Dermatoses and skin care in Graft versus Host Disease/GvHD

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Antwerp University Hospital (UZA)

Kennis / Ervaring / Zorg

UZA

Graft-Versus-Host Disease (GvHD)

Kennis / Ervaring / Zorg

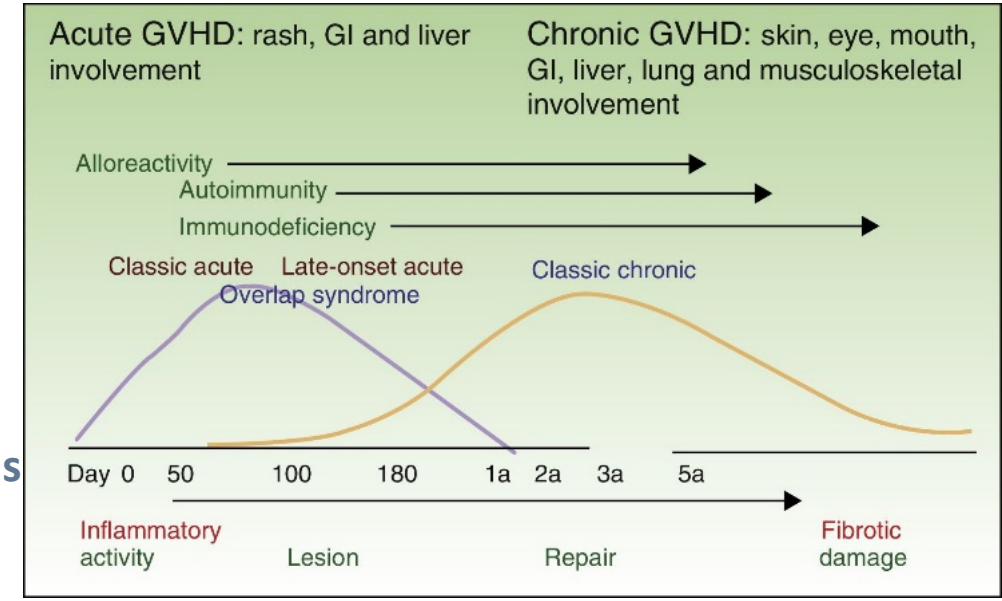
GvHD

- **GvHD**

  = Graft-versus-Host Disease

  - **donor immune cells mediate an immune attack to the host tissues/organs**

  - **Acute versus Chronic**
    - **Acute < 100**
    - **Chronic > 100**
    - **Overlap**
    - **Peak: Acute: after 4-6 weaks**
    - **Peak: Chronic: after 2-3 months**



GvHD: how frequent? And is skin affected frequently?

- YES!
- Skin is most frequently affected
- 80% of patients who develop aGvHD disease have SKIN affected at first presentation

- 40% of HLA identical HSCT (hematopoetic stem cell transplants) will develop GvHD
- 60-70% of HLA mismatched HSCT will develop GvHD

Clinical Study

Frequency and Outcome of Graft versus Host Disease after Stem Cell Transplantation: A Six-Year Experience from a Tertiary Care Center in Pakistan

Natasha Ali,[1] Salman Naseem Adil,[1] Mohammad Usman Shaikh,[1] and Nehal Masood[2]

Grade	*n* (%)
1	3 (16)
2	10 (53)
3	3 (16)
4	3 (16)

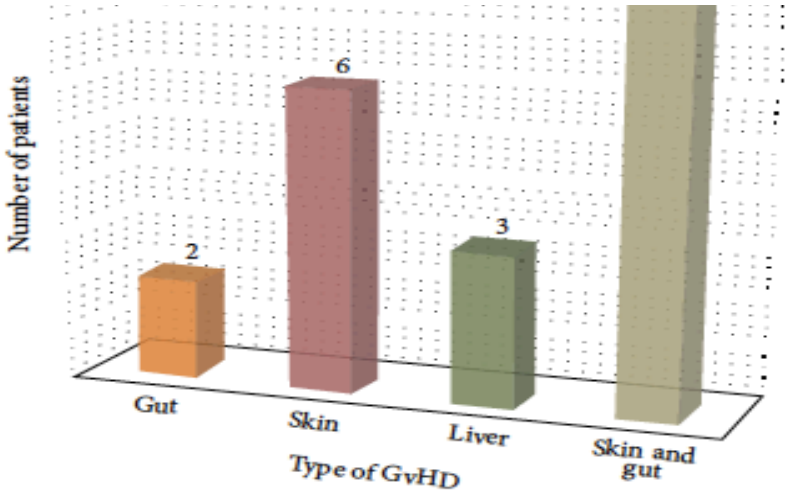


FIGURE 1: Acute GvHD grade and organ of involvement (n = 19/34).

Grade	*n* (%)
Limited	2 (13.3)
Extensive	13 (87)

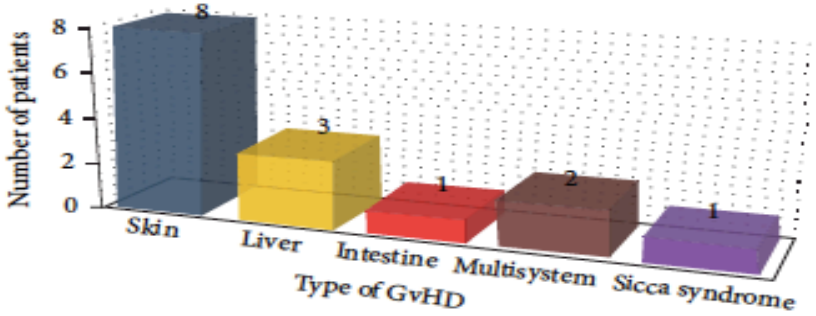


FIGURE 2: Chronic GvHD grade and organ of involvement (n = 15/34).

GvHD: Acute

- **Acute GvHD: STAGES 0-1-2-3-4**
  skin> liver and gut

Table II. Clinical staging of acute graft-versus-host disease

Stage	Skin	Liver	Gut
0	No rash related to GVHD	Bilirubin, <2 mg/dL	None
1	Maculopapular rash <25% of body surface area without associated symptoms	Bilirubin, 2 to <3 mg/dL	Diarrhea, >500 to 1000 mL/d, nausea and vomiting
2	Maculopapular rash or erythema with pruritus or other associated symptoms covering ≥25 and <50% of body surface area or localized desquamation	Bilirubin, 3 to <6 mg/dL	Diarrhea, >1000 to 1500 mL/d, nausea and vomiting
3	Generalized erythroderma or symptomatic macular, papular, or vesicular eruption with bullae or desquamation covering ≥50% of the body	Bilirubin, 6 to <15 mg/dL	Diarrhea, >1500 mL/d, nausea and vomiting
4	Generalized exfoliative dermatitis, ulcerative dermatitis or bullae	Bilirubin, ≥15 mg/dL	Severe abdominal pain with or without ileus

Grade 4:
Toxic epidermolytic necrosis-like

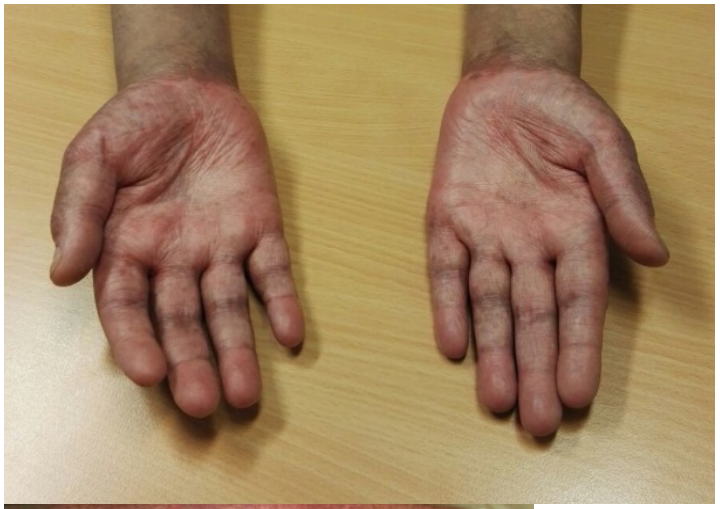
GvHD: Acute

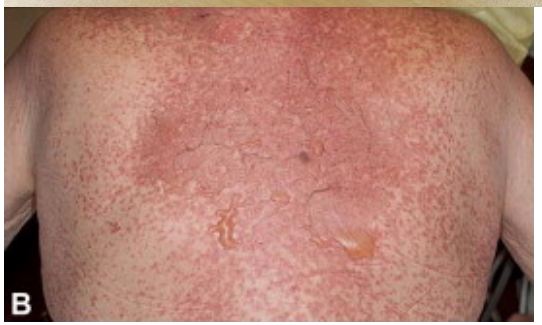
- Acute GvHD
  - Skin manifestations
    - Early: itching, dysesthesia/hyperesthesia, subtle erythema or edema
    - Typical:
      - Palmoplantar erythema
      - Maculopapular rash
      - Erythroderma, bullae development, desquamation, etc.

    CAVE: worst variant:

    Grade IV: TEN: toxic epidermolysis like:

    high mortality





GvHD: Chronic

- Chronic GvHD
  - Primary target tissues/organs: skin and mucosa
  - Can affect nearly every tissue/organ: liver, eye, GI tract/ esophagus, lung, GU tract, joints, etc.

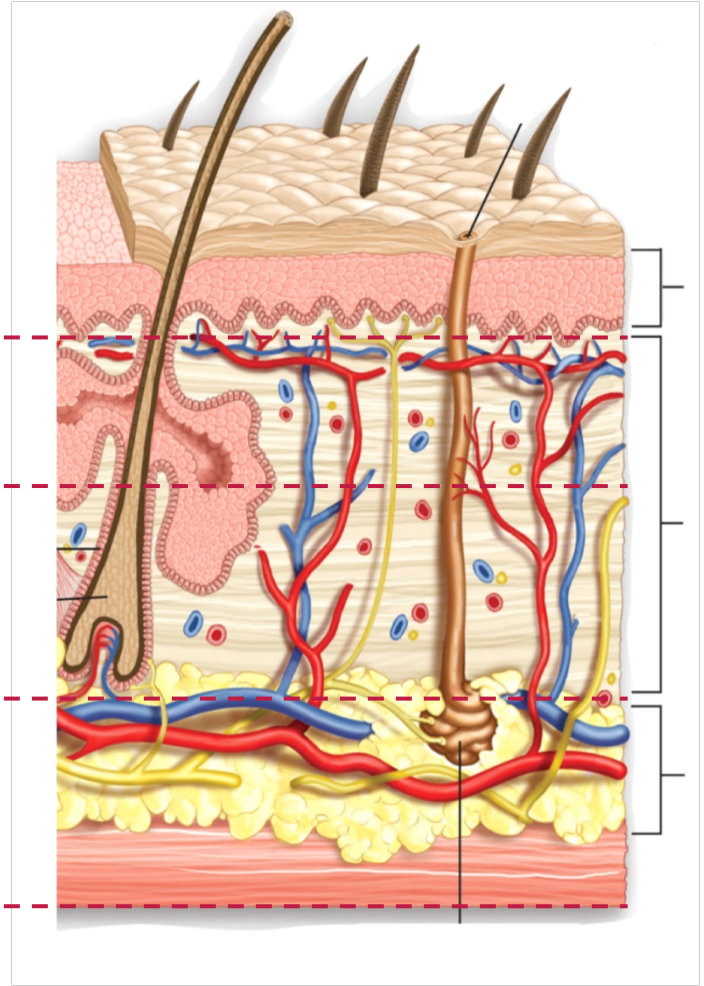
  - Skin manifestations in cGvHD = a wide range of presentations
    - Lichen planus-like: non-sclerotic
    - Sclerotic: lichen sclerosus, morpheaform, sclerosis/fasciitis

    - Leopard skin
    - Poikiloderma
    - Other: alopecia, graying hair, vitiligo, eczema, psoriasis

