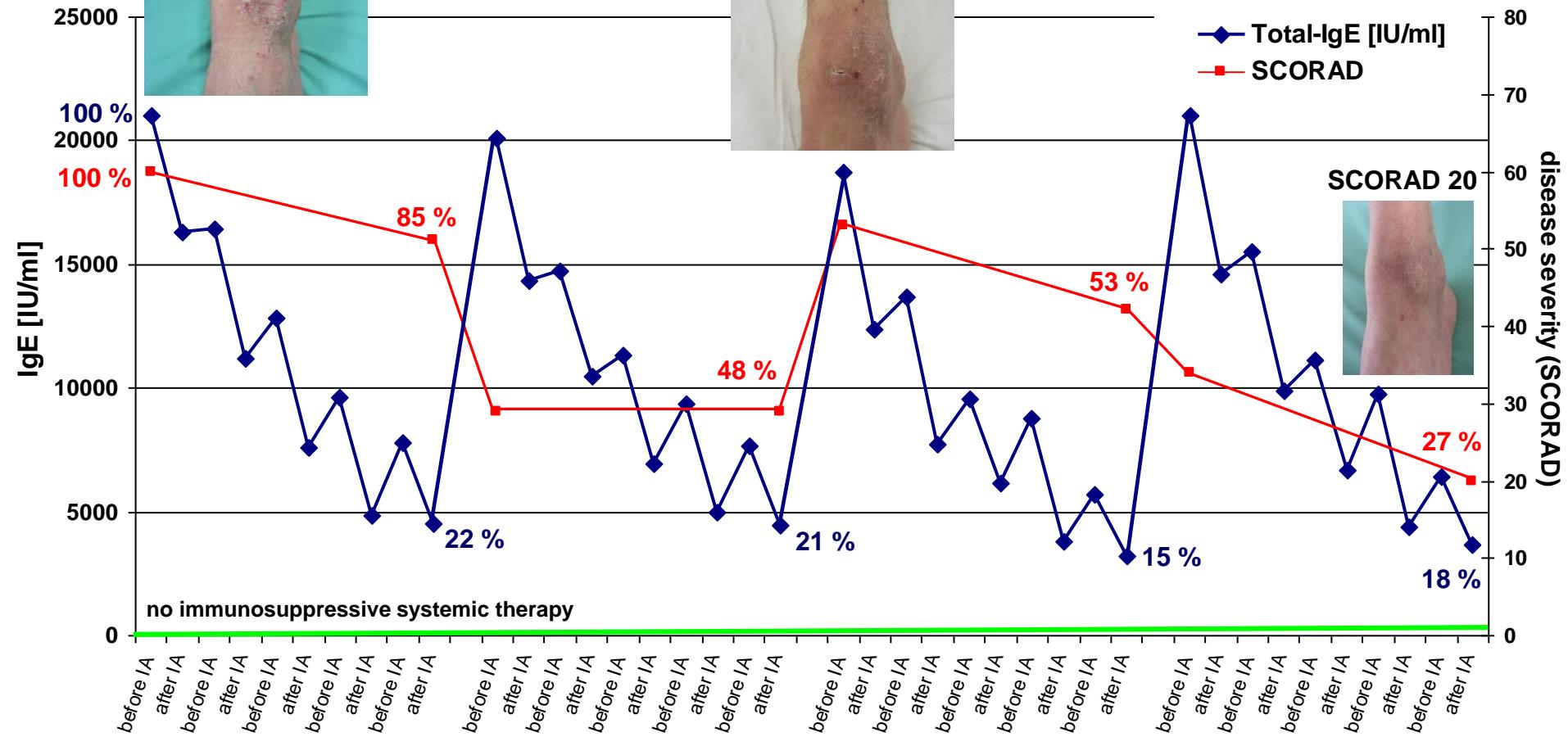


SCORAD 54



— Total-IgE [IU/ml]
— SCORAD

SCORAD 20

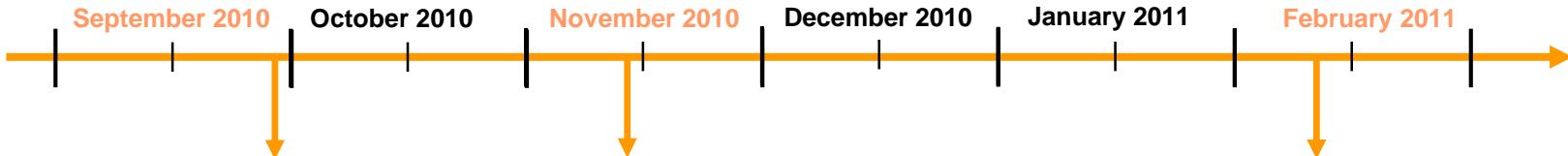


Atopic Dermatitis, 4 series, Patient-ID 03, male, 40 y



before 1st series

