



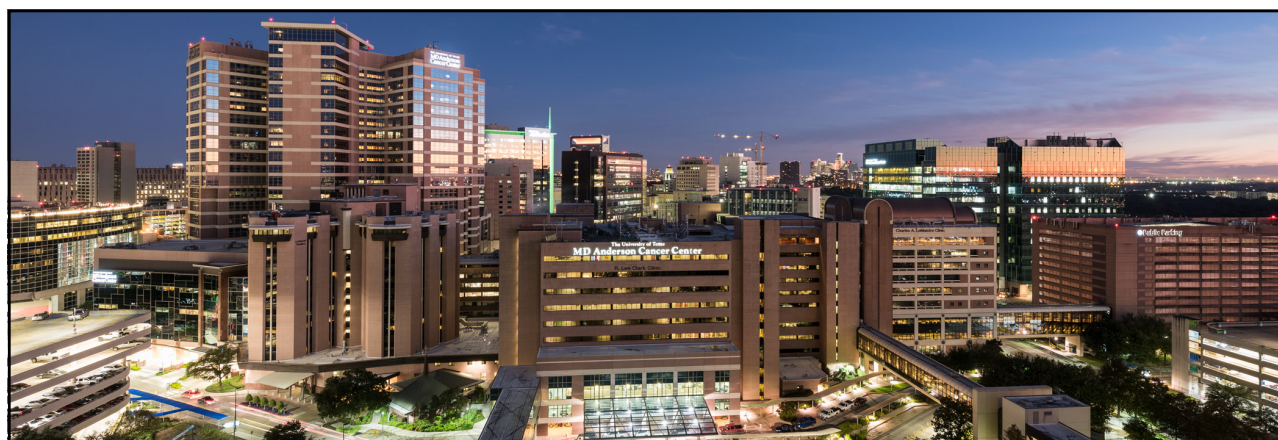
Introduction to Graft-versus-Host Disease

Celebrating a Second Chance at Life
Survivorship Symposium

April 30 - May 6, 2022



Amin Alousi MD
The University of Texas
MD Anderson Cancer Center



Graft-vs.-Host Disease *"It Takes a Village"*

Amin M. Alousi, MD
Professor of Medicine
Director of the Multidiscipline GVHD & Survivorship Program
Medical Director, Stem Cell Transplant Unit

THE UNIVERSITY OF TEXAS
**MD Anderson
Cancer Center**
Making Cancer History®

Graft-vs.-Host Disease (GVHD)

Multisystem Disorder that occurs when Immune Cells transplanted from a non-identical donor (the graft) recognize the recipient (host) as foreign resulting an immunologic process resulting in tissue injury.

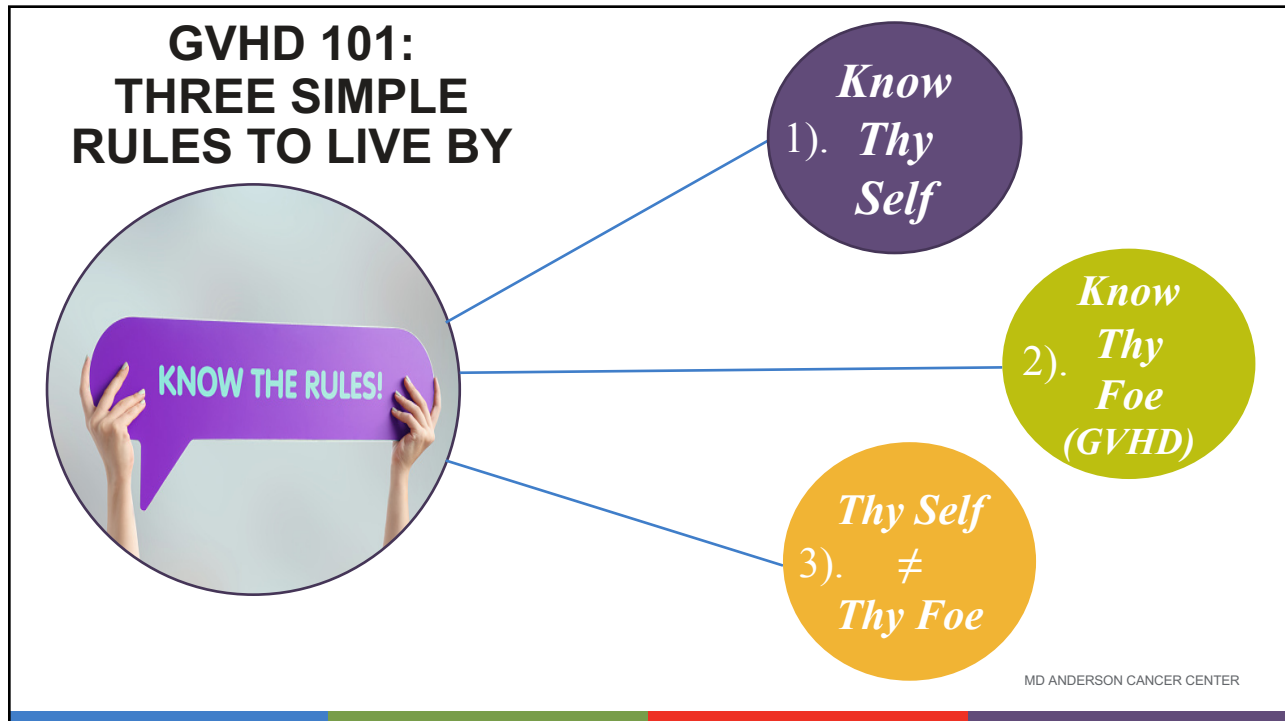
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Graft-vs.-Host Disease (GVHD)



WHAT SHOULD I KNOW ???

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Rule # 1

A large purple circle is centered on the page, containing the text "Know Thy Self" in a white, serif font.

Know Thy Self


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Know Thy Self

- **Examine your body weekly**
 - Mouth, Skin, Joints & Genitals
- **Pay attention to new symptoms**
 - Symptoms generally begin as subtle changes
- **Report new symptoms:**
 - Don't be afraid to ask
 - Don't assume

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Rule # 2



*Know
Thy
Foe
(GVHD)*

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Know Thy Foe (GVHD)

