Introduction to Graft-versus-Host Disease

Celebrating a Second Chance at Life
Survivorship Symposium

April 30 - May 6, 2022

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MD Anderson Cancer Center
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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WHAT SHOULD I KNOW ????
GVHD 101: THREE SIMPLE RULES TO LIVE BY

1). Know Thy Self

2). Know Thy Foe (GVHD)

3). Thy Self ≠ Thy Foe

Rule # 1

Know Thy Self
**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

**Rule #2**

*Know Thy Foe (GVHD)*
Know Thy Foe (GVHD)

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

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)
Graft-versus-Host Disease is actually two diseases: Acute & Chronic

Acute Graft-versus-Host Disease

- ACUTE GVHD
  - Typical Onset Shortly after Engraftment

- LATE ACUTE
  - Persistence of Earlier Symptoms
  - Recurrence of Previous Symptoms
  - New-Onset of Symptoms

GVHD PROPHYLAXIS (ex: tacrolimus, cyclosporine, sirolimus)

Day 0 Transplant
Day ~15 Engraftment
Day 100
Day 180
Chronic Graft-versus-Host Disease

**CHRONIC GVHD**
- Median onset 5-6 months
- 90% of onset by 1 year
- Rare onset beyond 2 years

The Finish Line is **Not** Day 100
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

Chronic GVHD: Organs Most Commonly Involved

Adapted from:
- Flowers et al. Blood, 2002
- Malard, Molty, Blood, 2017
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 your skin weekly
- Have a total skin exam by a transplant professional and/or dermatologist at least once yearly

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

“The Eyes Cannot See What the Eyes Cannot See.”
Disrobe!!!!
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 (hypo-pigmentation)
- Hair & nail changes
- Moles

Chronic GVHD of Skin: Rashes

- Macular-Papular (Acute GVHD)
- Keratosis Pilaris
- Poikilodermat
  - Atrophy (thinning)
  - Pigment Change
  - Small Blood Vessels (Telangiectasia)
- Ichthyosis
- Lichen-Planus-like
Chronic GVHD of Skin: Scarring (Fibrosis)

- Fixed Sclerosis
- Weit
- Lichen Sclerosis / Lichen Sclerosis et atrophicus
- Sclerotic, Dimpling, Fascilitis, Cellulite-like
- Morphea

Chronic GVHD of Skin: Pigment Changes

- NOT-ACTIVE ("post-inflammatory") GVHD
- Vitiligo
**Chronic GVHD of Skin: Hair**

- Non-Scarring Hair Loss (such as Telogen effluvium)
- Scarring Hair Loss (from Chronic GVHD)

**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)
Attention to Moles & Importance of Skin Cancer Prevention and Screening

Moles / Skin Lesions

** KNOW YOUR ABCDE’S **

- **A**symmetry: One half doesn’t match the other half
- **B**order: Irregular or notched border
- **C**olor: Varied colors like brown, tan, or black
- **D**iameter: Bigger than pencil eraser
- **E**volution: Changes in size, shape, color, or new lump or sore

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
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

Chronic GVHD of the Mouth

- Lacy- White Striations (lichen planus-like lesions)
- Mucoceles (fluid-filled lesions that come & go)
- Redness and Ulcerations

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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

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
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)
Chronic GVHD of the Joints / Fascia

Wrist and fingers

1 2 3 4 5 6 7

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)

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.
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).

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
Chronic GVHD of the Genitalia - Female

- Lacy White Striations and Redness
- Fusion of the labia minora and clitoris prepuce

Chronic GVHD of the Genitalia - Female

- Fissuring
- Atrophy and thinning; tear (arrow), scarring of canal (introitus)
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

Chronic GVHD of the Genitalia - Male
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)

Rule # 3

Thy Self ≠ Thy Foe
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

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
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)

Steroid-Refractory Acute GVHD

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

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
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)

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

GVHD CLINIC
- Transplant MD
  - Amin Alousi, MD
  - Rohitesh Mehta, MD
- Dermatologist
  - Sharon Hymes, MD
  - Joyce Neumann, PhD, APN
  - Tamera Plair, PA
- Occupational and Physical Therapist
  - Carly Cappuzzo, MS, OTR/L
  - Paulette Taku, PT, DPT
  - Jennifer Ramos
  - Lizette Martinez
  - Maria Alonso, RN

Transplant Medicine/Pulmonary Medicine
Dermatology
Dermatology/Nutrition
Pathology
Gastroenterology
Infectious Disease
Nursing
Pharmacy
Radiology
Nursing
Nutrition
Ophthalmology
Pulmonary Medicine
Ophthalmology/ENT
Transfusion Services
GVHD RESOURCES

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
bmtinfonet.org/GVHD-Patient-Handbook

Available in English and Spanish

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 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
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
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  

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
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

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
Questions?

Celebrating a Second Chance at Life Survivorship Symposium 2022
bmtinfonet.org  help@bmtinfonet.org  847-433-3313

Let Us Know How BMT InfoNet Can Help YOU!

Visit our website:  bmtinfonet.org
Email us: help@bmtinfonet.org
Give us call:  888-597-7674

We’re here to help every step of the way!