



A patient counseling resource to support

Early Identification of Symptoms Associated With Chronic Graft-Versus-Host Disease

Chronic graft-versus-host disease (GVHD) is a common immune-mediated complication of allogeneic hematopoietic stem cell transplantation that can affect multiple organs and may have a profound impact on patients' lives.¹

Help your transplant patients and their caregivers understand the initial signs and symptoms of chronic GVHD so they can take an active role in identifying the disease.

Actively Monitor All Your Transplant Patients for Chronic GVHD

Organ Involvement

Chronic GVHD may be restricted to a single organ or it may be widespread with varying degrees of severity and impact¹

Organ-Specific Manifestations of Chronic GVHD¹

Skin/Nails/Hair

- Poikiloderma^{a,b}
- Lichen planus–like features^{a,c}
- Sclerotic features^a
- Morphea–like features^a
- Lichen sclerosus–like features^{a,d}
- Nail ridging or splitting^e
- Alopecia; loss of body hair^e

Eyes

- New onset dry, gritty, or painful eyes^e
- Cicatricial conjunctivitis^e
- Keratoconjunctivitis sicca^e
- Confluent areas of punctate keratopathy^e
- Photophobia^g

Liverⁱ

- Total bilirubin, alkaline phosphatase $>2 \times$ ULN
- ALT $>2 \times$ ULN

Genitalia^a

- Lichen planus–like features
- Lichen sclerosus–like features
- Vaginal scarring or clitoral/labial agglutination (females)
- Phimosis or urethral/meatus scarring or stenosis (males)

Mouth

- Lichen planus–like changes^{a,f}
- Mucoceles or ulcers^e

Lungs

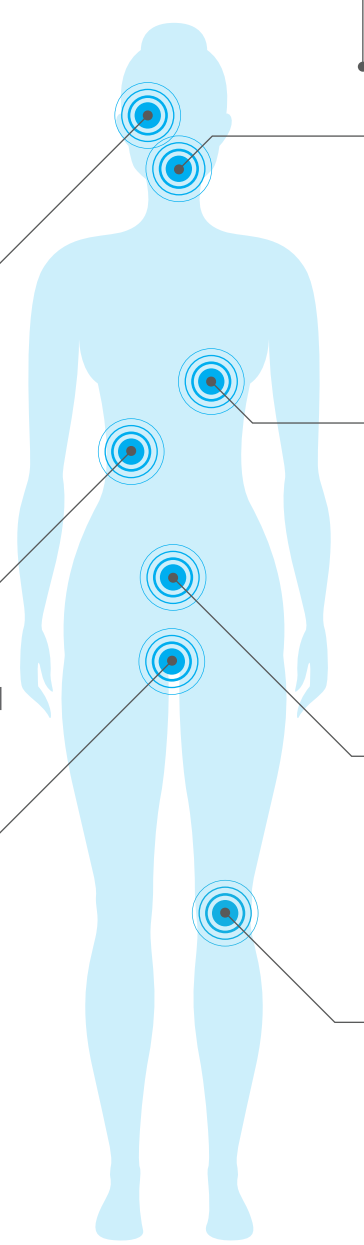
- Bronchiolitis obliterans diagnosed with lung biopsy^a
- Bronchiolitis obliterans syndrome^{a,h}
- Cryptogenic organizing pneumonia^g
- Air trapping^e

Gastrointestinal Tract^a

- Esophageal web
- Strictures or stenosis in the upper to mid third of the esophagus

Joints/Fascia^a

- Fasciitis^a
- Joint stiffness or contractures secondary to fasciitis or sclerosis^a
- Myositis^e
- Arthralgia^g



^aConsidered to be a diagnostic symptom per NIH consensus criteria (refers to manifestations that establish the presence of cGVHD without need for further testing or evidence of other organ involvement).¹

^bAtrophy, pigmentary changes and telangiectasia.¹

^cErythematous/violaceous flat-topped papules or plaques with or without surface reticulations or a silvery or shiny appearance.¹

^dDiscrete to coalescent, gray to white, moveable papules or plaques, often with follicular plugs, shiny appearance, and cigarette paper–like wrinkled texture.¹

^eConsidered to be a distinctive symptom of cGVHD per NIH consensus criteria (refers to manifestations that are typically found in cGVHD but are not sufficient in isolation to establish a diagnosis). Additional laboratory testing, biopsy, specialist evaluation, or radiographic imaging showing cGVHD in the same or another organ is required.¹

^fHyperkeratotic white lines and lacy-appearing lesions on the oral mucosa.¹

^gConsidered to be rare, controversial, or nonspecific features that cannot be used to establish the diagnosis of cGVHD, per NIH consensus criteria.¹

^hBOS can be diagnostic for lung cGVHD only if distinctive signs or symptoms of cGVHD are present in another organ.¹

