

# Graft-versus-Host Disease: How it Affects Skin, Nails and Hair

**Celebrating a Second Chance at Life  
Survivorship Symposium**

April 27 – May 3, 2024



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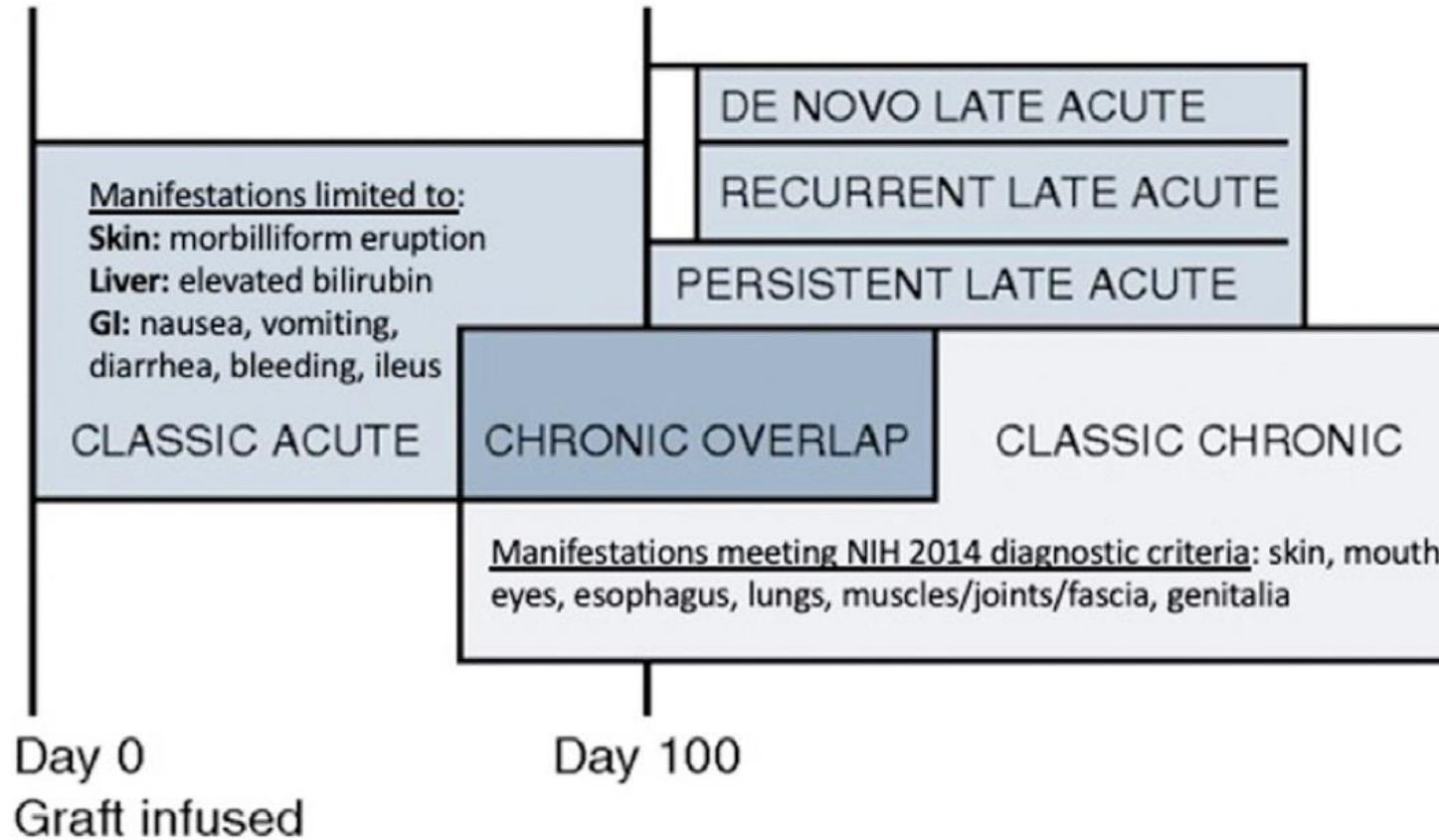
# Learning Objectives

1. Identify skin symptoms of acute GVHD and treatment options for acute skin GVHD.
2. Recognize the many ways that chronic GVHD can appear on the skin and how it may affect the mouth, genital skin, hair, and nails.
3. Identify treatment options for various forms of chronic skin GVHD.
4. Review dry skin care and sun avoidance/protection in patients with chronic skin GVHD.
5. Emphasize the importance of monitoring for skin wounds and skin cancers.

# What is Graft-Versus-Host-Disease (GVHD)?

- GVHD occurs when donor stem cells (**graft**) view the recipient cells (**host**) as foreign
- We'll focus on **skin GVHD**
- We'll discuss both **acute skin GVHD** and **chronic skin GVHD**

# Time to Onset



Baumrin et al. J Am Acad Dermatol. 2024 Jan;90(1):1-16.

# Acute GVHD

- The incidence rate for acute GVHD affecting any organ varies widely and is up to 50%
- We classically viewed this as occurring during the first 100 days after transplant, but now know this is not always the case
- Skin + gut + liver
- Skin involvement can occur at the same time as gut involvement (diarrhea)
- Lab tests may show signs of liver injury

# Acute Skin GVHD – what it looks like

- Pink, red, purple “measles-like” rash
- Can affect the hands and feet
- Can be itchy or have no symptoms

# Acute Skin GVHD



VisualDx.