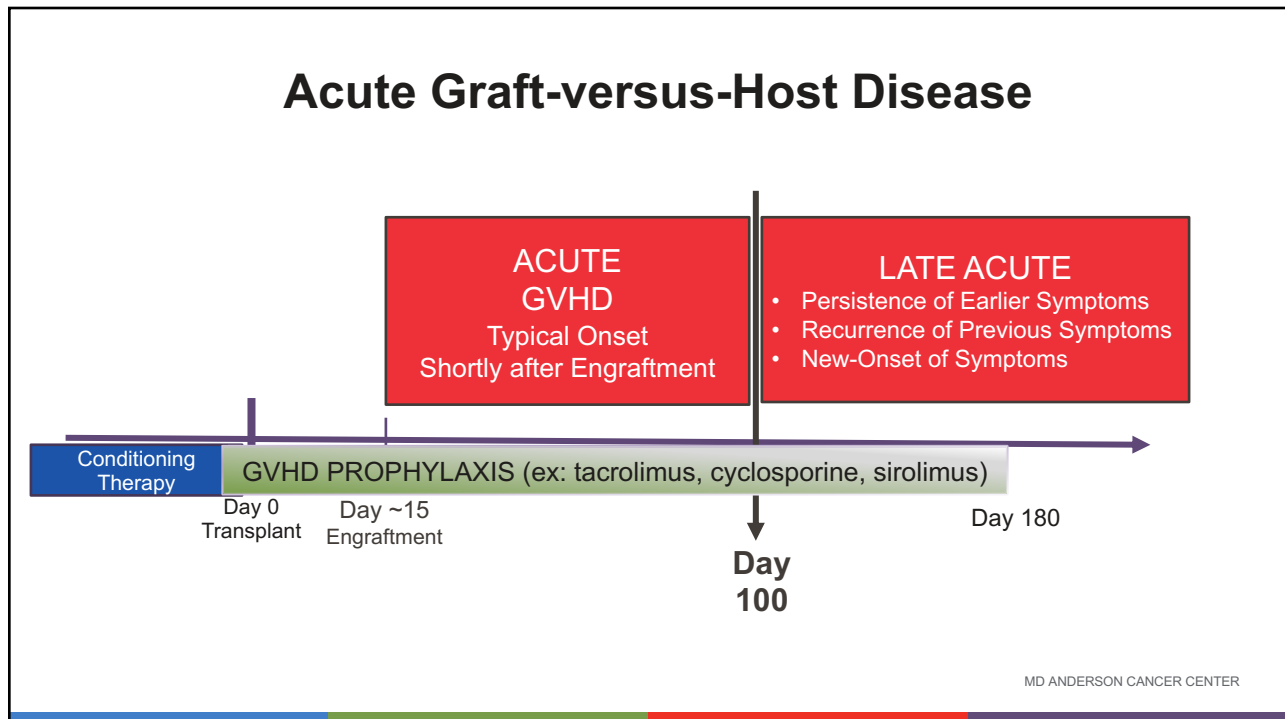
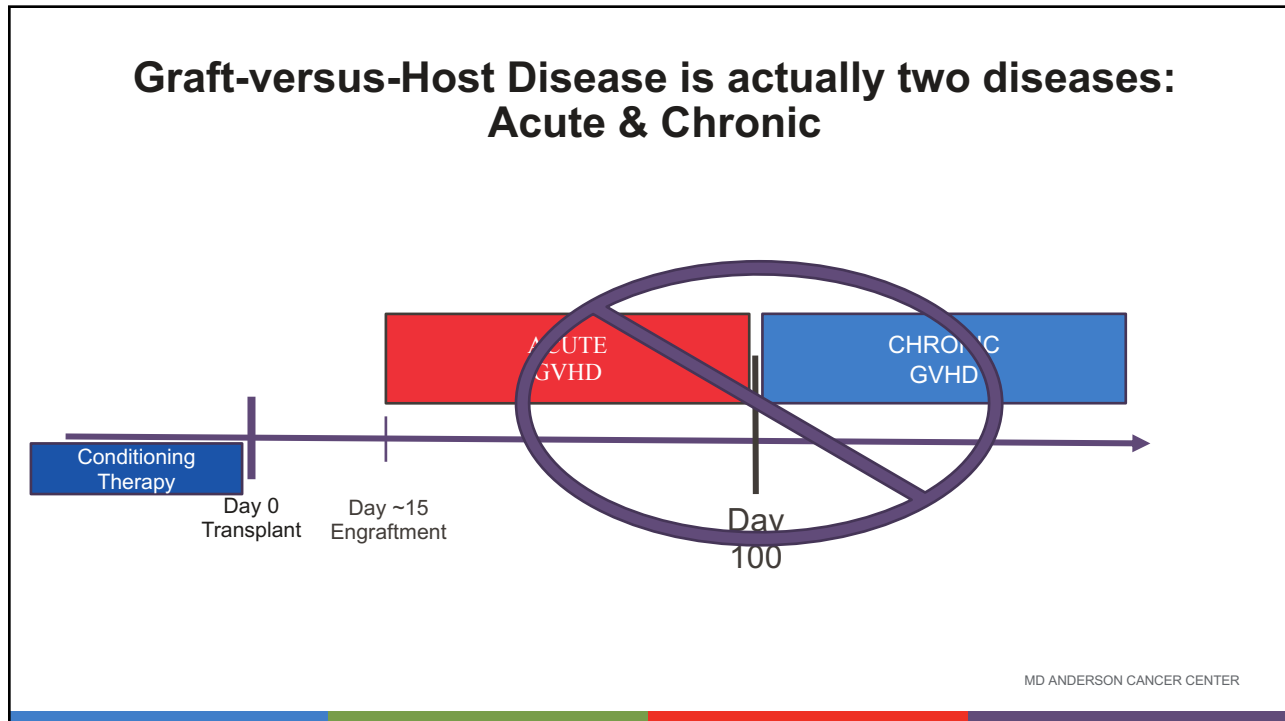
- Graft-versus-Host Disease is actually two diseases
 - acute GVHD
 - chronic GVHD
- Acute GVHD mainly affects three organs
 - Skin:
 - macular-papular rash
 - **Gastrointestinal (GI) Tract:**
 - upper GI symptoms: nausea, vomiting, poor appetite (*failure-to-thrive*)
 - lower GI: secretory diarrhea
 - Liver:
 - abnormal liver labs (typically total bilirubin)

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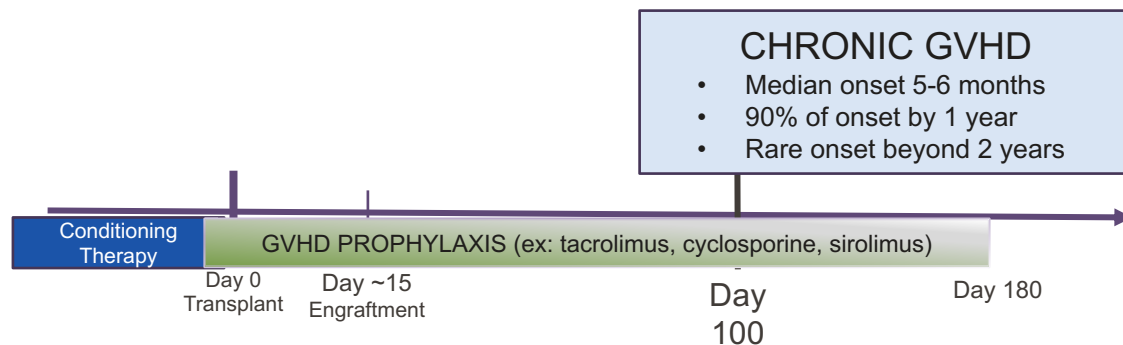
Know Thy Foe (GVHD)