    - Non-sclerotic often earlier than sclerotic disease

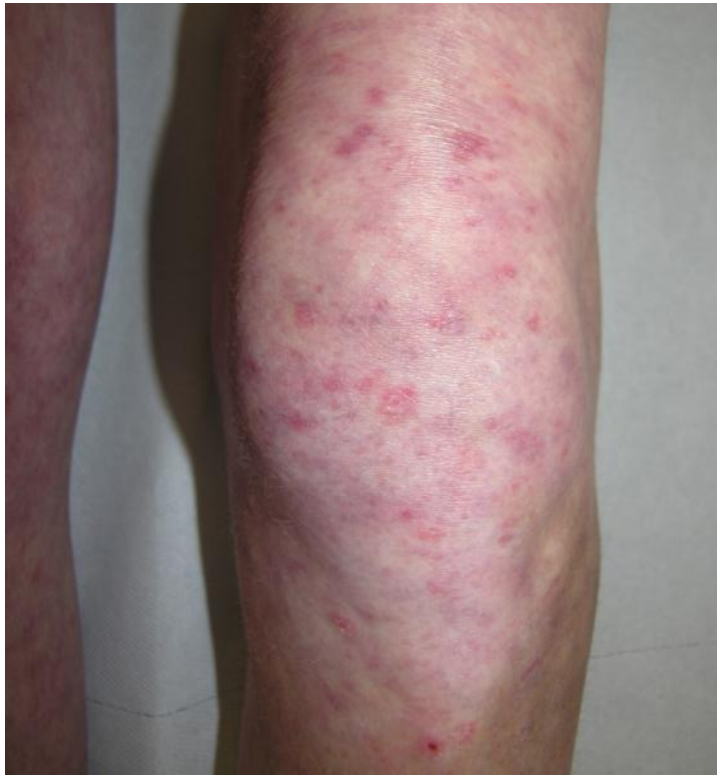
GvHD: Chronic

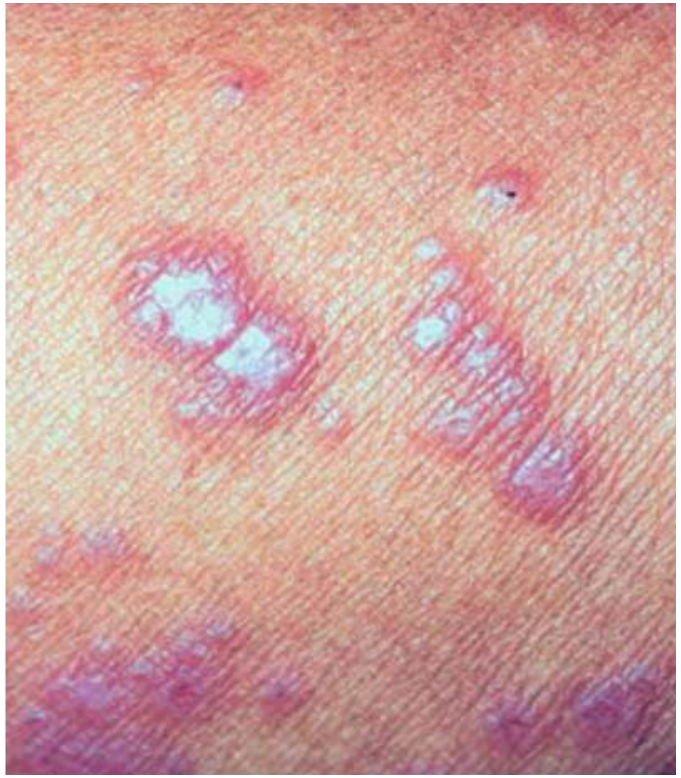
- Chronic GvHD
  - Skin manifestations in cGvHD
    - Lichen planus-like
    - Sclerotic
      - Lichen sclerosus-like
      - Morpheaform
      - Deep sclerosis/fasciitis
    - Poikiloderma
    - Other



GvHD: Chronic

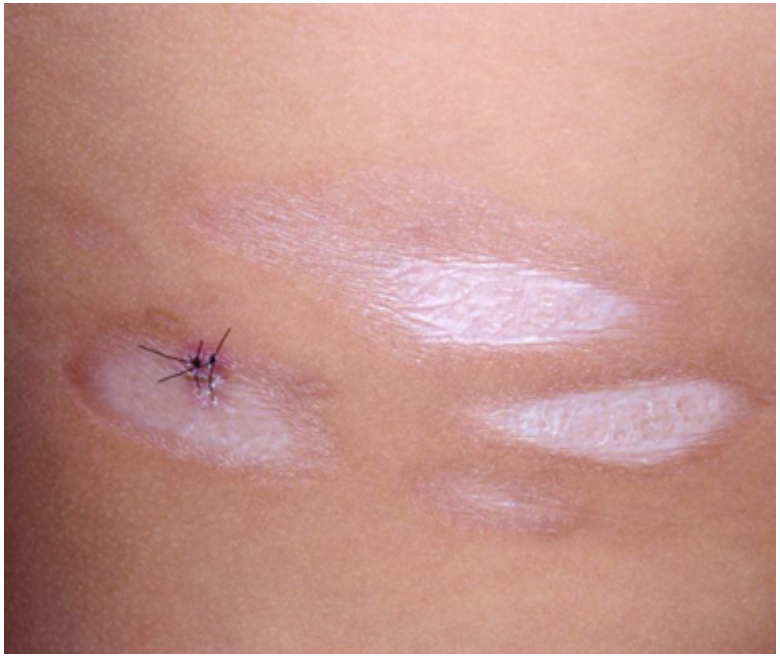
- Chronic GvHD
  - Lichen planus-like
    - Purple, papules, prurigo, polygonal, planar: predominantly on dorsal hands/feet, extremities and trunk-koebnerization





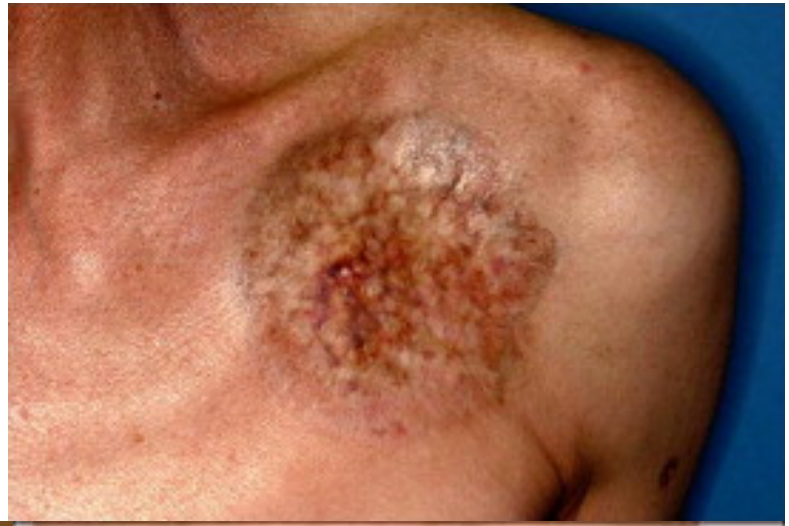
GvHD: Chronic

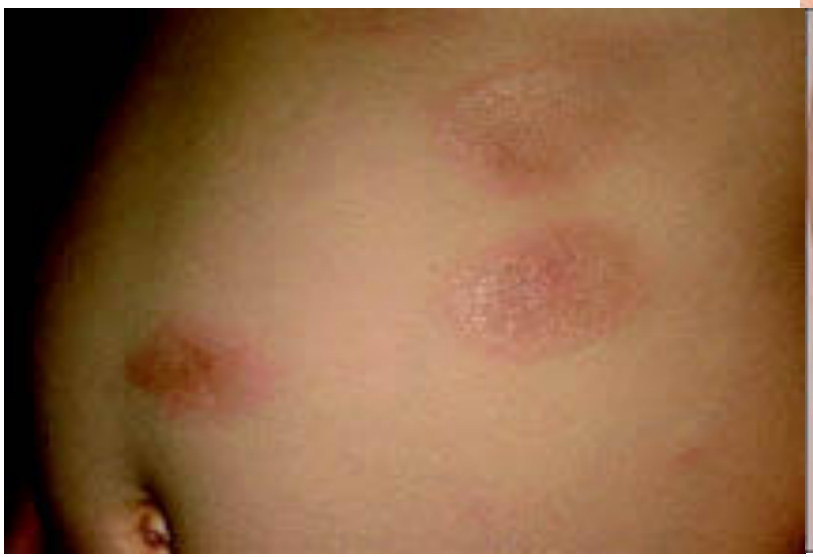
- Chronic GvHD
  - Sclerotic
    - Lichen sclerosus-like

