(Chronic) Graft Versus Host Disease: When the transplant is just the beginning of the journey

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Disclosure

- No relevant conflict of interest to disclose
Spectrum of GVHD: Before NIH Consensus 2005

- **Old day:**
  - Acute before day +100
  - Chronic after day +100
  - Arbitrary

- **Current:**
  - Reduced intensity conditioning regimens
  - Symptoms defined

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Day 0
Graft infused

Day 100

Classic ACUTE GVHD

Classical CHRONIC GVHD
Spectrum of GVHD: After NIH Consensus 2005

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  - Acute before day +100
  - Chronic after day +100
  - Arbitrary

- **Current:**
  - Reduced intensity conditioning regimens
  - Symptoms defined

Lee SJ. Blood. 2017 Jan 5;129(1):30-37
Spectrum of GVHD

- **Acute GVHD**: Rash, GI, Liver
- **Chronic GVHD**: Skin, Eyes, Mouth, GI, Liver, Musculoskeletal, Lungs, GU

Alloreactivity → Immunodeficiency → Autoimmunity

- **Classic acute**
- **Late acute**: Chronic overlap
- **Classic chronic**

Day 0 → 50 → 100 → 180 → 1 Yr → 2 Yr → 3 Yr → 5 Yr

Activity (Inflammation) → Injury → Repair → Damage (Fibrosis)
Chronic GVHD

- Multi-organ
- Autoimmune
- Sclerosis
- Fibrosis

Ocular sicca
Oral ulcers
Nail dystrophy
Skin sclerosis
Deep sclerosis
Bronchiolitis obliterans
Loss of bile ducts
Fasciitis
Skin ulcers
Chronic Graft versus Host Diseases

- Major barrier to an otherwise successful HSCT
- Incidence: 30-70% of patients who have undergone allo HSCT develop cGVHD
- Onset: As early as 2 months and as late as 7 years after HCT, although onset at >1 year from HCT occurs in <10% of cases
- Patients with cGVHD have reduced QoL & increased risk of morbidity and mortality
- Resembles autoimmune disease

### Risk factors for development of chronic GVHD

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Description</th>
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<tbody>
<tr>
<td>Prior acute GVHD</td>
<td>Older age of recipient</td>
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<tr>
<td>Peripheral blood stem cell graft</td>
<td>Diagnosis of chronic myeloid leukemia</td>
</tr>
<tr>
<td>Female donor to male host</td>
<td>HLA disparity between recipient and donor</td>
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</tbody>
</table>

Incidence of chronic GVHD

- 1995-1999 (n=10444)
- 2000-2003 (n=6573)
- 2004-2007 (n=6711)

Distribution of cGVHD by organ

- Dermal: 80%
- Oral: 75%
- Hepatic: 75%
- Infection: 60%
- Pulmo: 10%
- GI: 12%
- Wt Loss: 18%
- Myofas: 10%
- Contract: 5%
- Esoph: 5%
- Ocular: 10%
- Serosal: 1%
Pathogenesis of chronic graft versus host diseases

- Complex
- Continuum from aGVHD
- T cells
- B cells
- Myo-fibroblast
- Cytokines
Phases of chronic GVHD

- **Phase I**: Acute inflammation & Tissue injury
  - Innate immunity
    - Cytokines
    - TLR agonists
    - Neutrophils
    - Platelet
    - Vascular
    - Inflammation

- **Phase 2**: Chronic inflammation & dysregulated immunity
  - Adaptive immunity
    - Thymic injury and dysfunction
    - T cells
    - B cells
    - NK cells
    - APC
    - Regulatory Cells
      - Treg, Breg
      - Tr1

