Graft-versus-Host Disease: Gastrointestinal Tract

Celebrating a Second Chance at Life Survivorship Symposium

May 3-9, 2025

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Graft-versus-Host Disease: Gastrointestinal Track

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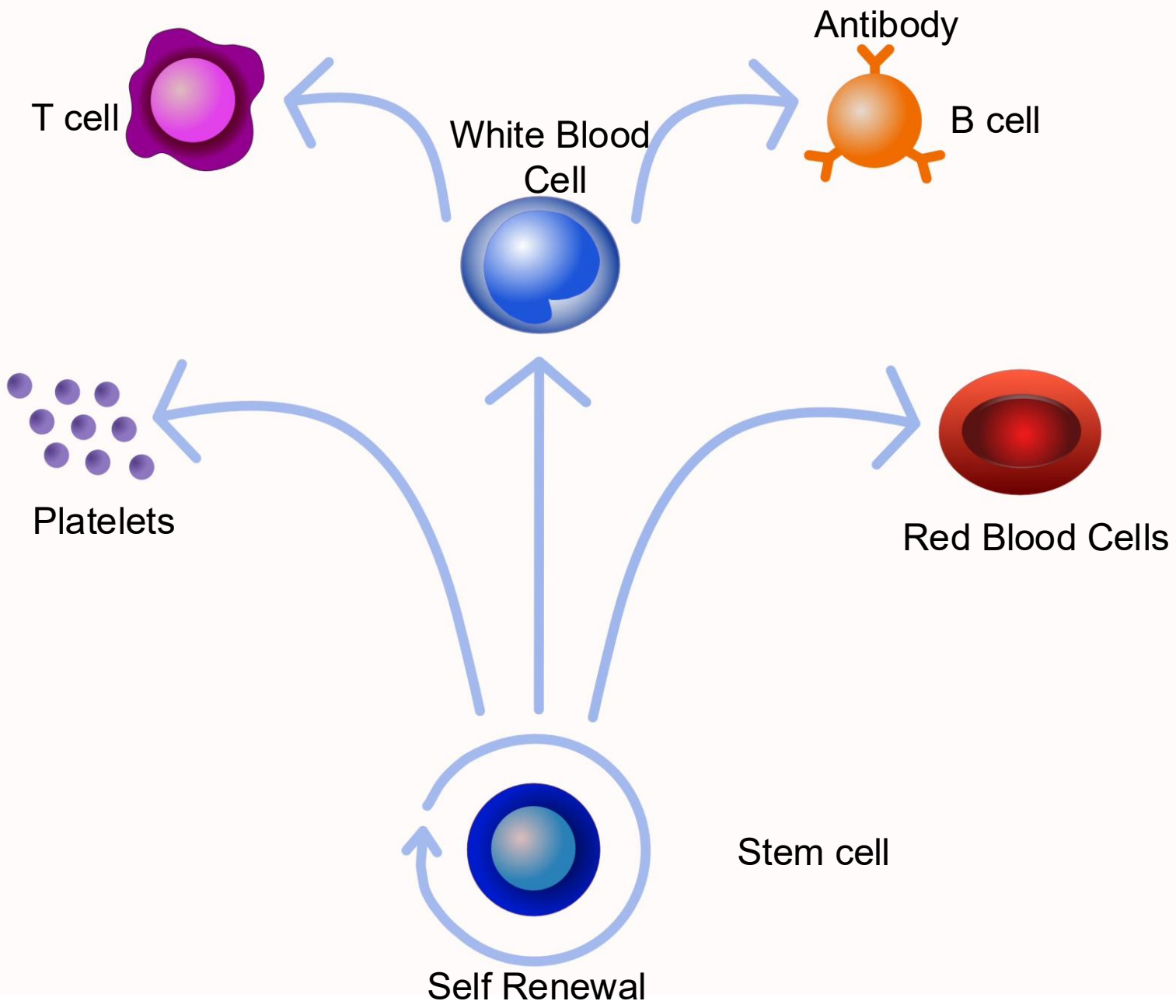
Learning Objectives

