

# Graft-versus-Host-Disease of the Gastrointestinal Tract and Liver

Celebrating a Second Chance at Life  
Survivorship Symposium

July 11-17, 2020



**Zachariah DeFilipp, MD**  
Massachusetts General  
Hospital



# Graft-Versus-Host Disease: Gastrointestinal Tract and Liver



MASSACHUSETTS  
GENERAL HOSPITAL

CANCER CENTER



Zachariah DeFilipp, MD  
Blood and Marrow Transplant Program  
Massachusetts General Hospital  
Assistant Professor, Harvard Medical School

2020 Celebrating a Second Chance at Life  
Survivorship Symposium  
July 12, 2020

# Agenda

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- What is graft-versus-host disease?
- What are the symptoms of does graft-versus-host disease in the gastrointestinal tract and liver?
- What is involved in the work up and how do we make a diagnosis?
- How do we try to prevent graft-versus-host disease?
- How do we treat graft-versus-host disease once it occurs?



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# Overview of Graft-Versus-Host Disease



# Graft-Versus-Host Disease

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- Graft-versus-host disease (GVHD) is a common complication in transplant recipients.
- It can only occur in patients receiving transplants using donor cells (allogeneic transplants).
- Graft-versus-host disease (GVHD) occurs when the donated cells (**the graft**) recognize the transplant recipient's body (**the host**) as foreign, leading the donated cells to attack and damage.



# Graft-Versus-Host Disease

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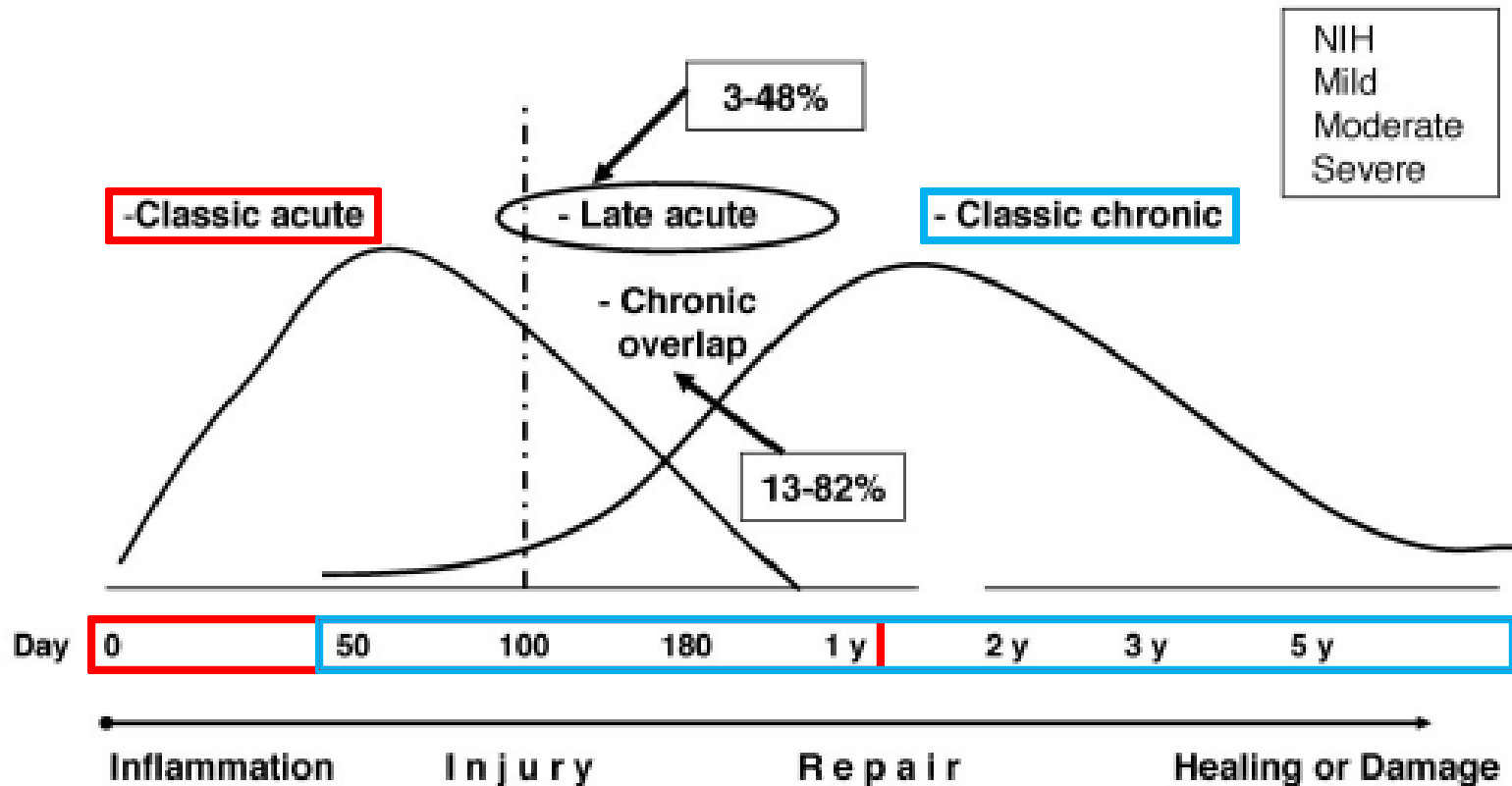
- Graft-versus-host disease has 2 major forms:
  - 1) Acute graft-versus-host disease**
  - 2) Chronic graft-versus-host disease**
- Both acute and chronic forms of graft-versus-host disease can affect the gastrointestinal tract and liver.
  - Sometimes patients only have involvement of one organ system.
  - Sometimes patients have multi-organ involvement of the disease.