before therapy



after 2nd series

1.5 month later



after 4th series

4.5 month later



SCORAD 60



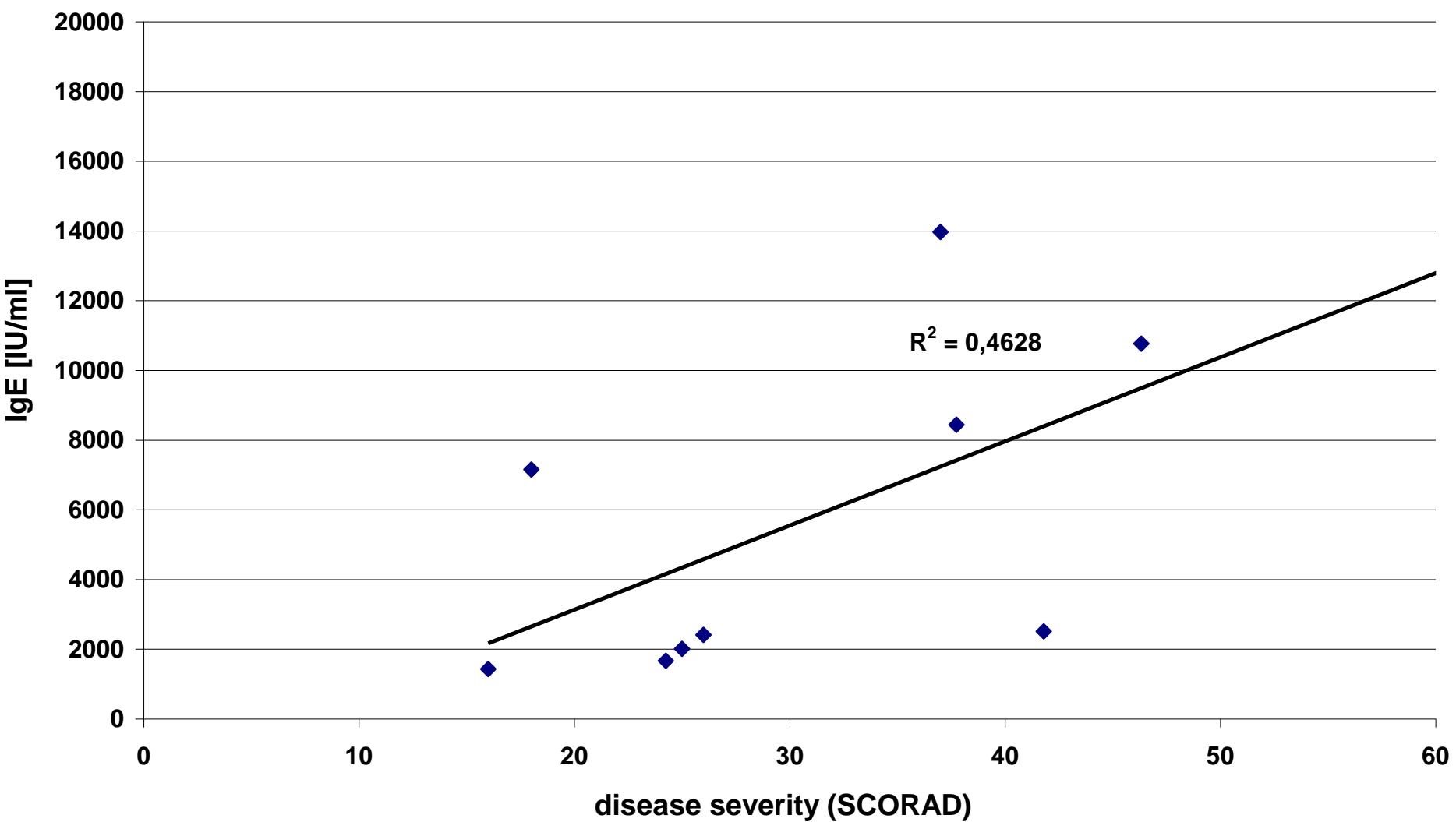
SCORAD 54



SCORAD 20

Correlation of IgE [mean IU/ml] with SCORAD (mean)