# Skin-directed treatment of acute GVHD

1. Topical steroids
2. Topical calcineurin inhibitors
3. Topical Janus kinase (JAK) inhibitors
4. Narrowband ultraviolet B (nbUVB)
5. Wound care if skin is open
6. Anti-itch medication if skin is itchy



# Topical steroids

- Creams, ointments, solutions (liquids), oils, sprays
- Ointments absorb best into the skin
- Solutions and oils work better in areas with hair (scalp)
- Steroids vary in strength depending on the name, NOT the %



Ointment



Cream

# Topical steroid side effects

- Skin thinning
- Stretch marks
- Bruising
- Acne
- Rash (contact allergy)



[dermnetnz.org/cme/dermatitis/corticosteroids](http://dermnetnz.org/cme/dermatitis/corticosteroids)

# How to treat steroid side effects

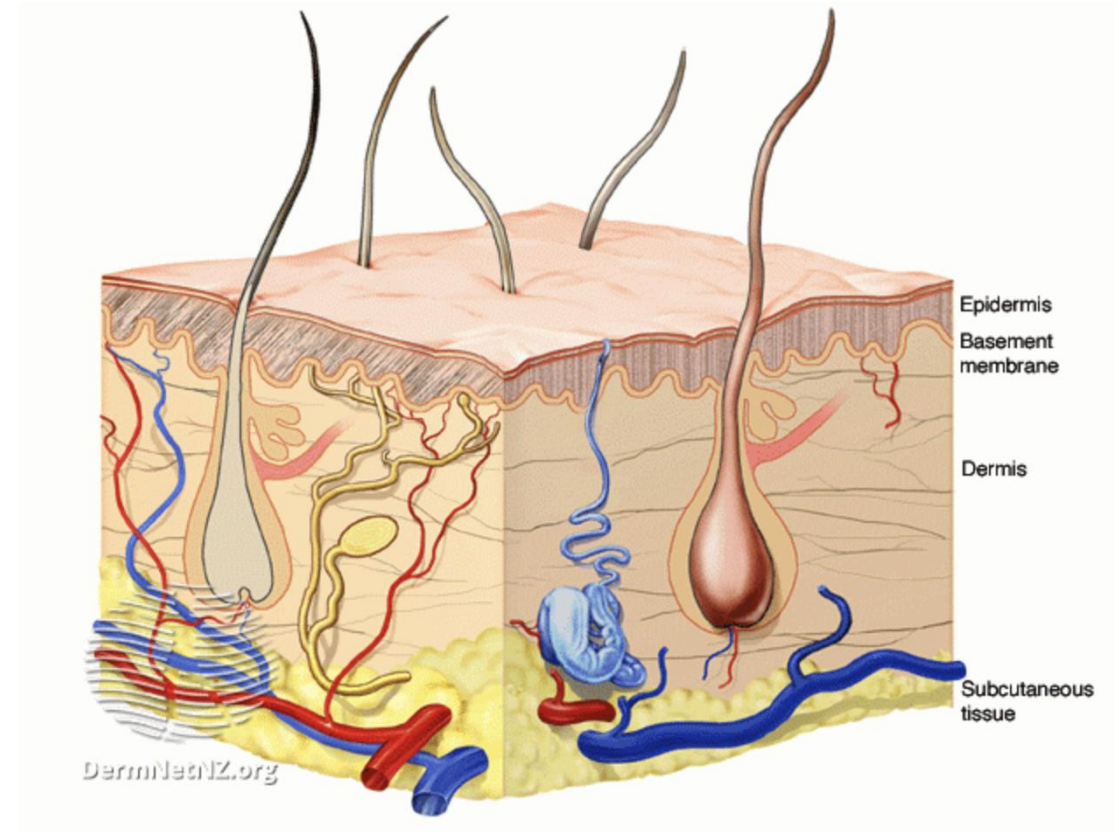
- **Skin thinning:** stop topical steroids
- **Stretch marks:** stop topical steroids, consider creams (tretinoin, glycolic acid, L-ascorbic acid) and lasers (work best on red stretch marks)
- **Bruising:** stop topical steroids, moisturize, physically protect
- **Acne:** stop topical steroids, use acne washes like benzoyl peroxide, salicylic acid, glycolic acid, use topical or oral antibiotics
- **Rash (contact allergy):** switch to another topical steroid class, consider non-steroidal topicals (pimecrolimus, tacrolimus)

# Chronic GVHD

- Occurs in 30-70% of transplant patients who receive donor cells
  - Of these patients, 60-80% will have skin involvement
- We classically viewed this as occurring 100 days after transplant, but now know this is not always the case
- Affects multiple organ systems
- Dermatologists are involved in diagnosis and treatment because it can affect the [skin, mouth, genitals, nails, and hair](#)

