



## Chronic Graft-versus-Host Disease of Skin and Connective Tissues

Celebrating a Second Chance at Life  
Survivorship Symposium

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# Chronic Graft-versus-Host Disease of the Skin and Connective Tissue

2022 Celebrating a Second Chance at Life Survivorship Symposium

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# No Disclosures

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## Learning Objectives

- Define GVHD as it relates to the skin
- Recognize the skin changes of chronic graft-vs-host disease (cGVHD)
- Understand how the diagnosis is made
- Review skin directed management of cGHVD
- Be familiar with other skin problems post transplant

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## What is GVHD?

- Multi-organ disorder
- Immunocompetent donor T cells “graft” are given to immunocompromised “host”
- Major cause of morbidity and mortality
- Skin changes are very common
- Often resembles autoimmune or connective tissue disease

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## What is Chronic Skin GVHD?

### Traditional definition

- Skin findings that look inflammatory (lichen planus) or fibrotic/scar-like (scleroderma) that occur 100 or more days post transplant

### Current definition

- Long term complication of allogeneic stem cell transplantation characterized by inflammatory or fibrotic skin problems that are not defined by time after transplant
- Most of these changes are diagnosed on clinical examination
- There may be no preceding acute GVHD

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## Chronic Cutaneous (skin) GVHD

- What does it look like?
- How do we grade and document these changes?

NIH Consensus Criteria....

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## NIH Consensus Criteria

**Attempt to categorize features of cGVHD for clinical trials:**

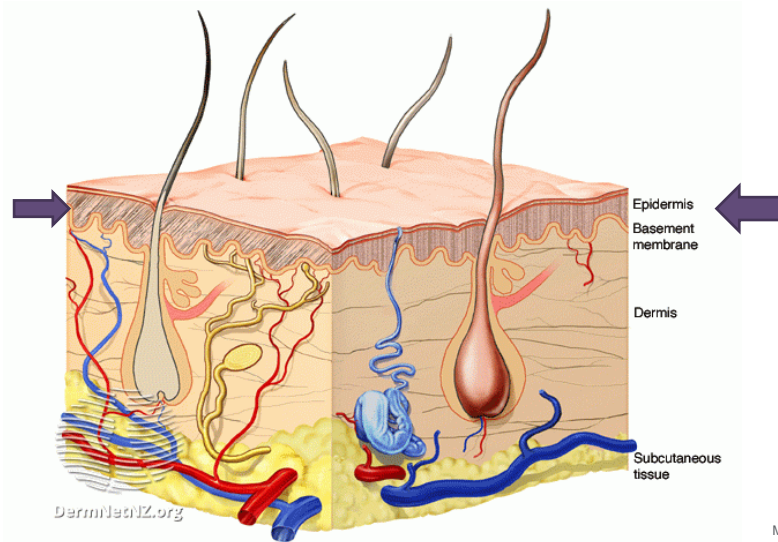
- **Diagnostic** features (sufficient to establish diagnosis)
- **Distinctive** features (insufficient alone to establish diagnosis)
- Other features

Biol Blood Marrow Transplant 2015. 21: 389

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## cGVHD changes of the epidermis



## cGVHD of the epidermis

- Symptomatic pruritis (itching) even without rash
- Dry “fish-scale” like skin called ichthyosis



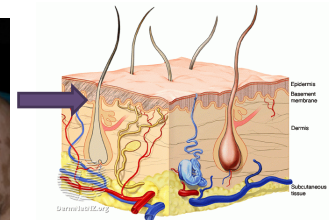
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## cGVHD of the epidermis

### Change of pigmentation

(hypo or hyperpigmentation, loss of pigment):

- Pigment cells (melanocytes) are located at the dermal-epidermal junction
- Anything that affects these cells may cause pigment disturbances.



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## GVHD of the epidermis and dermis

Purple polygonal papules are a diagnostic feature of lichen planus-like cGVHD



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## Body Surface Area

Localized



versus

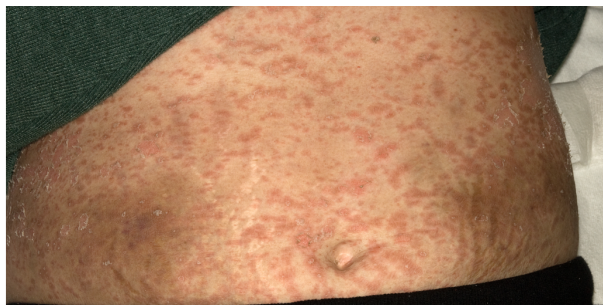
Widespread



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## GVHD of the epidermis and dermis