# Graft-Versus-Host Disease

Acute GVHD:  
Red skin rash, GI symptoms, liver

Chronic GVHD  
Skin, eyes, mouth, gastrointestinal, liver,  
musculoskeletal, lung, genitourinary



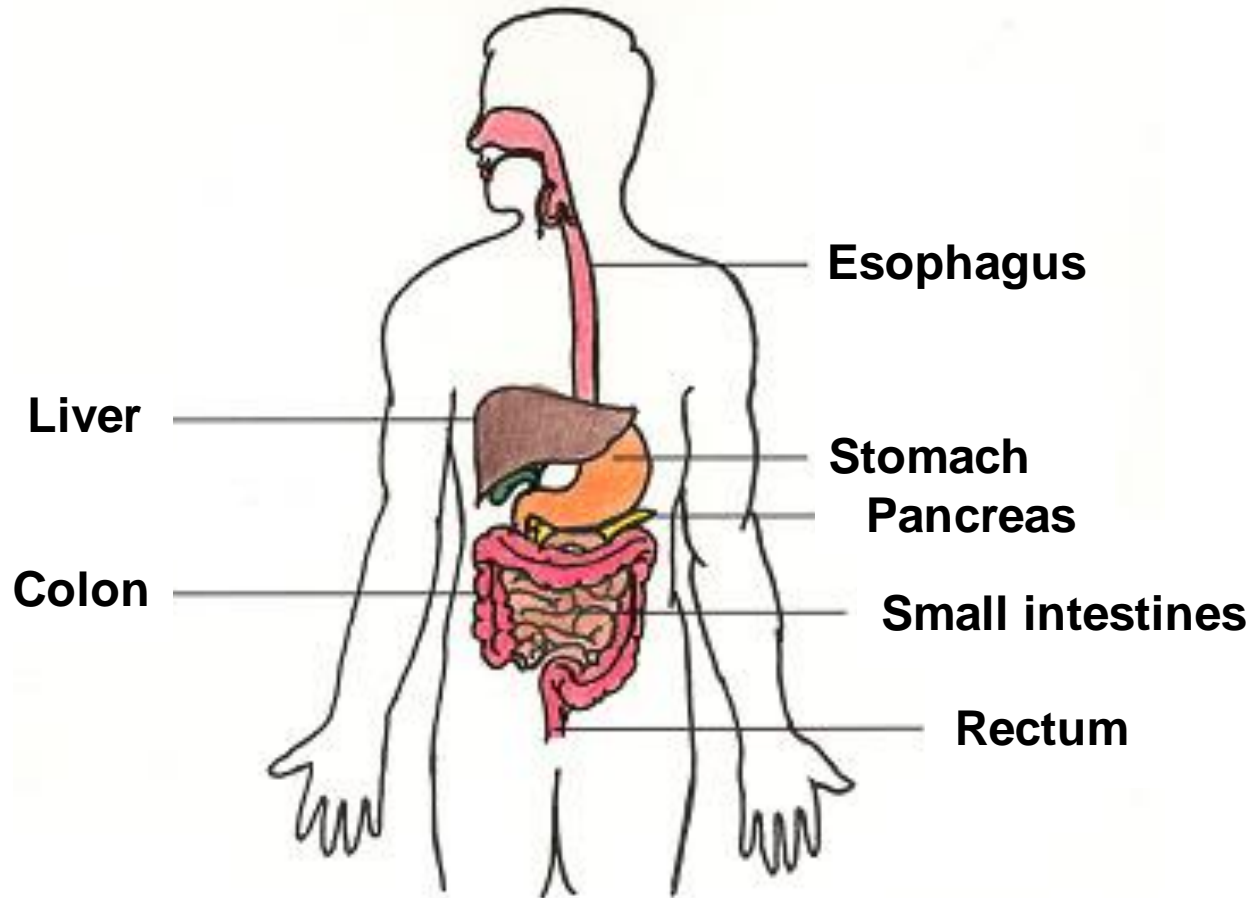
# Graft-Versus-Host Disease

<b>Acute GVHD</b>	<b>Chronic GVHD</b>
<b>Occurs “earlier” after transplant</b>	<b>Occurs “later” after transplant</b>
<b>Skin</b> <b>Gastrointestinal tract</b> <b>Liver</b>	<b>Skin</b> <b>Nails</b> <b>Mouth</b> <b>Eyes</b> <b>Gastrointestinal tract</b> <b>Liver</b> <b>Lung</b> <b>Muscles and joints</b>