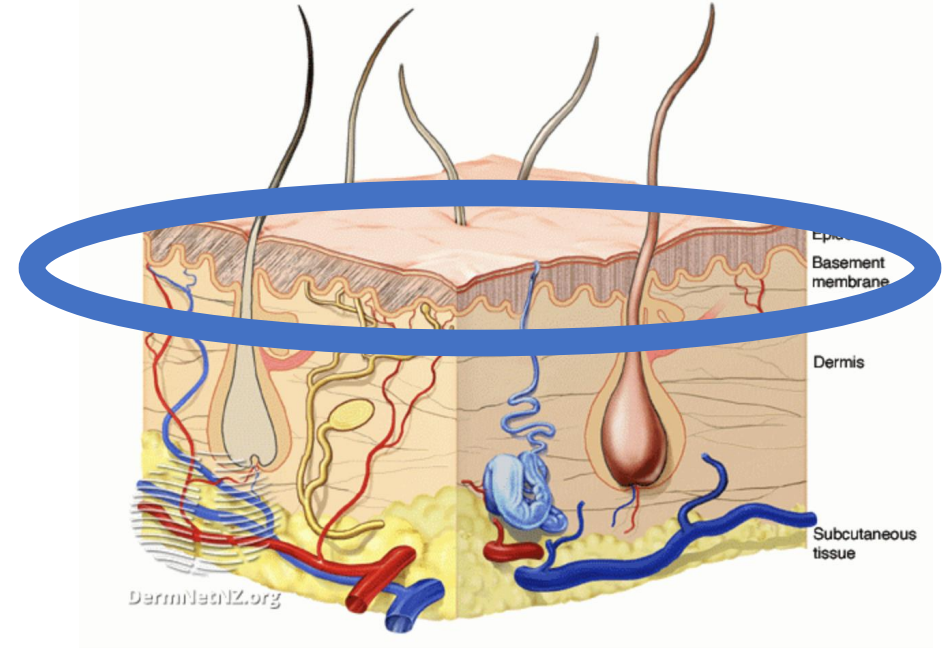
# Chronic GVHD is polymorphous

- Polymorphous: occurring in different forms
- The appearance depends partly on which layers of the skin are affected
- It looks very different from acute GVHD
- It can also look like other skin conditions



[dermnetnz.org/cme/principles/structure-of-the-epidermis](https://dermnetnz.org/cme/principles/structure-of-the-epidermis)

# Chronic GVHD affecting the outermost skin layer



Baumrin et al. *J Am Acad Dermatol.* 2024 Jan;90(1):1-16.  
[dermnetnz.org/cme/principles/structure-of-the-epidermis](https://dermnetnz.org/cme/principles/structure-of-the-epidermis)

# Skin-directed treatment for this type of cGVHD

1. Topical steroids
2. Topical calcineurin inhibitors
3. Topical Janus-kinase (JAK) inhibitors
4. Narrowband ultraviolet B (nbUVB)
5. Wound care if skin is open
6. Anti-itch medication if skin is itchy

# Other topicals

## Topical calcineurin inhibitors

- Tacrolimus ointment, pimecrolimus cream
- Can have burning sensation upon application

## Topical JAK inhibitors

- Ruxolitinib cream
- Best for very limited involvement, risk of systemic absorption and more serious side effects with widespread application



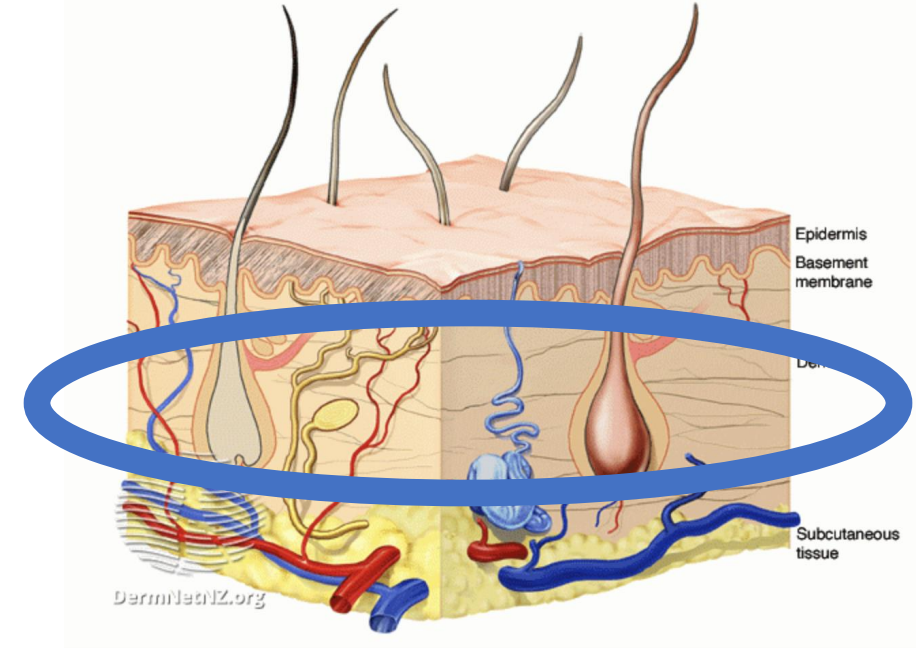
# Narrowband UVB

- 311–312 nanometer (nm)
- 3x/week
- Sessions are short (few seconds to minutes)
- Treatment course is a few months
- <https://find-a-derm.aad.org>
  - “phototherapy”



[dermnetnz.org/topics/uvb-phototherapy](https://dermnetnz.org/topics/uvb-phototherapy)

# Chronic GVHD affecting the middle layer of skin



Baumrin et al. *J Am Acad Dermatol.* 2024 Jan;90(1):1-16.  
<https://dermnetnz.org/cme/principles/structure-of-the-epidermis>

