

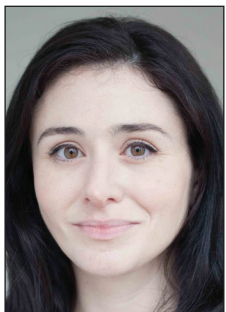
## boards fodder

### Graft-versus-host disease (GVHD)

By Abdulhadi Jfri, MD, MSc, FRCPC, FAAD, and Rachel Meltzer, MD, MPH, FAAD



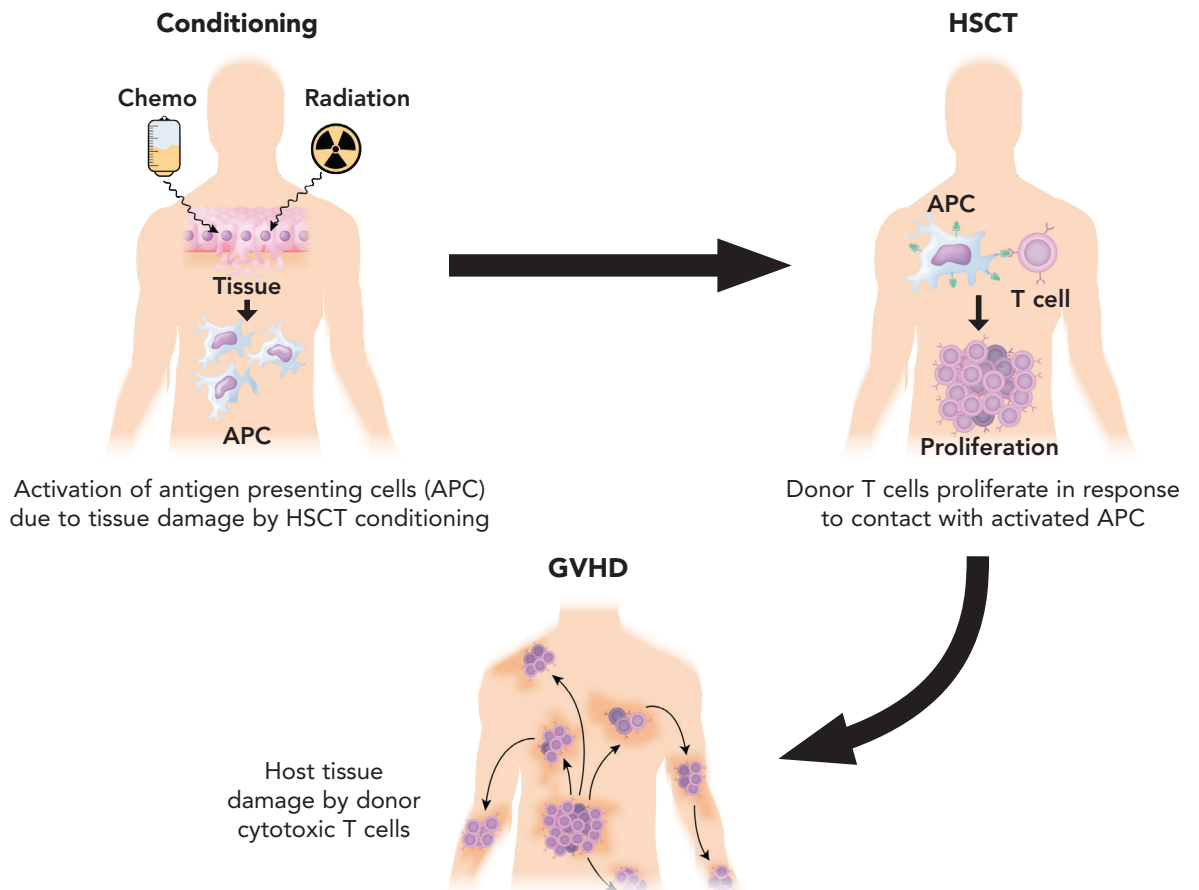
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The causes of GVHD	The risk factors for developing GVHD
<ol style="list-style-type: none"> <li>1. Allogeneic hematopoietic stem cell transplant (HSCT) (<b>most common</b>)</li> <li>2. Transfusion of non-irradiated blood to immunocompromised host.</li> <li>3. Maternal fetal transmission</li> <li>4. Solid organ transplant (intestine&gt;liver&gt;kidney&gt;heart)</li> </ol>	<ol style="list-style-type: none"> <li>1. HLA incompatibility 60-70% (<b>most important</b>)</li> <li>2. Female donor (especially multiparous) with male receipt</li> <li>3. Older age</li> <li>4. Myeloablative preconditioning regimen</li> <li>5. Stem cell source Peripheral blood &gt; bone marrow &gt; cord blood</li> </ol>
Types of HSCT	
<ul style="list-style-type: none"> <li>• <b>Auto(self)logous:</b> patient stem cells are harvested, frozen, and thawed and given back after the myeloablative preconditioning. The patient is their own donor.</li> <li>• <b>Allo(other)genic:</b> patient receives healthy stem cells from a donor to replace their own stem cells that have been destroyed by the <b>myeloablative preconditioning</b> with total body irradiation and/or alkylating agents.</li> </ul>	
The risk of developing GVHD in HSCT	The top 3 organs affected by GVHD
<ul style="list-style-type: none"> <li>• HLA-matched: 40%</li> <li>• HLA-mismatched: 60-70%</li> </ul>	<ol style="list-style-type: none"> <li>1. Skin (most common) (BSA%)</li> <li>2. Liver (bilirubin level mg/dl)</li> <li>3. GI (diarrhea volume ml/day) <ul style="list-style-type: none"> <li>• Used for staging acute GVHD</li> </ul> </li> </ol>

