Chronic GVHD

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No Conflicts of Interest
Chronic GVHD

• Most common long-term complication of allogeneic hematopoietic cell infusion
  – Affects 10-50% of allogeneic recipients
  – Median onset 4-6 months after HCT
  – 90-95% of cases diagnosed within first year

– Clinical implications:
  • Leading cause of non-relapse mortality
  • Associated with worse quality of life and functional status (e.g., inability to return to work)

• New CIBMTR forms incorporate the 2014 NIH Consensus recommendations
National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: I. The 2014 Diagnosis and Staging Working Group Report

Acute and Chronic GVHD

Day 0
Graft infused

Day 100

ACUTE

CHRONIC
Acute and Chronic GVHD
Diagnosis of Chronic GVHD

• Distinction from acute GVHD
• Presence of at least one diagnostic clinical manifestation OR at least one distinct manifestation confirmed by pertinent biopsy or other relevant tests
• Exclusion of other possible etiologies for the clinical manifestation (e.g., infection, drug toxicity)
• (Clinical care may deviate from this definition)
## Diagnostic vs. Distinctive

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<thead>
<tr>
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<th>Diagnostic</th>
<th>Distinctive</th>
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<tr>
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<td>myositis, polymyositis</td>
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</table>
# NIH Skin Score

<table>
<thead>
<tr>
<th>Score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>% BSA</td>
<td>☐ No BSA</td>
<td>☐ 1-18% BSA</td>
<td>☐ 19-50% BSA</td>
<td>☐ &gt;50% BSA</td>
</tr>
</tbody>
</table>

**GVHD features to be scored by BSA:**

**Check all that apply:**

☐ Maculopapular rash/erythema
☐ Lichen planus-like
☐ Sclerotic features
☐ Papulosquamous lesions or ichthyosis
☐ Keratosis pilaris-like

☐ No sclerotic features

☐ Superficial sclerotic features “not hidebound” (able to pinch)

**Check all that apply:**

☐ Deep sclerotic features
☐ “Hidebound” (unable to pinch)
☐ Impaired mobility
☐ Ulceration

☐ Abnormality present but explained entirely by non-GVHD documented cause (specify) ____________________________

♦ % BSA and degree of sclerosis
Skin:

1. Skin
   - Yes – *Go to question 253*
   - No – *Go to question 261*

2. Score percent BSA involved:
   - Score 0 – No BSA involved, no sclerotic features
   - Score 1 – 1-18% BSA
   - Score 2 – 19-50% BSA, or superficial sclerotic features “not hidebound” (able to pinch)
   - Score 3 - >50% BSA, deep sclerotic features, hidebound, impaired mobility, or ulceration

3. Skin features score:
   - No sclerotic features
   - Superficial sclerotic features “not hidebound” (able to pinch)
   - Deep sclerotic features, hidebound (unable to pinch), impaired mobility, or ulceration

Y/N:
- maculopapular rash/erythema
- lichen planus-like features
- sclerotic features
- papulosquamous lesions or ichthyosis
- keratosis pilaris-like

https://bethematchclinical.org/Post-Transplant-Care/Chronic-GVHD/Skin/
## NIH Mouth Score

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</thead>
<tbody>
<tr>
<td><strong>No Symptoms</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Lichen-planus like features present:</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not examined</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mild symptoms with disease signs but not limiting oral intake significantly</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Moderate symptoms with disease signs with partial limitation of oral intake</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Severe symptoms with disease signs on examination with major limitation of oral intake</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
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☐ Abnormality present but explained entirely by non-GVHD documented cause (specify) ______________

♦ Symptoms and limitation of oral intake
Mouth

8.    Mouth
       □ Yes
       □ No

9.    Mouth score:
       □ Score 0 – No symptoms
       □ Score 1 – Mild symptoms with disease signs but not limiting oral intake significantly
       □ Score 2 – Moderate symptoms with disease signs with partial limitation of oral intake
       □ Score 3 – Severe symptoms with disease signs on examination with major limitation of oral intake

10.   Lichen planus-like features
       □ Yes
       □ No

Specify if any mouth abnormalities were present, but explained entirely by non-GVHD causes:

11.   Abnormality present but explained entirely by non-GVHD documented cause
       □ Yes – Go to question 265
       □ No – Go to question 266