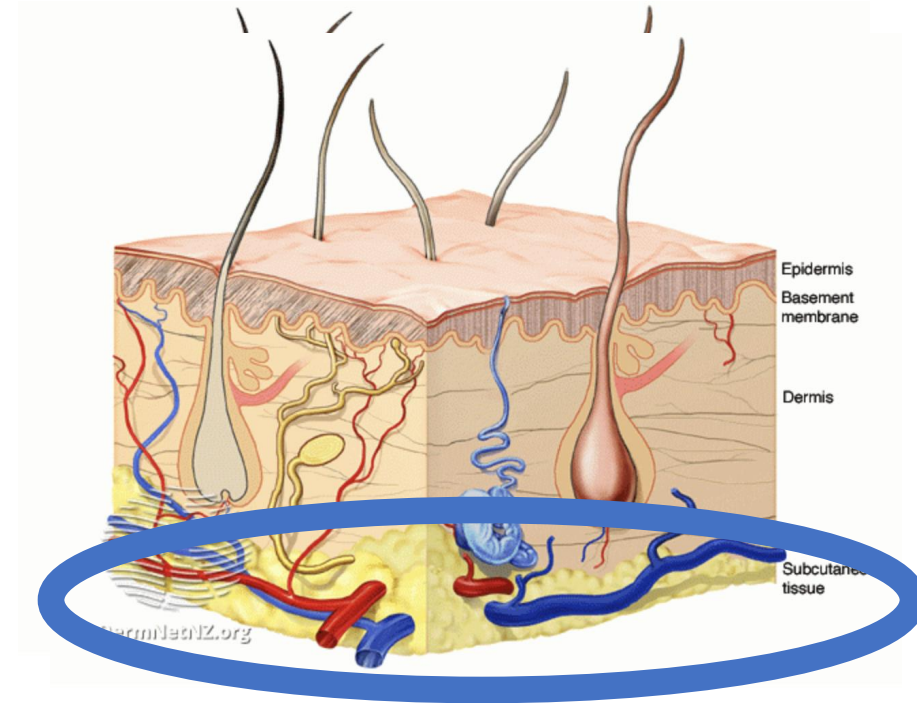
# Chronic GVHD affecting the deepest layer of skin



**Fig. 3** Rippling and groove sign on the inner arm of EF-like associated to skin sclerosis



**Fig. 4** Chronic GVHD-related EF: skin rippling on the anterior aspect of the thighs and on the abdomen. Skin is not involvement



Hidalgo Calleja et al. Adv Rheumatol. 2022 08 23;62(1):33.  
<https://dermnetz.org/cme/principles/structure-of-the-epidermis>

# Skin-directed treatment of “deeper” cGVHD

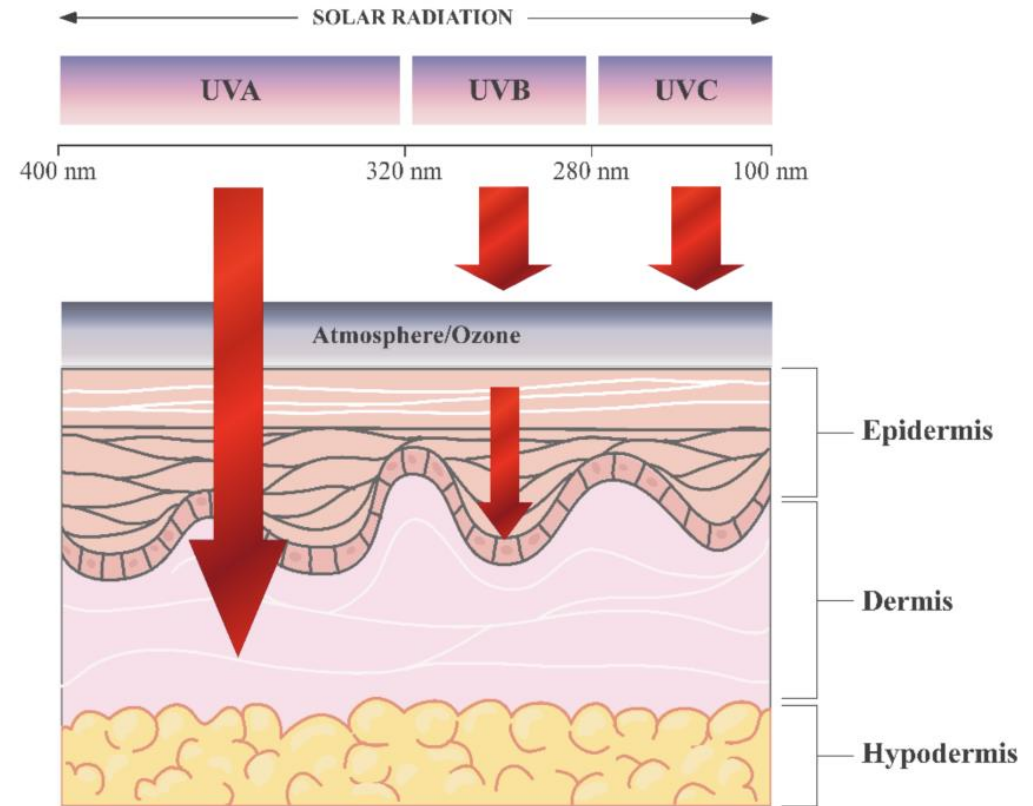
1. Topical medications “under occlusion”
2. Steroid injections into the skin
3. UVA (ultraviolet A)
4. Wound care if skin is open
5. Anti-itch medication if skin is itchy