Scaly thick plaques and papules





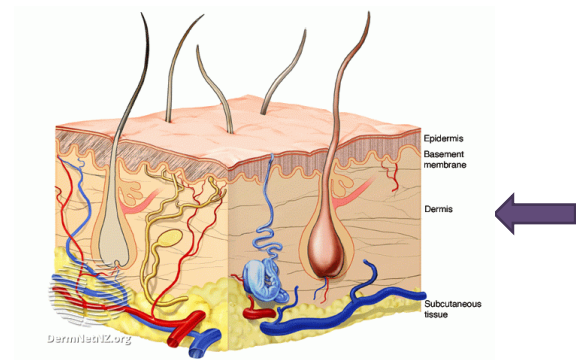
## GVHD of the epidermis and dermis

- May present with skin thinning
- Poikiloderma:
  - atrophy
  - hypo and hyperpigmentation
  - telangiectasia



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## GVHD of the hair follicles



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## GVHD of the hair follicles may cause hair loss



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## Changes in Nails

Over 50% patients with cGVHD develop nail changes:

### Dystrophy

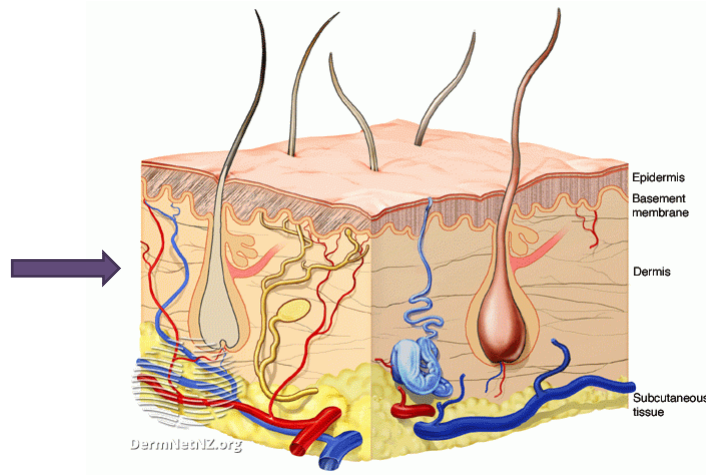
- Thickening and thinning
- Ridging
- Pterygium (scarring at nail bed)
- Nail destruction

**These may be treatable early on**

- Systemic agents
- Injected corticosteroids



## Sclerotic (scar-like) changes

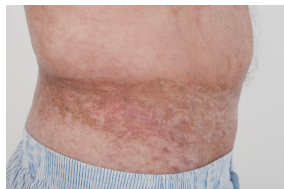


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## Sclerotic (scar-like, fibrotic, scleroderma-like):

- Occurs in the dermis but may extend deeper
  - Superficial morphea (sclerosis) is often “pinchable”, localized and moveable
- May occur in areas of trauma



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## Deep sclerosis

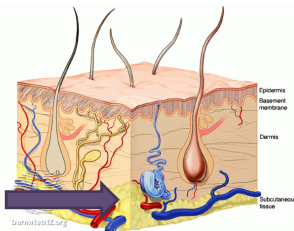
- "Hidebound" skin
- Sclerosis may extend through the dermis and to deeper layers
- May have epidermal changes characterized by erosions and scaling
- Skin is fragile and prone to injury



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## Deep sclerosis without epidermal change

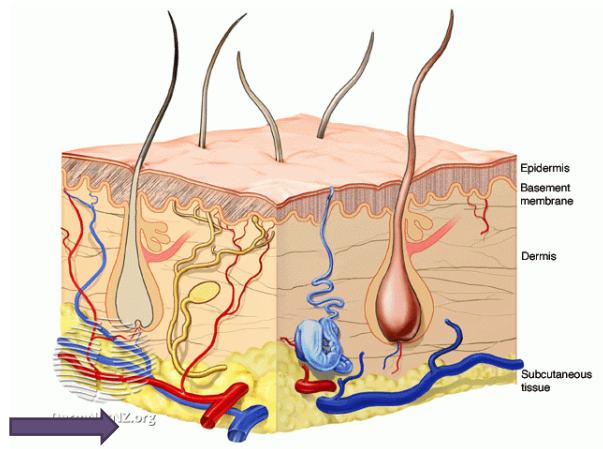
Cellulite-like changes



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## Fasciitis

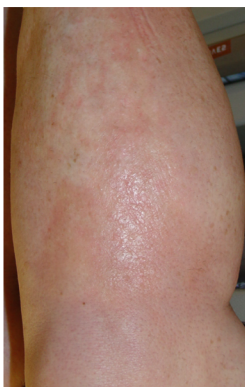
Inflammation of the layer of the skin overlying the muscles and tendons