- Chronic GVHD can affect many different organs
- Most common organs affected:
 - Eyes
 - Mouth
 - Skin
 - Joint/ Fascia
 - Gastrointestinal tract
 - Liver
 - Lungs
 - Genitals (vulva/vagina or penis/ foreskin)

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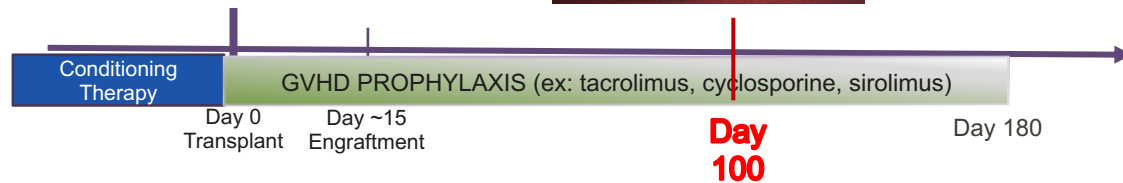


Chronic Graft-versus-Host Disease



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The Finish Line
is **Not** Day 100

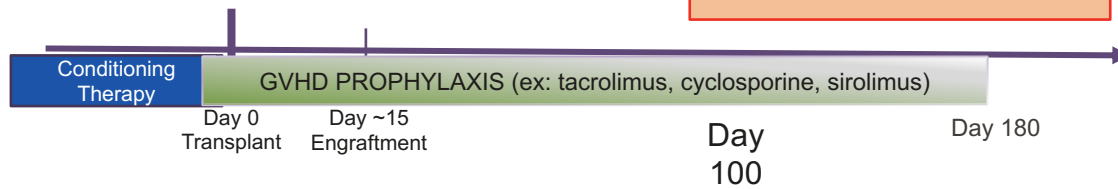


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Importance of Self Monitoring Days 100 to 360: **PERIOD OF HIGH ALERT**

- You may be at home and being seen by transplant providers less frequently
- Immunosuppression is being tapered
- Period when chronic GVHD is most likely to begin

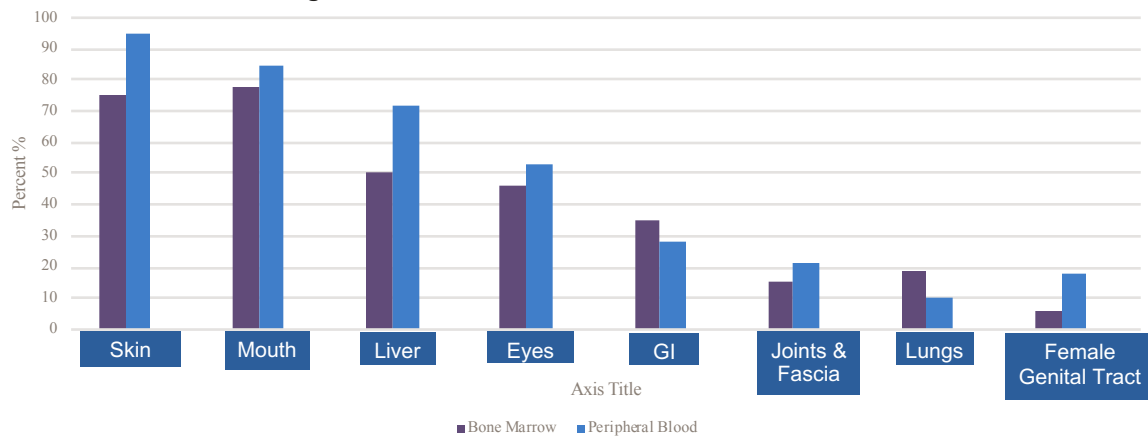
**ON HIGH ALERT
TAPERING
IMMUNOSUPPRESSION**



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Chronic GVHD: Organs Most Commonly Involved

Organ Involvement in Patients with Chronic GVHD



Adapted from:
• Flowers et. al. *Blood*. 2002
• Malard, Mohty. *Blood*. 2017

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Rule #1: Know Thy Skin

- Your skin is one of the most common organs involved by GVHD
- Your skin is also a common site for secondary cancers (skin cancers).
- Inspect of your skin weekly
- Have a total skin exam by a transplant professional and/or dermatologist at least once yearly

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Medical School Proverb:
"The Eyes Cannot See What the Brain Does not Know!"



"The Eyes Cannot See What the Eyes Cannot See."
Disrobe !!!!



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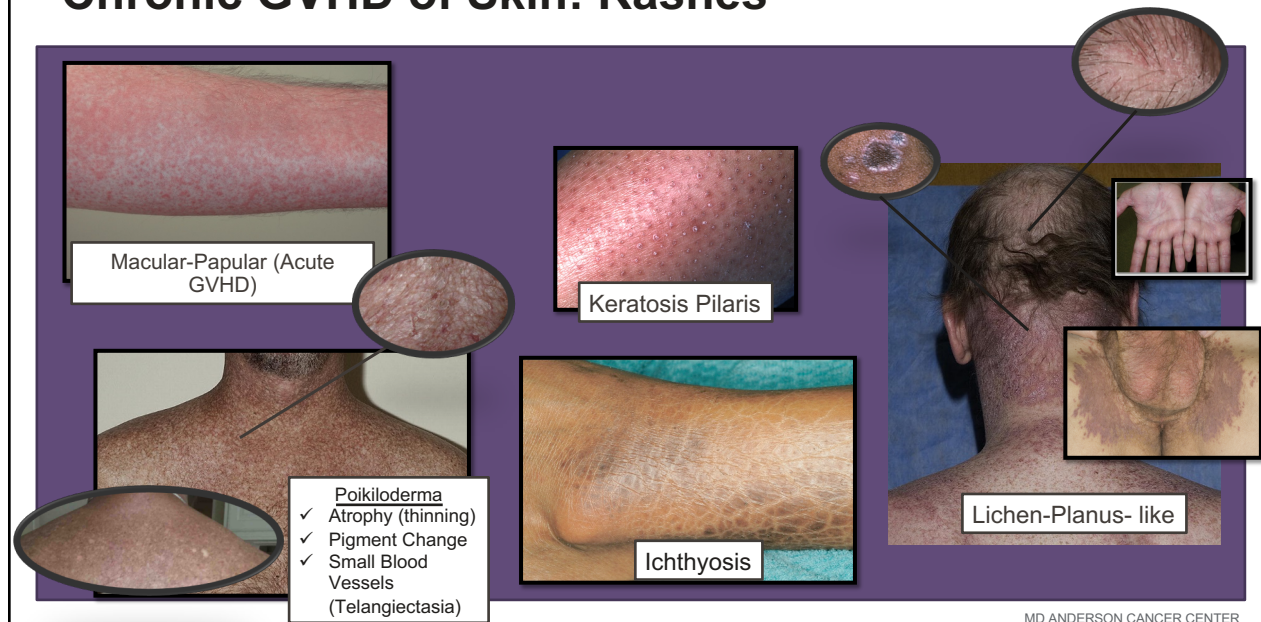
Chronic GVHD of Skin: What am I looking For?