*[dermnetz.org/topics/intralesional-injection](https://dermnetz.org/topics/intralesional-injection)*

# UVA

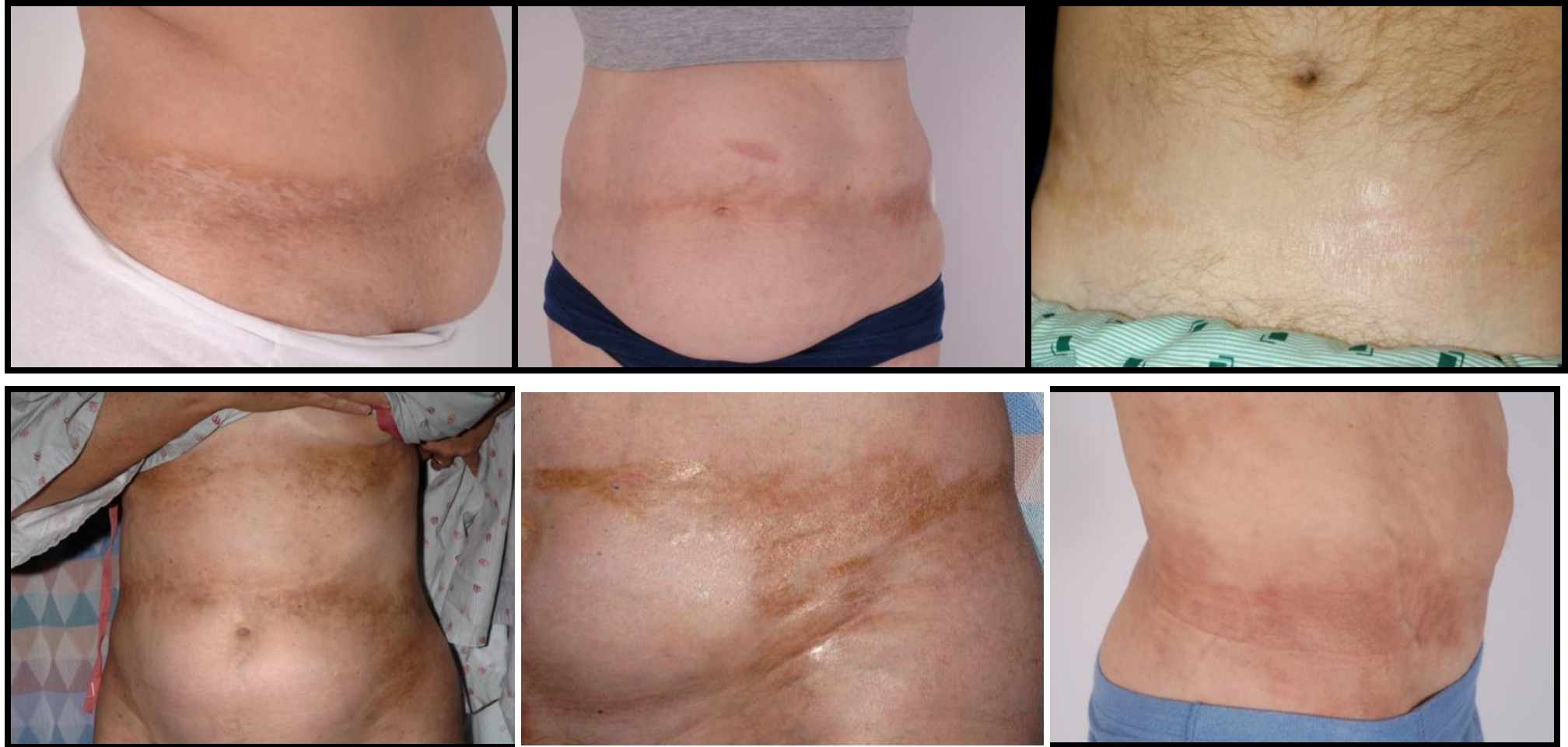
- UVA1: 340-400nm
- Longer wavelength, penetrates deeper into the skin
- Reaches the dermis



**Figure 2.** UV penetration into the layers of the skin. The figure was created using Servier Medical Art [19], licensed under the Creative Commons Attribution 3.0 Unported License ([www.creativecommons.org/licenses/by/3.0/](http://www.creativecommons.org/licenses/by/3.0/)).