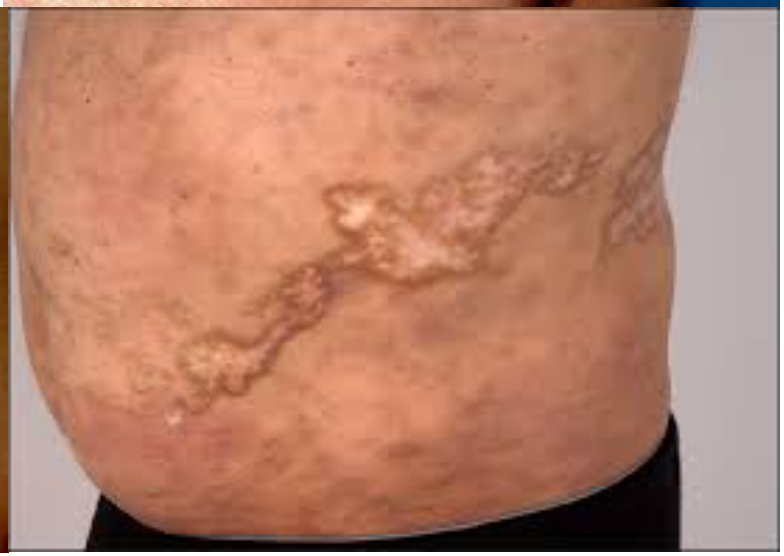


GvHD: Chronic

- Chronic GvHD
  - Sclerotic
    - Morphea-like

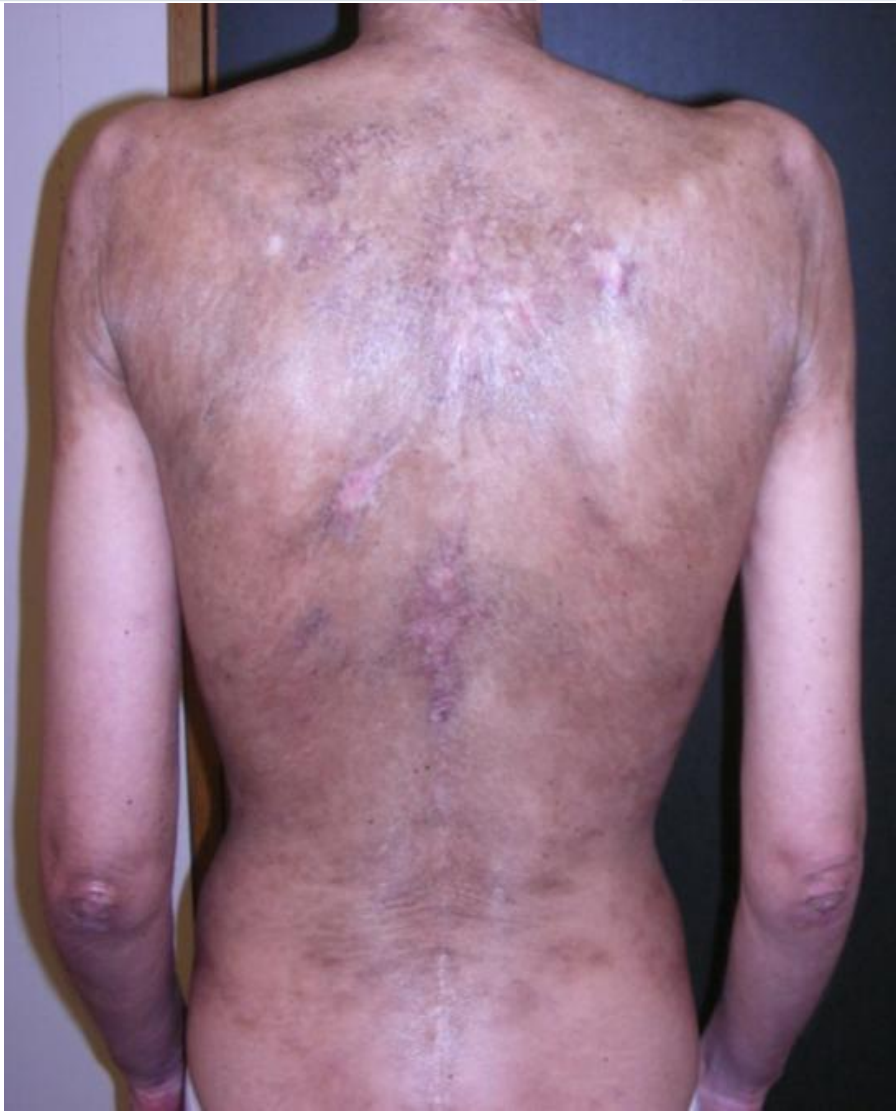






GvHD: Chronic

- Chronic GvHD
  - Sclerotic
    - Deep sclerosis/eosinophilic fasciitis



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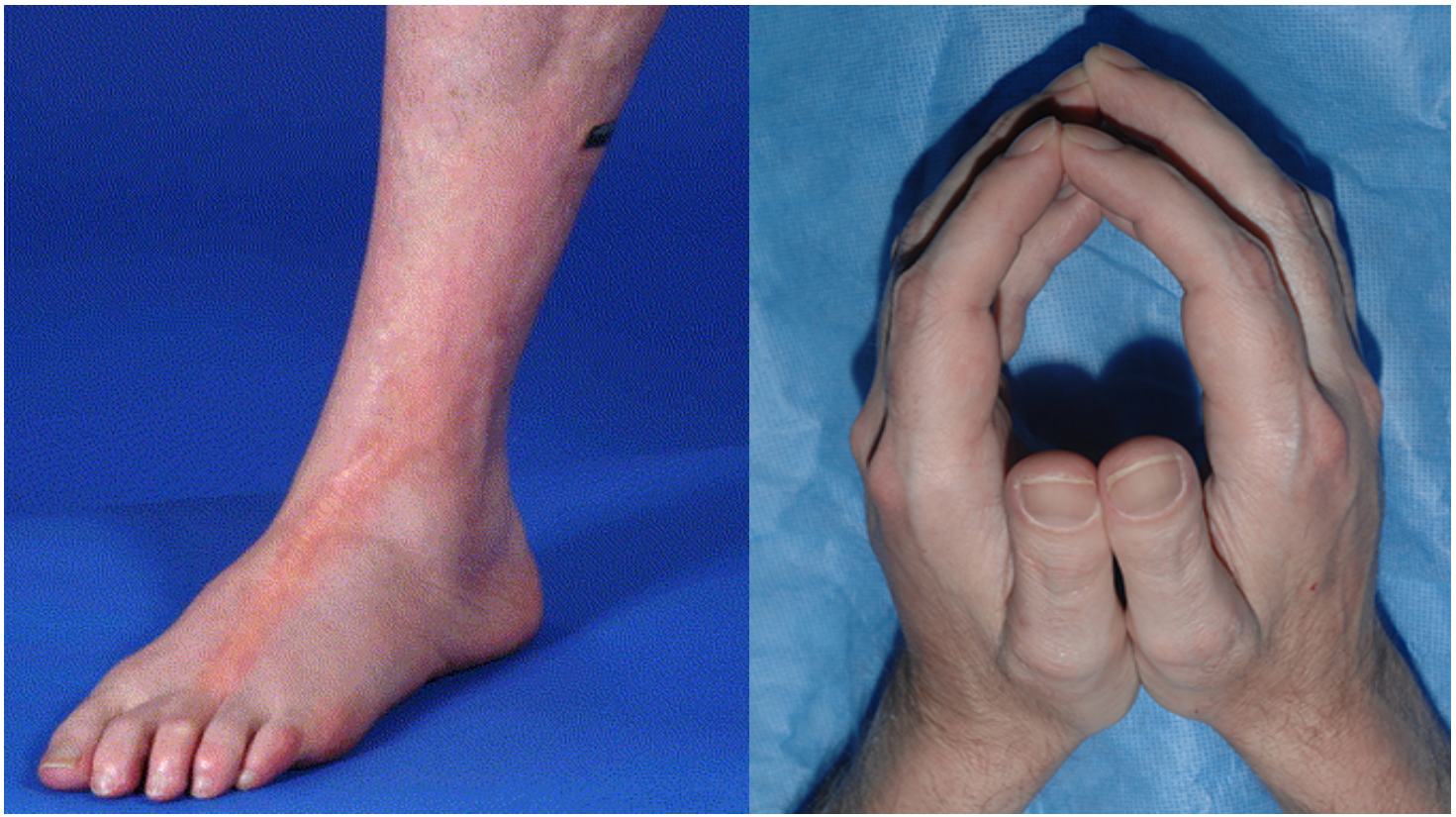

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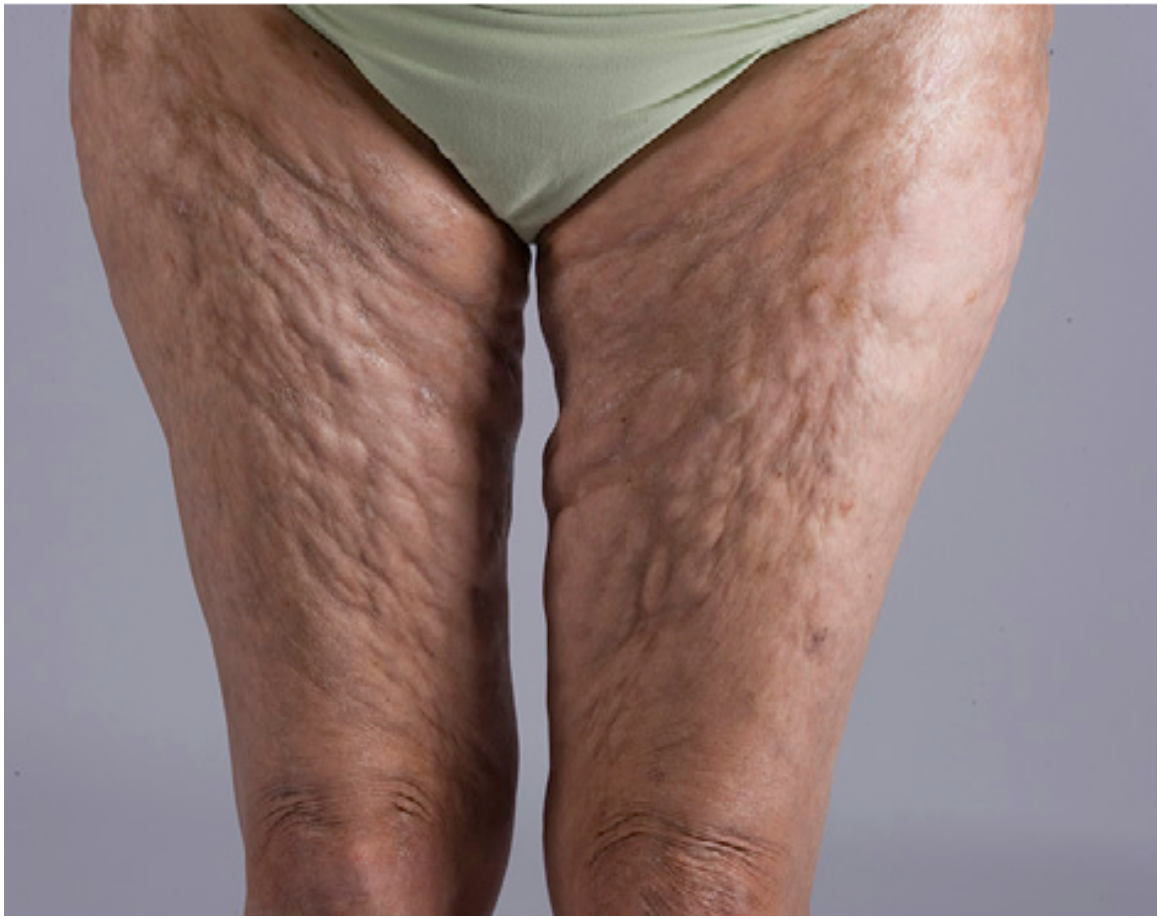
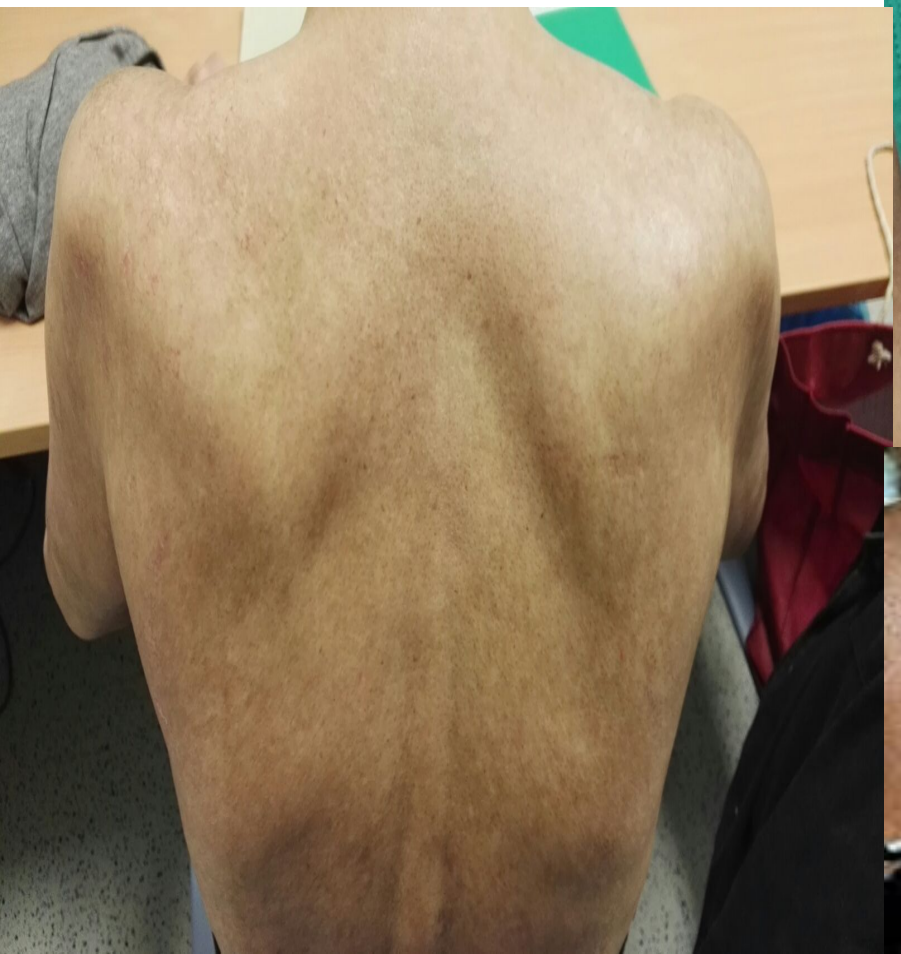
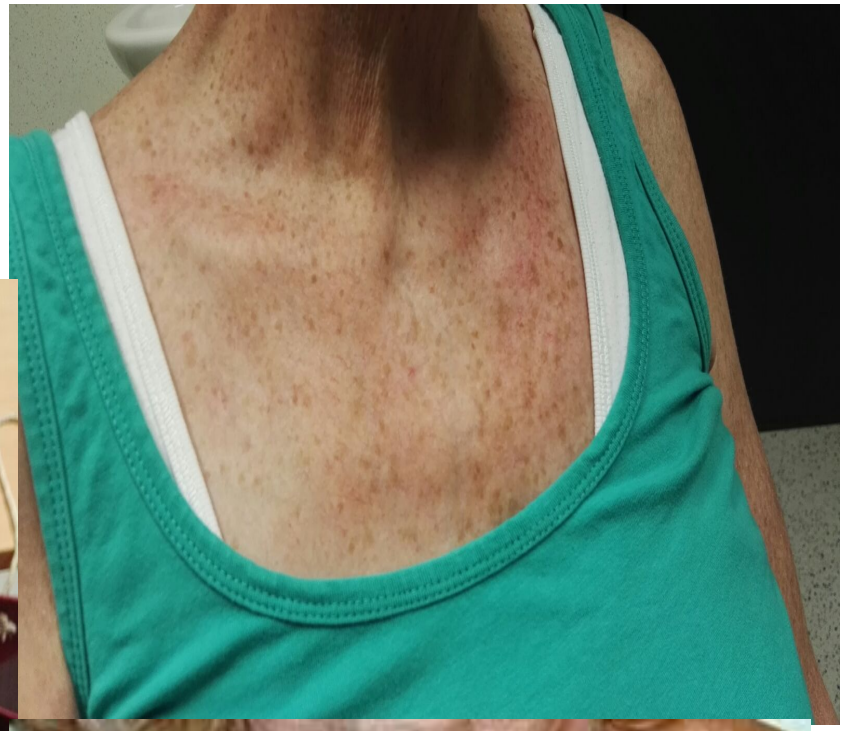
- Chronic GvHD
  - Sclerotic
    - Deep sclerosis/eosinophilic fasciitis