- ✓ Rashes
- ✓ Skin Texture
 - Scarring
 - New “cellulite-like” changes
 - Swelling
 - Limited mobility (skin feeling tight)
- ✓ Pigment Changes:
 - Darkening of skin (hyperpigmentation)
 - Lightening of skin (hypopigmentation)
- ✓ Hair & nail changes
- ✓ Moles



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Chronic GVHD of Skin: Rashes



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Chronic GVHD of Skin: Scarring (Fibrosis)



Chronic GVHD of Skin: Pigment Changes



Chronic GVHD of Skin: Hair



Non-Scarring Hair Loss (such as Telogen effluvium)



Scarring Hair Loss (from Chronic GVHD)

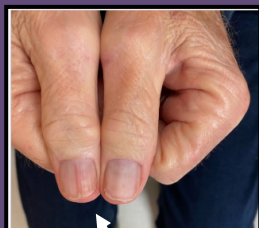


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Chronic GVHD of Skin: Nails



Longitudinal Ridging and Nail Splitting



Early to More Severe Scarring (pterygium) and (permanent) Nail Loss

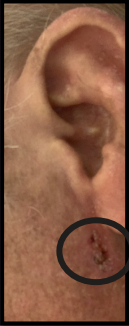



(Mild to More Severe Manifestations)


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Attention to Moles & Importance of Skin Cancer Prevention and Screening






Moles / Skin Lesions








KNOW YOUR ABCDE'S

A	B	C	D	E
ASYMMETRY	BORDER	COLOR	DIAMETER	EVOLUTION
				
One half does not match the other half	Uneven borders	Variety of colors like brown, tan, or black	Grows larger than the size of a pencil eraser (¼ inch)	Change in size, shape, color, elevation, another trait, or new symptom

Sun Protectants



**** See a dermatologist regularly (every 6-12 months) especially if have history of skin cancers**

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For More Information on Skin GVHD

- **BMT InfoNet Survivorship Symposium Workshop: Sharon Hymes, MD**
Skin GVHD (Tuesday, May 3, 2:45 pm Central)
Video at bmtinfonet.org/video/2022-GVHD-skin
- **BE THE MATCH®: Screening Skin for Chronic GVHD**
bethematchclinical.org/post-transplant-care/chronic-gvhd/skin
- **BE THE MATCH®: Fast Facts- Chronic GVHD of the Skin**
bethematchclinical.org/resources-and-education/materials-catalog/fast-facts---chronic-gvhd-of-the-skin

BE THE MATCH

FAST FACTS: CHRONIC GVHD OF THE SKIN AND DEEPER TISSUES

Learning more about graft-versus-host disease (GVHD) can help you make informed decisions and manage symptoms.

THIS FACT SHEET TELLS YOU:

- What chronic GVHD of the skin is
- How to assess chronic GVHD of the skin
- When to call your doctor

WHAT IS CHRONIC GVHD OF THE SKIN?

- Chronic GVHD of the skin happens when the donor's cells attack your skin. It is the most common type of chronic GVHD.
- Chronic GVHD of the skin can cause color changes (red, pink, purple, brown, or white), itching, dryness, scaling, sores, blisters, bumps, sores or blisters (small patches) of fluid. The skin may itch, feel like a sunburn, feel "wooly" like a sock, or you may have a scaling or flaking feeling underneath your skin.
- Chronic chronic GVHD is a specific type of skin GVHD. "Skinward" means hardening or thickening. This form of skin GVHD causes thickening, tightness, and hardening of the skin and deeper tissues. Skinless can also make it hard to move your joints.

HOW CAN I DECREASE SYMPTOMS?

- If your skin is itchy or irritated. The itch helps to keep your skin flexible and ease itching. Apply moisturizer right after you shower or bath to keep moisture from the water on your skin. Creams and ointments are better than lotions.
- If your skin or tissues are light, gentle, stretching, sensitive, numb, or painful. Physical therapy may help to ease the tightness. These activities should be gentle and not too much, otherwise you may be causing more irritation that could worsen GVHD.
- Avoid the sun, particularly during peak hours of ultraviolet radiation (10am-4pm). Use sunscreen and wear sun-protective clothes. Skin reactions can worsen chronic GVHD and cause skin cancer and wrinkles.
- If you have sores on your skin, keep the sores clean and protected from further injury. Ask your doctor if bandages or medicines applied to your skin may help.
- Avoid problems that decrease blood flow to your legs like smoking, crossing your legs or sitting for a long time.

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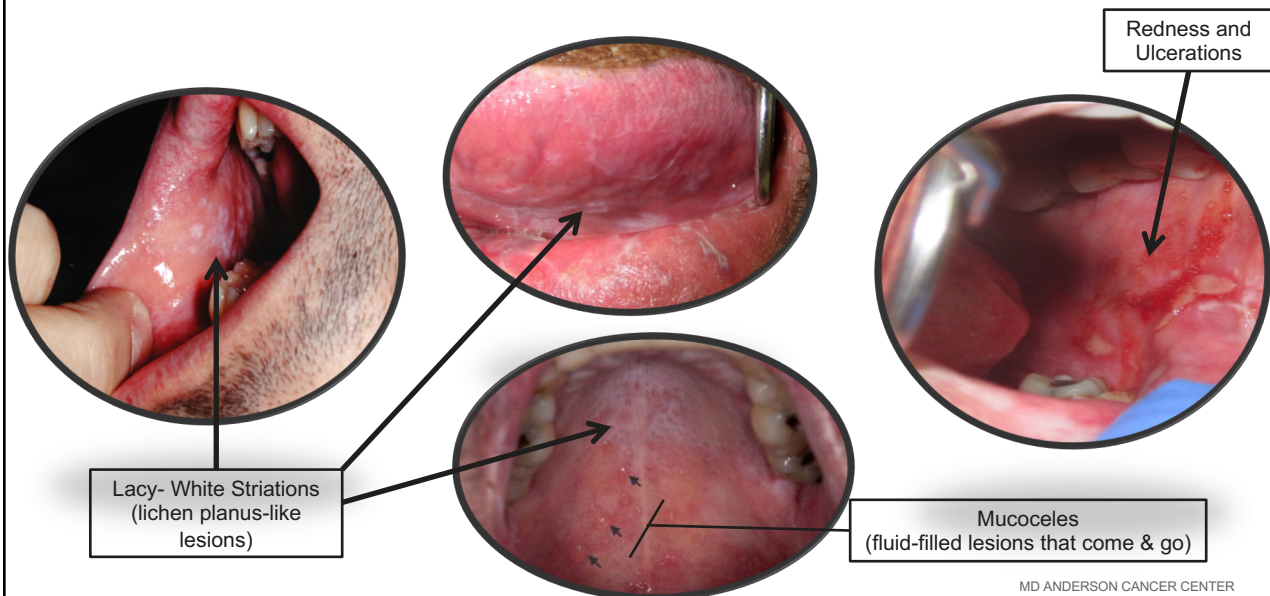
Chronic GVHD of the Mouth: What am I looking for?