- Overview of allogeneic transplant
- Risk factors for acute graft-versus-host disease (GVHD)
- Colon biology and the microbiome
- Diagnosing and assessing acute GVHD of the gut
- Prevention of acute GVHD
- Treating acute GVHD

Stem Cells


Antibody
T cell
White Blood Cell
B cell
Platelets
Red Blood Cells
Stem cell
Self Renewal

Allogeneic Stem Cell Transplant: Initial Consult

- Evaluate the fitness of the patient
- HLA typing and donor search
  - Sibling donors
  - Unrelated donors
  - Mismatched donors
- Important factors in choosing a donor
  - Age
  - Gender
  - Blood type
  - Bone Marrow versus peripheral blood stem cells

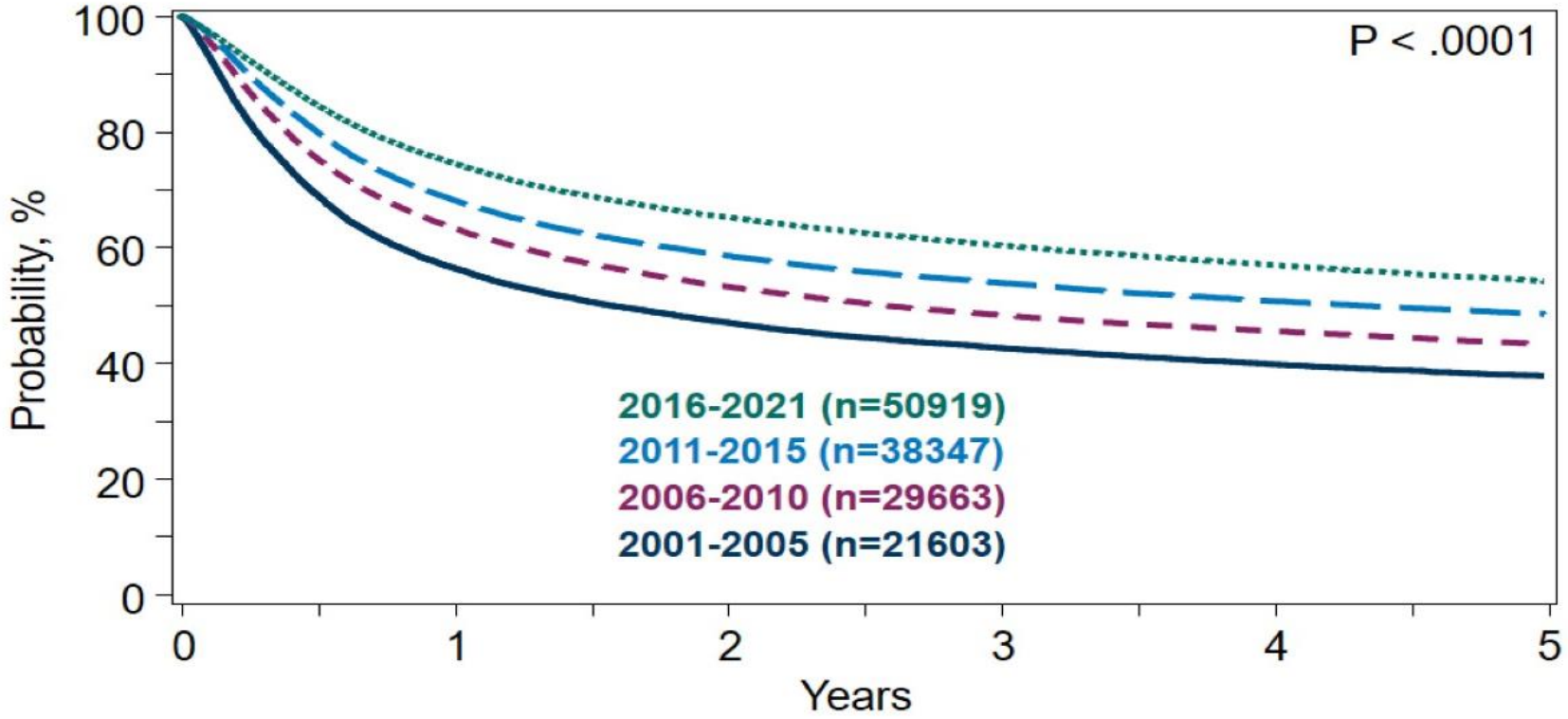
Allogeneic Stem Cell Transplant: Signing Consent