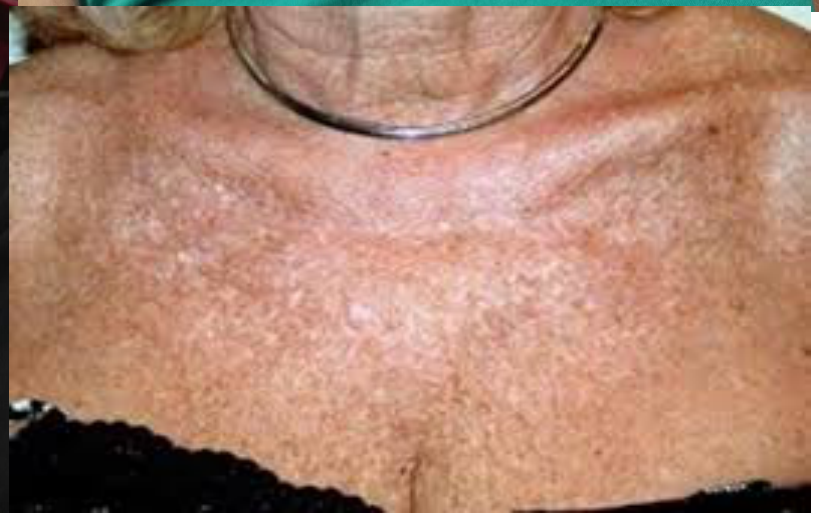


GvHD: Chronic

- Chronic GvHD
  - **Poikiloderma**

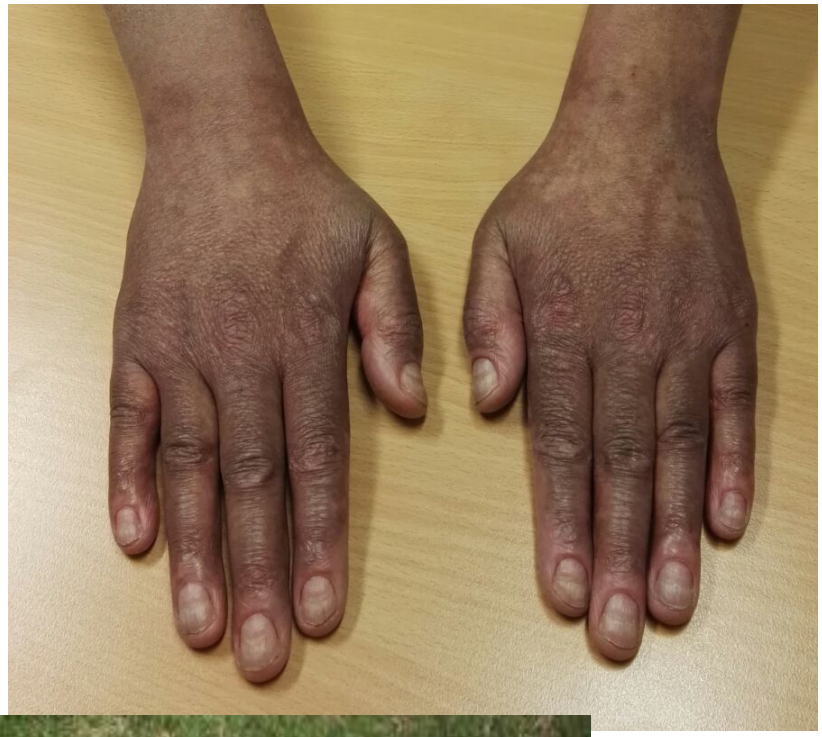


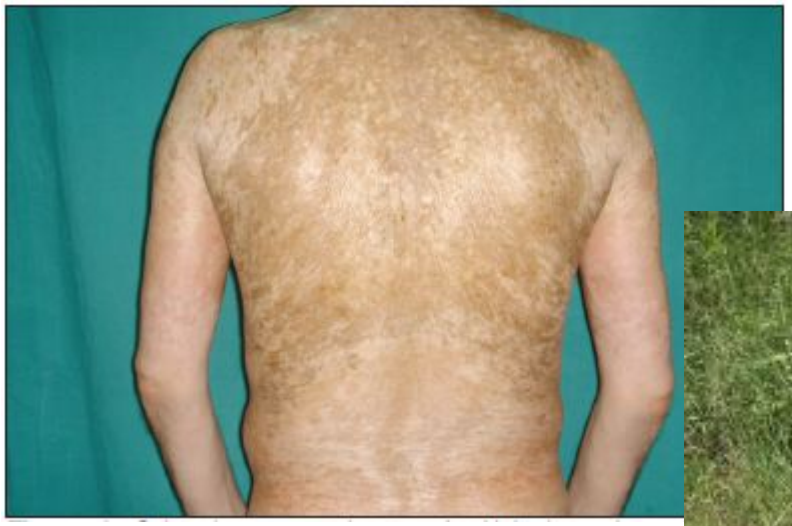




GvHD: Chronic

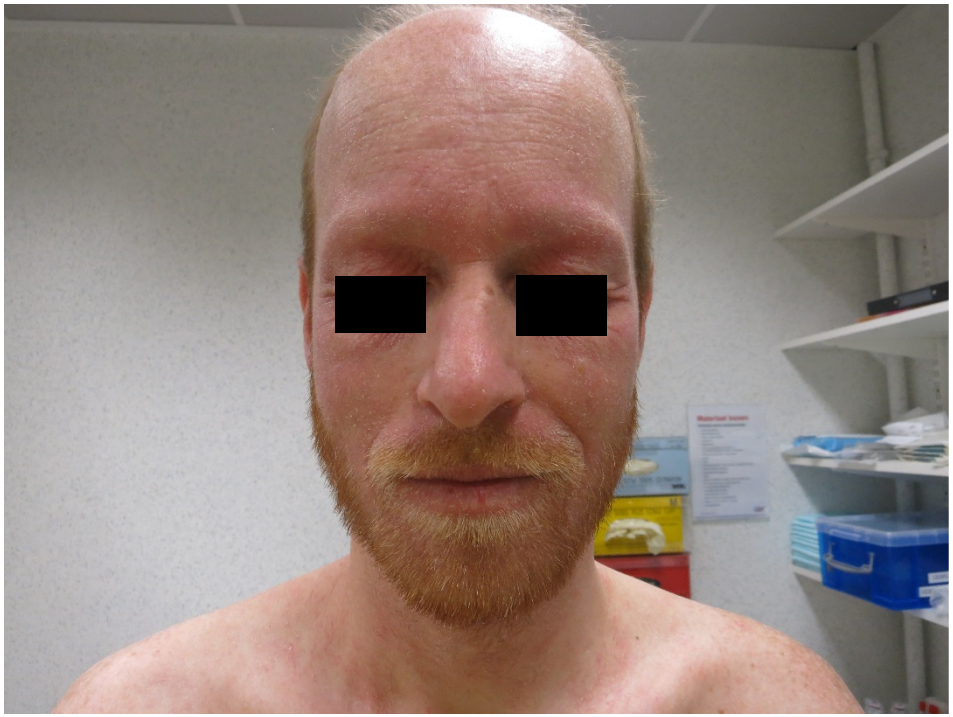
- Chronic GvHD
  - Other cutaneous manifestations
    - Hypopigmentation
    - Hyperpigmentation (leopard skin)

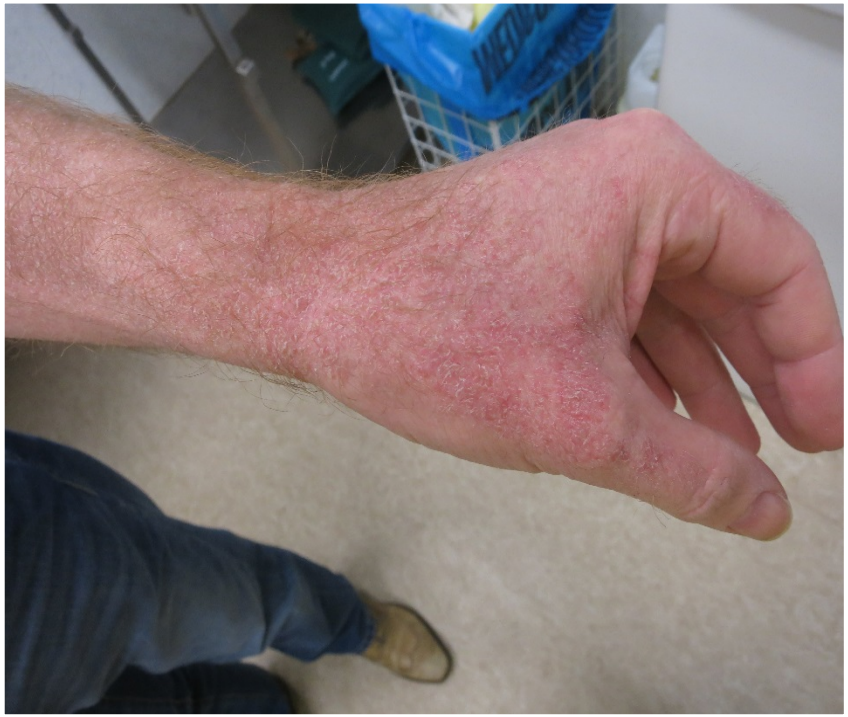




GvHD: Chronic

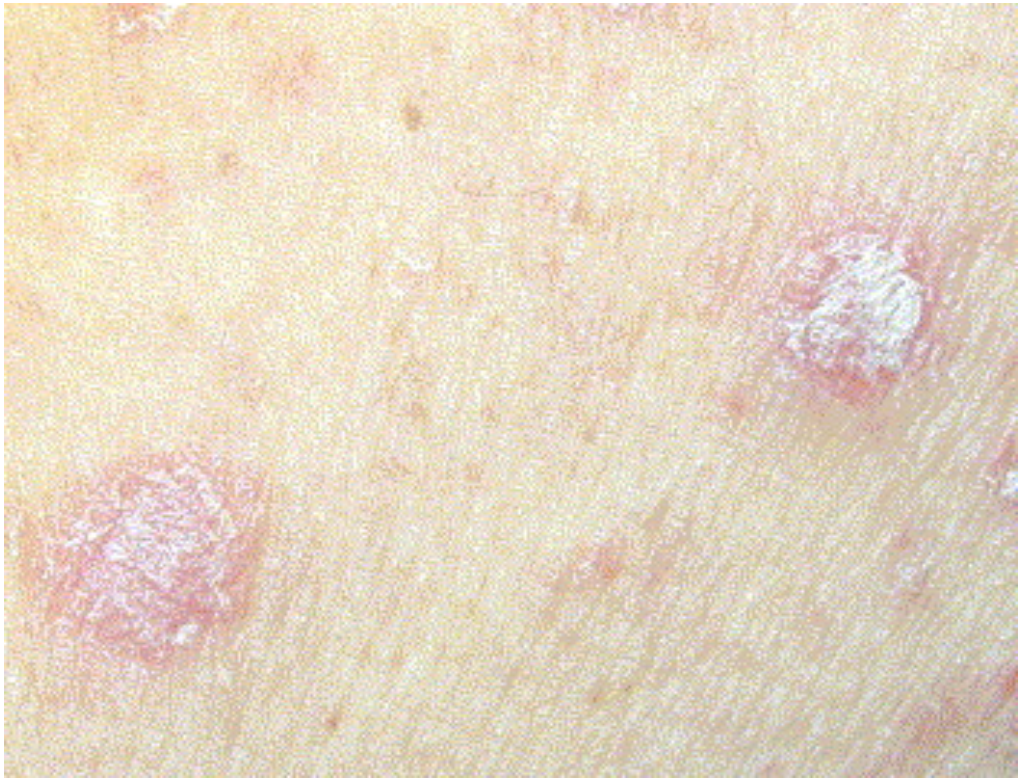
- Chronic GvHD
  - Other cutaneous manifestations
    - Eczematous or psoriasiform