- **Phase 3**: Aberrant tissue repair & fibrosis
  - Innate & adaptive

- Divide into 3 phases
  - Inflammation
  - Dysregulation
  - Fibrosis

Clinical presentation according to cGVHD phases

<table>
<thead>
<tr>
<th>Manifestations</th>
<th>Inflammatory (Phase 1)</th>
<th>Immune Dysregulatory (Phase 2)</th>
<th>Fibrotic/Sclerotic (Phase 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucocutaneous</td>
<td>Oral lichen planus-like erythema/ulcers; erythematosus skin rashes; conjunctival erythema; genital/vaginal erythema, lichen planus-like or ulcerations</td>
<td>Chronically infected ulcers</td>
<td>Salivary dysfunction; limitation of mouth opening; lacrimal dysfunction; cutaneous sclerosis; labial agglutination; vaginal stenosis; phimosis</td>
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<tr>
<td>Lung</td>
<td>Pulmonary inflammation (clinical or subclinical)</td>
<td>Chronic lymphocytic bronchiolitis; chronic interstitial pneumonitis; recurrent sinopulmonary infections</td>
<td>Bronchiolitis obliterans syndrome; interstitial fibrosis</td>
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<tr>
<td>Myofascial</td>
<td>Extremity edema, fasciitis</td>
<td>Myositis; myasthenia gravis; chronic inflammatory demyelinating polyneuropathy</td>
<td>Subcutaneous deep fibrosis; joint contractures</td>
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<tr>
<td>Liver</td>
<td>Cholestatic or hepatitic GVHD</td>
<td>Autoimmune hepatitis</td>
<td>Advanced liver GVHD with periportal fibrosis, ductopenia</td>
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<tr>
<td>Gastrointestinal Hematopoietic system</td>
<td>Colitis, epithelial cell injury Neutrophilia; elevated platelet counts; anemia of chronic disease</td>
<td>Chronic colitis, malabsorption Lymphopenia; immune neutropenia or thrombocytopenia; eosinophilia; autoimmune hemolytic anemia</td>
<td>Esophageal web, stricture formation Marrow failure/fibrosis</td>
</tr>
<tr>
<td>Immune system</td>
<td>Acute-phase reactants</td>
<td>Infections, especially with encapsulated bacteria; hypogammaglobulinemia or hypergammaglobulinemia; autoimmune phenomena (renal, thyroid, polyserositis, other)</td>
<td>Functional asplenia; opportunistic infections</td>
</tr>
</tbody>
</table>

Signs and Symptoms of Chronic Graft Versus Host Diseases

Diagnostic: Sufficient to Establish the Diagnosis of chronic GVHD

Distinctive: Seen in chronic GVHD, but not Sufficient Alone to Establish a Diagnosis