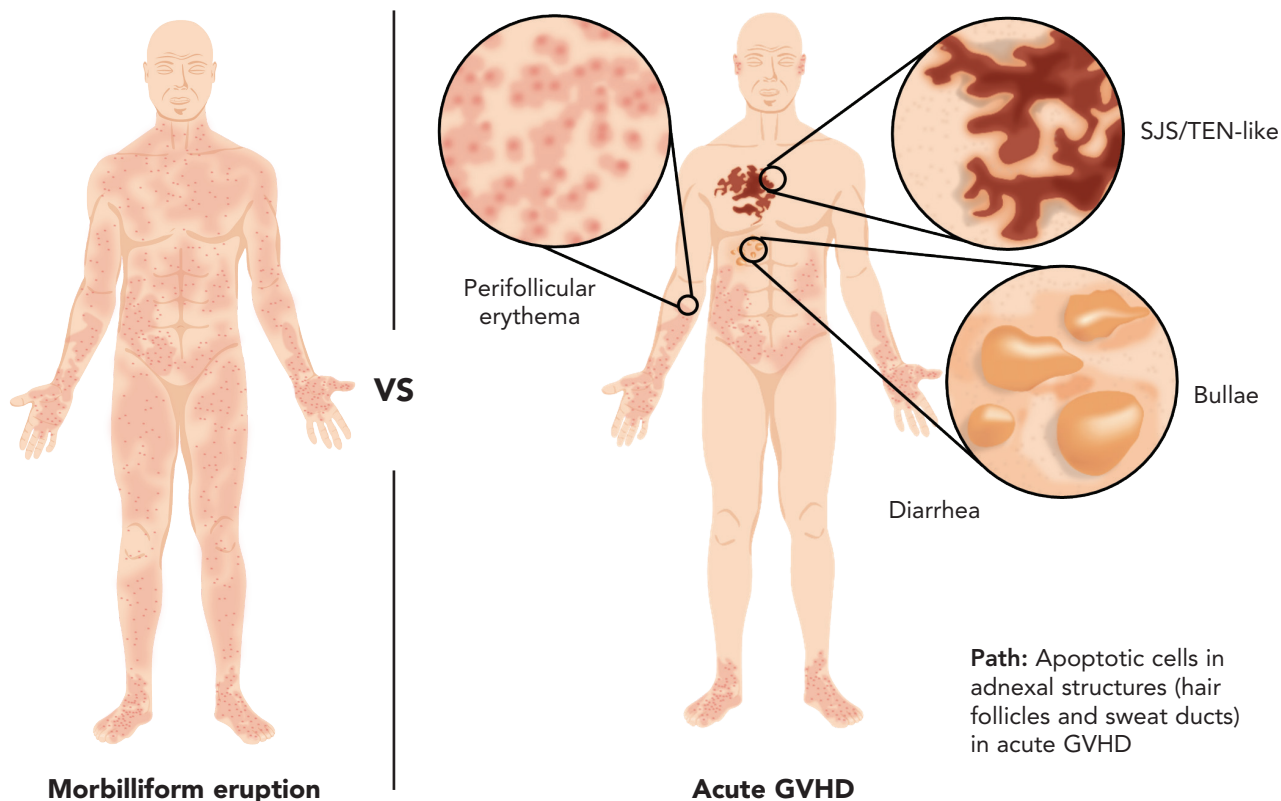
### ACUTE GVHD:



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Acute GVHD can appear morbilliform but has some distinguishing features.