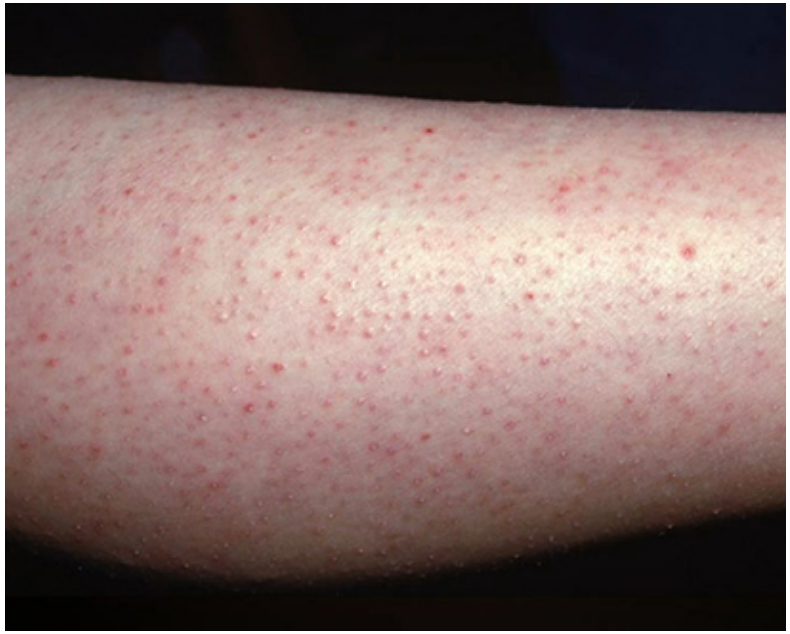
GvHD: Chronic

- Chronic GvHD
  - Other cutaneous manifestations
    - Eczematous or psoriasiform

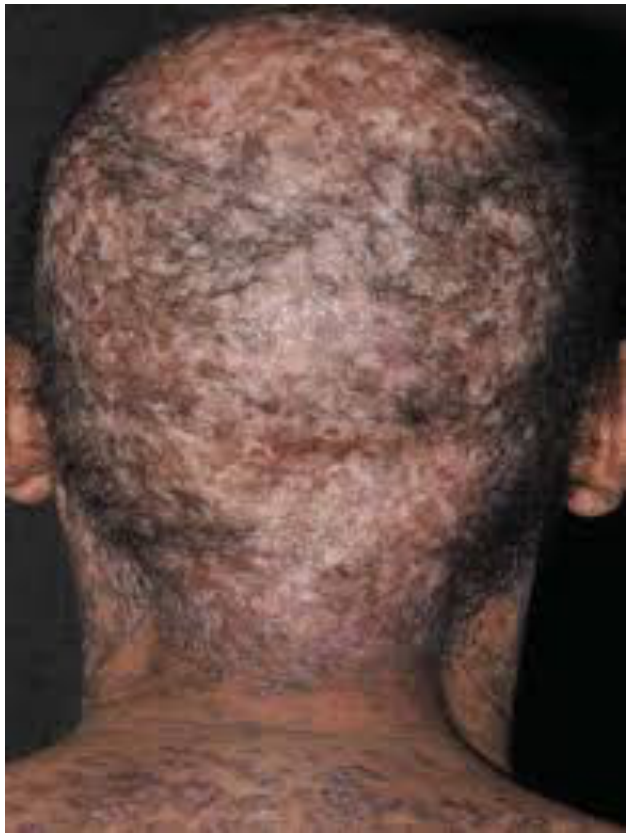


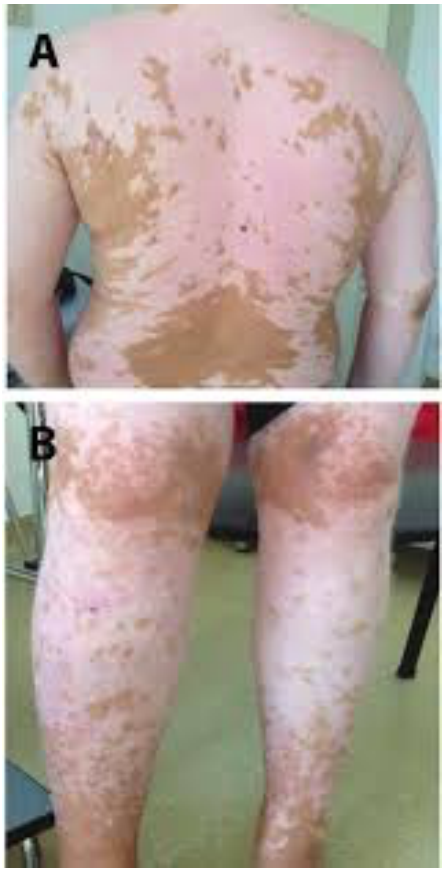
GvHD: Chronic

- Chronic GvHD
  - **Other cutaneous manifestations**
    - Erythematous folliculaly-based papules ~ keratosis pilaris



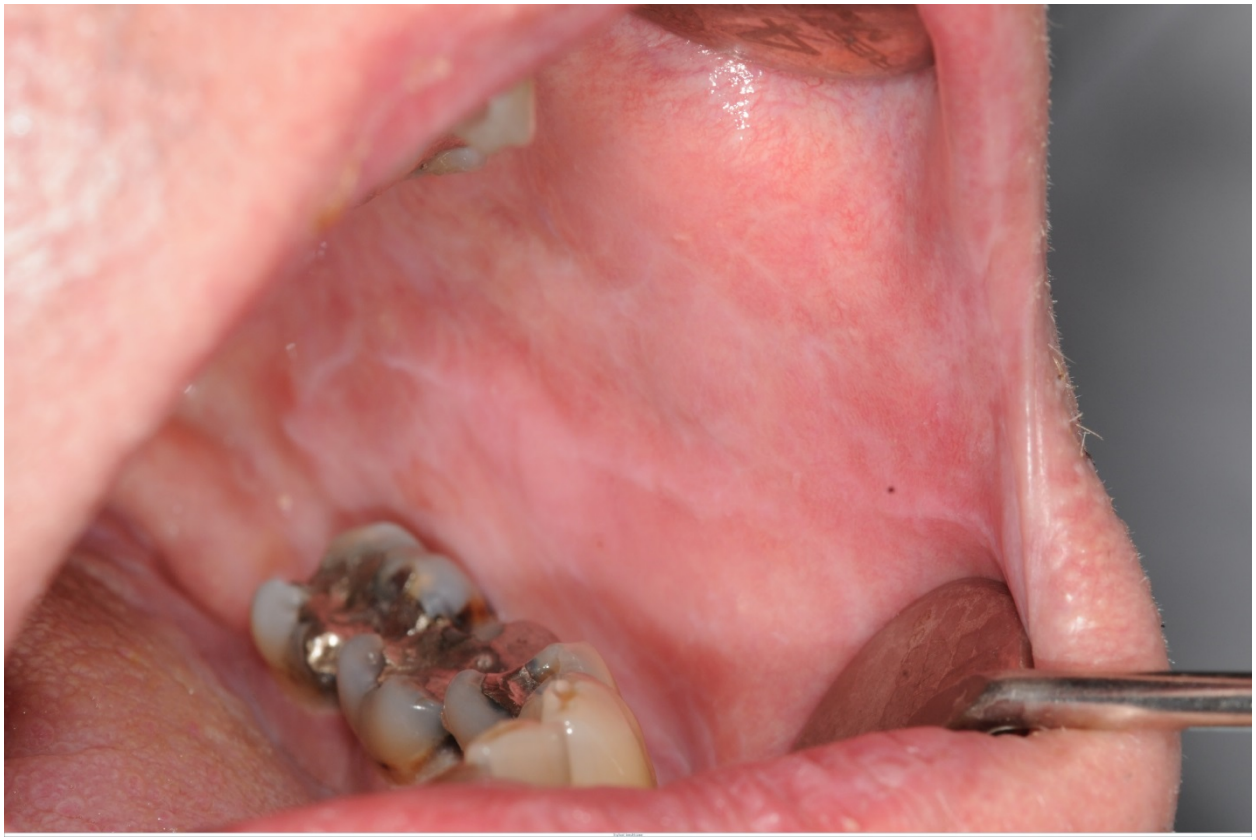
Chronic GvHD: Alopecia / Vitiligo in GvHD





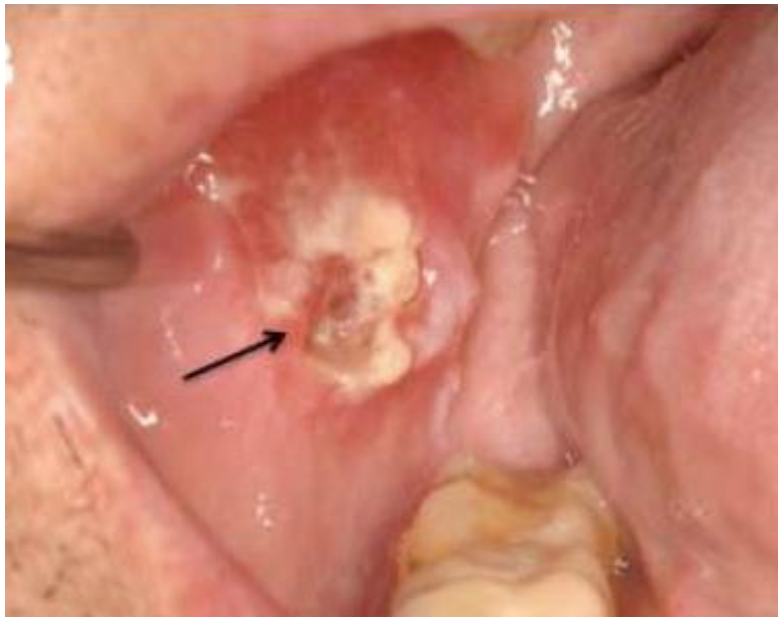
GvHD: Chronic

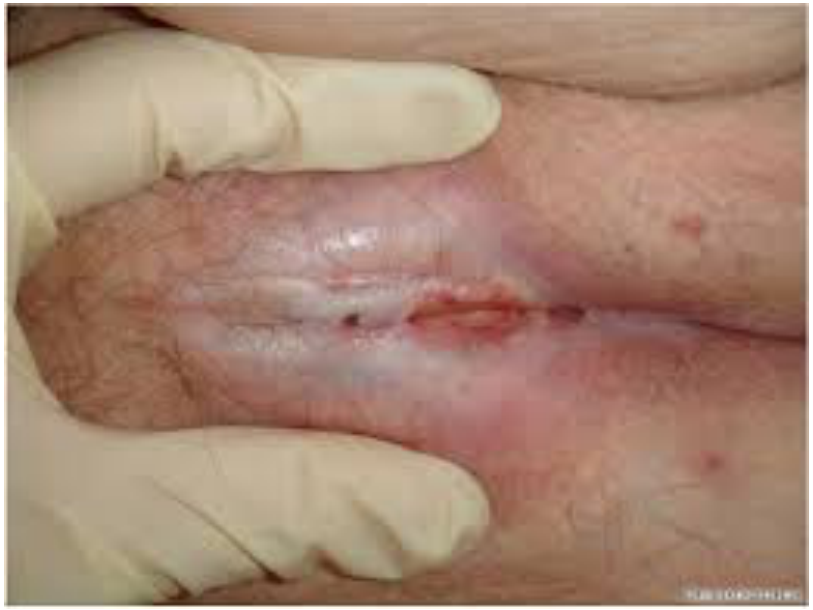
- Chronic GvHD
  - Oral mucosa



GvHD: Chronic

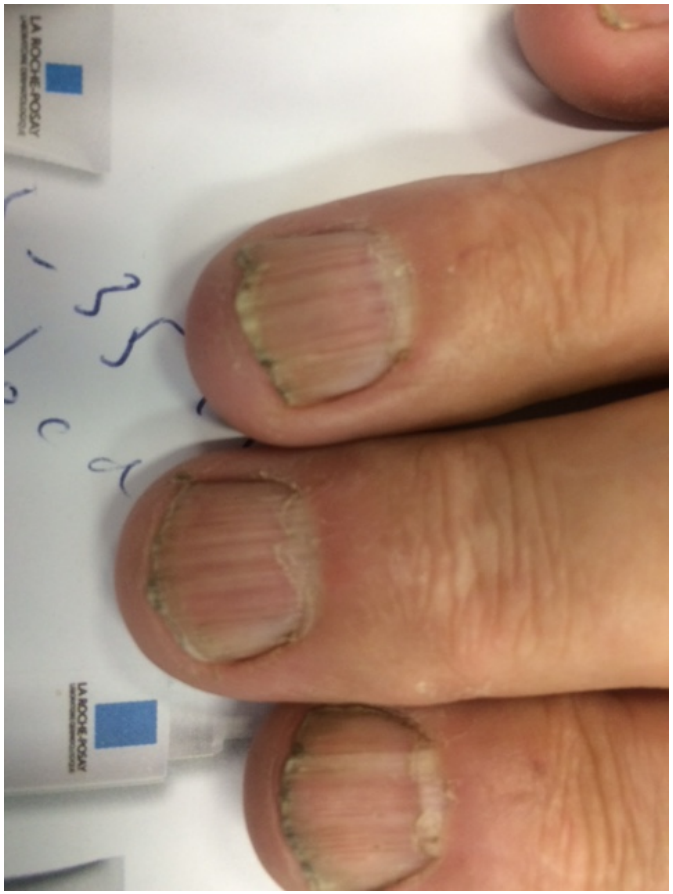
- Chronic GvHD
  - Oral mucosa / genital mucosa