# Graft-Versus-Host Disease

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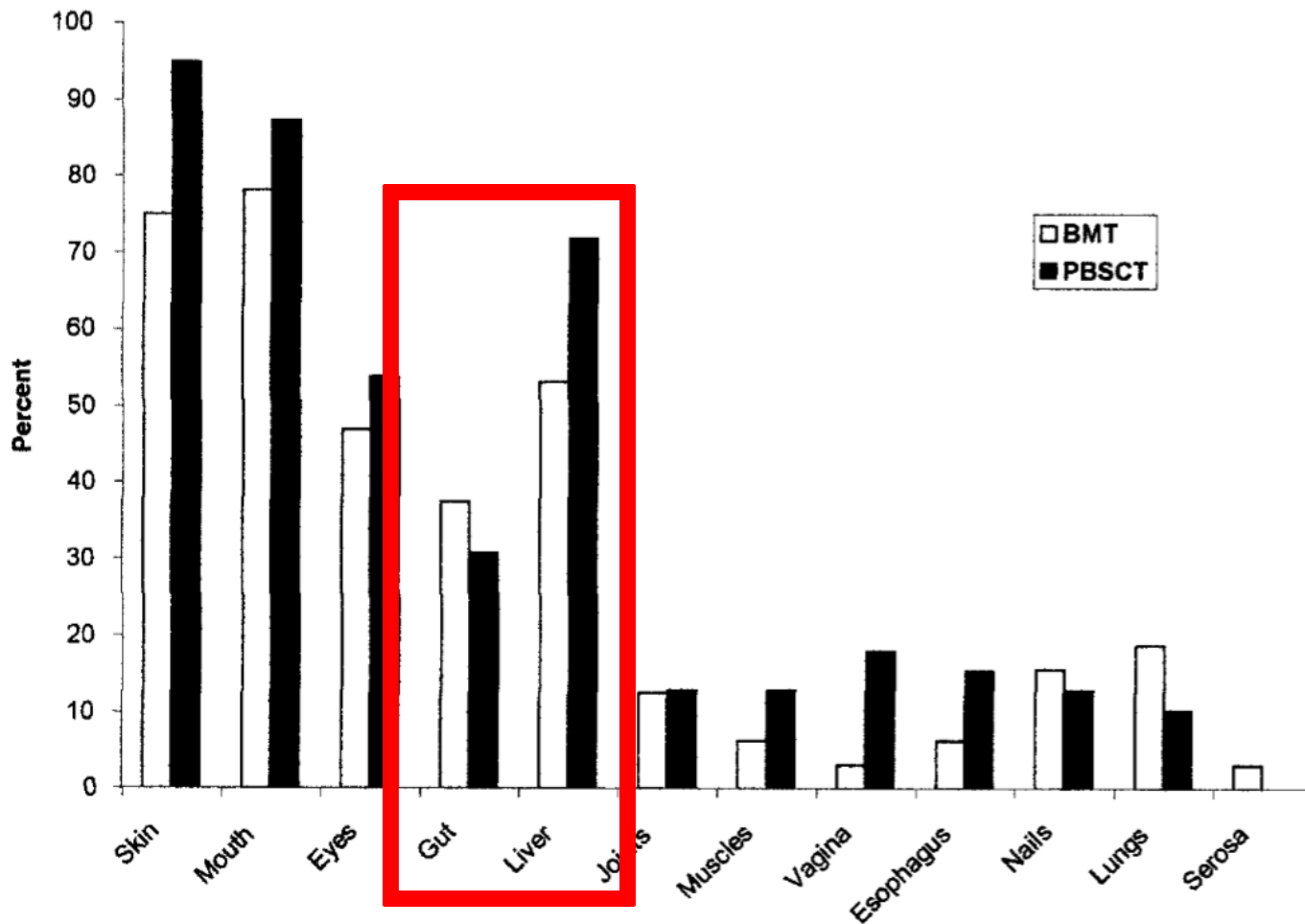
# Acute Graft-Versus-Host Disease

Organs involved	1999-2001	2002-2005	2006-2012
Skin + <b>GI + Liver</b>	27%	20%	13%
Skin + <b>GI</b>	25%	30%	39%
Skin + <b>Liver</b>	14%	7%	4%
<b>Gut + Liver</b>	4%	4%	3%
Skin only	17%	21%	15%
<b>GI only</b>	11%	16%	24%
<b>Liver only</b>	1%	2%	1%

- 80-85% of patients with acute graft-versus-host disease will have involvement of the gastrointestinal tract or liver.



