



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

Celebrating a Second Chance at Life Survivorship Symposium

April 17- 23, 2021



Badri Modi MD
City of Hope

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Your Skin and Chronic Graft-versus-Host Disease

Celebrating a Second Chance at Life Symposium

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Financial Disclosures

I have received honoraria as a consultant and/or speaker in the past from the following:

- Sanofi Genzyme – unrelated to GVHD
- Regeneron – unrelated to GVHD
- Kadmon – I participated in an advisory board to discuss a medication in development for chronic graft versus host disease



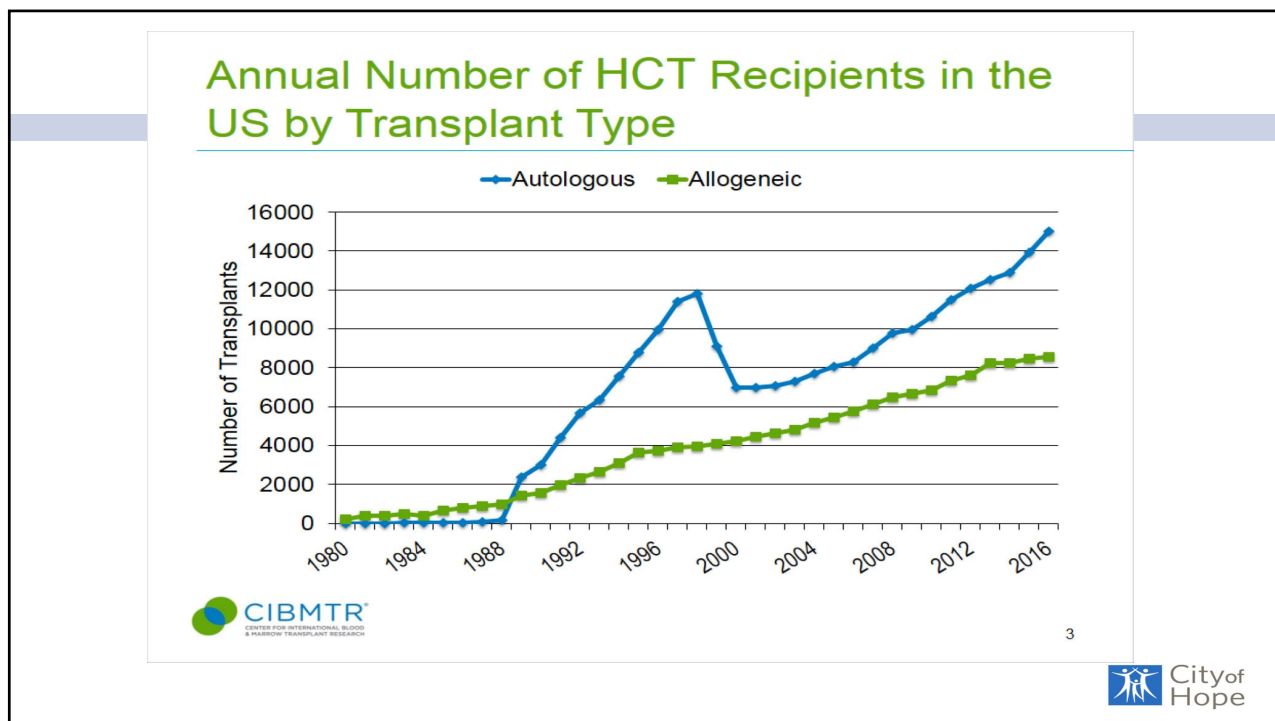
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Learning Objectives

- Risk factors for developing cGvHD of skin
- Review the various manifestations of cGvHD on skin
- Review the therapies available to manage cGvHD of skin
- Skin cancer after bone marrow transplantation



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Chronic Graft-versus-Host Disease

- Major barrier to an otherwise successful HSCT
- 30-70% of patients who have undergone allogeneic HSCT develop cGvHD
- Patients with cGvHD have reduced quality of life and increased risk of morbidity and mortality
- Resembles autoimmune disease

Zeiser, et al. "Pathophysiology of chronic graft versus host disease..." *NEJM*. 2017. [PMID: 29281578](https://pubmed.ncbi.nlm.nih.gov/29281578/).