Other Features or Unclassified Entities

Common: Seen with Both Acute and Chronic GVHD

Lee S. Blood. 2017 Jan 5; 129(1): 30–7
<table>
<thead>
<tr>
<th>Organ or Site</th>
<th>Diagnostic (Sufficient to Establish the Diagnosis of chronic GVHD)</th>
<th>Distinctive* (Seen in chronic GVHD, but Insufficient Alone to Establish a Diagnosis)</th>
<th>Other Features or Unclassified Entities†</th>
<th>Common‡ (Seen with Both Acute and chronic GVHD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>Poikiloderma—like features</td>
<td>Depigmentation</td>
<td>Sweat impairment</td>
<td>Erythema</td>
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<tr>
<td></td>
<td>Lichen planus—like features</td>
<td>Papulosquamous lesions</td>
<td>Ichthyosis</td>
<td>Maculopapular rash</td>
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<td>Sclerotic features Morphea-like features</td>
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<td>Keratosis pilaris</td>
<td>Pruritus</td>
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<td>Lichen sclerosus—like features</td>
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<td>Hypopigmentation</td>
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<td>Hyperpigmentation</td>
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<td>Nails</td>
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<td>Dystrophy</td>
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<td>Longitudinal ridging, splitting or brittle features</td>
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<td></td>
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<td>Onycholysis</td>
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<td>Pterygium unguis</td>
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<td>Nail loss (usually symmetric, affects most nails)</td>
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<td>Scalp and body hair</td>
<td>New onset of scarring or nonscarring scalp alopecia (after recovery from chemoradiotherapy)</td>
<td>Thinning scalp hair, typically patchy, coarse or dull (not explained by endocrine or other causes)</td>
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<td>Loss of body hair</td>
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<td></td>
<td>Scaling</td>
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<td>Mouth</td>
<td>Lichen planus—like changes</td>
<td>Xerostomia</td>
<td>Gingivitis</td>
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<td>Mucoceles</td>
<td>Mucositis</td>
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<td>Mucosal atrophy</td>
<td>Erythema</td>
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<td>Ulcers</td>
<td>Pain</td>
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<td></td>
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<td>Pseudomembranes</td>
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<td>Eyes</td>
<td>New onset dry, gritty, or painful eyes</td>
<td>Photophobia</td>
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<td>Cicatricial conjunctivitis</td>
<td>Periorbital hyperpigmentation</td>
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<td>KCS</td>
<td>Blepharitis (erythema of the eyelids with edema)</td>
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<td>Confluent areas of punctate keratopathy</td>
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<tr>
<td>Organ or Site</td>
<td>Diagnostic (Sufficient to Establish the Diagnosis of chronic GVHD)</td>
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<tr>
<td>Genitalia</td>
<td>Lichen planus—like features</td>
<td>Erosions</td>
<td>Exocrine pancreatic insufficiency</td>
<td>Anorexia</td>
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<tr>
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<td>Lichen sclerosus—like features</td>
<td>Fissures</td>
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<td>Nausea</td>
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<td>Vaginal scarring or clitoral/labial agglutination</td>
<td>Ulcers</td>
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<td>Vomiting</td>
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<td>Phimosis or urethral/meatus scarring or stenosis</td>
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<td>Diarrhea</td>
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<td>Esophageal web</td>
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<td>Weight loss</td>
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<td>Strictures or stenosis in the upper to mid third of the esophagus</td>
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<td>Failure to thrive (infants and children</td>
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<td>Total bilirubin, alkaline phosphatase &gt; 2 × upper limit of normal</td>
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<td>Liver</td>
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<td>ALT &gt; 2 × upper limit of normal</td>
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<tr>
<td>Lung</td>
<td>Bronchiolitis obliterans diagnosed with lung biopsy</td>
<td>Air trapping and bronchiectasis on chest CT</td>
<td>Cryptogenic organizing pneumonia</td>
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<td></td>
<td>BOS§</td>
<td></td>
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<td>Restrictive lung disease†</td>
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<td>Muscles, fascia, joints</td>
<td>Fascitis</td>
<td>Myositis or polymyositis‡</td>
<td>Edema</td>
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<td>Joint stiffness or contractures secondary to fasciitis or sclerosis</td>
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<td>Muscle cramps</td>
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<td>Hematopoietic and Immune</td>
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<td>Articulargia or arthritis</td>
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<td>Thrombocytopenia</td>
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<td>Eosinophilia</td>
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<td>Lymphopenia</td>
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<td>Hypo- or hyper-gammaglobulinemia</td>
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<td>Autoantibodies (AIHA, ITP)</td>
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<td>Raynaud's phenomenon</td>
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<td>Other</td>
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<td>Pericardial or pleural effusions</td>
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<td>Ascites</td>
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<td>Peripheral neuropathy</td>
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<td>Nephrotic syndrome</td>
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<td>Myasthenia gravis</td>
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<td>Cardiac conduction abnormality or cardiomyopathy</td>
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</tbody>
</table>
Diagnostic Features of chronic GVHD: Skin

Poikiloderma
Diagnostic Features of chronic GVHD: Soft tissue

- Subcutaneous fibrosis
- Ripping & Dimpling
- Fasciitis
- Depigmentation
- Nail Change
- Joint Stiffness
Chronic GVHD of oral cavity

Role of biopsy: diagnostic or non-specific for cGVHD mostly done for DDx
cGVHD of pulmonary system

- Bronchiolitis obliterans w/o organizing pneumonia
- Interstitial lung disease
- Pleural diseases
Bronchiolitis obliterans

- **Criteria diagnosis:**
  - FEV1<75% predicted or decline > 10%
  - Sign of obstruction:
    - FEV1/FVC < 0.7
    - RV>120% and HR CT inspiratory and expiratory cuts (air trapping, small airway thickening or bronchiectasis)
  - No evidence of active respiratory infection
  - >1 distinctive cGVHD manifestation in a separate organ

- Most patients with prior diagnosis of GvHD prior onset of BOS
- Mostly occurring within 18 months after HSCT
- Incidence likely to be underestimated
- Poor prognosis: 2-yr OS 45%, 5-yr OS 13%
- Often insidious onset. Might be misinterpreted or starts as protracted viral infection of the respiratory tract
- Assess for subtle signs: Chronic dry cough, exercise intolerance, decreased activity
Chronic GVHD of ocular and adnexa

- Dry eyes: Irritating – sand paper like, inability to tolerate light or wind
- Painful eyes
- Corneal ulcers due to very severe dry eyes

Other systemic involvement by cGVHD

- **Joint/Muscle cGVHD**
  - Up to 50% patients
  - Fasciitis: Joint ROM limitation often in the continuum of skin
  - Myositis: Weakness with or without myalgia, symmetrical proximal muscles
    - Check serum CPK
  - Extremity edema: Generally non-pitting
  - Muscle atrophy
  - Muscle cramping