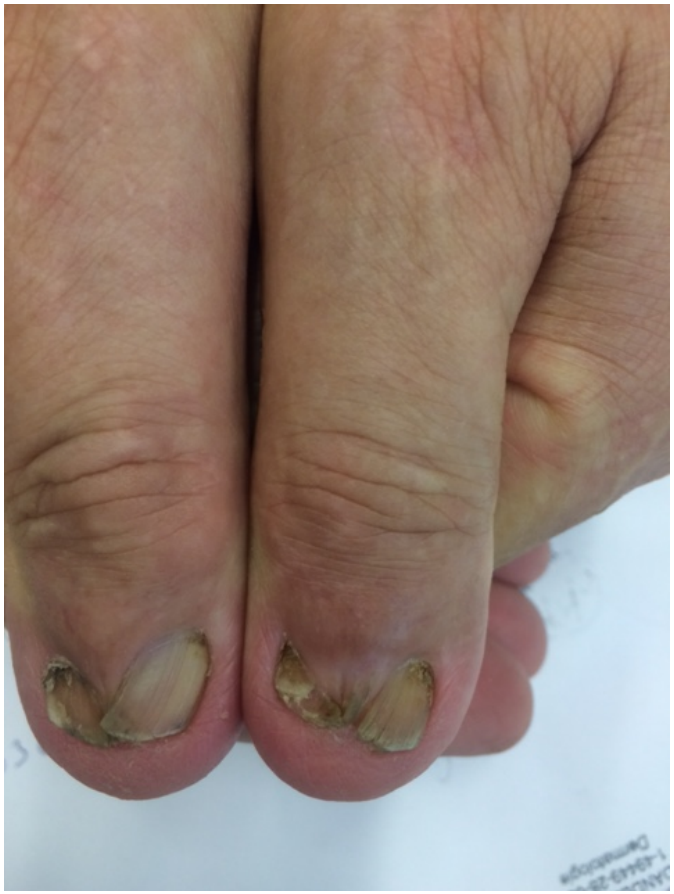




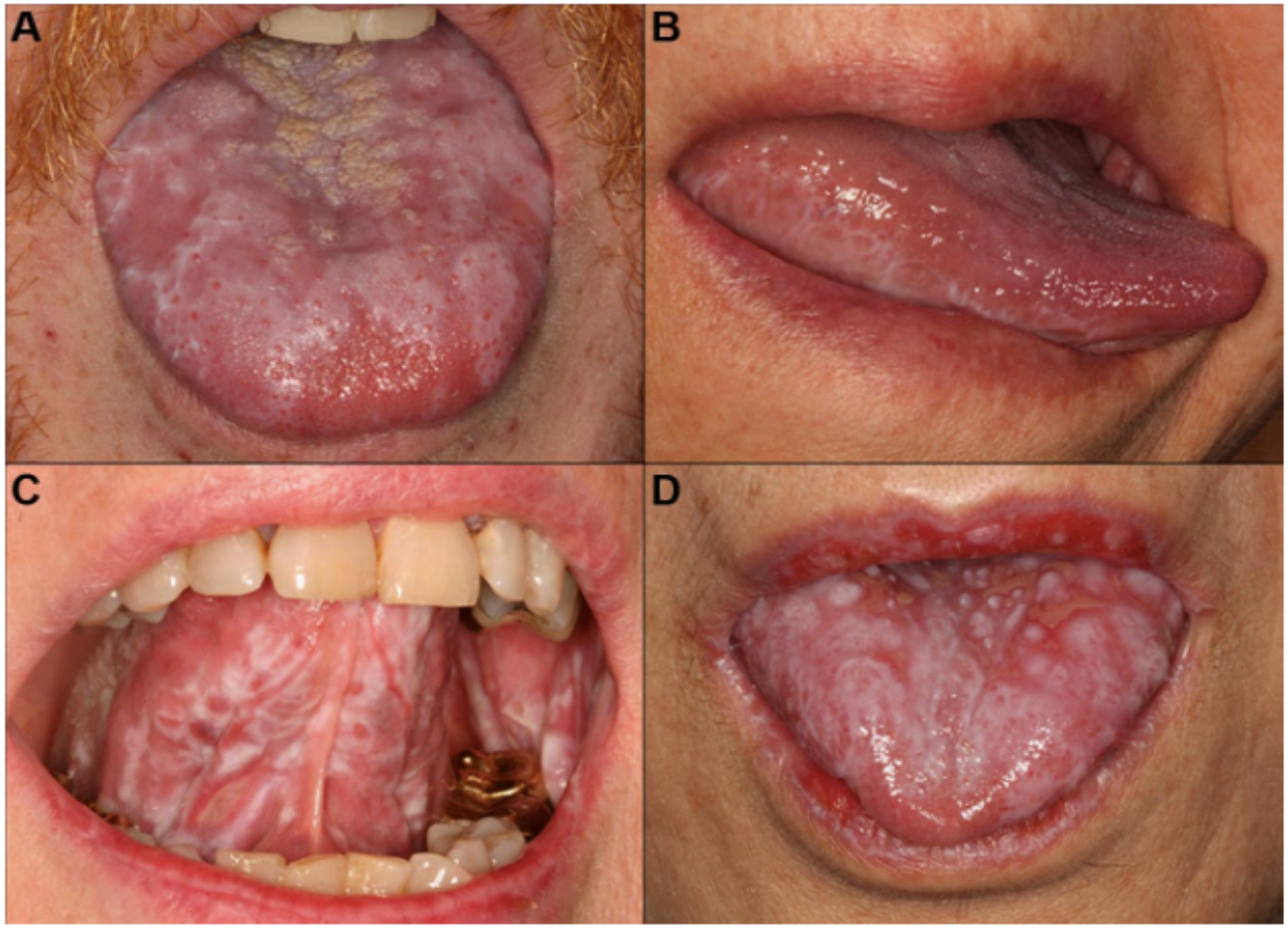
GvHD: Chronic

- Chronic GvHD
  - nails





Mucosal: Lichenoid features of tongue



How we treat oral chronic graft-versus-host disease

Nathaniel Treister,[1,2] Christine Duncan,[3,4] Corey Cutler,[4,5] and Leslie Lehmann[3,4]

[1]Division of Oral Medicine and Dentistry, Brigham and Women's Hospital, Boston, MA; [2]Department of Oral Medicine, Infection and Immunity, Harvard School of Dental Medicine, Boston, MA; [3]Department of Pediatric Oncology, Dana-Farber Cancer Institute, Boston, MA; [4]Department of Medicine, Harvard Medical School, Boston, MA; and [5]Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA

Treatment of Graft-Versus-Host Disease (GvHD)

Kennis / Ervaring / Zorg

GvHD Treatment: General Measures

- Prevent or relieve dry skin
  - **Bathing instructions**
    - Not too long and not too hot
    - Use bath or shower oils / soapfree body wash

      e.g. Xeracalm AD, Lipikar syndet, etc.
  - **Skin hydration**
    - On a daily basis
    - Emollients (creams or ointments) are necessary !
      - Magistral formulas : less expensive, but often very greasy: vaseline/ paraffine/AVA
      - Pharmacy: e.g. Epaderm, Dexeryl, Xeracalm AD baume, Lipikar AP+ baume, etc.

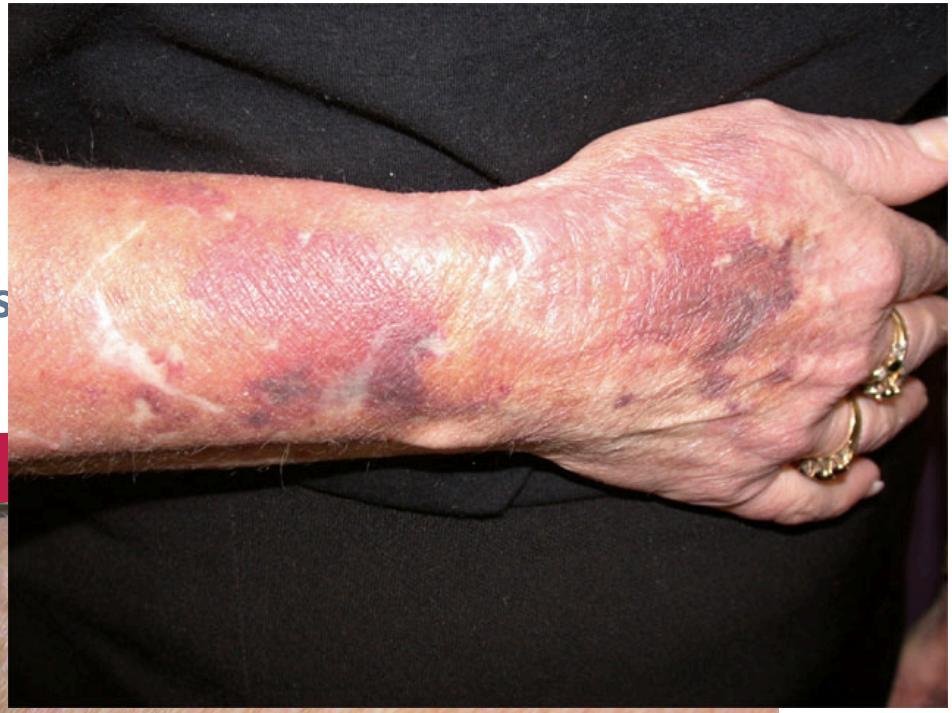
      Tips for use: after shower/bath: do not rub, apply to affected and not affected skin

GvHD Treatment: Topical

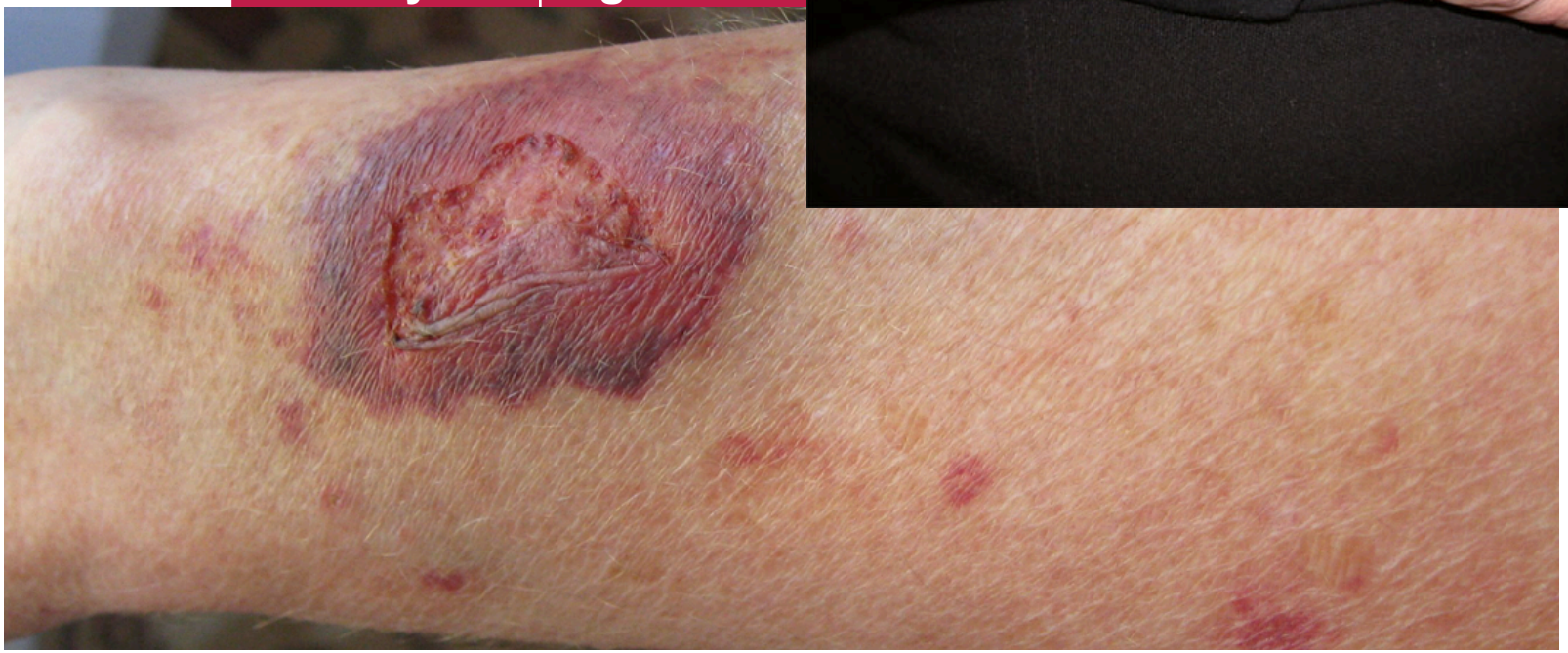
- **Topical corticosteroids**
  - Acute GvHD
  - Chronic GvHD: non-sclerotic

  Psoriasis, eczema, lichen planus

  Vitiligo..