12.   Specify cause:______________________________
<table>
<thead>
<tr>
<th>NIH Eye Score</th>
</tr>
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<tr>
<td>□ No Symptoms</td>
</tr>
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*Keratoconjunctivitis confirmed by ophthalm:*

□ Yes
□ No
□ Not examined

□ Abnormality present but explained entirely by non-GVHD documented cause (specify) __________________

♦ Symptoms, ADLs, eyedrop frequency
## NIH Liver Score

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<tr>
<td>☐</td>
<td>Normal total bilirubin and ALT or AP &lt;3x ULN</td>
<td>☐ Normal total bilirubin with ALT 3-5x ULN or AP &gt;3x ULN</td>
<td>☐ Elevated total bilirubin but &lt;3 mg/dl or ALT &gt; 5x ULN</td>
<td>☐ Elevated total bilirubin &gt; 3 mg/dl</td>
</tr>
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☐ Abnormality present but explained entirely by non-GVHD documented cause (specify) ______________

♦ Liver function tests
# NIH GI Score

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</tr>
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<tbody>
<tr>
<td>☐ No Symptoms</td>
<td>☐ Symptoms without significant weight loss (&lt;5%)</td>
<td>☐ Symptoms associated with mild to moderate weight loss (5-15%) OR moderate diarrhea without significant interference with daily living</td>
<td>☐ Symptoms associated with significant weight loss (&gt;15%), requires nutritional supplementation for most calorie needs OR esophageal dilation OR severe diarrhea with significant interference with daily living</td>
</tr>
</tbody>
</table>

☐ Abnormality present but explained entirely by non-GVHD documented cause (specify) ________________

♦ Symptoms, weight loss, ADLs, esophageal dilation
## NIH Lung Score

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<tbody>
<tr>
<td>□ No Symptoms</td>
<td>□ Mild symptoms (shortness of breath after climbing one flight of steps)</td>
<td>□ Moderate symptoms (shortness of breath after walking on flat ground)</td>
<td>□ Severe symptoms (shortness of breath at rest; requiring O₂)</td>
<td></td>
</tr>
</tbody>
</table>

☐ Abnormality present but explained entirely by non-GVHD documented cause (specify) ______________

Were PFTs performed? Specify FEV1 % predicted ______________

♦ Symptoms and PFTs
## NIH Joint Score

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</tr>
</thead>
<tbody>
<tr>
<td>☐</td>
<td>No Symptoms</td>
<td>☐ Mild tightness of arms or legs, normal or mildly decreased range of motion not affecting ADL</td>
<td>☐ Tightness of arms or legs OR joint contractures, erythema thought due to fasciitis, moderate decrease ROM AND mild to moderate limitation of ADL</td>
<td>☐ Contractures WITH significantly decreased ROM AND significant limitation of ADL (unable to tie shoes, button shirts, dress self, etc.)</td>
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☐ Abnormality present but explained entirely by non-GVHD documented cause (specify) ______________

◆ Tightness, range of motion, ADLs
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<tbody>
<tr>
<td><strong>No Signs</strong></td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td><strong>Mild signs and females with or without discomfort on exam</strong></td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td><strong>Moderate signs and may have symptoms with discomfort on exam</strong></td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td><strong>Severe signs with or without symptoms</strong></td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
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Currently sexually active:
- ☐ Yes
- ☐ No
- ☐ Unknown

☐ Abnormality present but explained entirely by non-GVHD documented cause (specify) ______________

♦ Signs and symptoms on female exam
Maximum grade of chronic GVHD since the date of last report:

49. Maximum grade of chronic GVHD: (according to best clinical judgment)
   □ Mild
   □ Moderate
   □ Severe
   □ Unknown

50. Specify if chronic GVHD was limited or extensive:
   □ Limited – localized skin involvement and/or hepatic dysfunction due to chronic GVHD
   □ Extensive – one or more of the following:
     – generalized skin involvement; or,
     – liver histology showing chronic aggressive hepatitis, bridging necrosis or cirrhosis; or,
     – involvement of eye: Schirmer’s test with < 5 mm wetting; or
     – involvement of minor salivary glands or oral mucosa demonstrated on labial biopsy; or
     – involvement of any other target organ

51. Date of maximum grade of chronic GVHD: ___ ___ ___ ___ - ___ ___ - ___ ___ *

* Check boxes of individual signs/symptoms retained
Treatment

• Initial therapy is steroids at 0.5-1 mg/kg/d
  – About 30% of people respond and never need additional treatment (Flowers Blood 2002; 100: 415)