- **Hepatic cGVHD**
  - 50-70% of patients will have involvement of the liver
  - Mimic cholestasis
  - Abnormal LFTs: Elevation ALP, AST, ALT, and bilirubin
  - Can mimic other hepatic diseases
  - Rule out other potential causative factors

- **GI cGVHD**
  - Approximately 30% of patients
  - Upper vs Lower gut
  - Esophageal involvement leading to esophageal web and tapering of esophagus
    - Choking on pills/food, weight loss, painful ulcers
  - Small and large bowel involvement
    - Loose stools, malabsorption
    - Gastric pain, gastric bloating
    - Anorexia, nausea, vomiting, weight loss
  - Failure to thrive

Chronic Graft versus Host Assessment

Four Part Process

1. Not acute GVHD
2. Diagnostic or distinctive
3. Rule out other diseases

Organ Score

“As is”
Based on symptoms/signs, function, therapy
May not score if other cause obvious

Global Score

Prognosis
Therapeutic decision
Quality of life and function

Cumulative Data Completion (%)

0 12 52 91 100

Flowers ME and Martin PJ. Blood. 2015 Jan 22;125(4):606-15
## Severity assessment

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>▪ 1 or 2 organs or sites (except lung) with score 1</td>
</tr>
</tbody>
</table>
| Moderate | ▪ 3 or more organs with score 1  
            ▪ At least 1 organ or site with score 2  
            ▪ Lung score 1 (FEV1 60-79% or dyspnea with stairs) |
| Severe  | ▪ At least 1 organ or site with score 3  
            ▪ Lung score 2 (FEV1 40-59% or dyspnea walking on flat ground) |

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<table>
<thead>
<tr>
<th>PERFORMANCE SCORE</th>
<th>cGVHD assessment tool</th>
<th>SKIN</th>
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<tbody>
<tr>
<td><strong>SCORE 0</strong></td>
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<td><strong>SCORE 1</strong></td>
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<td><strong>SCORE 2</strong></td>
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<td><strong>SCORE 3</strong></td>
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<td><strong>KPS ECOG LPS</strong></td>
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<td><strong>SCORE 0</strong></td>
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Joint assessment & Skin assessment

NIH Assessment uses
Rule of 9s
8 body areas

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<table>
<thead>
<tr>
<th>Performance Score</th>
<th>Score 0</th>
<th>Score 1</th>
<th>Score 2</th>
<th>Score 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin Score % BSA</td>
<td>No BSA involved</td>
<td>1-18% BSA</td>
<td>19-50% BSA</td>
<td>&gt;50% BSA</td>
</tr>
<tr>
<td>Skin Features Score</td>
<td>No sclerotic features</td>
<td></td>
<td>Superficial sclerotic features &quot;not hidebound&quot; (able to pinch)</td>
<td>Deep sclerotic features &quot;hidebound&quot; (unable to pinch)</td>
</tr>
<tr>
<td>Mouth</td>
<td>No symptoms</td>
<td>Mild symptoms not limiting oral intake</td>
<td>Moderate symptoms with partial limitation to oral intake</td>
<td>Severe symptoms with major major limitation to oral intake</td>
</tr>
<tr>
<td>Eyes</td>
<td>No symptoms</td>
<td>Mild dry eye symptoms</td>
<td>Moderate dry eye symptoms</td>
<td>Severe dry eye symptoms</td>
</tr>
<tr>
<td>GI Tract</td>
<td>No symptoms</td>
<td>Symptoms without significant weight loss (&lt;5%)</td>
<td>Symptoms with mild to moderate weight loss (5-15%)</td>
<td>Symptoms with significant weight loss (&gt;15%)</td>
</tr>
<tr>
<td>Liver</td>
<td>Normal bilirubin and ALT/AT &lt;3xULN</td>
<td>Normal bilirubin and ALT &gt;3 &gt;3 to 5xULN</td>
<td>Elevated total I bilirubin &lt;3mg/dL or ALT &gt;5xULN</td>
<td>Elevated total bilirubin &gt;3mg</td>
</tr>
<tr>
<td>Lungs</td>
<td>No symptoms</td>
<td>Shortness of breath after climbing stairs</td>
<td>Shortness of breath after walking on flat ground</td>
<td>Shortness of breath requiring requiring oxygen</td>
</tr>
<tr>
<td>Joints and Fascia</td>
<td>No symptoms</td>
<td>Mild tightness of arms or legs</td>
<td>Tightness of arms or legs or joint contractures</td>
<td>Contractures with significant significant decrease in ROM</td>
</tr>
<tr>
<td>Genital Tract</td>
<td>No symptoms</td>
<td>Mild signs without discomfort on exam</td>
<td>Moderate signs and may have discomfort on exam</td>
<td>Severe signs with or without without symptoms</td>
</tr>
</tbody>
</table>