# Chronic Graft-Versus-Host Disease



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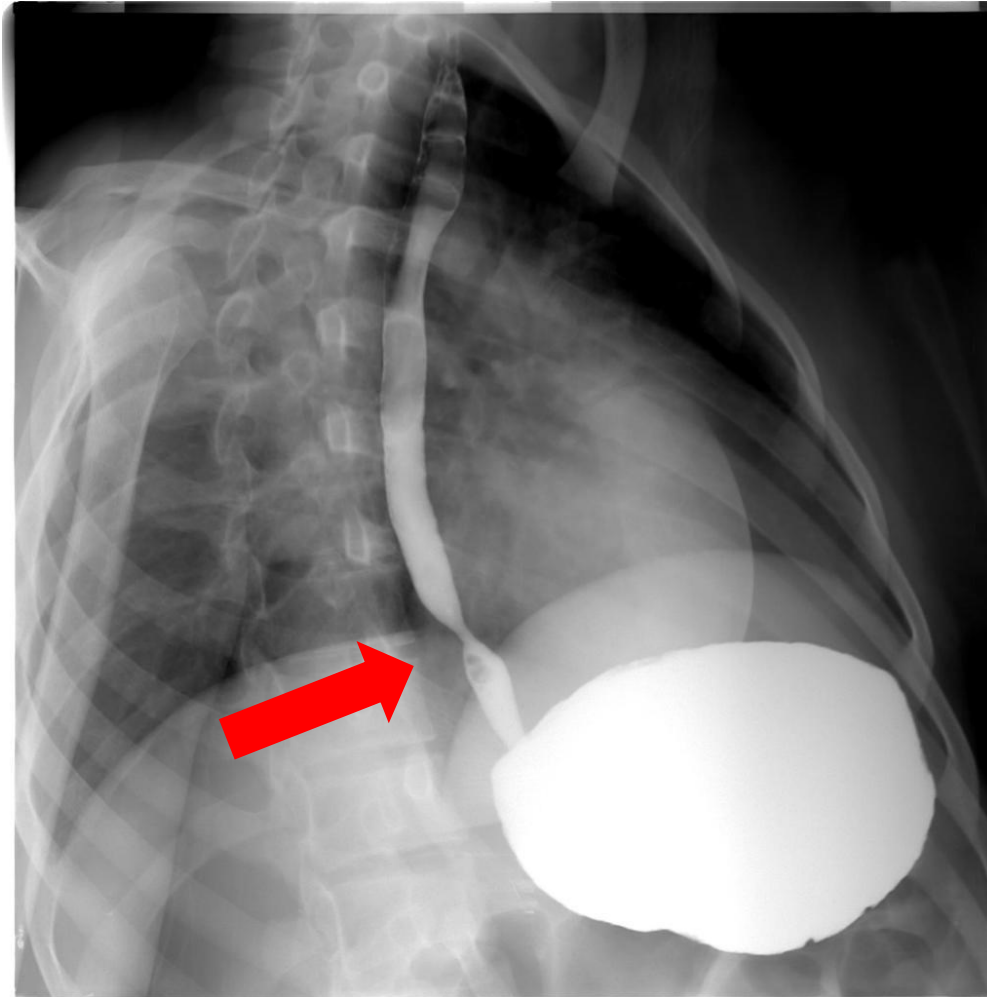
# **Presentation of Graft-Versus-Host Disease Gastrointestinal Tract and Liver**



# Graft-Versus-Host Disease

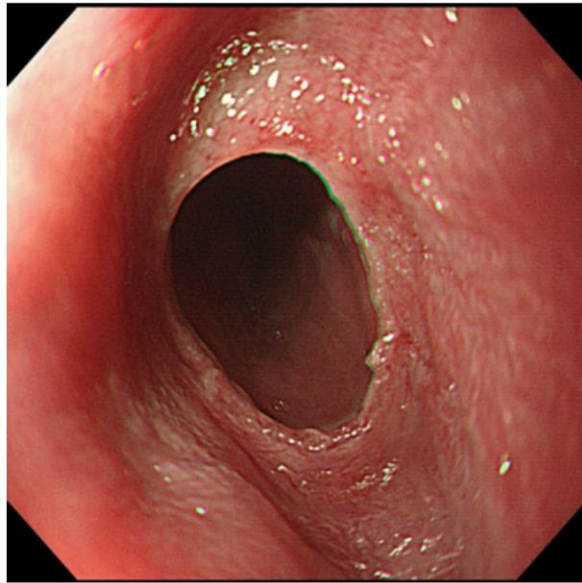
	Acute GVHD	Chronic GVHD
<b>Gastrointestinal tract</b>	<ul style="list-style-type: none"><li>• Diarrhea</li><li>• Abdominal pain or cramping</li><li>• Nausea or vomiting</li><li>• Poor appetite</li><li>• Weight loss</li></ul>	<ul style="list-style-type: none"><li>• Diarrhea</li><li>• Abdominal pain or cramping</li><li>• Nausea or vomiting</li><li>• Poor appetite</li><li>• Weight loss</li><li>• <b>Difficulty swallowing (due to esophageal web or strictures)</b></li></ul>
<b>Liver</b>	<ul style="list-style-type: none"><li>• No symptoms</li><li>• Jaundice (skin, eyes turn yellow)</li><li>• Dark urine</li></ul>	<ul style="list-style-type: none"><li>• No symptoms</li><li>• Jaundice (skin, eyes turn yellow)</li><li>• Dark urine</li></ul>