• Secondary therapy - >30 agents but no standard established
Current GVHD Status

147. Are symptoms of GVHD still present on the date of actual contact (or present at the time of death)?
   □ Yes
   □ No

148. Is the recipient still taking systemic steroids? (Do not report steroids for adrenal insufficiency, ≤10 mg/day for adults, <0.1 mg/kg/day for children)
   □ Yes – Go to question 404
   □ No – Go to question 402
   □ Not applicable – Go to question 404
   □ Unknown – Go to question 404

149. Date final treatment administered:
   □ Known – Go to question 40
   □ Unknown – Go to question 404
   □ Previously reported – Go to question 404

150. Date final treatment administered: ___ ___ ___ ___ — ___ ___ — ___ ___
     YYYY MM DD
Medical Records Conundrums

• Notes say the patient has chronic GVHD and prednisone was started. But she did not meet NIH criteria for chronic GVHD. *Do I check the chronic GVHD box?*

• Notes say that the patient has skin, eye and mouth involvement but no score is listed. *What should I record on the CRFs?*
Case #1

- 38 y/o woman with AML in first complete remission undergoing HLA-identical sibling transplantation using cytoxan/TBI
- Day +30, skin rash on 30% BSA, diarrhea ~1200 mL/d
- Despite treatment with steroids, mycophenolate mofetil, ATG and infliximab, she has lingering red skin and diarrhea on day +110

• **What is the significance of the rash and diarrhea on day +110?**
Acute and Chronic GVHD

Day 0
Graft infused

Day 100

CLASSIC ACUTE

CHRONIC OVERLAP

CLASSIC CHRONIC

DE NOVO LATE ACUTE
RECURRENT LATE ACUTE
PERSISTENT LATE ACUTE
Case #1

- Her skin rash and diarrhea resolve
- At day +150, she develops dry eyes, a dry and sensitive mouth, and lichen planus in her mouth. The notes state: “She has chronic GVHD and was started on prednisone. Tacrolimus was increased to full dose.”

- Does she have chronic GVHD?
## Diagnostic vs. Distinctive

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<tr>
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<td></td>
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**Maximum grade of chronic GVHD since the date of last report:**

49. **Maximum grade of chronic GVHD:** (according to best clinical judgment)
   - [X] Mild
   - [ ] Moderate
   - [ ] Severe
   - [ ] Unknown

50. **Specify if chronic GVHD was limited or extensive:**
   - [ ] Limited – localized skin involvement and/or hepatic dysfunction due to chronic GVHD
   - [X] Extensive – one or more of the following:
     - generalized skin involvement; or,
     - liver histology showing chronic aggressive hepatitis, bridging necrosis or cirrhosis; or,
     - involvement of eye: Schirmer’s test with < 5 mm wetting; or
     - involvement of minor salivary glands or oral mucosa demonstrated on labial biopsy; or
     - involvement of any other target organ

51. **Date of maximum grade of chronic GVHD:** ___ ___ ___ ___ - ___ ___ - ___ ___

* Check boxes of individual signs/symptoms retained
Case #2

• A 60 y/o man with CLL has a matched unrelated donor non-myeloablative transplant. He does not have any skin rash, liver function abnormalities, or diarrhea.

• On day +90 he develops mouth sensitivity with erythema and his absolute eosinophil count is 1200. The notes say he has chronic GVHD and his tacrolimus is increased.

• Does he have chronic GVHD?
Case #2

• At one year he has increased liver function tests (bili normal, ALT 4x ULN), lichen-sclerosis on his upper back and arms, and a painful mouth ulcer, although he is eating a normal diet.

• *Does he have chronic GVHD?*
## Diagnostic vs. Distinctive

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Body Surface Area

“lichen-sclerosis on his upper back and arms”
Skin:

1. Skin
   ☒ Yes – Go to question 253
   ☐ No – Go to question 261

2. Score percent BSA involved:
   ☐ Score 0 – No BSA involved, no sclerotic features
   ☐ Score 1 – 1-18% BSA
   ☒ Score 2 – 19-50% BSA, or superficial sclerotic features “not hidebound” (able to pinch)
   ☐ Score 3 - >50% BSA, deep sclerotic features, hidebound, impaired mobility, or ulceration