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Risk Factors for Developing Chronic GVHD

Risk factors for development of cGVHD	
Prior acute GVHD	Older age of recipient
Peripheral blood stem cell graft	Diagnosis of chronic myeloid leukemia
Female donor to male host	HLA disparity between recipient and donor

Inamoto, et al. "Incidence, risk factors, and outcomes of sclerosis in patients with chronic graft-versus-host disease." *Blood*. 2013. PMID: [23547053](#).



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Patient experience with cGvHD

- **1377** completed patient surveys about quality of life, symptoms, health status, comorbid conditions and medications
- Patients reported disease severity:
 - Mild: 18.7%
 - Moderate: 8%
 - Severe: 1.8%
 - Never had cGvHD: 27.4%
 - Had cGvHD, but has since resolved: 20.3%
 - Excluded for not completing surveys: 23.8%

More likely to report:

- Worse quality of life
- Lower performance status
- More likely to take prescription meds for pain, anxiety and depression

Self-reported measures were similar between those who had resolved cGvHD and those who never had it

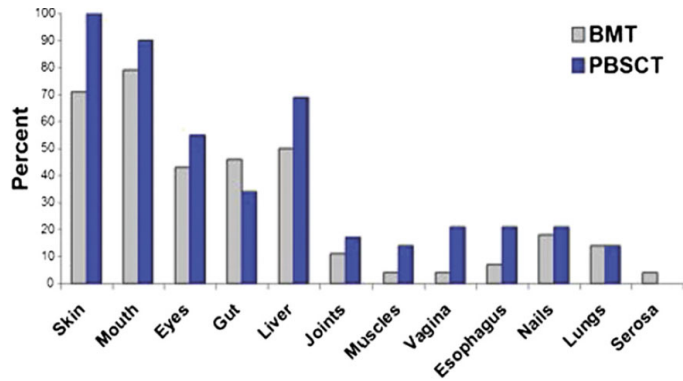
Lee, et al. "Patient-reported outcomes...." *Haematologica*. 2018. PMID: [29858386](#)



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What is Graft-versus-Host Disease?

- Graft (donor) versus host (recipient) disease
- New immune system cells attack tissues that appear foreign
- Skin is the most commonly involved organ