Patient ID: 02, 03, 05 and 09



Conclusion

1) IA beneficial for 6/6 patients

mean total-SCORAD lowering : 37 (± 17)

mean SCORAD lowering per series : 16 (± 14)

- 1) Prolongation of IA (>2 series, 3/6) associated with further Clinical improvement (SCORAD, 2 of 3 patients)
- 2) After final IA: Currently > 4 months remission (no systemic corticoids + saving of immune-suppressing ointments)
- 3) Despite relapsing IgE levels after IA (1 exception (9/10 possible weeks): SCORAD improvement (8/9)

Immunapheresis (IgG ↓, IG Flex, **Miltenyi**)



Simultaneous reduction of:

IgG (Subtypes 1-4)

IgM, IgA, IgE, IgD

Circ. immunocomplexes

Rheumatoid factors (IgG)

Fragments of immunglobulines

Coagulation-factors (?)

Pemphigus foliaceus

♂ , 57y

Desmoglein 1 – Autoantibody

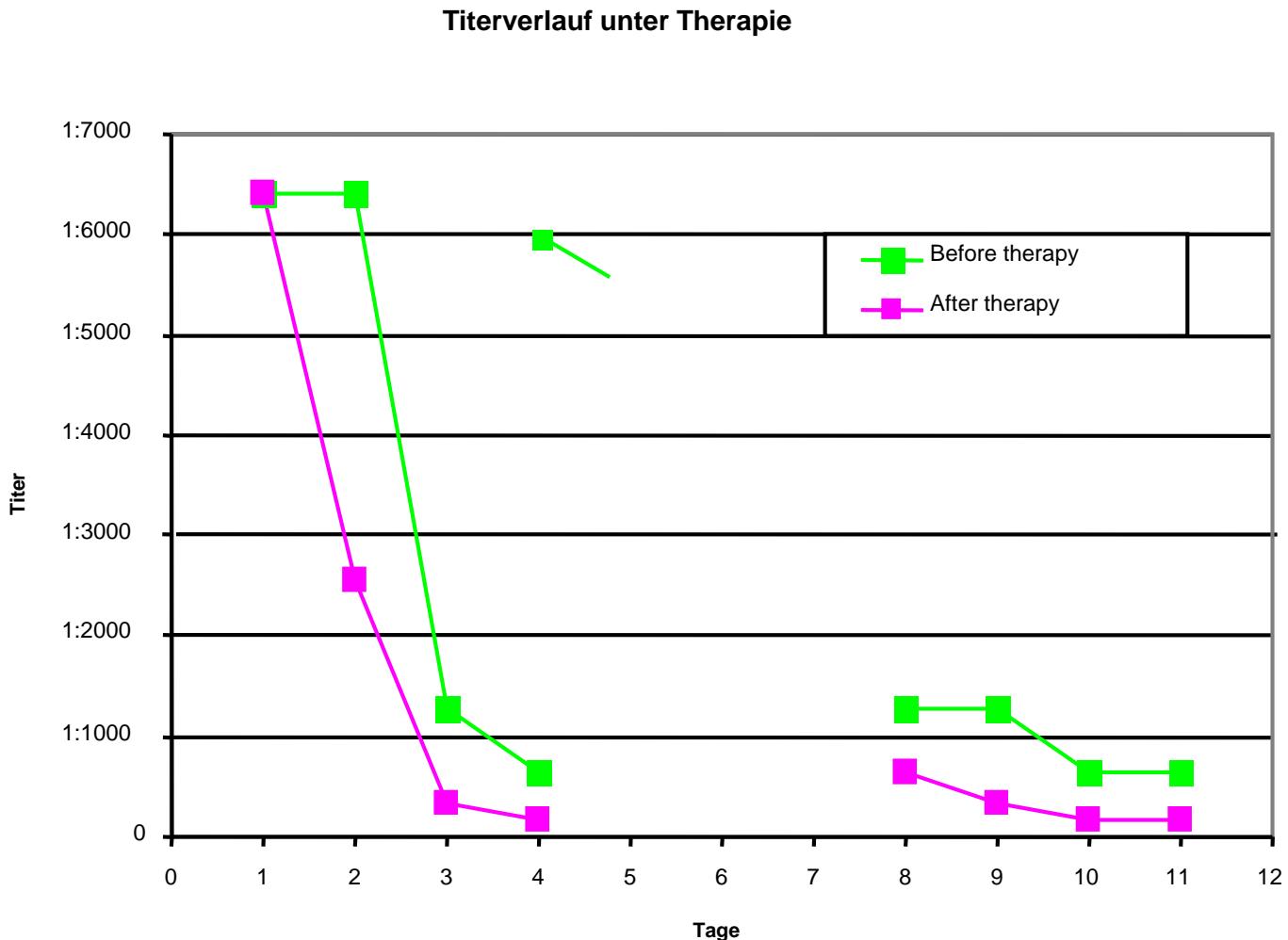
- Intermittend course (≥ 3 attacks/y)
- Systemically: Corticosteroids+Azathioprine
- Topically: Corticosteroids