*Pérez-Sánchez A, et al. Nutrients. 2018 Mar 24;10(4).*

# Can develop in areas of pressure



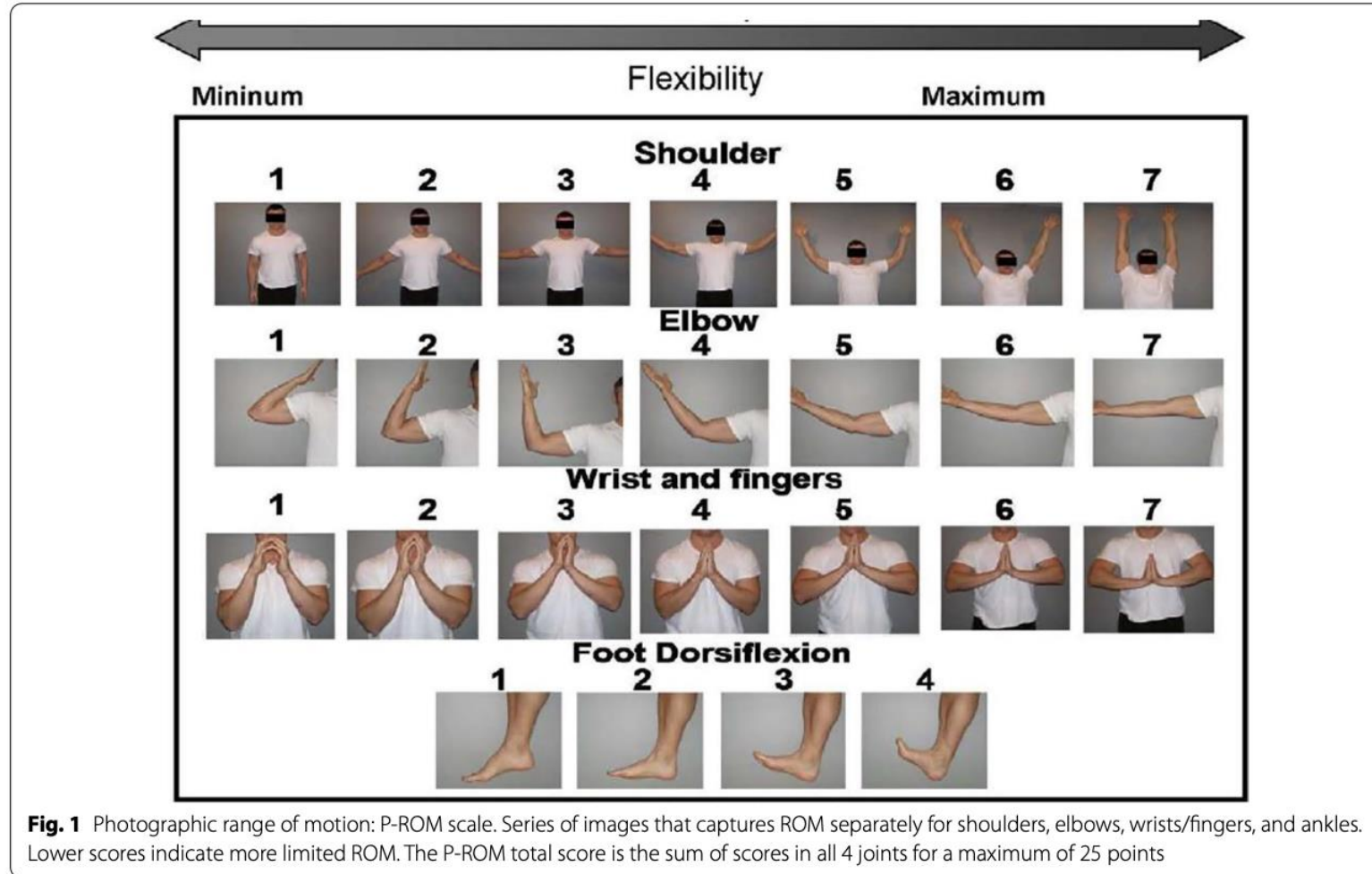
# Can develop in areas of skin injury

- In skin affected by shingles
- Where a line was
- After a blood draw
- In areas of prior radiation



Martires et al. Arch Dermatol. 2011;147(9):1081-1086.

# Can affect movement





# How Do We Diagnosis Chronic GVHD?

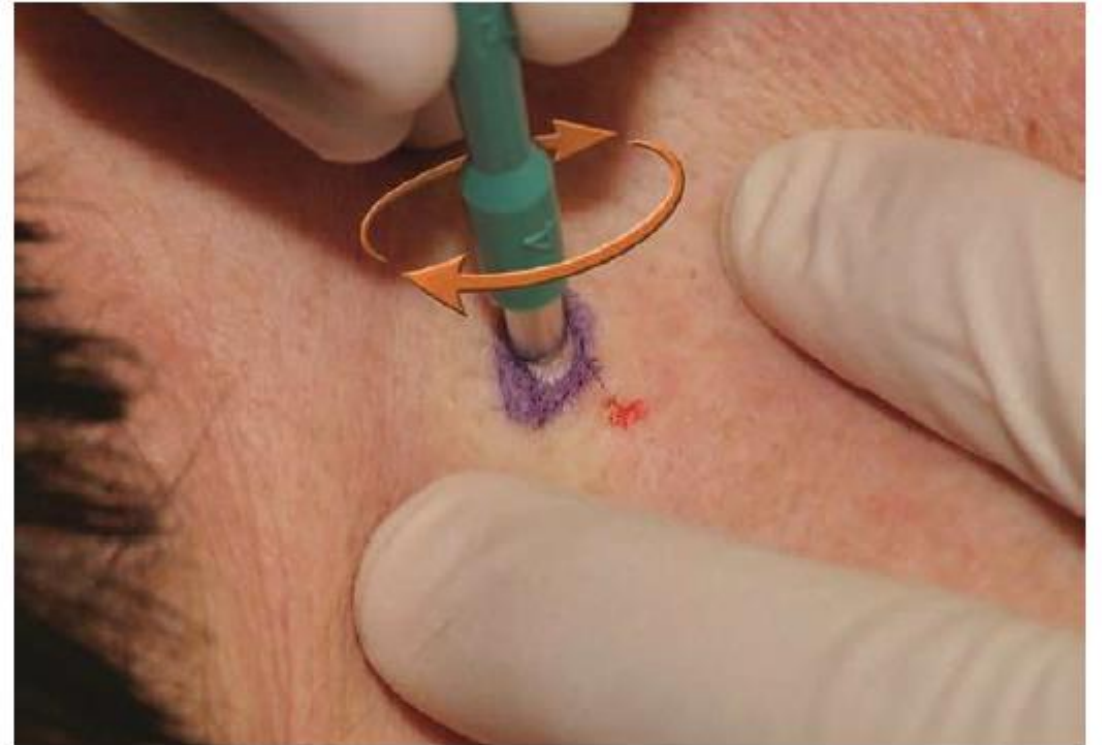
- There are some **diagnostic** skin findings
- A skin biopsy can be helpful in cases without diagnostic skin findings
- **Many skin conditions can mimic chronic GVHD**