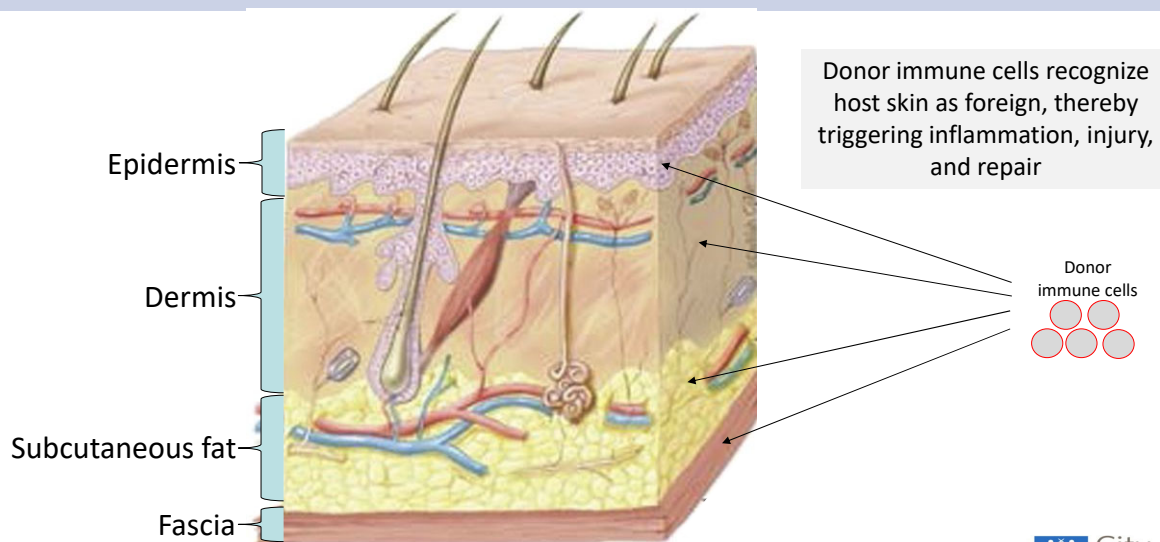


Flowers, M. and Martin, P. "How we treat chronic graft-versus-host disease." *Blood*. 2015. [PMID: 25398933](https://pubmed.ncbi.nlm.nih.gov/25398933/).



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Sections of Skin Affected by cGVHD



Flowers, M. and Martin, P. "How we treat chronic graft-versus-host disease." *Blood*. 2015. [PMID: 25398933](https://pubmed.ncbi.nlm.nih.gov/25398933/).



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Symptoms of Skin GVHD

- Rash
- Itching
- Changes in skin color
- Sweat gland and hair follicle damage
- Skin sores and ulcerations
- Tightening of the skin
 - Mouth and around joints
 - Pseudo-cellulite
 - Difficulty with taking deep breath



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Morphologies of Skin cGvHD

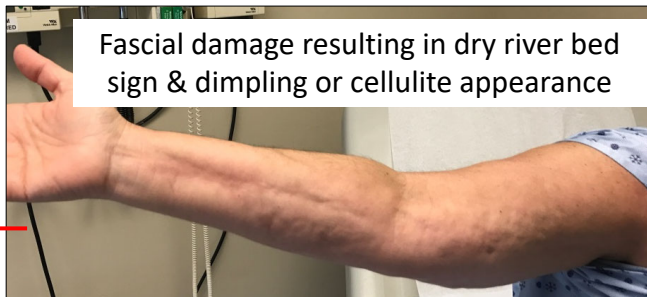
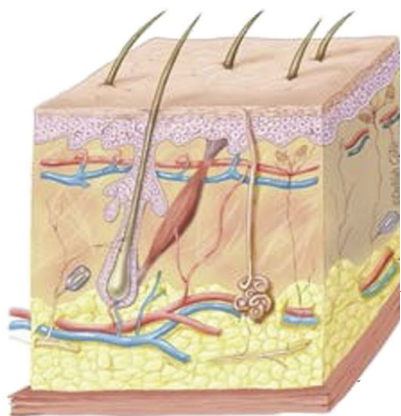
Historically, skin cGvHD has been described as either
scleroderma or lichen planus

- Sclerotic
- Morphea-like
- Lichen planus
- Lichen sclerosus et atrophicus- like
- Dyspigmentation
- Vitiligo
- Eczema like
- Papulosquamous-like



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Sclerotic



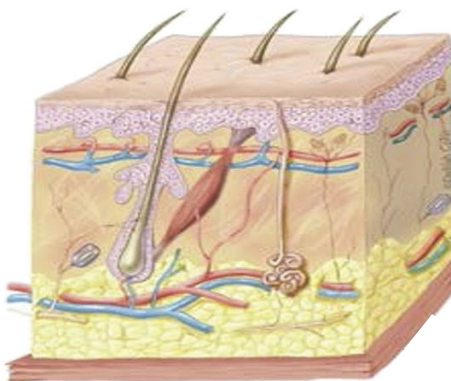
Reduced "pinch-ability"

Flowers, M. and Martin, P. "How we treat chronic graft-versus-host disease." *Blood*. 2015. [PMID: 25398933](https://pubmed.ncbi.nlm.nih.gov/25398933/).