- ✓ Dry mouth
- ✓ Rough sensation (scalded mouth sensation)
- ✓ Painless small fluid-filled lesions that come and go throughout the day
- ✓ Sensitivity to spicy or acidic foods, toothpaste, carbonated beverages
- ✓ Swelling, redness, pain or bleeding gums
- ✓ Ulcers, pain



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Chronic GVHD of the Mouth



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Chronic GVHD of the Eyes: What am I looking for?

- ✓ Excessive tearing (early symptom)
- ✓ Decreased tearing
- ✓ Dry, burning, gritty eyes
- ✓ Itching
- ✓ Difficulty opening eyes in morning (eye discharge)
- ✓ Sensitivity to light and wind
- ✓ Diminished visual acuity / blurred vision



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Chronic GVHD of the GI Tract: What am I looking For?

- ✓ Anorexia (no desire to eat)
- ✓ Nausea, vomiting
- ✓ Abdominal pain, bloating, cramping
- ✓ Diarrhea
- ✓ Greasy stools, undigested food in stool
- ✓ Painful swallowing
- ✓ Difficulty swallowing dry foods, pills including esophageal strictures (narrowing of the esophagus)
- ✓ Weight loss



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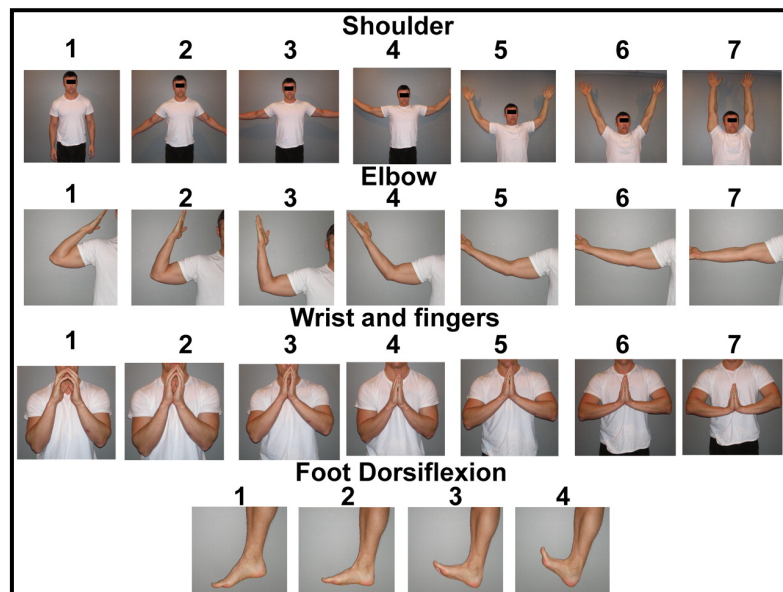
Chronic GVHD of Joints, Fascia, Muscles: What am I Looking For?

- ✓ Joint stiffness
- ✓ Reduced range of motion
- ✓ Tightened muscles, tendons
- ✓ Muscle cramps / spasms
- ✓ Contractures (joints in a fixed, flexed position)
- ✓ Edema (swelling)
- ✓ Joint Pain / Swelling (rare)



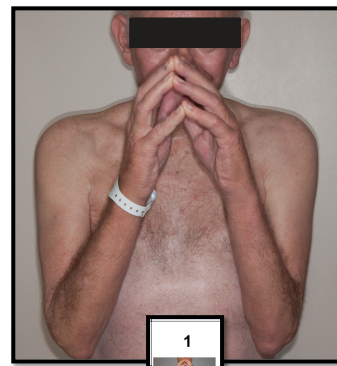
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Chronic GVHD of the Joints and Fascia



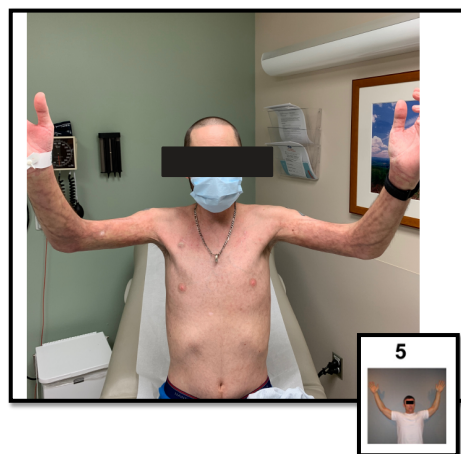
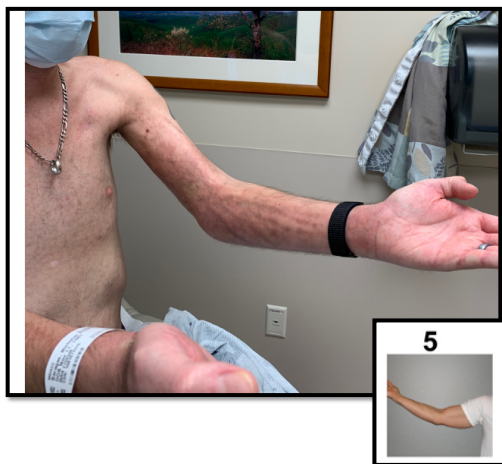
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Chronic GVHD of the Joints / Fascia



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Chronic GVHD of the Joints / Fascia



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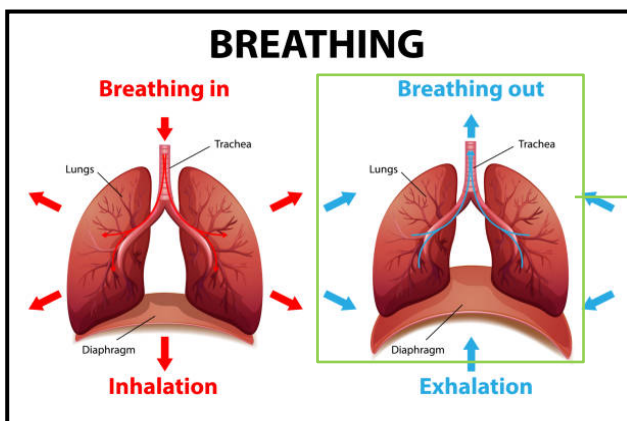
Chronic GVHD of the Lungs: What am I Looking For?