Some examples include:

- Eczema
- Psoriasis
- Drug rashes
- Lichen planus
- Vitiligo
- Keratosis pilaris

# What is a skin biopsy?

- “Punch” biopsy for rashes
- In-office procedure
- Numbing medication is injected into the skin
- A small piece of skin is removed
- 1-3 stitches are placed
- Side effects: scar, bleeding, infection



# Hints to diagnosis: triggers

- Decrease in immunosuppression
- Donor lymphocyte infusion
- CAR-T cell therapy
- Sunburn / UV exposure
- Infection (e.g. virus)
- New medication causing a drug rash

# Chronic GVHD affecting the mouth

- Dry mouth, dry lips
- Sores
- White lines/streaks
- Puffy gums
- Pain
- Trouble eating
- Sensitivity to food



# Treatment of cGVHD of the mouth

- Topical steroids (liquids/”swish & spit”, gels, dental paste)
- Topical calcineurin inhibitors (capsule contents in water)
- Topical lidocaine (to help with eating)

# Chronic GVHD affecting the genitals

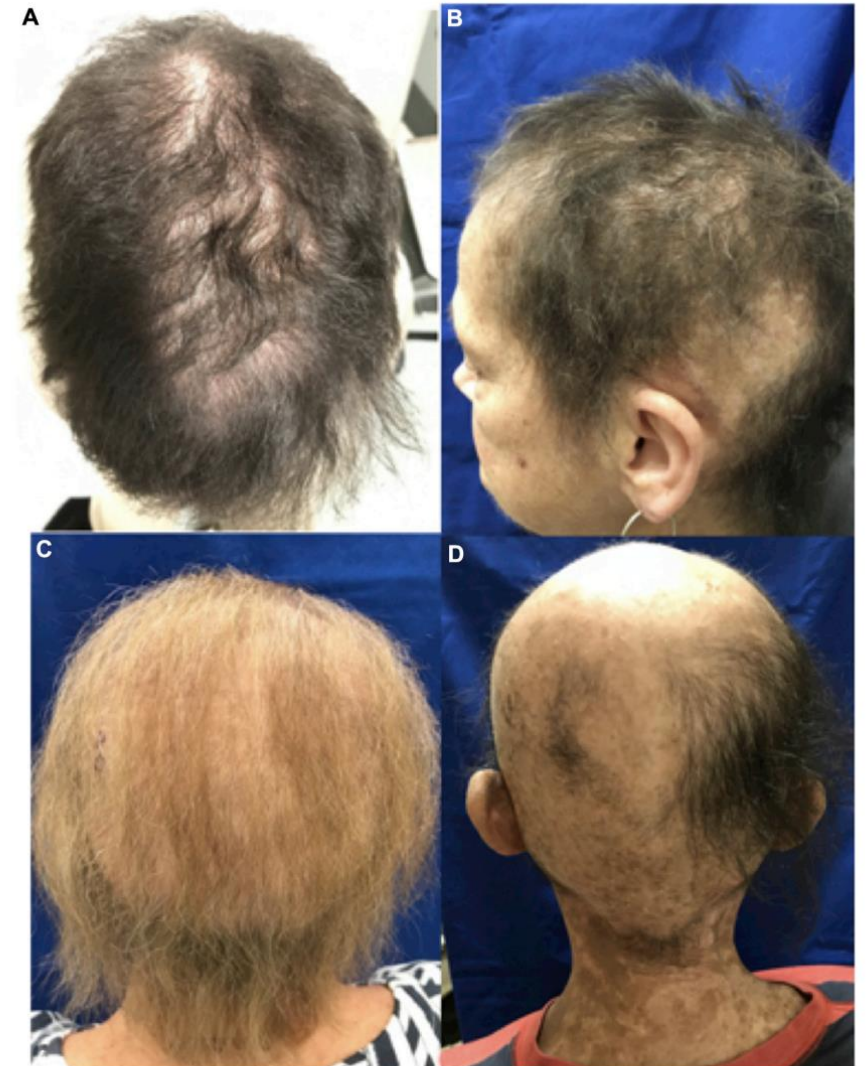
- Some patients may feel uncomfortable discussing genital symptoms with their doctors, but cGVHD of genital skin can have a significant impact on quality of life
- Symptoms include:
  - vaginal or penile pain
  - pain with sexual intercourse
  - pain/burning sensation when urinating
- Patients may see skin changes on their penis or vulva

# Treatment of cGVHD of genital skin

- Topical steroids
- Topical calcineurin inhibitors
- Referral to gynecology or urology
- Pelvic floor physical therapy
- Some centers have dermatologists who specialize in genital skin

# Chronic GVHD affecting the hair

- Can be **scarring** or **non-scarring**
  - Scarring: redness, flaking, scale, loss of hair follicles
  - Non-scarring: loss of hair throughout scalp
- Can affect hair from scalp, eyebrows, eyelashes, and anywhere on the body



**Fig 1.** Clinical hair findings in patients with chronic graft-versus-host disease. **A**, Patchy nonscarring alopecia. **B**, Patchy sclerotic alopecia. **C**, Diffuse nonscarring alopecia. **D**, Diffuse sclerotic alopecia.