3. Skin features score:
   ☐ No sclerotic features
   ☒ Superficial sclerotic features “not hidebound” (able to pinch)
   ☐ Deep sclerotic features, hidebound (unable to pinch), impaired mobility, or ulceration

Y/N:
□ maculopapular rash/erythema
□ lichen planus-like features
☒ sclerotic features
□ papulosquamous lesions or ichthyosis
□ keratosis pilaris-like

https://bethematchclinical.org/Post-Transplant-Care/Chronic-GVHD/Skin/
8. Mouth
   ☒ Yes
   ☐ No

9. Mouth score:
   ☐ Score 0 – No symptoms
   ☒ Score 1 – Mild symptoms with disease signs but not limiting oral intake significantly
   ☐ Score 2 – Moderate symptoms with disease signs with partial limitation of oral intake
   ☐ Score 3 – Severe symptoms with disease signs on examination with major limitation of oral intake

10. Lichen planus-like features
    ☐ Yes
        ☒ No

Specify if any mouth abnormalities were present, but explained entirely by non-GVHD causes:

11. Abnormality present but explained entirely by non-GVHD documented cause
    ☐ Yes – Go to question 265
        ☒ No – Go to question 266

12. Specify cause: ________________________________

“a painful mouth ulcer, although he is eating a normal diet”
“increased liver function tests (bili normal, ALT 4x ULN)”

30. Liver
   ✗ Yes – Go to question 284
   ☐ No – Go to question 287

31. Liver score
   ☐ Score 0 – Normal total bilirubin and ALT or AP < 3 x ULN
   ✗ Score 1 – Normal total bilirubin with ALT ≥ 3 to 5 x ULN or AP ≥ 3 x ULN
   ☐ Score 2 – Elevated total bilirubin but ≤ 3 mg/dL or ALT > 5 ULN
   ☐ Score 3 – Elevated total bilirubin > 3 mg/dL

Specify if any liver abnormalities were present, but explained entirely by non-GVHD causes:

32. Abnormality present but explained entirely by non-GVHD documented cause
   ☐ Yes – Go to question 286
   ✗ No – Go to question 287

33. Specify cause: ________________________________
Case #2

• At one year he has increased liver function tests (bili normal, ALT 4x ULN), lichen-sclerosis on his upper back and arms, and a painful mouth ulcer, although he is eating a normal diet.

• He is started on prednisone with some improvement but when the prednisone is tapered he develops dry eyes requiring eyedrops every 4 hours.

• He then starts sirolimus.

What other manifestations does he have?

What treatments are used?
Eyes

13. Eyes

☒ Yes – Go to question 267
☐ No – Go to question 271

14. Eyes score

☐ Score 0 – No symptoms

☐ Score 1 – Mild dry eye symptoms not affecting ADL (requirement of lubricant eye drops ≤ 3x per day)

☒ Score 2 – Moderate dry eye symptoms partially affecting ADL (requiring lubricant eye drops >3x per day or punctal plugs), without new vision impairment due to keratoconjunctivitis sicca (KCS)

☐ Score 3 – Severe dry eye symptoms significantly affecting ADL (special eyewear to relieve pain) OR unable to work because of ocular symptoms OR loss of vision due to keratoconjunctivitis sicca (KCS)

15. Keratoconjunctivitis sicca (KCS) confirmed by ophthalmologist?

☐ Yes
☐ No
☒ Not done
Maximum grade of chronic GVHD since the date of last report:

49. Maximum grade of chronic GVHD: (according to best clinical judgment)
   - □ Mild
   - ☒ Moderate
   - □ Severe
   - □ Unknown

50. Specify if chronic GVHD was limited or extensive:
   - □ Limited – localized skin involvement and/or hepatic dysfunction due to chronic GVHD
   - ☒ Extensive – one or more of the following:
     - generalized skin involvement; or,
     - liver histology showing chronic aggressive hepatitis, bridging necrosis or cirrhosis; or,
     - involvement of eye: Schirmer’s test with < 5 mm wetting; or
     - involvement of minor salivary glands or oral mucosa demonstrated on labial biopsy; or
     - involvement of any other target organ

51. Date of maximum grade of chronic GVHD: ___ ___ ___ ___ - ___ ___ - ___ ___

* Check boxes of individual signs/symptoms retained
Case #3

- A 48 y/o woman with MDS has a mismatched unrelated donor peripheral blood transplant using busulfan and Cytoxan
- On day +276 she notes dry eyes and a sensitive mouth. The physician note says that this could be chronic GVHD, and prescribes topical cyclosporine for her eyes and dexamethasone for her mouth. In addition, she is using eyedrops every 3-4 hours.