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## Fasciitis



Painful edema



Positive prayer sign



Fasciitis + Sclerosis

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## Diagnosing skin cGVHD

- Clinical impression +/- skin biopsy
- Characterize the morphology & extent of involvement
- Determine other organs that are involved
- Identify secondary skin problems



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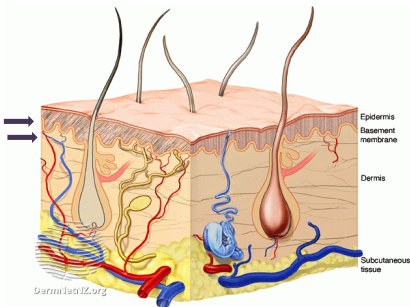
## Chronic skin GVHD: It takes a village....



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## Topical Treatment

- GVHD affecting the **epidermis and superficial dermis** may be amenable to topical therapy
- Topical corticosteroids and topical calcineurin inhibitors (tacrolimus and pimecrolimus) are useful for short-term treatment of localized disease
- Phototherapy



## Topical Therapies

### Steroids

- Many different formulations and many different strengths
- Common measures of potency:
  - Anti-inflammatory properties.
  - Vasoconstriction assay
  - Atrophogenicity (thinning of the skin)

### Calcineurin Inhibitors

- Use in areas of high risk for atrophy
- Poorly tolerated on erosions
- Possibility of significant systemic drug levels in children

# Phototherapy



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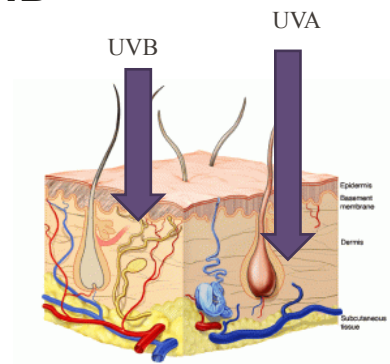
## Ultraviolet radiation (UVR) for cGVHD

### Types of UVR

- PUVA (330-400nm)
- NBUVB (311-313nm)
- UVA1(340-400nm)

### Mechanism of action

- modify inflammatory response
- modifies cells in the epidermis which help regulate the immune system
- modifies circulating cells



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## Light Therapy for Cutaneous GVHD: NB UVB



10 treatments



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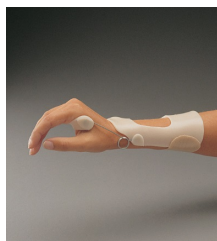
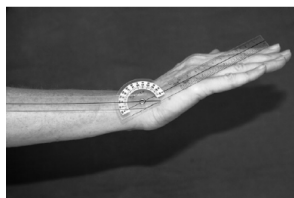
## Fasciitis

- Topical therapy not effective
- Consider systemic therapy
- Physical and occupational therapy



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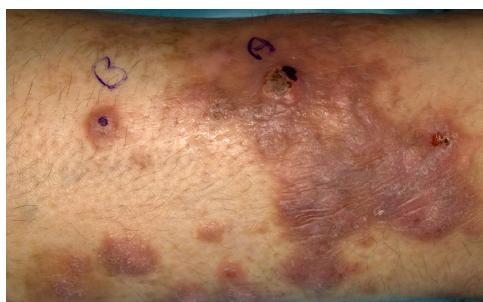
## Fasciitis: Importance of supportive care



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## Other skin problems related to transplant and GVHD

- Tumors of the skin (benign and malignant)
- Skin infections
- Hard to heal wounds



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## Malignant Tumors of the Skin

### Related to:

- Long term immune suppression or chemotherapy
- Persistent inflammation
- Preceding sun damage
- Ionizing radiation

### Leads to:

- Increased risk of squamous cell carcinoma, basal cell carcinoma and melanoma
- Curable when found early



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## How to protect your skin

### Early recognition is important

- Get undressed for a full skin examination
- Tell your provider about any skin concerns
- Check your range of motion
- Protect your skin from trauma
- Treat skin cuts and scrapes early
- Use photoprotection:
  - protective clothing
  - sunscreen



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## Review Objectives

### Define GVHD as it relates to the skin:

- long term complication of allogeneic stem cell transplantation characterized by inflammatory or fibrotic skin problems

### Recognize the skin changes of cGVHD

- Epidermal, dermal, subcutaneous & fascial inflammatory or fibrotic changes

### Understand how the diagnosis is made

- Clinical, biopsy and correlation with other organ systems

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## Review Objectives

### Skin directed management of cGHVD

- Topical therapy and UVR

### Other skin problems post transplant

- Infection, wounds and skin cancers

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# Questions?



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