# Graft-Versus-Host Disease: Esophagus



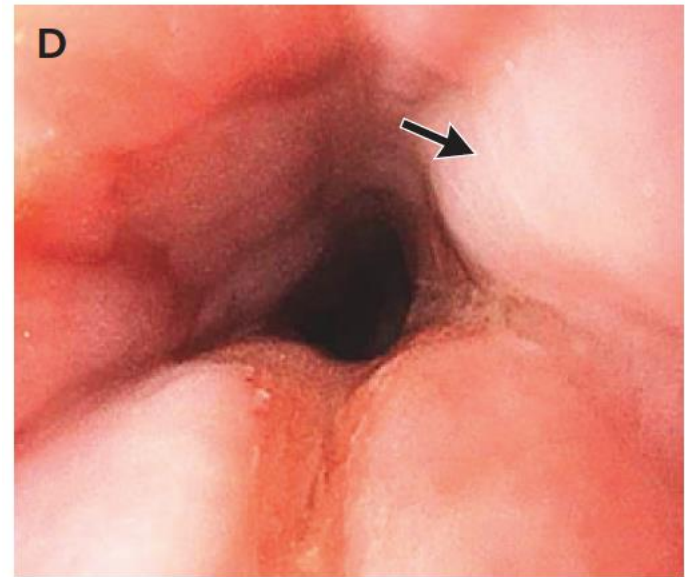
# Graft-Versus-Host Disease: Esophagus

Esophageal web



Watari T. JGFM. 2018

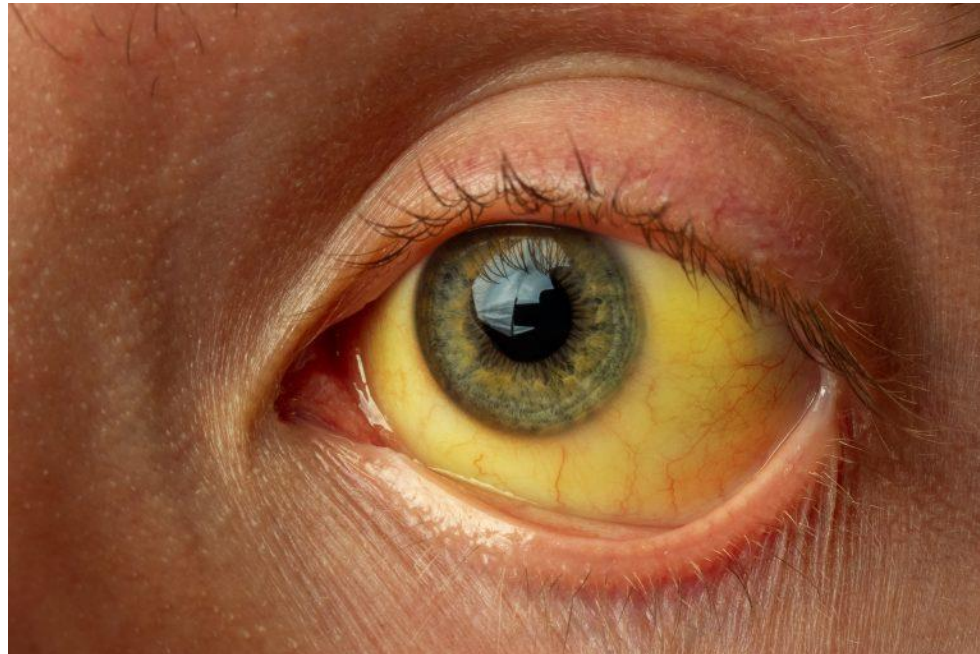
Sclerotic changes  
in the esophagus



Zeiser R. NEJM. 2017

# Graft-Versus-Host Disease: Liver

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# Diagnosis of Graft-Versus-Host Disease



# Diagnosis

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- Graft-versus-host disease is a clinical diagnosis. Tests and biopsies can help support the diagnosis, but the ultimate determination is made by the BMT clinicians.
- Most symptoms require work up to help rule out causes other than graft-versus-host disease.
- These clinical scenarios can include:
  - Infection (viral, fungal, bacterial)
  - Transplant-specific complications
  - Medication side effect
  - Other medical conditions



# Other Diagnoses

Other Causes	
<b>Difficulty swallowing</b>	<ul style="list-style-type: none"><li>• Esophageal reflux</li><li>• Hiatal hernia</li><li>• Infections</li></ul>
<b>Nausea +/- abdominal pain</b>	<ul style="list-style-type: none"><li>• Esophageal reflux</li><li>• Peptic ulcer disease</li><li>• Gastritis</li><li>• Medications</li></ul>
<b>Diarrhea +/- abdominal pain</b>	<ul style="list-style-type: none"><li>• Infections (C diff infection, viral infections)</li><li>• Medications</li></ul>
<b>Liver inflammation</b>	<ul style="list-style-type: none"><li>• Infections (viral infections)</li><li>• Gallstones</li><li>• Medications</li></ul>