Does she have chronic GVHD?
## Diagnostic vs. Distinctive

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Case #3

- On day +365 sclerosis (skin thickening) around her waistline and lower leg is seen. Dry eyes worsen and she uses eyedrops every 2 hours. Prednisone is started. In retrospect, she first noticed problems with her skin 2 months before.

- On day +400 she reports difficulty swallowing. EGD shows an esophageal web which is dilated. She is scheduled to start ECP

- Does she have chronic GVHD? What is the date of diagnosis?
## Diagnostic vs. Distinct

<table>
<thead>
<tr>
<th>Organ</th>
<th>Diagnostic</th>
<th>Distinctive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>poikiloderma, <strong>sclerosis</strong>, morphea, lichen-planus, lichen-sclerosis</td>
<td>depigmentation, papulo-squamous</td>
</tr>
<tr>
<td>Nails</td>
<td>GVHD onset day 365 (not 2 mo before when symptoms developed)</td>
<td>dystrophy, ridging, onycholysis</td>
</tr>
<tr>
<td>Mouth</td>
<td>lichen planus</td>
<td>xerostomia, mucoceles, ulcers, atrophy</td>
</tr>
<tr>
<td>Eyes</td>
<td>-</td>
<td>new onset dry eyes, keratoconjunctivitis sicca</td>
</tr>
<tr>
<td>Genitalia</td>
<td>lichen planus</td>
<td>erosions, fissures, ulcers</td>
</tr>
<tr>
<td>GI tract</td>
<td><strong>esophageal web</strong> or strictures</td>
<td>-</td>
</tr>
<tr>
<td>Liver</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Lung</td>
<td>bronchiolitis obliterans (bx proven)</td>
<td>air trapping and bronchiectasis</td>
</tr>
<tr>
<td>Musculo-</td>
<td>fasciitis, contractures</td>
<td>myositis, polymyositis</td>
</tr>
<tr>
<td>Skeletal</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Skin:

1. Skin

   X Yes – *Go to question 253*
   
   □ No – *Go to question 261*

2. Score percent BSA involved:

   □ Score 0 – No BSA involved, no sclerotic features
   
   □ Score 1 – 1-18% BSA
   
   □ Score 2 – 19-50% BSA, or superficial sclerotic features “not hidebound” (able to pinch)
   
   X Score 3 - >50% BSA, deep sclerotic features, hidebound, impaired mobility, or ulceration

3. Skin features score:

   □ No sclerotic features
   
   □ Superficial sclerotic features “not hidebound” (able to pinch)
   
   X Deep sclerotic features, hidebound (unable to pinch), impaired mobility, or ulceration
Dry eyes worsen and she uses eyedrops every 2 hours

14. Eyes score
   - Score 0 – No symptoms
   - Score 1 – Mild dry eye symptoms not affecting ADL (requirement of lubricant eye drops ≤ 3x per day)
   - Score 2 – Moderate dry eye symptoms partially affecting ADL (requiring lubricant eye drops >3x per day or punctal plugs), without new vision impairment due to keratoconjunctivitis sicca (KCS)
     - Score 2 – Moderate dry eye symptoms partially affecting ADL (requiring lubricant eye drops >3x per day or punctal plugs), without new vision impairment due to keratoconjunctivitis sicca (KCS)
   - Score 3 – Severe dry eye symptoms significantly affecting ADL (special eyewear to relieve pain) OR unable to work because of ocular symptoms OR loss of vision due to keratoconjunctivitis sicca (KCS)

15. Keratoconjunctivitis sicca (KCS) confirmed by ophthalmologist?
   - Yes
   - No
   - Not done
“she reports difficulty swallowing. EGD shows an esophageal web which is dilated”

Specify if any GI abnormalities were present, but explained entirely by non-GVHD causes:

20. Abnormality present but explained entirely by non-GVHD documented cause
   □ Yes – Go to question 274
   □ No – Go to question 275

21. Specify cause: ____________________________

   □ Y/N
   □ Esophageal web
   □ Dysphagia
   □ Anorexia
   □ N/V/D
   □ Weight loss > 5%
   □ Failure to thrive
Joints and fascia