Features of engraftment syndrome relative to GVHD	GVHD prophylaxis
<ol style="list-style-type: none"> <li>Occurs earlier (10-12 days) than acute GVHD</li> <li>Less likely to have diarrhea</li> <li>Fever +</li> <li>Pulmonary edema +</li> <li>Weight gain +</li> </ol>	<ul style="list-style-type: none"> <li>Methotrexate + cyclosporine or</li> <li>Methotrexate + tacrolimus</li> </ul>

### CHRONIC GVHD:

The main cellular difference between chronic and acute GVHD: Possible role of B cells in chronic GVHD

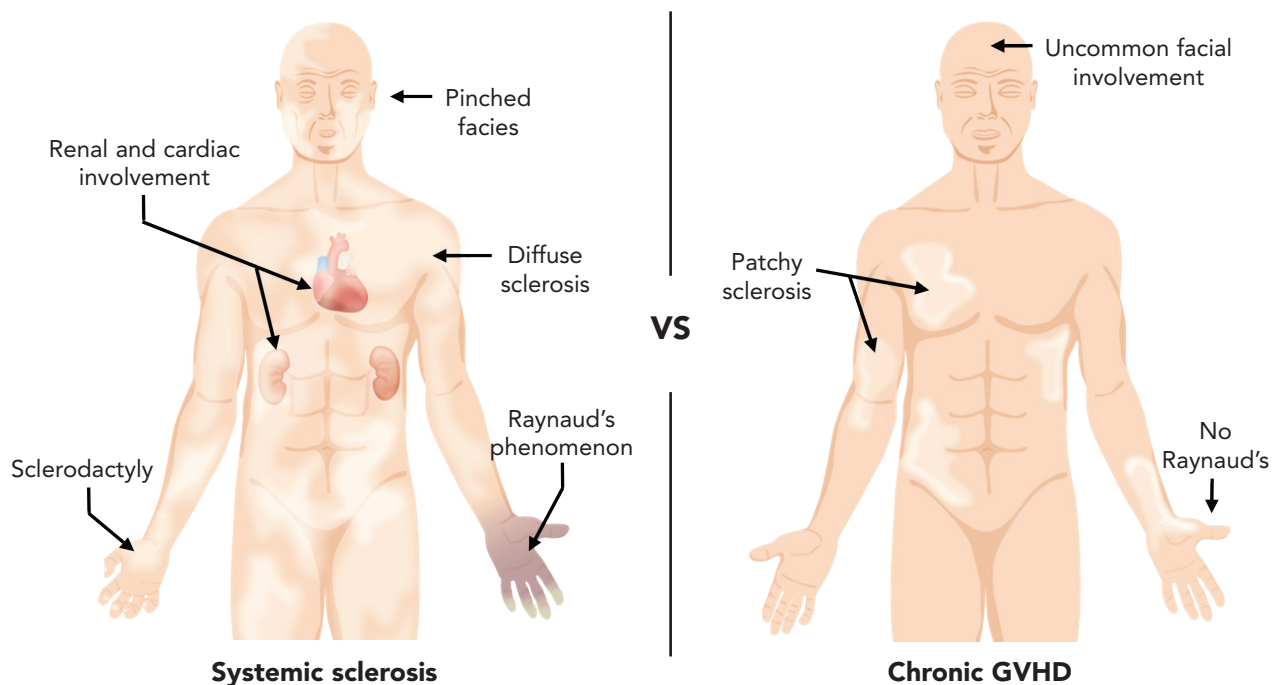
Cutaneous manifestations of chronic GVHD		
COMMON	UNCOMMON	
<ol style="list-style-type: none"> <li>Lichen planus-like</li> <li>Lichen sclerosus-like</li> <li>Morphea-like</li> <li>Scleroderma-like</li> <li>Fasciitis</li> <li>Poikiloderma</li> </ol>	<ol style="list-style-type: none"> <li>Psoriasis/psoriasiform</li> <li>SCLE-like</li> <li>PR-like</li> <li>Eczema craquelé</li> <li>Eczematous/dyshidrotic</li> <li>Ichthyosis-like</li> </ol>	<ol style="list-style-type: none"> <li>Keratosis pilaris-like follicular erythema</li> <li>Hypo/hyperpigmentation</li> <li>Vitiligo</li> <li>Angiomatous nodules</li> </ol>