# Graft-Versus-Host Disease

## Work up

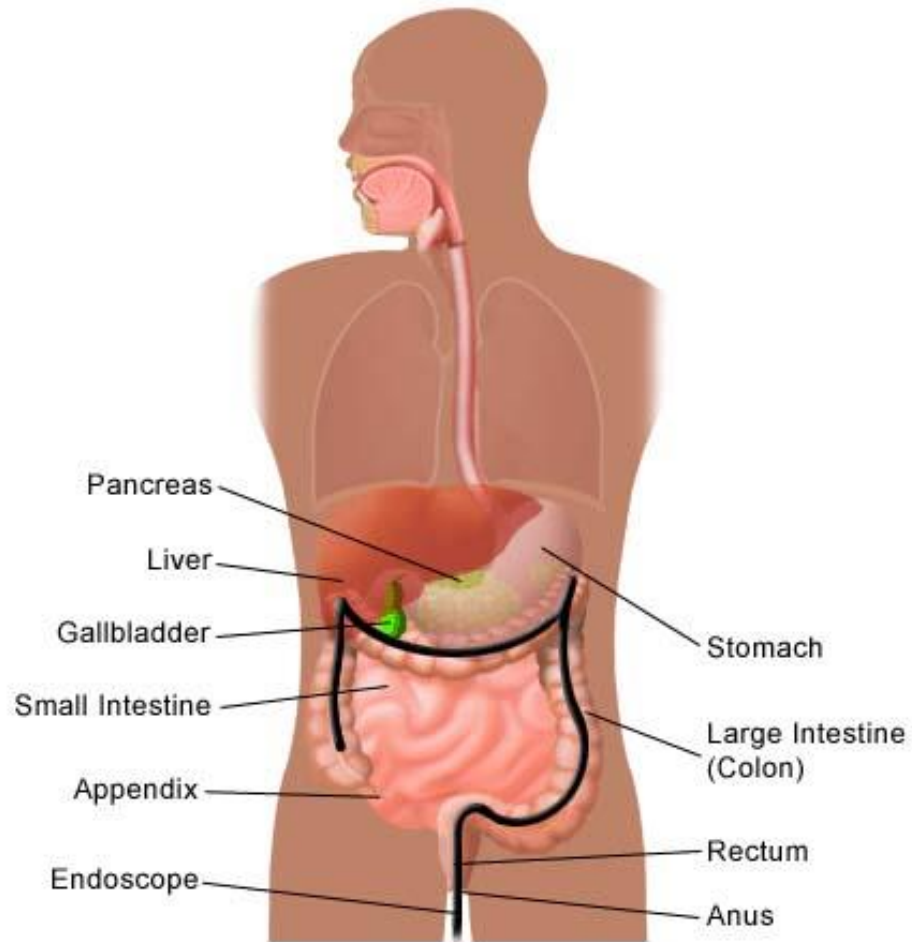
### Gastrointestinal tract

- History
- Physical exam
- Blood tests
- **Colonoscopy** (visualization of large intestines and rectum)
  - *consider for diarrhea*
- **Upper endoscopy** (visualization of esophagus, stomach, and small intestines)
  - *consider for nausea / vomiting, poor appetite / weight loss, difficulty swallowing*
- Biopsies are often taken during colonoscopy and endoscopy procedures