40. Joints and fascia

☑ Yes – Go to question 294
☐ No – Go to question 297

41. Joints and fascia score

☐ Score 0 – No symptoms
☑ Score 1 – Mild tightness of arms or legs, normal or mild decreased range of motion (ROM) AND not affecting ADL
☐ Score 2 – Tightness of arms or legs OR joint contractures, erythema thought due to fasciitis, moderate decrease ROM AND mild to moderate limitation of ADL
☐ Score 3 – Contractures WITH significant decrease ROM AND significant limitation of ADL (e.g. unable to tie shoes, button shirts, dress self, etc.)
Maximum grade of chronic GVHD since the date of last report:

49. Maximum grade of chronic GVHD: (according to best clinical judgment)
   □ Mild
   □ Moderate
   ✥ Severe
   □ Unknown

50. Specify if chronic GVHD was limited or extensive:
   □ Limited – localized skin involvement and/or hepatic dysfunction due to chronic GVHD
   ✥ Extensive – one or more of the following:
       – generalized skin involvement; or,
       – liver histology showing chronic aggressive hepatitis, bridging necrosis or cirrhosis; or,
       – involvement of eye: Schirmer’s test with < 5 mm wetting; or
       – involvement of minor salivary glands or oral mucosa demonstrated on labial biopsy; or
       – involvement of any other target organ

51. Date of maximum grade of chronic GVHD: ___ ___ ___ ___ - ___ ___ - ___ ___

* Check boxes of individual signs/symptoms retained
Case #4

• A 26 y/o man 8 mos post HCT is seen urgently for diarrhea. You notice oral lichen planus. He also reports a 2 lb weight loss and shortness of breath when walking up one flight of stairs. Stool studies show norovirus. Workup shows bronchiolitis obliterans with an FEV1% predicted of 45% and FEV1/FVC=0.5

• Two weeks later he reports worsening shortness of breath when walking on flat ground and is found to have a pulmonary embolus

How would you score his chronic GVHD?
You notice oral lichen planus

8. Mouth
   □ Yes
   □ No

9. Mouth score:
   □ Score 0 – No symptoms
   □ Score 1 – Mild symptoms with disease signs but not limiting oral intake significantly
   □ Score 2 – Moderate symptoms with disease signs with partial limitation of oral intake
   □ Score 3 – Severe symptoms with disease signs on examination with major limitation of oral intake

10. Lichen planus-like features
    □ Yes
    □ No

Specify if any mouth abnormalities were present, but explained entirely by non-GVHD causes:

11. Abnormality present but explained entirely by non-GVHD documented cause
    □ Yes – Go to question 265
    □ No – Go to question 266

12. Specify cause: ______________________________
18. Gastrointestinal (GI) tract
   - Yes – Go to question 272
   - No – Go to question 283

19. Gastrointestinal (GI) tract score
   - Score 0 – No symptoms
   - Score 1 – Symptoms without significant weight loss (<5%)
   - Score 2 – Symptoms associated with mild to moderate weight loss (5-15%) OR moderate diarrhea without significant interference with daily living
   - Score 3 – Symptoms associated with significant weight loss (>15%), requires nutritional supplementation for most calorie needs OR esophageal dilation OR severe diarrhea with significant interference with daily living

Specify if any GI abnormalities were present, but explained entirely by non-GVHD causes:

20. Abnormality present but explained entirely by non-GVHD documented cause
   - Yes – Go to question 274
   - No – Go to question 275

21. Specify cause: norovirus

“diarrhea….2 lb weight loss...norovirus”
Lungs

34. Lungs
   □ Yes – Go to question 288
   □ No – Go to question 293

35. Lung score
   □ Score 0 – No symptoms
   □ Score 1 – Mild symptoms (shortness of breath after climbing one flight of steps)
   X Score 2 – Moderate symptoms (shortness of breath after walking on flat ground)
   □ Score 3 – Severe symptoms (shortness of breath at rest; requiring oxygen)

36. Were pulmonary function tests performed?
   □ Yes – Go to question 290
   □ No – Go to question 291

37. Specify FEV1 percent: 45 %
Summary

• New CRFs
  – Acute GVHD section minimally changed
  – Chronic GVHD section significantly different
• New cGVHD questions based on the 2014 NIH consensus conference
  – Allow better understanding of organ severity and overall prognosis
  – Likely to have difficulty finding information in medical records