Immunapheresis in erythroderma





Desmoglein 1 – Autoantibody in relation to apheretic courses





After two courses remission

Cellapheresis

Principle

- Selective removal of leucocytes, monocytes
- Induction of antiinflammatory Interleukin-1-Receptor-Antagonist (IL-1ra)
- Apoptosis of leucocytes

Indikationen

- Colitis ulcerosa
- s LE
- SSc
- Severe Atopic Dermatitis
- Severe Psoriasis

Case 1

44-y female patient

Mixed connective disease for 10 y

Raynaud Phenomenon

GI-Disease

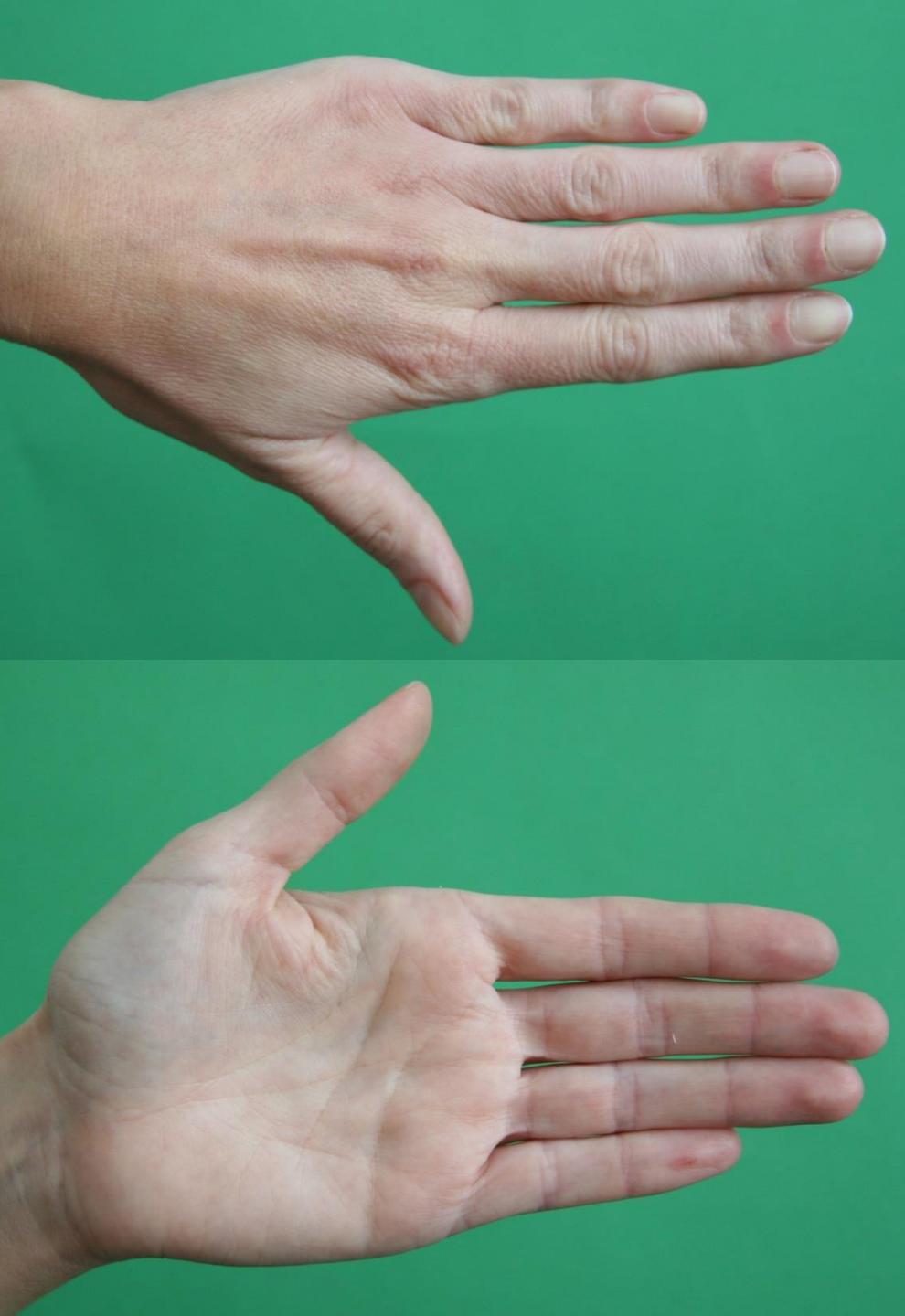
↑ ANA

No former immunosuppressive therapy

12/2009 - 01/2010 1. cycle cellapheresis

