

# Graft versus Host disease

Occurs following allogeneic stem cell transplantation, and solid organ transplants (when some lymphoid tissue gets a ride across into the new patient)

**Clinical triad of GVHD:**  
Dermatitis, Hepatitis, Enteritis

**HYPER-ACUTE:** within 7-14 days  
**ACUTE GVHD:** in the first 100 days after transplant  
**CHRONIC GVHD:** after the first 100 days

**PATHOPHYSIOLOGY:**

The **graft, containing immune cells**, is implanted into an **immunosuppressed host**;  
The cells react with the antigens of the host, and the graft attacks.

**Sites by frequency:**

Skin → liver → gut

**WHAT IS THE RISK?**

HLA-identical sibling donor = 19-66%  
HLA matched unrelated donor = 70-90%

**Clinical Picture of Symptoms:**

**20 days post transplant: ACUTE GVHD**

**THE RASH →**

Red to violaceous in colour  
First on palms of hands  
Then soles of feet  
Then cheeks, neck, ears, and upper trunk.  
Vesicles and bullae may form.

CHRONIC GVHD causes the formation of lichenoid plaques and possibly limb contractures due to skin thickening.

- a pruritic or painful rash
- generalised erythroderma
- Fever
- Diarrhea
- intestinal bleeding
- cramping abdominal pain
- ileus
- Diarrhea is green, mucoid, watery, and mixed with exfoliated cells, Voluminous secretory diarrhea may persist despite no oral intake.
- older patients = anorexia and dyspepsia without diarrhea.

**Rising LFTS**

- ALT
  - AST
  - AP
  - Bilirubin
- ← Cholestatic Picture  
← bilirubinaemia causes the pruritis

**CHRONIC GVHD**

- burning sensation in eyes
- irritation, photophobia, and pain occur from lack of tear secretion.
- Dry mouth,
- sensitivity to acidic or spicy foods,
- dysphagia
- odynophagia
- insidious weight loss.
- wheezing, dyspnea, and chronic cough
- **OBSTRUCTIVE lung disease nonresponsive to bronchodilators**
- Weakness
- neuropathic pain
- muscle cramps

**INVESTIGATIONS**

LFT, FBC, EUC, liver ultrasound, spirometry.  
**SKIN BIOPSY IS DIAGNOSTIC**

**MANAGEMENT (acute)**

KEEP the original immune suppressive drugs eg.

**TACROLIMUS**

= macrolide immunomodulator, inhibits calcineurin phosphatase in T-cells, thus → decreased cytokine synthesis  
...But also add

**METHYLPREDNISONE**

Not working after 7 days of Tx?  
→ try **Monoclonal antibodies to TNF or IL-1 and IL-2 receptor**

**MANAGEMENT (chronic)**

**Thalidamide, cyclosporin, prednisone, azathioprine**

**PHYSICAL EXAM FINDINGS**

**EYES**

hemorrhagic conjunctivitis, pseudomembrane formation, inability to close upper lid erosions of the cornea = associated with poorer prognosis

**MOUTH**

Atrophy of oral mucosa  
Mouth + lip erythema + lichenus (more chronic)

**LUNGS**

Bronchiolitis obliterans → wheezes.

**ABDOMEN**

Diffuse tenderness with hyperactive bowel sounds  
Severe ileus = abdo silent and distended.

**LIVER:**

Jaundice, pruritis

**OTHER:**

RASH, Polymyositis, Vaginitis and vaginal strictures, Autoimmune thrombocytopenia and anaemia

Stage	Skin	Liver (Bilirubin)	Gut	
+	Maculopapular rash on <25% of body surface	2-3 mg/dL	Diarrhea 500-1000 mL/d or persistent nausea	
++	Maculopapular rash on 25-50% of body surface	3-6 mg/dL	Diarrhea 1000-1500 mL/d	
+++	Generalized erythroderma	6-15 mg/dL	Diarrhea >1500 mL/d	
++++	Desquamation and bullae	>15 mg/dL	Pain with or without ileus	
Overall Grade	Stage			
	Skin	Liver	Gut	Functional Impairment
0 (None)	0	0	0	0
I (Mild)	+ to ++	0	0	0
II (Moderate)	+ to +++	+	+	+
III (Severe)	++ to +++	++ to +++	++ to +++	++
IV (Life threatening)	++ to ++++	++ to ++++	++ to ++++	+++

~Median time to resolution of acute GVHD is 30-42 days