Lee SJ. Blood. 2017 Jan 5;129(1):30-37
Prognostic factors of cGVHD

- Thrombocytopenia < 100,000/ul
- Clinical score: NIH severity index, CIBMTR cGVHD score
- Lymphocyte & Eosinophil counts
- Extensive skin involvement, lung involvement, GI- involvement (diarrhea)
- Type of onset (progressive and overlap): Overlap & Late acute worse
Treatment of chronic graft versus host diseases

- GVHD specific treatment
  - Local/Topical treatment
  - Systemic treatment
- Supportive/Symptomatic treatment
- Lifestyle modification
Mechanistic approaches for cGVHD

**Stem cell graft engineering**
- ATG
- Post Tx Cyc
- CD34 selection
- Ex vivo pan-T cell depletion
- Ex vivo selective T cell depletion
- Donor IL-2 therapy

**Inhibit T cell signaling**
- ITK inhibition - Ibrutinib
- JAK ½ inhibition - ruxolitinib
- ROCK2 inhibition – KD025
- Bortezomib

**Adoptive Treg Therapy**
- Purified donor Treg
- Ex vivo expanded Treg
- Antigen-specific Treg

**Inhibit B cell signaling**
- BTK inhibition – ibrutinib
- SYK inhibition – fostamatinib

**B cell depletion in vivo**
- Rituximab
- Ofatumumab
- Obinutuzumab

**Allo & Auto-reactive B cells**

**CD4+ FoxP3+ Treg cells**

**Treg-sparing therapy**
- Sirolimus
- Mycophenolate mofetil
- Ruxolitinib
- Bortezomib

**In vivo Treg expansion**
- ECP
- Low-dose IL-2

**Cutler CS et al. Blood. 2017 Jan 5;129(1):22-2**
Treatment of Mild Chronic GVHD

- Topical immunosuppressive agents alone
  - Recommend close follow-up to screen for disease progression
  - Preferred in patients at high risk for disease relapse (to avoid abrogation of GvL effect)
  - Preferred in pediatric patients
    - Corticosteroids have deleterious effects on growing child
    - On the other hand, non-malignant indications for transplant do not benefit from GvL effect
  - Treat until symptoms improve and taper as able

- In areas where topical agents have no effect (liver, fascia), low dose systemic corticosteroids is preferred. No evidence for or against this recommendation of lower dose
Treatment of Moderate to severe cGVHD

- Severe cGVHD is associated with increased mortality
  - In general, systemic corticosteroids are recommended first line therapy, established from trials in the 1980s
  - Clinical trials that suggest benefit of combination therapy (i.e. steroids + non-steroidal option) as first line therapy are lacking

- No randomized trials comparing varying doses of corticosteroids
  - Expert recommendation: 1mg/kg/day for moderate to severe symptoms
  - Maintain this dose x 2 weeks
  - Then taper to 1mg/kg every other day over 2 months, if symptoms remain stable
  - Then taper every 10-20% per month

Natural course & Treatment of cGVHD

- Steroid remains the mainstay of cGVHD treatment
- Tapering to minimum dose sufficient to control cGvHD activity
- Steroid sparing: CNI
- Patients usually on immunosuppressants for about 3-5 years

Flowers ME and Martin PJ. Blood. 2015 Jan 22;125(4):606-15
Failure-free survival after cGVHD treatment

- 4 risk factors associated with initial Rx failure:
  - Time interval <12 months from HCT to initial Rx
  - Age ≥ 60 years
  - Severe involvement of the GI tract, liver or lungs
  - Karnofsky score <80% at initial Rx

Second line treatment of cGHVD

- When to start second line treatment:
  - Worsening manifestations
  - Lack of improvement after at least 1 month of treatment
  - Inability to decrease the dose of prednisone to <1mg/kg/d within 2 months
  - (New manifestations in a new organ)

- Choice for second line treatment:
  - Consider availability, costs, co-morbidities
  - “Try and error” – wait for effect for 3 months