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Sclerotic

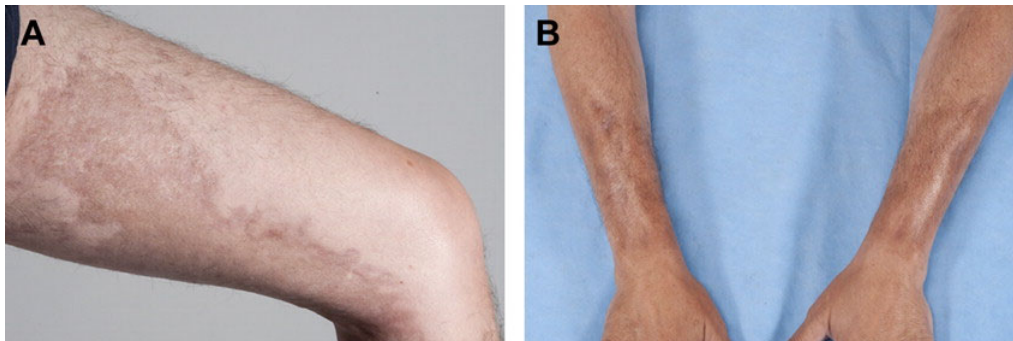


Flowers, M. and Martin, P. "How we treat chronic graft-versus-host disease." *Blood*. 2015. [PMID: 25398933](https://pubmed.ncbi.nlm.nih.gov/25398933/).



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Morphea-Like



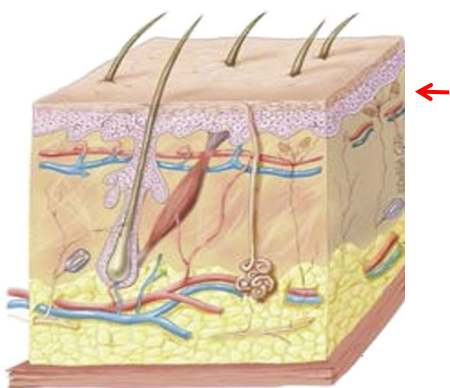
Localized areas of sclerosis

Hymes, et al. "Graft-versus-host disease...." *JAAD*. 2012. [PMID: 22421124](#).



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Lichen sclerosis

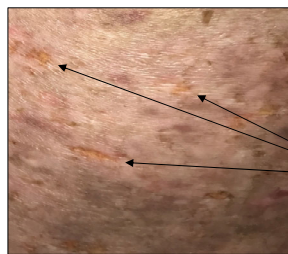


Flowers, M. and Martin, P. "How we treat chronic graft-versus-host disease." *Blood*. 2015. [PMID: 25398933](#).



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Lichen sclerosus



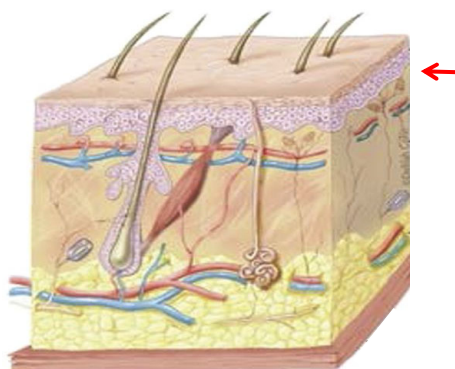
Thinning and fibrosis of the superficial skin that leads to a “cigarette-paper” like wrinkled appearance

Easily breaks down



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Lichen Planus



Flowers, M. and Martin, P. “How we treat chronic graft-versus-host disease.” *Blood*. 2015. [PMID: 25398933](https://pubmed.ncbi.nlm.nih.gov/25398933/).