ⁱThere are no hepatic manifestations that are considered distinctive or diagnostic of cGVHD per NIH consensus criteria. Manifestations listed here are common to both aGVHD and cGVHD.¹

Identify Chronic GVHD Early to Avoid Organ Damage and Preserve Organ Function²⁻⁵

Importance of Early Identification in Chronic GVHD

Subtle manifestations of chronic GVHD may go undiagnosed for months, and this delay may worsen prognosis. Timely diagnosis is important to minimize irreversible tissue damage.²⁻⁵ New signs and symptoms post transplant should be evaluated as potential chronic GVHD.⁵

Leading Cause of Post-Transplant Mortality

- Chronic GVHD is a leading cause of nonrelapse mortality in patients post transplant⁶
- More severe chronic GVHD is associated with higher mortality²
- Chronic GVHD is associated with a higher infection rate, and this contributes to increased mortality⁷

According to the NIH Consensus on Diagnosis and Staging of Chronic GVHD¹

Early intervention may

- Prevent progression to severe chronic GVHD
- Relieve symptoms
- Potentially prolong survival

Hear how Linda M. Perry, MS, PA-C, identifies the early signs and symptoms of chronic GVHD in her practice



Enhance Your Conversations With Patients About Symptoms Using Contextual Questions

Patients may not recognize that their symptoms could be linked to chronic GVHD. Open-ended questions can encourage your patients to share any changes to their overall wellness that may be an early indication of chronic GVHD

Caregivers can also be a valuable source of information on subtle changes to a patient's quality of life and daily activity

Skin/Nails/Hair^{1,8}



- Do you experience the following on any part of your skin?
 - Dryness, itchiness, rawness or soreness
 - Scaly, flaky, lighter, or darker in appearance
 - Rash or shiny scar
- Have you noticed any unusual thinning of scalp hair, loss of body hair, or premature graying?
- Have you noticed any changes to your nails (ridges or brittleness)?
- Have you experienced any dimpling or weight gain around abdomen or thighs?

Mouth^{1,8}



- Do pills or food get stuck in your mouth (and drinking water doesn't help)?
- Does your mouth feel dry most of the time despite drinking water?
- Do you experience any oral discomfort with spicy or acidic foods, sweet food, hot/cold food, or when you drink soda?
- Are there any recent changes in taste or sensitivity to toothpaste?
- Do you have mouth ulcers/sores or any difficulty when opening your mouth wide?

Joints/Fascia^{1,8}



- Have you noticed any pain, swelling, or stiffness in your feet, ankles, or other joints?
- Have you experienced any recent changes/difficulty in ability to move your body (eg, pulling up socks or reaching the cabinet top)?
- Are you experiencing any muscle cramps, pain, tenderness, or weakness?

Gastrointestinal Tract^{1,8}



- Have you had any recent weight loss?
- Are there any changes in your appetite? —poor, or reduced, or increased? Do you feel full with less food than before (early satiety)?
- Have you recently experienced any abdominal pain, cramping or bloating, nausea, vomiting, or diarrhea?

Eyes^{1,8}



- Do your eyes burn or feel dry, sandy or gritty, or itchy?
- Have you been using eye drops more frequently compared with 3 months ago?
- Are you experiencing any sensitivity to light or wind (eg, bothered by indoor light or ceiling fan)?
- Have you noticed excessive tearing of your eyes?

Genitals^{1,8}



- Do you have vaginal (or penile) dryness, burning, rash, ulcers, sores, or pigmentation changes?
- Are you sexually active? Do you have any discomfort during sexual activity, urination, gynecologic examination, or when wiping the area?
- Do you have any difficulty in retracting penile foreskin (in uncircumcised males)?

Lungs^{1,8}



- Do you find it difficult to catch your breath after minimal activity, take deep breaths, or perform daily activities because of shortness of breath?
- Are you experiencing any coughing or wheezing?
- Have you had a pulmonary function test done since the transplant?

Take an Active Role in Your Care: Communicate Your Symptoms to Your Healthcare Team

- Chronic graft-versus-host disease is a condition that develops when donor cells (called the *graft*) attack the organs and tissues of the patient who received them (or the *host*)
- Chronic GVHD may occur at any time after transplant, but most patients develop symptoms after 100 days post transplant. The organs most commonly affected are the skin, mouth, gastrointestinal tract, genitalia, liver, and eyes

GET TO KNOW THESE CHRONIC GVHD–RELATED SYMPTOMS:

Skin/Nails/Hair



- Dryness, itching, tightness (hard to pinch), dimpling, or thickening of skin
- Any color changes (lighter or darker than usual), rashes, scaly or flaky areas, shiny scars, sores, or blisters on your skin
- Thinning of scalp hair, or loss of body hair
- Weak or brittle nails; nail ridges
- Inability to sweat or keep body warm