Flower ME and Martin PJ. Blood. 2015 Jan 22;125(4):606-15
Plausible targets of chronic graft vs host diseases

- How to choose 2nd line treatment for cGVHD
  - Clinical efficacy
  - Toxicity profile
  - Mechanism of action
  - Mode of delivery
  - Patient compliance
  - Cost

Non-lymphocyte targets:
- Hedgehog inhibitors
- Neutrophil elastase inhibitors

Block T activation & cytokine-induced lineages:
- JAK inhibitors
  - (Ruxolitinib, Baricitinib)
- Proteasome inhibitors
- CTLA4-Ig fusion protein

Expand Tregs:
- IL-2

Block trafficking of effectors from LN:
- Ponesimod (S1P1R)

Expand thymopoiesis:
- KGF
- IGF
- IL-7
- Steroid blockade

Deplete B cells:
- Rituximab
- Block B activation:
  - Belimumab (BAFF)
  - Fostamatinib (Syk)
  - Cerdulatinib (Syk)
  - Ibrutinib (BTK)

1. APC activated, move to LN
2. APC activate Th1, Th17, TfH T cells
3. TfH support Ab-producing B cells
4. T & B-cells infiltrate tissue
5. Ab deposition and cytotoxic attack
## Second line treatment of cGVHD

<table>
<thead>
<tr>
<th>Treatment Modalities</th>
<th>%ORR</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECP</td>
<td>65-70</td>
<td>70-78% at 1 yr</td>
</tr>
<tr>
<td>Rituximab</td>
<td>66-86</td>
<td>72% at 1 year</td>
</tr>
<tr>
<td>Imatinib</td>
<td>22-79</td>
<td>75-84% at 1.5 year</td>
</tr>
<tr>
<td>Pentostatin</td>
<td>53-56</td>
<td>34-60% at 1-3 year</td>
</tr>
<tr>
<td>Mesenchymal stem cell</td>
<td>50-74</td>
<td>78% at 2 year</td>
</tr>
<tr>
<td>Mycophenolate mofetil</td>
<td>26-64</td>
<td>67-96% at 1 year</td>
</tr>
<tr>
<td>mTOR inhibitor</td>
<td>76</td>
<td>72% at 3 year</td>
</tr>
<tr>
<td>Interleukin-2</td>
<td>52</td>
<td>Not reported</td>
</tr>
</tbody>
</table>

### Other therapies:
- Calcineurin inhibitor
- High dose MTP
- Methotrexate
- Thalidomide
- Hydroxychloroquine
- Clofazimine
- Thoraco-abdominal XRT
- Alefacept
- Infliximab
- Etanercept
- JAK-2 inhibitor

Flower ME and Martin PJ. Blood. 2015 Jan 22;125(4):606-15
Outcome after 1\textsuperscript{st} line cGVHD Rx

- Increased risks of Rx failure after 1\textsuperscript{st} line treatment:
  - High-risk disease at transplant
  - Lower GI involvement at 2\textsuperscript{nd} line treatment
  - Severe NIH global score at second-line treatment
Bruton tyrosine kinase inhibitor: Ibrutinib

- BCR signaling is required for tumor expansion and proliferation
- BTK: Essential element of the BCR signaling pathway
- Inhibitors of BTK block BCR signaling and induce apoptosis
Ibrutinib in steroid non-responsive cGVHD

80% of patients ≥ 2 involved organs at baseline responded in ≥ 2 organs
56% (5/9) of patients ≥ 3 involved organs at baseline responded in ≥ 3 organs
62% - steroid dose < 0.15 mkd
5 pts able to discontinue all steroid treatment

Supportive and ancillary treatment for cGVHD

- Mainstay of cGVHD treatment
- Optimize nutrition, exercise, symptom management, drug interactions, infection prophylaxis, health maintenance including disease prevention and management of comorbidities
- Patient education and care coordination
- Organ system approach
Conclusion

- Chronic GVHD common after transplant and major barrier to health after relapsed mortality
- Pleomorphic, autoimmune disease with many manifestations
- Diagnosis is clinical with assistance of histology
- Important to grade severity of disease to determine type of therapy
  - Site-directed treatment
  - Systemic
- Systemic therapy must weigh risks / benefits of intervention
  - Corticosteroids are first-line therapy
  - Multiple 2ndline options, with varying advantages and disadvantages
- Chronic syndrome – cure may not always be possible, but improvement of quality of life can be achieved