- ✓ Dry cough
- ✓ Wheezing
- ✓ Cough that persists after a cold (lasting longer than 2-4 weeks)
- ✓ Shortness of breath
- ✓ Feeling like you can't take a deep breath
- ✓ Asymptomatic (no symptoms; importance of screening)



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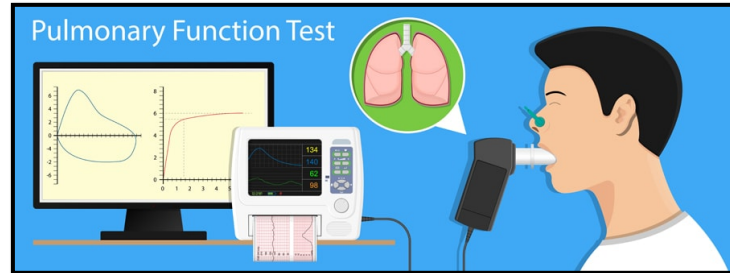
Chronic GVHD of the Lungs



- ✓ Hallmark of lung GVHD is impaired exhalation.
- ✓ Air gets trapped in lungs.
- ✓ One of the most serious forms of chronic GVHD.
- ✓ Patients with chronic GVHD involving other organs (skin, eyes, etc.) are at highest risk for developing lung involvement.
- ✓ Can be triggered by common community respiratory viruses like RSV and Parainfluenza.

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Importance of Screening for Lung GVHD



- Patients with early Lung GVHD may have few or no symptoms.
- Catching it early is felt to be important.
- Routine (screening) PFT's should be done for the first 2-3 years (or longer).
- Screening pulmonary function tests (PFT) especially important in those with active GVHD outside of the lung
- The role of at-home monitoring is being studied (handheld PFT).

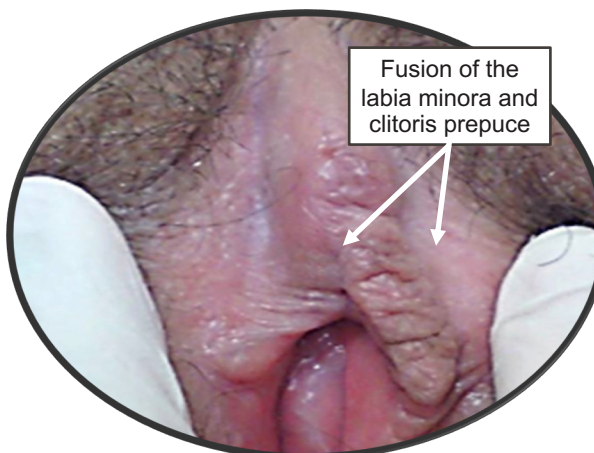
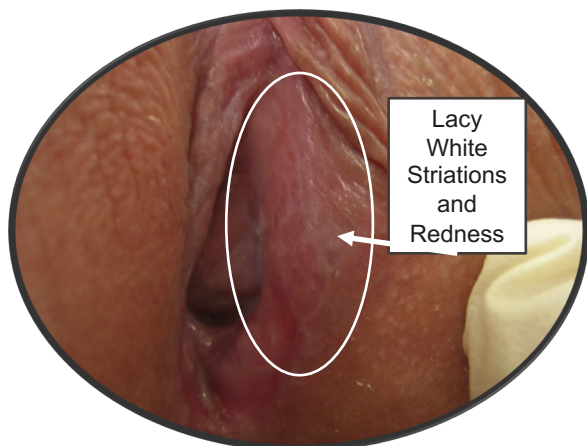
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Rule # 1: Know Thy Genitals - Females

- ✓ **Examine (external) vulva**
 - Note areas of redness, focal areas of white plaques or thinning
- ✓ **Examine (internal) vaginal mucosa (use a hand mirror).**
 - Is the tissue uniform in color?
 - Note areas of redness, white striations, scarring, adhesions, loss of elasticity, narrowing of the vaginal canal
- ✓ **Note symptoms:**
 - Itching
 - Burning
 - Dryness
 - Painful Intercourse
 - Pain with urination
 - Bleeding

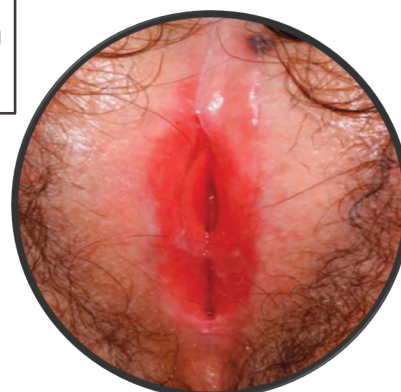
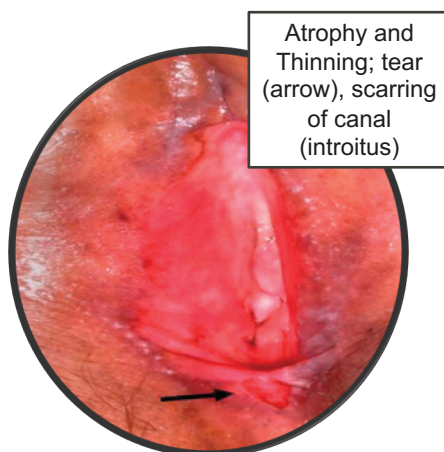
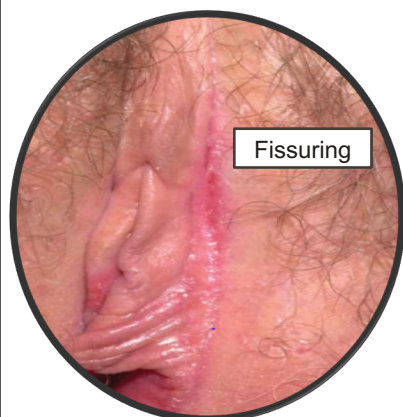
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Chronic GVHD of the Genitalia - Female



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Chronic GVHD of the Genitalia - Female



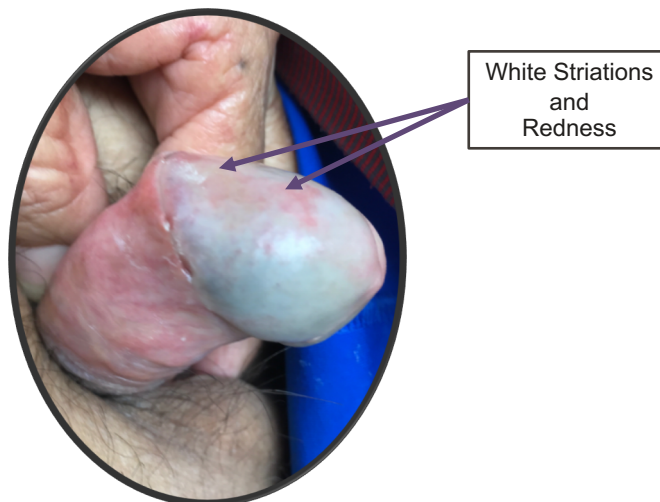
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Rule # 1: Know Thy Genitals - Males