Marks D, et al. *J Am Acad Dermatol.* 2019 Nov;81(5):1134-1141.

**2024 SURVIVORSHIP SYMPOSIUM**



# Treatment of hair loss

- If itch, scale, or redness exist, certain topicals (such as **topical steroids**) can be used
- Steroids can also be injected into the scalp (**intralesional**)
- Topical **minoxidil** foam or solution
- Oral **minoxidil**
- Powders/lotions/sprays to mask thinning hair
- Hair/cranial prosthesis
- Hair transplant

# Chronic GVHD affecting the nails

- Nail lifting
- Lines running throughout the nail
- Loss of nails
- Can be painful and significantly impact daily, routine activities



# Treatment of cGVHD of the nails

- Topical steroids
- Injection of steroids into the nail
- Topical antifungals to prevent fungal infection
- Biotin (2500mcg) to make the nails stronger
- Avoid washing your hands with hot water
- Moisturize with cream-based moisturizer
- Petroleum jelly around the nail folds

# General skin care for patients with chronic GVHD

- Dry skin care
  - Helps to prevent/treat: itch, rashes, bruising, open skin
- Sun protection
  - Helps to prevent/treat:
    - *sun freckles*
    - *skin discoloration*
    - *skin aging*
    - *skin cancer*
    - *flares of chronic GVHD*

# Habits To Improve Dry Skin

- Shower/wash hands with lukewarm water (not hot!)
- Keep showers/baths short
- Wear gloves when washing dishes
- Avoid harsh soaps
- Avoid fragrances
- Moisturize daily
- Use cream-based moisturizers
- Use ointment moisturizers at night with white cotton gloves

# Sun avoidance and protection

- Comprehensive approach
  - Avoidance: seek shade, avoid high UV index (10am-4pm)
  - Protection: UPF clothing + SPF sunscreen
- There are two main sunscreens: chemical blockers, physical blockers
  - The best sunscreen is the one you will wear
  - Broad-spectrum (blocks UVA + UVB)
  - At least SPF 30 (choose a bit higher to account for imperfect application)
  - Consider water-resistant depending on your activities

# Monitor your skin for wounds

- The same factors that contribute to wound development can contribute to delayed wound healing
  - Status of chronic GVHD
  - Nutrition
  - Injury
  - Circulation
  - Infection
- Wounds that don't heal as expected should be evaluated for skin cancer

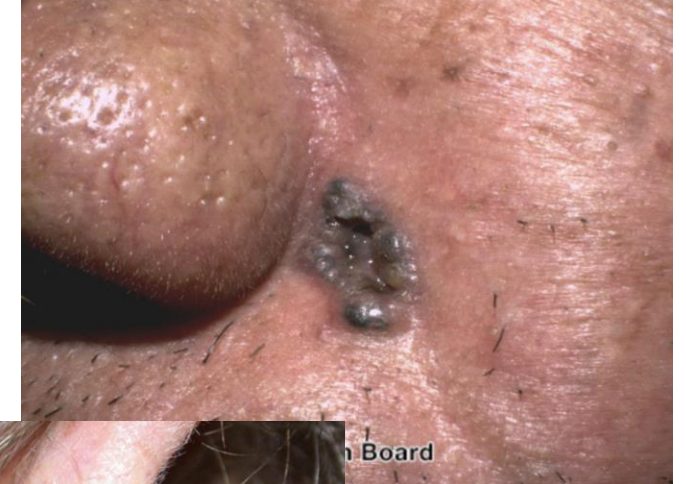


**Fig 5.** Full-thickness ulcer on posterior scalp in a patient with chronic GVHD. *GVHD*, Graft-versus-host disease.

Baumrin et al. *J Am Acad Dermatol.* 2024 Jan;90(1):1-16.

# Identifying skin cancers

- Patients who have undergone bone marrow transplants have an increased risk of developing skin cancer
- Chronic GVHD increases the risk of skin cancer development
- Look for:
  - pink, red, purple, shiny or scaly bumps
  - spots that bleed or are painful
  - wounds that don't heal
  - scars that open up



[dermnetnz.org/topics/cutaneous-squamous-cell-carcinoma](http://dermnetnz.org/topics/cutaneous-squamous-cell-carcinoma)  
[dermnetnz.org/topics/basal-cell-carcinoma](http://dermnetnz.org/topics/basal-cell-carcinoma)



# Find a dermatologist familiar with GVHD

BMT InfoNet Directory of GVHD Clinics and Specialists

[bmtinfonet.org/gvhd-directory](https://bmtinfonet.org/gvhd-directory)



# Questions?



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