Joints



- Difficulty in bending or stiffness/pain in your arms, wrists, fingers, or other joints
- Muscle pain, cramps, or weakness in your joints and muscles

Eyes



- Dry or itchy eyes
- Gritty or sandy eyes; excessive crustiness in the morning
- Sensitivity to light or wind (eg, bothered by indoor light or wind from the ceiling fan)
- Excessive tearing
- Blurred vision

Lungs



- Shortness of breath after mild activity (eg, climbing one flight of steps); inability to take deep breaths; or difficulty getting breath out
- Decreased stamina or trouble walking distances that were previously managed without stopping

Mouth



- Difficulty swallowing or opening mouth wide; food or pills get stuck
- Persistent dry mouth; altered taste; redness, ulcers, sores, or bumps in the mouth
- Sensitivity to spicy or acidic food, hot food or drink, soda, or toothpaste

Gastrointestinal Tract



- Abdominal discomfort, cramping and bloating, nausea, vomiting, or changes in appetite
- Diarrhea or changes in the number or consistency of bowel movements that don't improve over time
- Unexplained weight loss (such as recent changes in how clothes fit)

Genitals



- Dryness, burning, itching, sores, or pigmentation changes
- Changes in appearance (eg, redness, white thick skin)
- Discomfort during sexual activity, urination, gynecologic examination, or when wiping the area

Talk to your healthcare professional within 1-2 days of occurrence, about new or changing symptoms you may be experiencing, even if you think they are not related to chronic GVHD. Remember, chronic GVHD may occur at any time, even years, after transplant.



Share Your Symptoms

Please help us care for you. First, fill out the blue box. Then, provide more details by answering on the right. No symptom is too small, so there are multiple sections if you're experiencing more than one.

Check all symptoms that apply:

- Hair loss
- Dry or gritty eyes
- Brittle nails
- Red or dark skin patches
- Rash
- Coughing/wheezing
- Joint stiffness
- Pain
- Mouth sores
- Other

Please confirm the location of the symptom(s) (check all that apply):

- Hair
- Nails
- Eyes
- Mouth
- Chest
- Skin (please specify where)
- Joints
- Genitals
- Stomach
- Other

Please specify the time and date the symptom(s) first occurred:

..... / / ;
Month Day Year
..... : AM/PM
Time event occurred

If I were to further describe this , it felt or looked like

(Name of symptom)

..... I experience it

(Describe the symptom)

(Describe the frequency. Is it constant or intermittent?)

When the symptom first began, I was

(Share what you were doing when the symptom first occurred)

worsened when

(Describe the activities and/or specific times when the symptom felt worse)

If I were to rate the severity of the symptom from 1 to 7, 1 being mild and 7 being severe, I'd give it a

(1-7)

This symptom has affected my ability to

(Share details of the impact the symptom has had on your life and day-to-day activities)

Example: tie shoes, wear contact lenses, eat spicy food, fold clothes, drive a car

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Contact your healthcare team if you start to experience any new symptoms or changes to existing symptoms.



“ While the presence of chronic graft-versus-host disease is associated with decreased risk of relapse, the disease can lead to significant impairment in quality of life and decreased survival. **Early detection of chronic GVHD may lead to improved outcomes.** The multitude of potential manifestations and the often insidious onset of chronic GVHD can make early detection a challenge. Educating providers about the various symptoms, and encouraging them to query their patients, is critical to early detection. Equally as important is educating patients and caregivers so they can report symptoms suggestive of chronic GVHD in a timely fashion. ”

—Linda M. Perry, MS, PA-C, Abramson Cancer Center, University of Pennsylvania

Be sure to watch Linda M. Perry’s videos on the importance of symptom recognition and early identification of chronic GVHD



Abbreviations:

aGVHD, acute graft-versus-host disease; ALT, alanine aminotransferase; BOS, bronchiolitis obliterans syndrome; cGVHD, chronic graft-versus-host disease; GVHD, graft-versus-host disease; NIH, National Institutes of Health; ULN, upper limit of normal.

References:

1. Jagasia MH, et al. *Biol Blood Marrow Transplant.* 2015;21(3):389-401. 2. Lee SJ, et al. *Biol Blood Marrow Transplant.* 2003;9(4):215-233. 3. Hildebrandt GC, et al. *Bone Marrow Transplant.* 2011;46(10):1283-1295. 4. Nassiri N, et al. *J Ophthalmic Vis Res.* 2013;8(84):351-358. 5. Lee SJ, Flowers MED. *Hematology Am Soc Hematol Educ Program.* 2008;2008(1):134-141. 6. MacDonald KPA, et al. *Blood.* 2017;129(1):13-21. 7. Flowers MED, et al. *Blood.* 2015;125(4):606-615. 8. Carpenter PA. *Blood.* 2011;118(10):2679-2687.



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