The significance of autoantibodies in chronic GVHD:
<ol style="list-style-type: none"> <li>Presence of more than one antibody correlates with risk of extensive of disease.</li> <li>Autoantibodies lack specificity for GVHD and no antibody has been found to correlate with severity.</li> </ol>

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### Clinical features to differentiate systemic sclerosis from chronic GVHD



Acute versus chronic GVHD:		
	Acute GVHD	Chronic GVHD
Onset	Usually first 100 days post-transplant Can happen after 100 days → delayed acute GVHD Most commonly 4-6 weeks	Time is not essential for diagnosis 50% follow acute 50% de novo
Initial presentation	Morbilliform eruption	Sclerotic vs. non-sclerotic eruptions
Most common sites	Acral (hands, feet, ears) and upper trunk. May progress to SJS/TEN-like	Dorsal hands/feet, forearms, and trunk. Lesions can be widespread
Organs involved other than the skin	Liver (transaminitis) GI (nausea, abdominal pain, and voluminous diarrhea)	Eye (keratoconjunctivitis sicca, blepharitis, corneal erosions) Salivary glands (sicca syndrome) Lungs (bronchiolitis obliterans) Liver (transaminitis) Pancreas
Histopathology	<ul style="list-style-type: none"> <li>Vacuolar interface dermatitis with necrotic keratinocytes and lymphohistiocytic infiltrate in upper dermis with sparse perivascular infiltrate</li> <li>Apoptotic cells in <b>adnexal structures</b> - helpful to differentiate from drug eruption</li> </ul>	<ul style="list-style-type: none"> <li>Depends on the clinical phenotype</li> <li>Lichenoid/vacuolar interface dermatitis with perivascular lymphohistiocytic infiltrate, keratinocyte apoptosis, and sclerosis at different levels</li> </ul>

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Acute versus chronic GVHD:		
	Acute GVHD	Chronic GVHD
Treatment	<p><b>First line is systemic corticosteroids:</b> oral prednisone or IV methylprednisone + ongoing prophylaxis including calcineurin inhibitors (tacrolimus, cyclosporine)</p> <p>Skin-directed therapies:</p> <ol style="list-style-type: none"> <li>1. Medium-high potency topical corticosteroids</li> <li>2. Topical calcineurin inhibitors</li> <li>3. Phototherapy (PUVA, UVB, NB-UVB, UVA1)</li> </ol> <p>Others:</p> <ul style="list-style-type: none"> <li>• Ruxolitinib (JAK 1/2 inhibitor)</li> <li>• Mycophenolate mofetil</li> <li>• Extracorporeal photopheresis (ECP)</li> </ul>	<p><b>First line is systemic corticosteroids</b></p> <p>Skin directed therapies</p> <ol style="list-style-type: none"> <li>1. Medium-high potency topical corticosteroids</li> <li>2. Topical calcineurin inhibitors</li> <li>3. Phototherapy (PUVA, UVB, NB-UVB, UVA1)</li> </ol> <p>Others:</p> <ul style="list-style-type: none"> <li>• Ruxolitinib</li> <li>• Belumosodil (ROCK2 inhibitor)</li> <li>• Rituximab (Anti-CD20):</li> <li>• Ibrutinib (BTK inhibitor)</li> <li>• Hydroxychloroquine</li> <li>• Mycophenolate mofetil</li> <li>• Acitretin</li> <li>• ECP</li> </ul>
Prognosis	<p><b>Prognosis: depends on the GVHD stage</b></p> <p>In general:</p> <ul style="list-style-type: none"> <li>• 50-60% respond to steroid in 4 weeks</li> <li>• Steroid-refractory acute GVHD has 45-65% 6-month mortality rate</li> </ul>	

### References:

1. Fitzpatrick's Dermatology in General Medicine, 9th edition
2. Bologna. Dermatology, 4th edition
3. Sharon Hymes, Amin Alousi, Edward Cowen. Graft-versus-host disease: Part I. Pathogenesis and clinical manifestations of current Graft-versus-host disease. *J Am Acad Dermatol.* 2012 Apr;66(4):515.e1-18; quiz 533-4. doi: 10.1016/j.jaad.2011.11.960.
4. Sharon Hymes, Amin Alousi, Edward Cowen. Graft-versus-host disease: Part II. Management of current Graft-versus-host disease. *J Am Acad Dermatol.* 2012 Apr;66(4):535.e1-16; quiz 551-2. doi: 10.1016/j.jaad.2011.11.961.