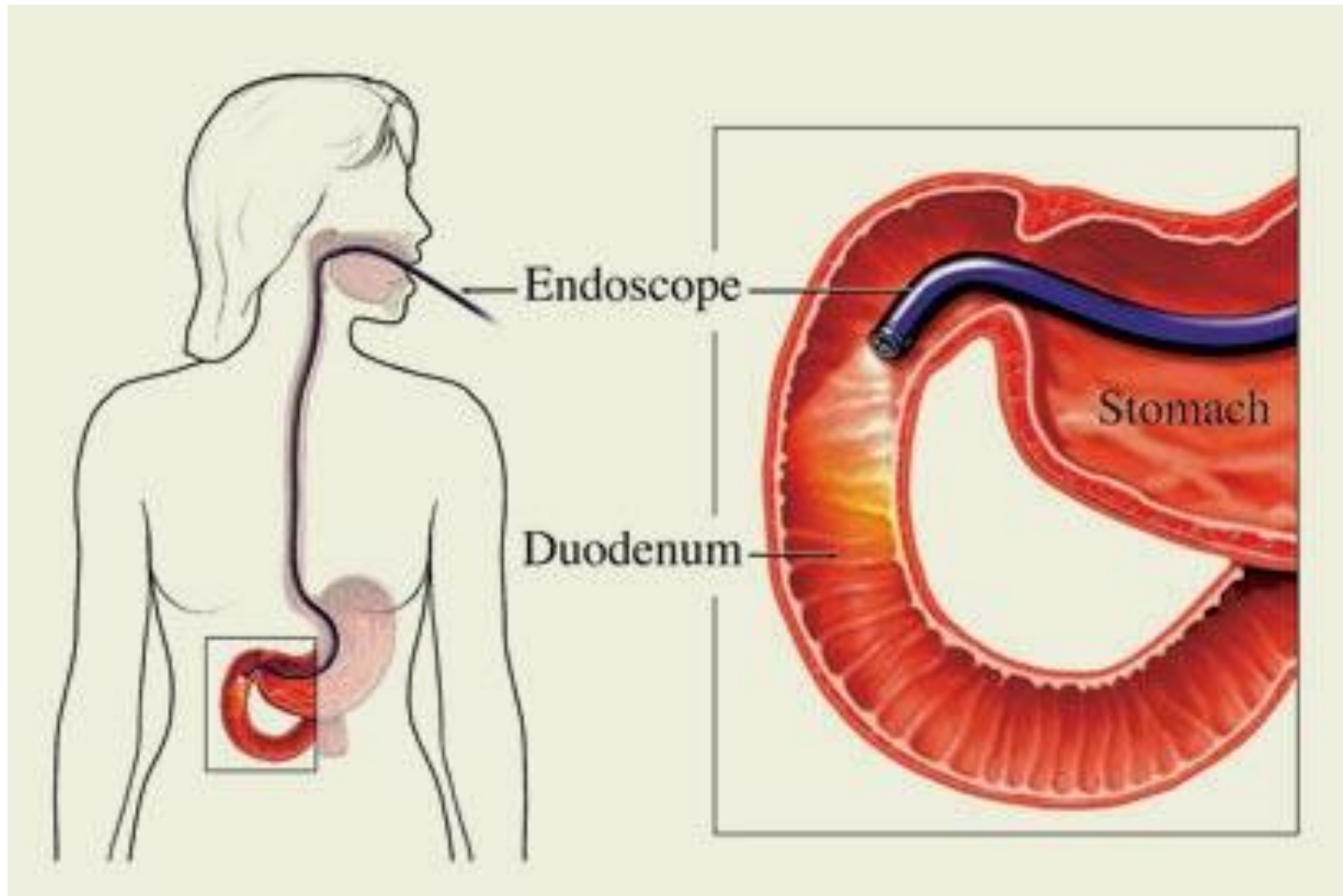
# Endoscopy



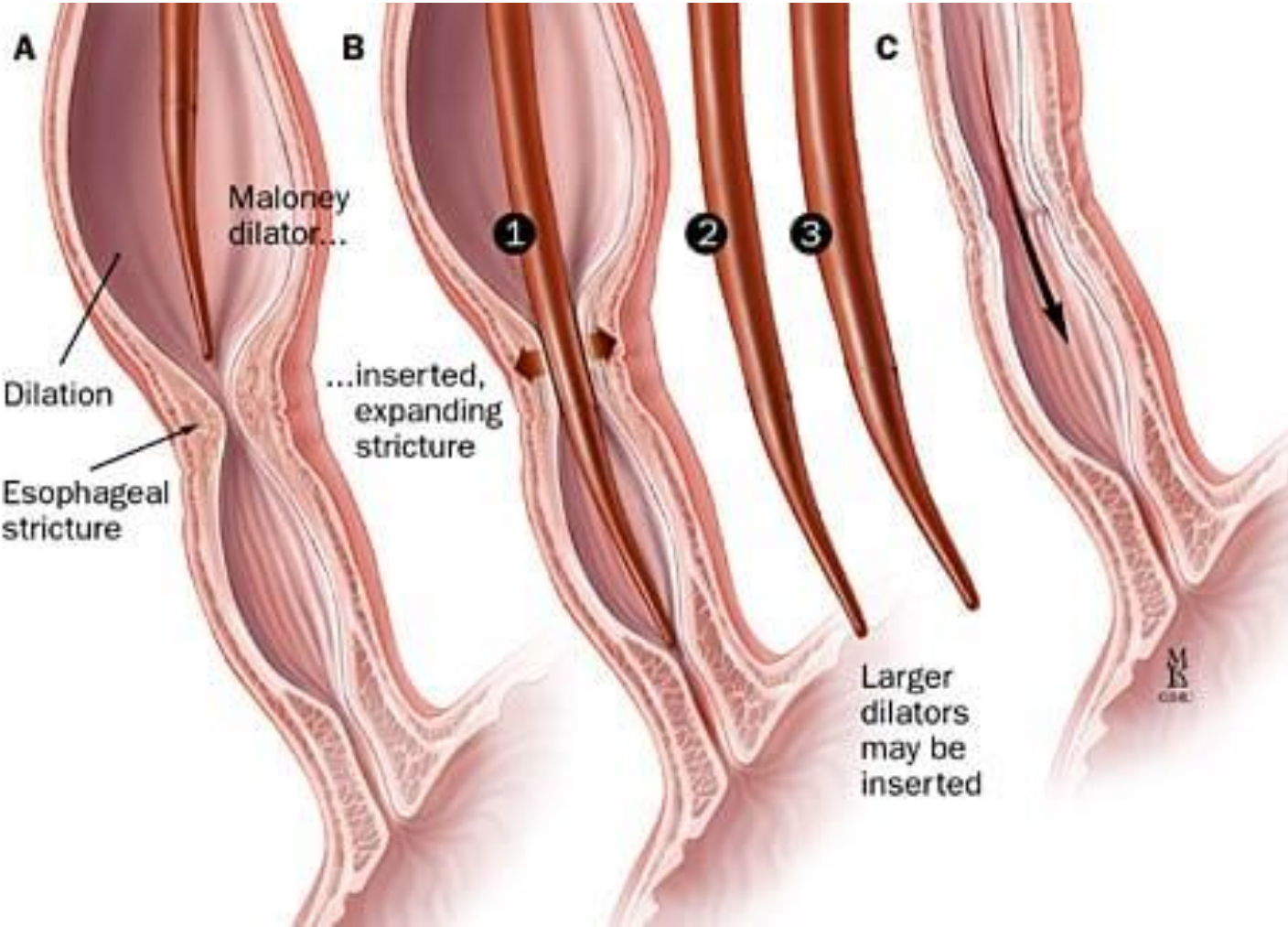
# Colonoscopy



# Upper Endoscopy



# Esophageal dilation





# Graft-Versus-Host Disease

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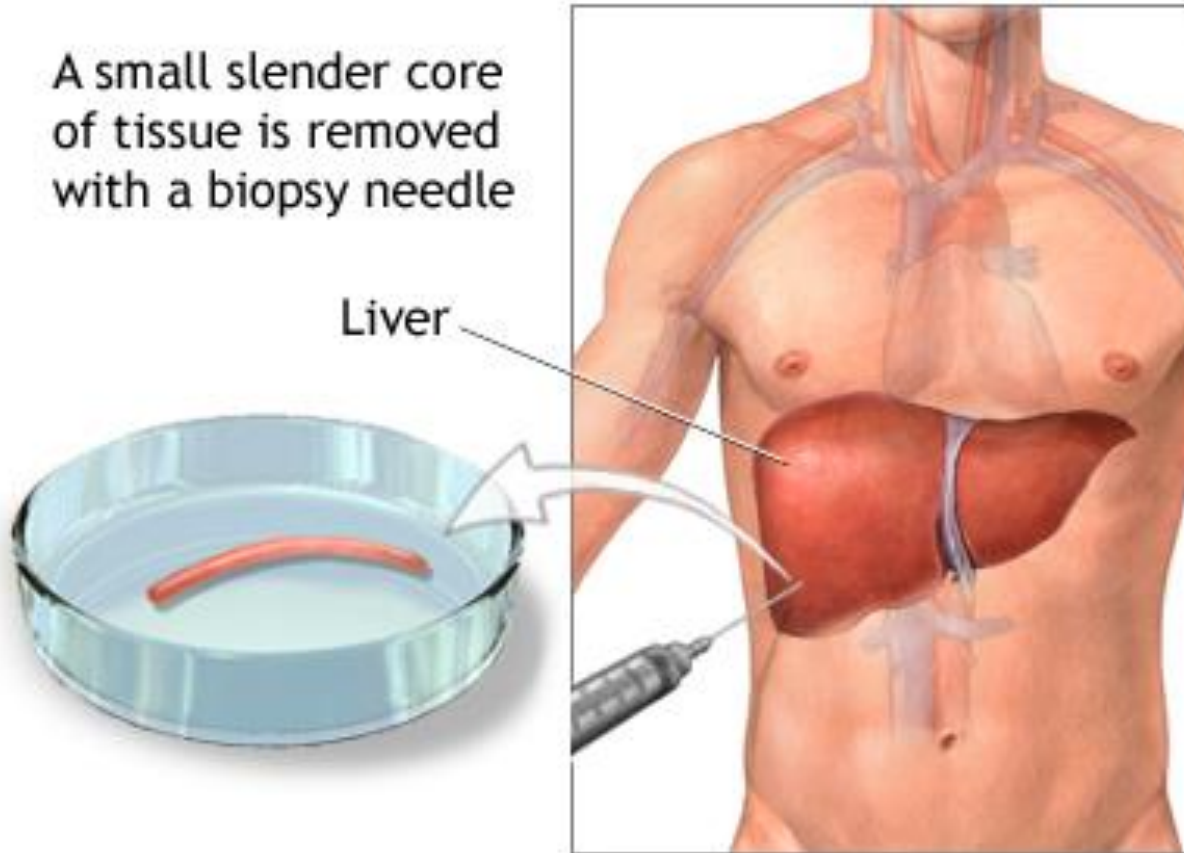
## Work up

### Liver

- History
- Physical exam
- Blood tests
- Imaging (ultrasound, CT scan, MRI)
- **Liver biopsy**

# Liver Biopsy

A small slender core of tissue is removed with a biopsy needle



ADAM.

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# Prevention of Graft-Versus-Host Disease



# Prevention

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- There are no organ specific approaches to preventing graft-versus-host disease.
- However, all transplants using donor cells (allogeneic transplants) will include an approach to prevent graft-versus-host disease.
- These approaches may include:
  - Standard combinations of immunosuppressive agents
  - Manipulation of the donor cells
  - Experimental agents in combination with traditional approaches



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# Treatment of Graft-Versus-Host Disease



# Treatment of GVHD

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- Almost all cases of GVHD involving the GI tract and/or liver require intervention.
- The majority of cases can be treated in the outpatient setting, although some patient may need to be admitted to the hospital.
- Treatments can be categorized as:
  - Local therapies
  - Systemic therapies
  - Procedural interventions
  - Supportive measures



# Treatment

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## Local therapies

- Budesonide (non-absorbed corticosteroid)

## Systemic therapies

- Prednisone (corticosteroid)