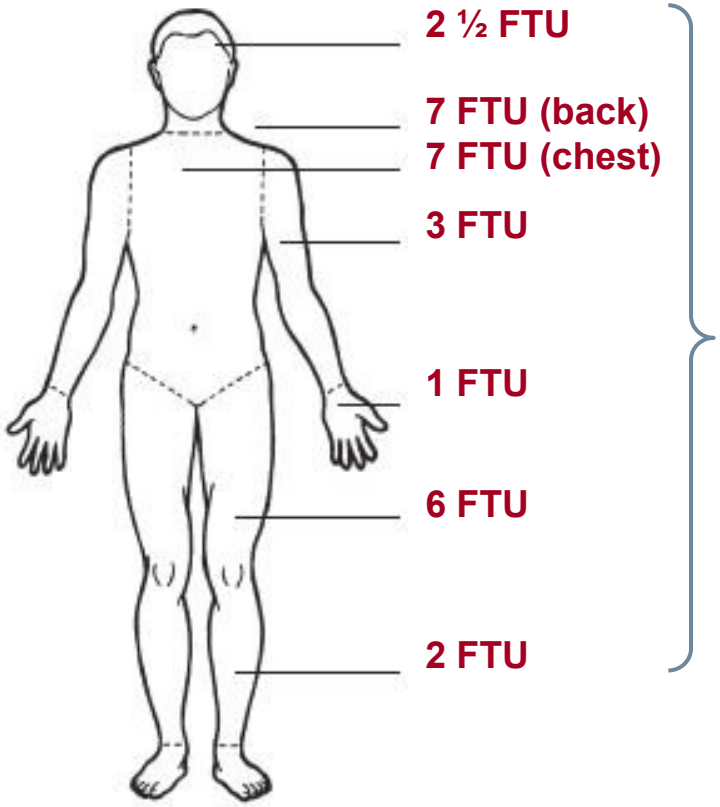


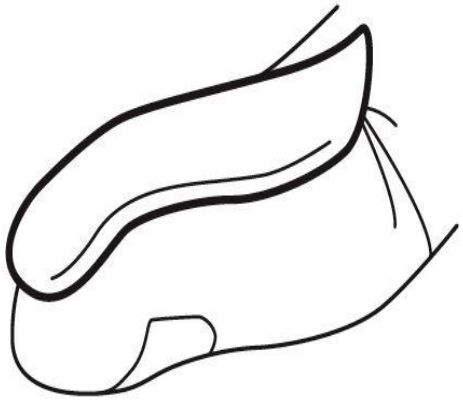
Potency	e.g.



GvHD Treatment: Topical

- **Topical corticosteroids**
  - Potency CAVE! Dermovate versus Elocom





= 0.5 g

Entire body = app. 40 FTU = 20 g

UZA

GvHD Treatment: Topical

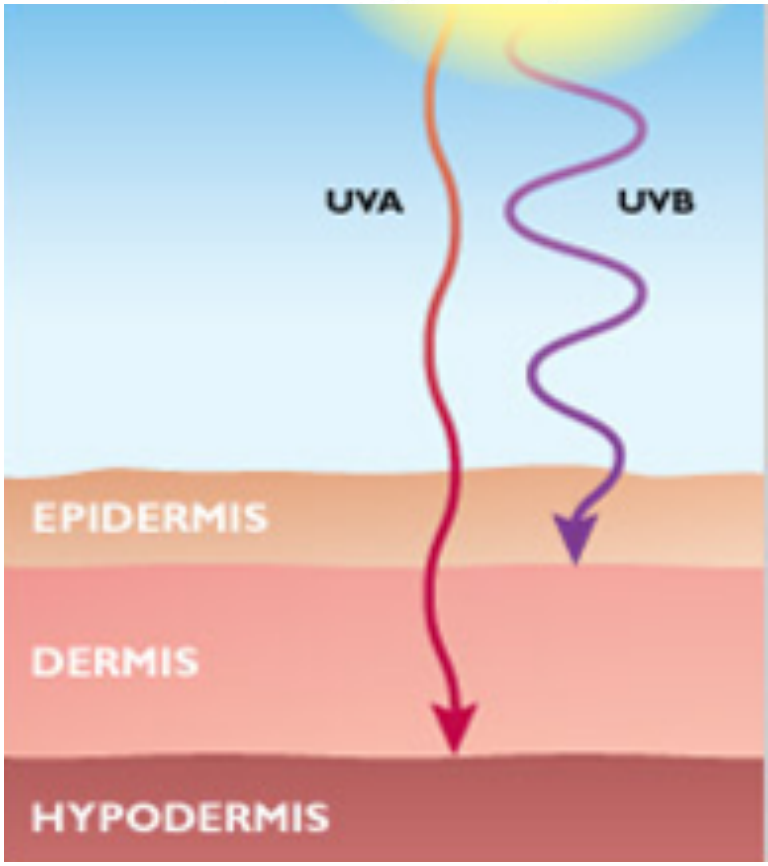
- **Topical immunomodulators**
  - Chronic GvHD (off-label): more specifically useful for sensitive skin (e.g. face)
  - Which formulation?
    - Tacrolimus [Protopic®], Pimecrolimus [Elidel®]
    - Less potent than topical CS
    - No skin atrophy (can be used for a longer period of time and also on sensitive skin)
    - Flushing can be a side effect (temporary)
    - Black box warning with regard to increased risk of lymphomas has been withdrawn

GvHD Treatment: Topical

- **Topical corticosteroids + vitamin D**
  - Chronic GvHD : sclerotic (lichen sclerosus-like or morphea)
  - Which formulation?
    - Betamethason + calcipotriol [Dovobet®, Xamiol®, Enstilum®] -> vitamin D analogue with ***antifibrotic action***
    - No effect on existing sclerosis

GvHD Treatment: Phototherapy

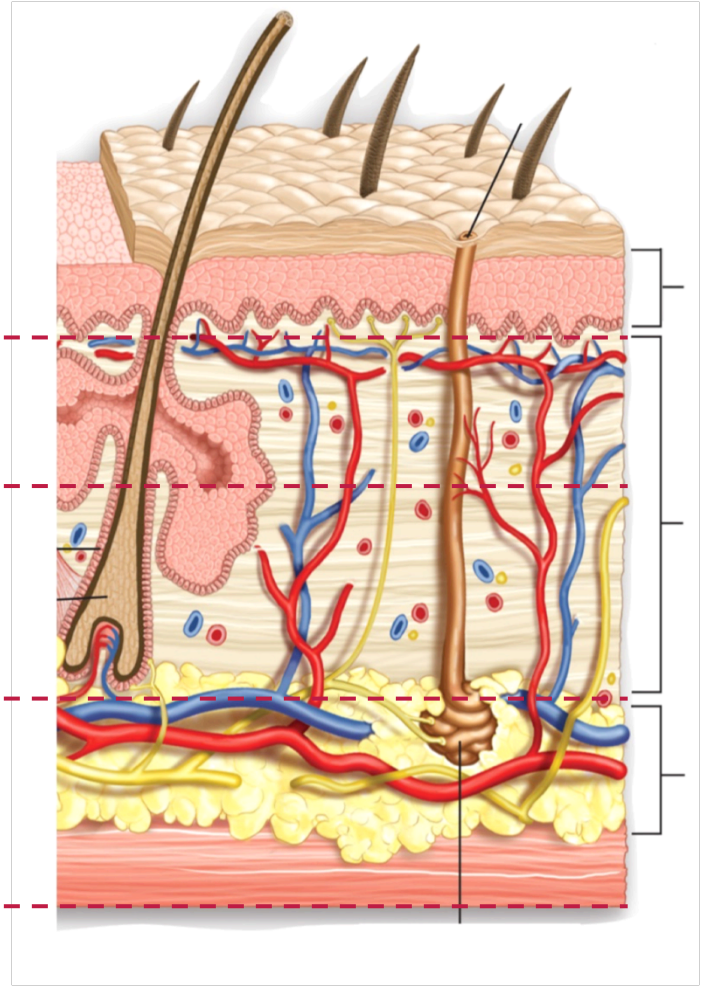
- **Phototherapy**
  - Chronic GvHD: lichen planus-like > UVB
  - Chronic GvHD: sclerotic > PUVA and UVA-1
  - Corticosteroid-sparing
  - Dose modifications:
    - Concomitant photosensitizing medication



  - ↑ risk of skin malignancies (PUVA > UVB >> UVA-1)
  - PUVA: psoralen can cause GI disturbances and liver toxicity
  - UVA-1: only available in UZ Leuven (Prof De Haes), no need to use psoralen

GvHD: Chronic

- Chronic GvHD
  - Skin manifestations in cGvHD
    - Lichen planus-like
    - Sclerotic
      - Lichen sclerosus-like
      - Morpheaform
      - Deep sclerosis/fasciitis
    - Poikiloderma
    - Other



GvHD-Related: Systemic

- **Systemic corticosteroids**
- **Immunosuppressants**
  - Cyclosporine, tacrolimus
  - Mycophenolate mofetil
  - mTOR inhibitors (rapamycin)
- **Other strategies**
  - Imatinib and Rituximab see Arai et al. Clin Cancer Res 2016
    - Antifibrotic properties: sclerotic type cGvHD
    - Significant clinical response ~25%
  - Mesenchymal stem cells (Prof Beguin, CHU Liège)
  - Ruxolitinib (Jakavi®) see Takahashi et al. Blood 2018

JAK inhibitor/ruxolitinib: protein kinase inhibitor

Immunotherapy. 2018 Apr;10(5):391-402. doi: 10.2217/imt-2017-0156. Epub 2018 Jan 10.

Ruxolitinib for the treatment of patients with steroid-refractory GVHD: an introduction to the REACH trials.

Jagasia M[1], Zeiser R[2], Arbushites M[3], Delaite P[3], Gadbaw B[4], Bubnoff NV[2].

⊕ Author information

JAK inhibitor in
world of polycythemia vera
and
myeloproliferative disorders

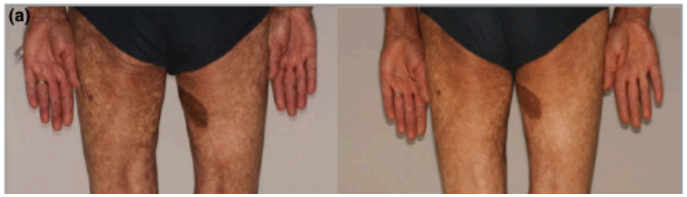
Works on gene pathways!