02/2010 – 04/2010 2. cycle cellapheresis





**At the end of
2. cycle
1 minute cold
stress test by
water bath**

no vasospasms

Case 2

- 55-y female patient
- sLE for 10 Y
 - involved:
 - skin
 - lung
 - Raynaud's-Phenomenon
- ↑ ANA
- Former immunosuppressive therapy:
 - MTX,
 - Azathioprine
 - Prednisolon
- 10/2009 - 11/2009 1.cycle of cellapheresis
- 01/2010 - 02/2010 2.cycle of cellapheresis





Conclusion

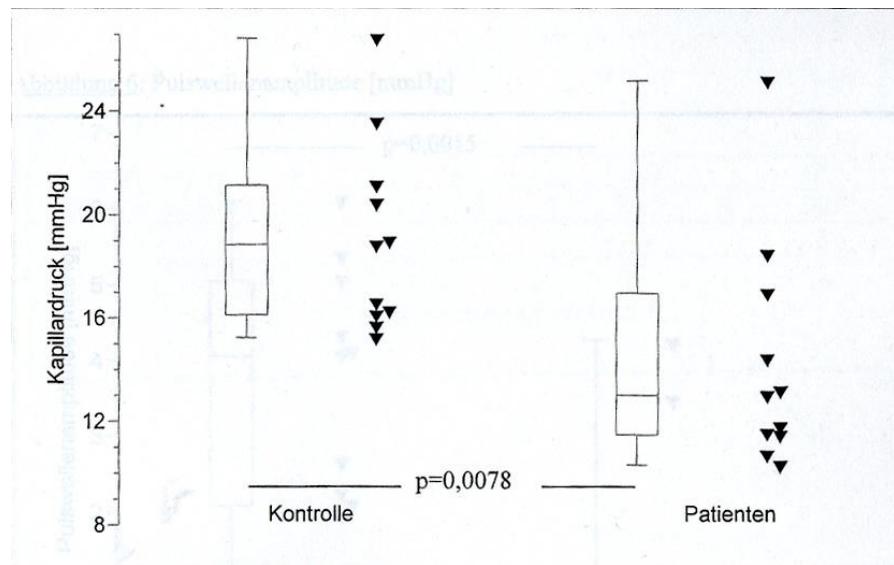
- > **Systemic Sclerosis:** Raynaud Phenomenon
Acral Necrosis
PF, FA, IGG-IA
- > **Hard to Heal Leg Ulcers:** FA
- > **Atopic Eczema:** IGG-IA