- ✓ **Examine the glans (the *head* of the penis)**
 - Is it uniform in color?
 - Note areas of redness or white striations, burning or pain
- ✓ **Retract the foreskin**
 - It should retract easily and without pain
 - Note scar tissue / adhesions
- ✓ **Note Symptoms**
 - Pain and burning on the head of penis (glans)
 - (Rare) scarring of the meatus (where the urine comes out)
 - (Rare) abnormal/new bending of the penis when erect

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Chronic GVHD of the Genitalia - Male



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Chronic GVHD Laboratory Monitoring

- ✓ Labs are an important part of monitoring for Chronic GVHD.
- ✓ Particularly important when tapering immunosuppression.
- ✓ Routine labs should be obtained at least monthly between days 100 to 365 (and sometimes more frequently).
- ✓ Liver test results including: ALT/AST, Alkaline Phosphatase, Total Bilirubin.
- ✓ Other markers of chronic GVHD may include:
 - Elevated eosinophil count (an increase in the absolute number of these white blood cells)
 - New fall in blood counts (neutrophils, platelets)



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Rule # 3

Thy Self
≠
Thy Foe

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Rule #3: Thy Self Must NEVER Be Thy Foe

- ✓ Takes thy meds
- ✓ Monitor and report
- ✓ When feasible, travel to see transplant provider and sub-specialists who best know and can treat GVHD
- ✓ Don't resist starting and taking therapy:
 - Steroids
 - Other GVHD Therapy
 - Physical / Occupational Therapy

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Chronic GVHD Treatment: Supportive Care

- It's more than just taking a drug
- Organ specific therapies (therapies to improve symptoms and/or organ function) e.g.
 - Ocular GVHD: topical agents, punctal plugs/ cautery, scleral lenses
 - Lung GVHD: Inhaled steroids, Montelukast (*Singulair*)
 - Genital GVHD: topical agents
 - Skin: topical therapies and emollients
- Drugs to prevent infections
- Occupational, physical and pelvic floor therapy
- Nutritional support

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Chronic GVHD Treatment: Systemic Therapy

- Steroids (prednisone or methylprednisolone) are the first line treatment for acute and chronic GVHD
- Patients who fail to get better or have GVHD recur with lowering or stopping the steroids will require additional therapy (Steroid-Refractory or Dependent GVHD)

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Steroid-Refractory Acute GVHD

- Ruxolitinib (*Jakafi/Jakavi*) is the only FDA-approved therapy
- New therapies are being studied
- Importance of clinical trials

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Steroid-Refractory Chronic GVHD

- Three FDA-approved therapies
 - Ibrutinib (*Imbruvica*)
 - Belumosudil (Rezurock)
 - Ruxolitinib (Jakafi/Jakavi)
- A number of agents are used for Non-FDA approved indications
 - Sirolimus
 - Extracorporeal phototherapy (ECP)
 - Rituximab
 - IL-2
 - Methotrexate
 - Abetacept
- A number of new, exciting drugs are being studied
- Importance of clinical trials

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Ibrutinib (*Imbruvica*™)

- First FDA-approved Therapy for Patients with Steroid-Refractory Chronic
 - Inhibits the immune cells that drives chronic GVHD
 - Studied in patients ≥ 18 years who failed steroids and had red rash or oral GVHD
 - 67% of patients had a GVHD response and roughly 25% had meaningful improvement in symptoms.
- Side Effects
 - Infections requiring hospitalization (36%)
 - Fatigue (roughly half of patients reported)
 - Diarrhea (roughly 1/3rd of patients reported)
- Commonly patients need a lower dose due to side effects

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Belumosudil (*Rezurock*[™])

- FDA approved in 2021 for patients failing more than 2 prior therapies
 - First of its kind drug - inhibits the ROCK2 protein
 - Believed to restore immune balance as well as inhibit fibrosis (scarring)
 - Studied in patients ≥ 12 years with very advanced / severe chronic GVHD
 - 74% of patients had a GVHD response and roughly 60% had meaningful improvement in symptoms.
- Side Effects
 - Pneumonia requiring hospitalization (roughly 10%)
 - Elevated liver tests (roughly 20%)
 - Fatigue (roughly half of patients reported)
 - Nausea/ Diarrhea (roughly 1/3rd of patients reported)

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Ruxolitinib (*Jakafi*[™])

- FDA approved in 2021 for patients failing one or more prior therapies
 - Previously FDA approved for Steroid-Refractory Acute GVHD
 - Only FDA-approved, Chronic GVHD drug tested in a randomized trial against other (“best-available”) therapies
 - Studied in patients ≥ 12 years with moderate to severe chronic GVHD
 - ~ 50% of patients had a GVHD response compared to ~25% for patients who received other therapies (control-arm).
 - ~ 25% had meaningful improvement in symptoms vs. 11% for control-arm.
- Side Effects
 - Pneumonia requiring hospitalization (8.5%)
 - Anemia (29%), lowering of platelets (21%) or neutrophils (11%)

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“It Takes a Medical Village to Care for a BMT Patient”

Gynecology Nursing Pharmacy

Pulmonology Pathology

Medicine

Dermatology

Ophthalmology

Gastroenterology

Infectious Disease Nutrition

Transfusion Services

Medicine/Pharmacy

GVHD CLINIC

Transplant MD

- **Amin Alousi, MD**
- **Rohtesh Mehta, MD**

Dermatologist

- **Sharon Hymes, MD**

Mid-level Team

- **Joyce Neumann, PhD, APN**
- **Tamera Plair, PA**

Occupational and Physical Therapist

- **Carly Cappozzo, MS, OTR/L**
- **Paulette Taku, PT, DPT**

Research Nurse & Data Manager

- **Jennifer Ramos**
- **Lizette Martinez**

Clinic Nurse

- **Maria Alonso, RN**



GVHD RESOURCES

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More GVHD Information and Resources

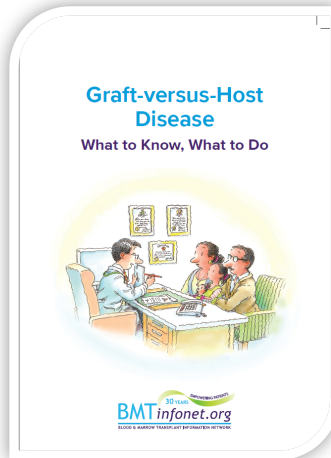
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Graft-versus-Host Disease: What to Know, What to Do