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Lichen Planus

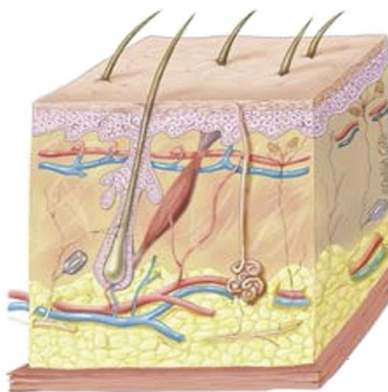


- Violaceous papules that may have thin scale
- “5 P’s”: purple, polygonal, planar, pruritus, papule



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Papulosquamous



Papulosquamous

Flowers, M. and Martin, P. "How we treat chronic graft-versus-host disease." *Blood*. 2015. [PMID: 25398933](https://pubmed.ncbi.nlm.nih.gov/25398933/).



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Pigmentary changes




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Nail Changes



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TREATMENT OF SKIN CHRONIC GVHD

Optimize skin-directed therapy  **Systemic therapy**




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Optimize Skin Directed Therapies

- **Topical anti-inflammatory medications**
 - Steroids
 - Non-steroids (calcineurin inhibitors)
- **Phototherapy**
 - Psoralen + UVA
 - UVA alone
 - UVB

Higher efficacy for superficial subtypes of chronic GvHD including lichen planus, lichenoid, psoriasiform, eczematous.

Sclerotic subtypes are less likely to improve with skin-directed therapy, although there are reports.



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Topical Therapies

- Considerations for steroids
 - Potency: mild to super-potent
 - Vehicle: ointment, cream, solution
 - Site specific
 - Side effects from overuse: skin thinning, atrophy
- Calcineurin inhibitors (tacrolimus, pimecrolimus)
 - Safe alternative to topical steroids
 - Expensive



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Dry Skin Care

- Helpful for itch and hyperkeratotic skin lesions (heaped up skin)
- By “exfoliating” the excess skin in these lesions, you make it less likely to tear and leave behind a sore



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Phototherapy

- Psoralen + UVA

- Penetrates into the dermis
- Limited availability due to shortage of facilities that have UVA machine

- UVB

- More superficial penetration into the skin



Koo, et al. "Evidence-based, skin-directed treatments for cutaneous chronic GVHD." *Cureus*. 2019. [PMID: 32025391](https://pubmed.ncbi.nlm.nih.gov/32025391/)



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Systemic Therapies

- Systemic corticosteroids

- Other immune modulating options

- Ruxolitinib
- Ibrutinib
- Imatinib
- TNF-inhibitors
- Rituximab
- Sirolimus
- Tacrolimus
- Mycophenolate mofetil
- Cyclosporine
- Photopheresis



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Watch Out for Skin Cancer

- Nonmelanoma and melanoma skin cancers occur at a higher rate in patients who undergo bone marrow transplantation than the general population
- Self monitor every 1-2 months
- At least annual screening with a dermatologist
- Practice sun safety – UV exposure is only modifiable risk factor
- No tanning booths!



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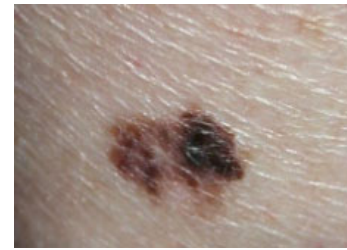
Skin cancer after bone marrow transplant



Basal cell carcinoma



Squamous cell carcinoma



Melanoma

Clinical images courtesy of www.dermnetz.org



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Skin cancer prevention



Common sunscreen mistakes

- Forgetting to re-apply
- Missing areas



Courtesy of The American Academy of Dermatology



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Summary

- Chronic GvHD is common after transplant and a major barrier to health
- The skin is the most-likely involved organ, with symptoms manifesting in one of several morphologies
- Treatment:
 - Skin directed
 - Systemic
- Chronic syndrome – improvement of symptoms and quality of life can be achieved



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Questions?



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