- > **Pemphigus vulgaris:** IGG-IA
- > **Systemic lupus erythematoses:** CA

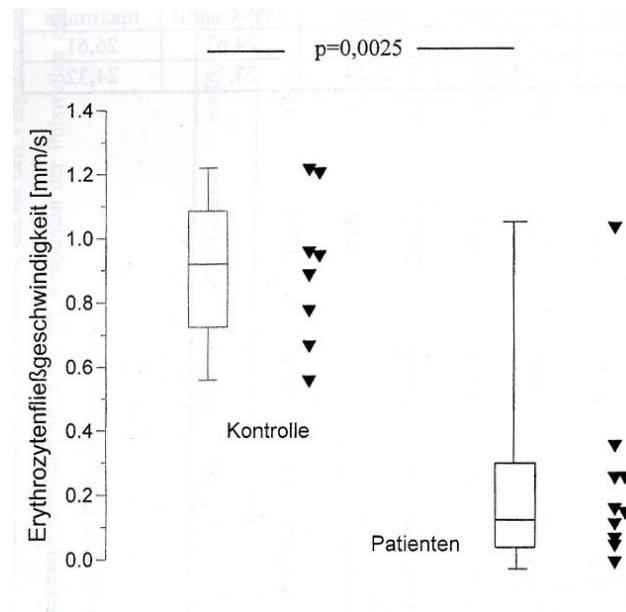


Systemic Sclerosis

Capillary Pressure



Capillary Bloodflow velocity

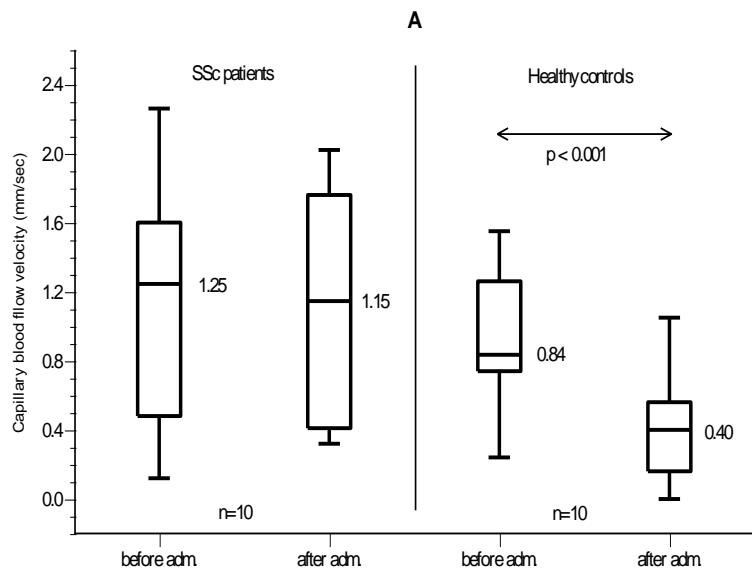


Hahn M, Heubach T, Steins A, Jünger M: J Invest Dermatol (1998) 110:982-985

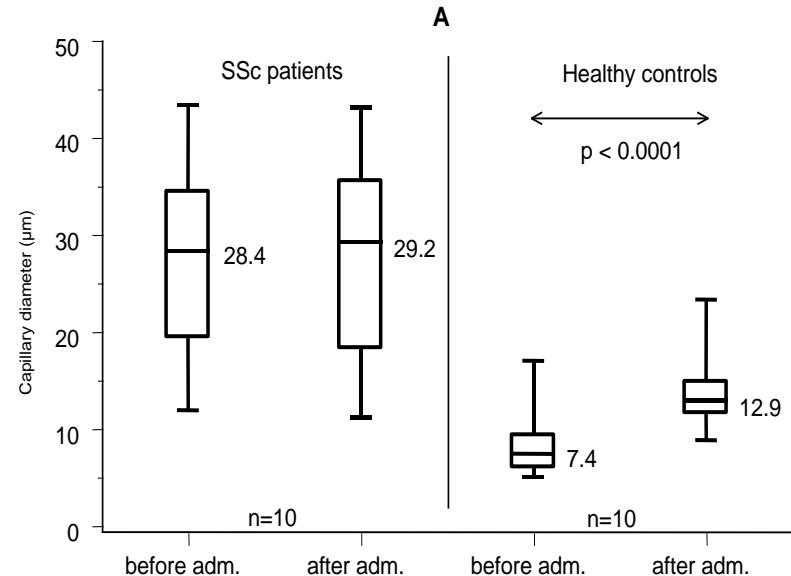
Endothelial Dysfunction in SSc: Pathological Reaction of Blood Flow in Nailfoldcapillaries to Acetylcholine



Capillary Blood Flow Velocity



Capillary Diameter



A Schlez, M Kittel, S Braun, HM Häfner, M Jünger J Invest Dermatol 2003 120: 332-334