Free booklet from BMT infonet.org

bmtinfont.org/GVHD-Patient-Handbook



Available in English
and Spanish

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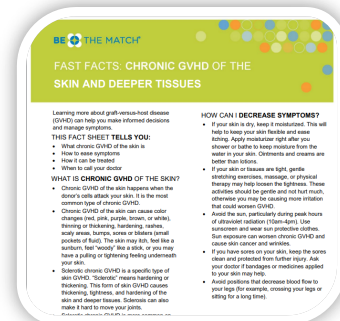
For More Information on Skin GVHD

- **BMT InfoNet Survivorship Symposium Workshop: Sharon Hymes, MD**
Skin GVHD (Tuesday, May 3, 2:45 pm Central)

Video after symposium at bmtinfont.org/video/2022-GVHD-skin

- **BE THE MATCH®: Screening Skin for Chronic GVHD**
bethematchclinical.org/post-transplant-care/chronic-gvhd/skin

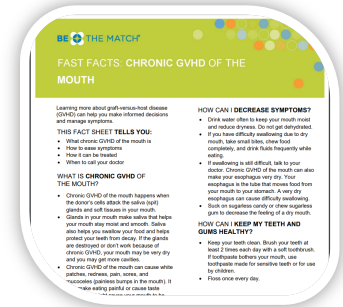
- **BE THE MATCH®: Fast Facts- Chronic GVHD of the Skin**
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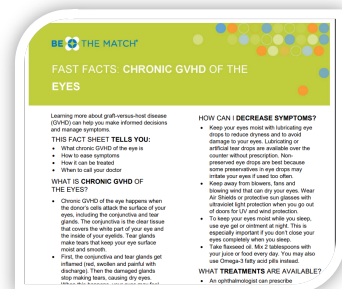
For More Information on Oral GVHD

- **BMT InfoNet Symposium Workshop: Nadarajah Vigneswaran, BDS, DMD, Dr.Med.Dent Your Mouth and GVHD** (Wednesday, May 4, 11:00 am Central)
Video after symposium at bmtinfonet.org/video/2022-GVHD-mouth
- **BE THE MATCH®: Screening Mouth for Chronic GVHD**
bethematchclinical.org/post-transplant-care/chronic-gvhd/mouth
- **BE THE MATCH®: Fast Facts- Chronic GVHD of the Mouth**
bethematchclinical.org/resources-and-education/materials-catalog/fast-facts---chronic-gvhd-of-the-mouth



For More Information on Ocular GVHD

- **BMT InfoNet Survivorship Symposium Workshop: Zhonghui Katie Luo MD, PhD Your Eyes and GVHD** (Saturday, April 30, 2:45 pm)
Video after symposium at bmtinfonet.org/video/2022GVHD-Eyes
- **BE THE MATCH®: Screening Eyes for Chronic GVHD**
bethematchclinical.org/post-transplant-care/chronic-gvhd/eyes
- **BE THE MATCH®: Fast Facts- Chronic GVHD of the Eye**
bethematch.org/materials-catalog/items/fast-facts---chronic-gvhd-of-the-eye?pid=12884



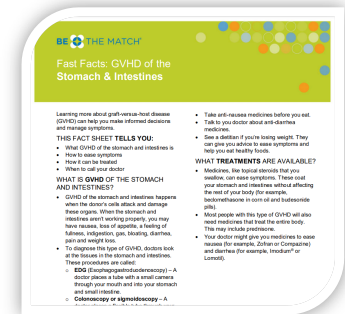
For More Information on GVHD of the GI Tract and Liver

- **BMT InfoNet Survivorship Symposium Workshop: Paul Shaughnessy MD**
GVHD of GI Tract and Liver (Sunday, May 1, 2022 11 AM Central)
Video after symposium at bmtinfonet.org/video/2022-GVHD-gastrointestinal-liver

- **BE THE MATCH®: Screening Skin for Chronic GVHD**
bethematchclinical.org/post-transplant-care/chronic-gvhd/gi-tract

- **BE THE MATCH®: Fast Facts- Chronic GVHD of the Skin**

bethematch.org/materials-catalog/items/fast-facts---ghvd-of-the-stomach-and-intestines/?pid=15558



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For More Information on Chronic GVHD of Joints and Fascia

- **BMT InfoNet Survivorship Symposium Workshops:**
Megan Nelson MD & Ekta Gupta MD
How Rehabilitation Medicine Helps GVHD Patients (Friday, May 6, 11:00 am)
Video after symposium at bmtinfonet.org/video/2022-GVHD-rehabilitation-medicine

Carly Cappozzo MSOT, OTR/L, Rachel Petrie MS, OTR/L, MSCS, and Paulette Taku, PT, DPT
Rehabilitation Therapies to Manage Side Effects of GVHD (Friday, May 6, 12:15 pm)
Video after symposium at bmtinfonet.org/video/2022-GVHD-rehab-exercises-and-devices

- **BE THE MATCH®: Screening Muscles, Fascia, Joints for Chronic GVHD**
bethematchclinical.org/post-transplant-care/chronic-gvhd/muscles,-fascia,-joints

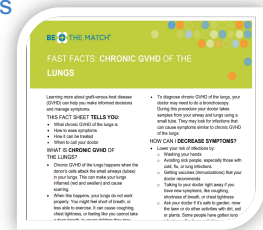
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For More Information on Chronic GVHD of the Lungs

- **BMT InfoNet Survivorship Symposium Workshop: Ajay Sheshadri MD, MSCI Pulmonary GVHD** (Monday, May 2, 1:30 pm)
Video after symposium at bmtinfonet.org/video/2022-lung-breathing-problems

- **BE THE MATCH®: Screening Lungs for Chronic GVHD**
bethematchclinical.org/post-transplant-care/chronic-gvhd/lungs

- **BE THE MATCH®: Fast Facts- Chronic GVHD of the Lungs**
bethematch.org/materials-catalog/items/fast-facts---gvhd-of-the-lungs?pid=13627



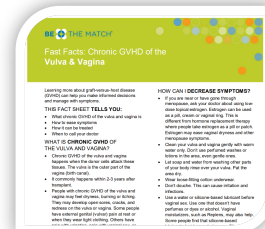
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For More Information on Chronic GVHD of the Genitals

- **BMT InfoNet Survivorship Workshop: Nikki Samms, PT, DPT Pelvic Floor Exercises for Vulvar GVHD** (Tuesday, May 3, 11 am)
Video after at bmtinfonet.org/video/2022-GVHD-pelvic-floor-exercise

- **BE THE MATCH®: Screening Genitalia for Chronic GVHD**
bethematchclinical.org/post-transplant-care/chronic-gvhd/genitalia

- **BE THE MATCH®: Fast Facts- Chronic GVHD of the Vulva & Vagina**
network.bethematchclinical.org/workarea/downloadasset.aspx?id=16426



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Questions?



Amin Alousi MD

Celebrating a Second Chance at Life Survivorship Symposium 2022

bmtinfonet.org ♦ help@bmtinfonet.org ♦ 847-433-3313



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