Efficacy and tolerance of ruxolitinib in refractory sclerodermatous chronic graft-versus-host disease

DOI: 10.1111/bjd.15593

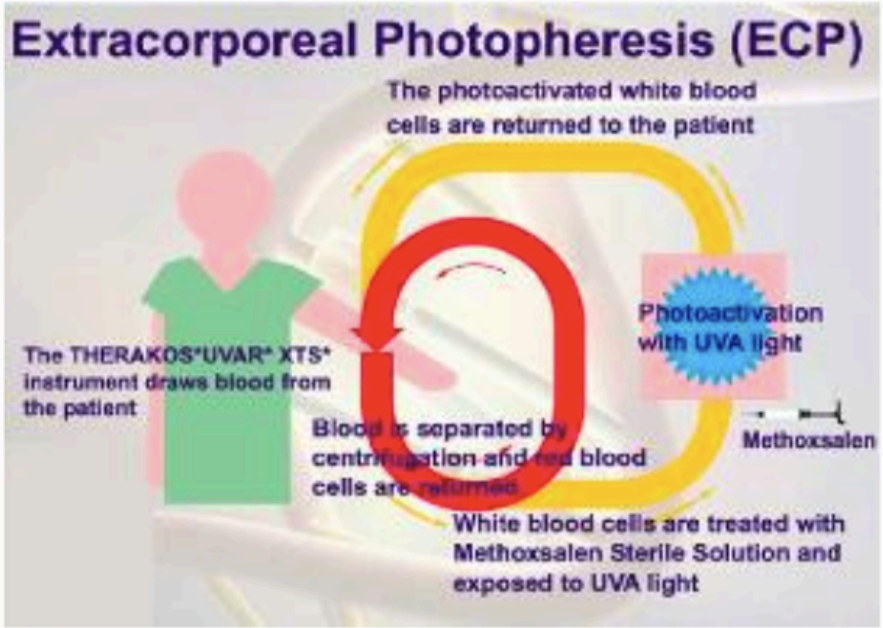
Dear Editor, Chronic graft-versus-host disease (cGVHD) occurs frequently following allogeneic haematopoietic stem cell transplantation (AHSCT). It can often be severe and there is currently an unmet therapeutic need.[1] A recent retrospective study has shown the potential efficacy of ruxolitinib, a selective Janus kinase (JAK)1/2 inhibitor, for the treatment of acute graft-versus-host disease (aGVHD) (n = 41), with an overall response r respectively.[2] There are no specific stud cacy of ruxolitinib in sclerodermatous rare and difficult to treat form of cGVH

This monocentric retrospective study 12) with severe sclerodermatous cGVH tinib between May 2015 and July 201 sclerodermatous cGVHD were defined modified Rodnan skin score (mRSS) ≥ to corticosteroids and at least one oth drug. All of the patients had a stabl

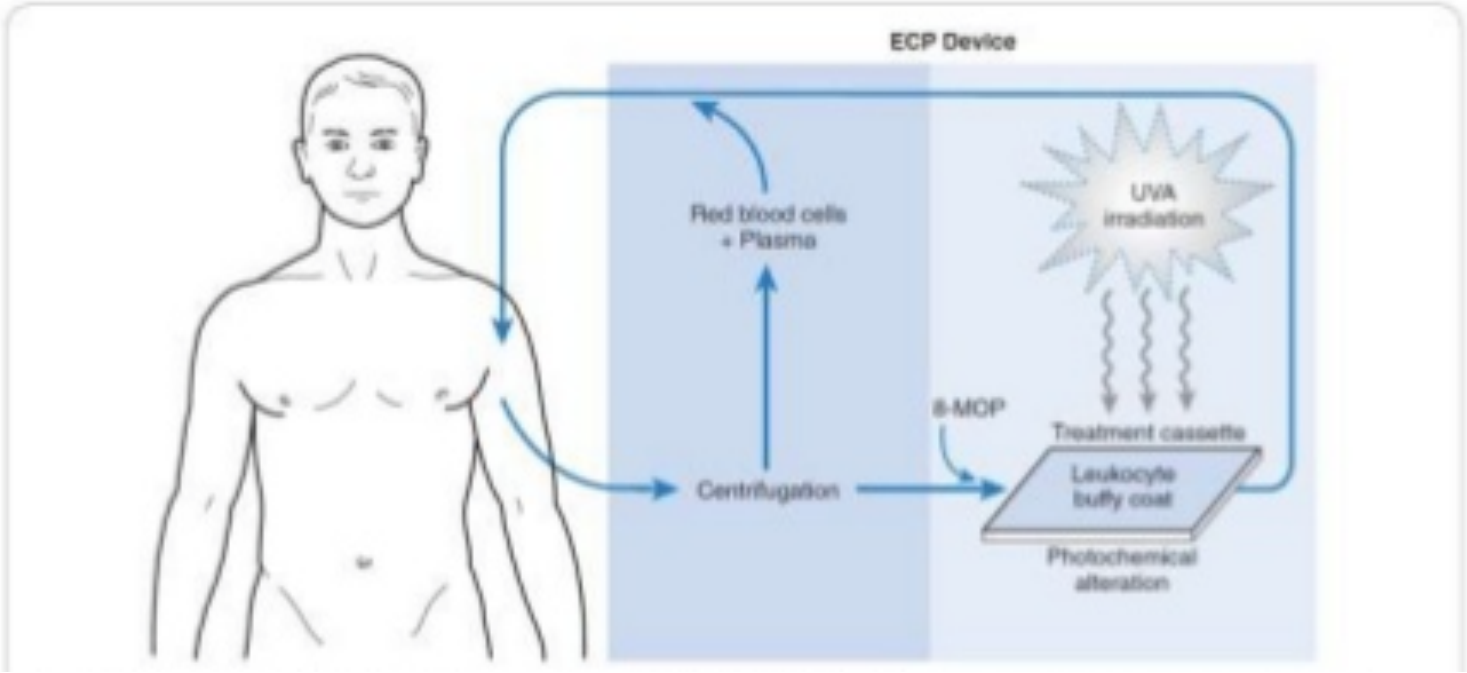


GvHD-Related: Systemic

- **Extracorporeal photopheresis: immunosupressive effects**
  - Steroid-refractory GvHD, sclerotic and non-sclerotic
  - Also in aGvHD
  - C TCell Lymphoma : also used: immunostimulatory effects against neoplastic cells



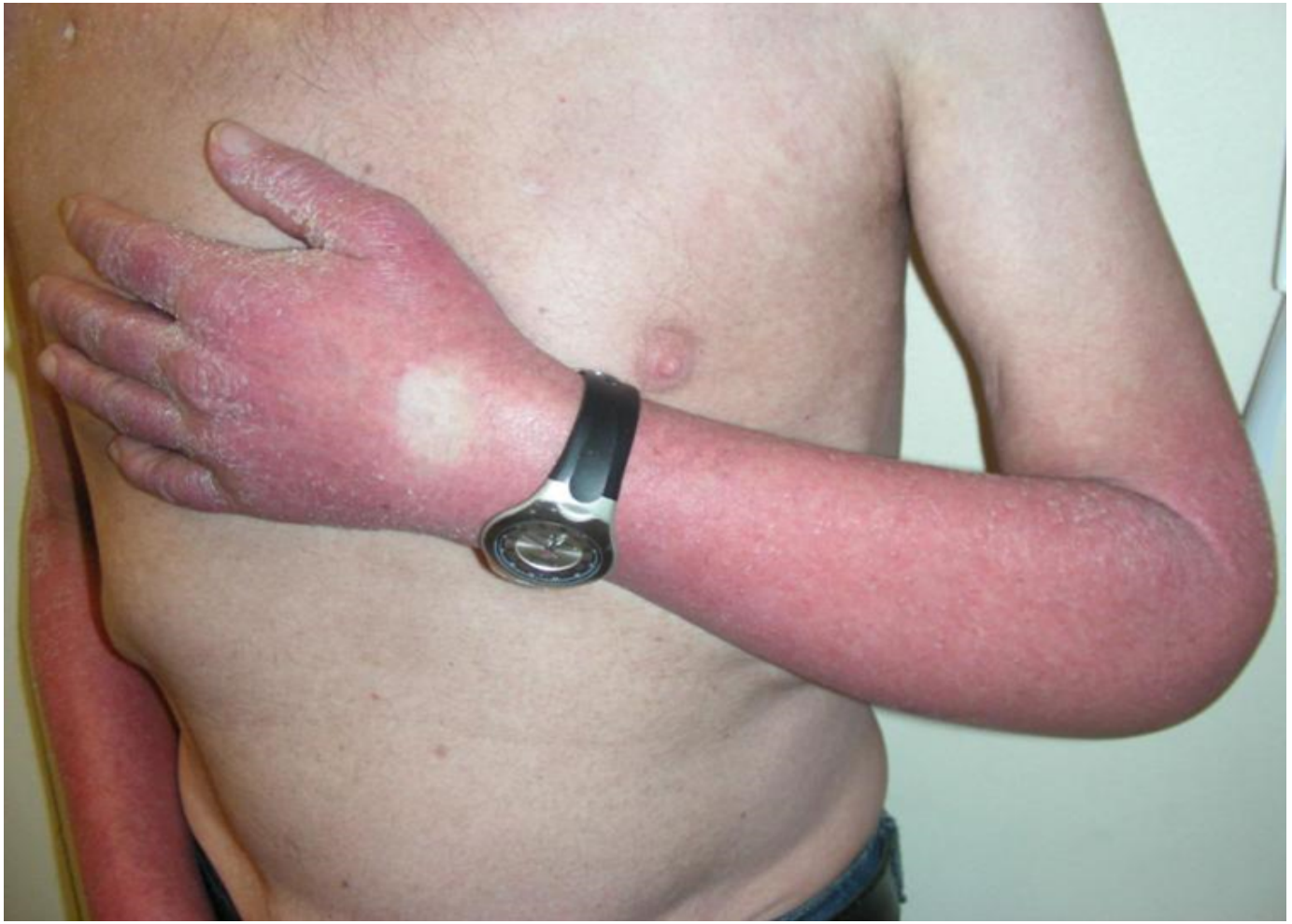
What is photopheresis?



Differential Diagnosis

Differential Diagnosis

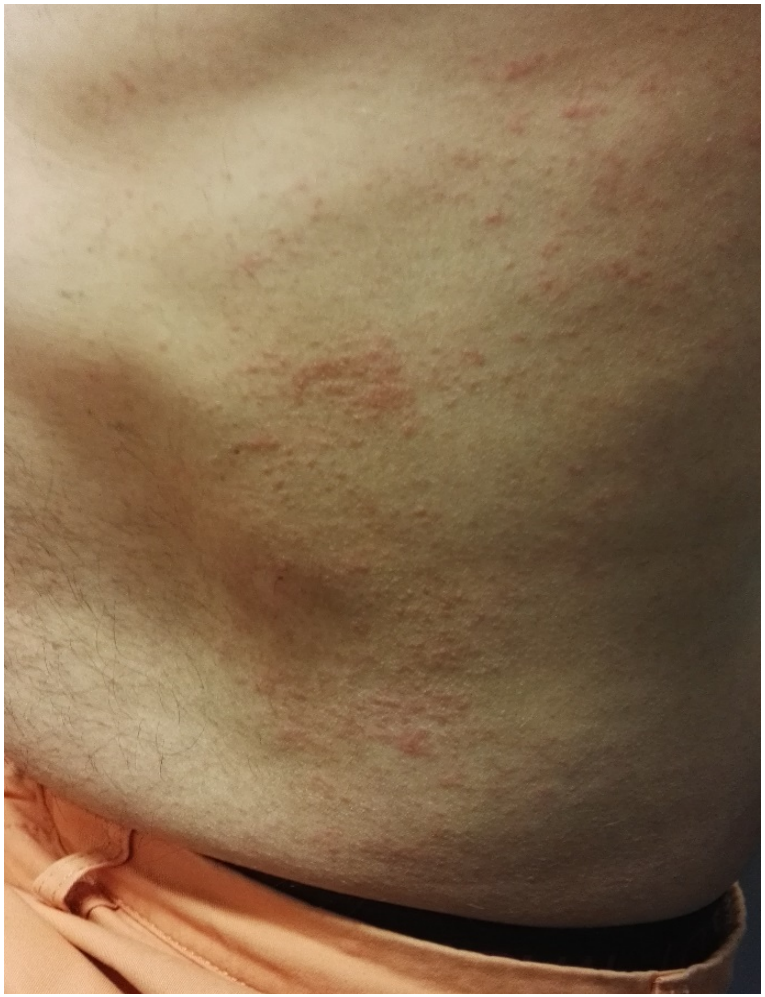
- **Phototoxic reactions**



UZA

Differential Diagnosis

- Not all skin rashes are GvHD…
- **Skin infections**



GvHD-Related

- **Drug eruption**
  - Maculopapular rash

aGvHD	Drug eruption
59% facial	24% facial
36% face, palms/soles	0% face, palms/soles
73% diarrhea	12% diarrhea
41% diarrhea + ↑ bilirubin	0% diarrhea + ↑ bilirubin

  - **Usually trunk –> extremities**
  - **40% caused by antibiotics**
  - **!Cave: NOT the same is Chemotherapy and drug eruptions: palms often affected: 3 graden van ernst (erytheem, dysesthesie, blaren..)= hand-voet syndroom**

GvHD:Differential Diagnosis

- Engraftment syndrome IS NOT THE SAME as acute GvHD
- Pulmonary edema!
- T°
- Skin involvement
- (myeloid recovery phase : 10-12 days)

Take home messages

- Skin: important affected organ in GvHD: in both acute and chronic form
- Early detection of skin GVhD important for prognosis: Skin is often first sign
- Treatment: Future Options?
- Pathways in other skin diseases, other hematological diseases, Genetic Diseases, Inflammatory Diseases, Autoimmune Diseases: it Opens a door for future treatments in GvHD

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