  - 1<sup>st</sup> line systemic therapy for acute and chronic GVHD
- Ruxolitinib (FDA approved for acute GVHD)
- Ibrutinib (FDA approved for chronic GVHD)
- Other established agents in GVHD treatments
- Enrollment in clinical trial

# Treatment

## **Procedural interventions**

- Esophageal dilation

## **Supportive measures**

- Ursodiol (decreased inflammation in liver)
- Medications for nausea, vomiting
- Medications for diarrhea
- IV fluids (to prevent dehydration)
- Nutritional support
- Dietary changes
- Physical therapy
- Psychological and social support



# GVHD Diet

- BMT patients are asked to follow a balanced diet.
- When patients develop GVHD of the GI tract:
  - Best to avoid fatty or spicy foods
  - Sometimes might need to eat bland diet
  - If inflammation severe, may require of bowel rest (no eating but nutrition by vein).

Have plenty of  
vegetables and fruits

Eat protein foods

Make water  
your drink  
of choice



Choose  
whole grain  
foods

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# Conclusions



# Conclusions

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- Graft-versus-host disease involving gastrointestinal tract and liver is common in transplant recipients.
- Both acute and chronic forms of GVHD can affect these organs.
- The diagnosis of GVHD is made after evaluating for other potential causes of symptoms.
- Majority of patients will require some form of treatment.
- The treatments and outcomes of patients with GVHD continue to improve.



# Do I have GVHD?

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# Questions?



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[bmtinfonet.org](http://bmtinfonet.org) ♦ [help@bmtinfonet.org](mailto:help@bmtinfonet.org) ♦ 847-433-3313