- Discuss the chemotherapy plan
  - Intensity of the chemotherapy with or without radiation
    - Full intensity, reduced intensity, and very reduced intensity
- Plan for prevention of GVHD
- Goals
  - Decrease risk of relapse
  - Decrease risk of GVHD
  - Decrease risk of infection
  - Improve survival and quality of life

Allogeneic Stem Cell Transplant: Conditioning, Transplant, and Follow-Up

- Chemotherapy
  - 4-7 days of chemotherapy with or without total body radiation
- Stem cell infusion: Day +0 “Your new Birthday!”
- Days +3 & +4 after infusion, start GVHD prevention
  - Post-transplant Cytoxan, IV chemotherapy
  - Day +5 start immune suppression, continues for 2-6 months
- Discharge - Ring the bell!
  - 2-4 weeks after infusion

Survival Trends after Transplant 2001-2021

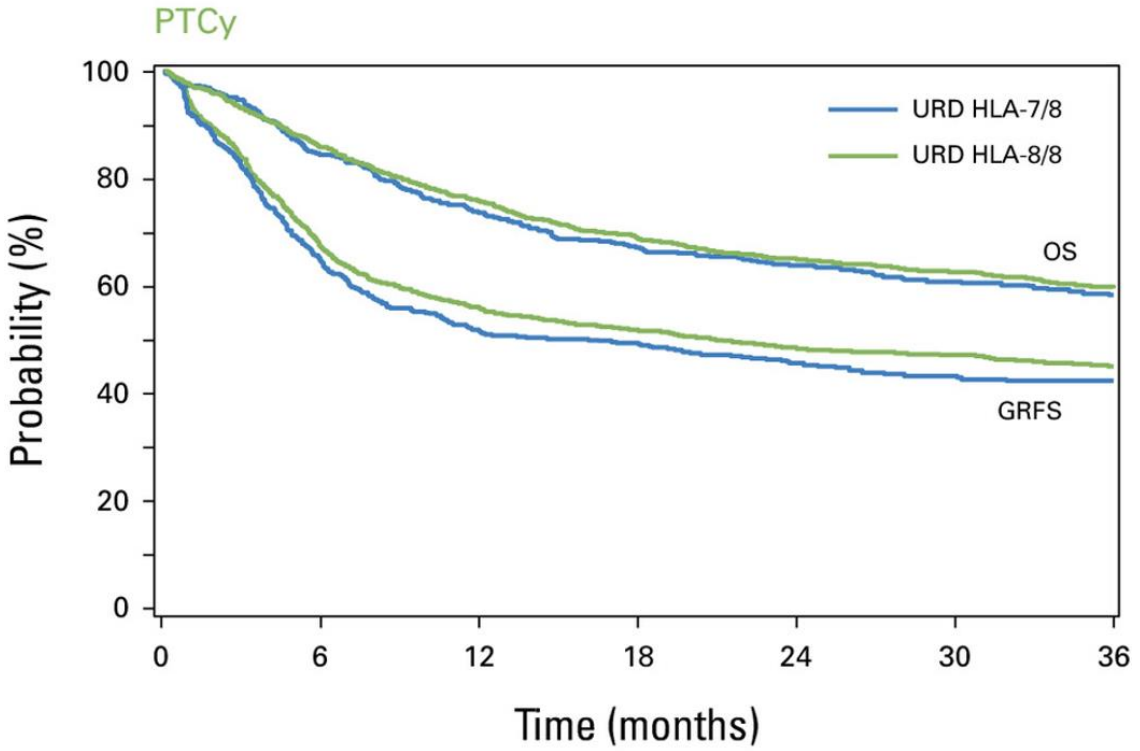


Survival has improved from 40% in 2001 to 60% in 2021.

CIBMTR.org

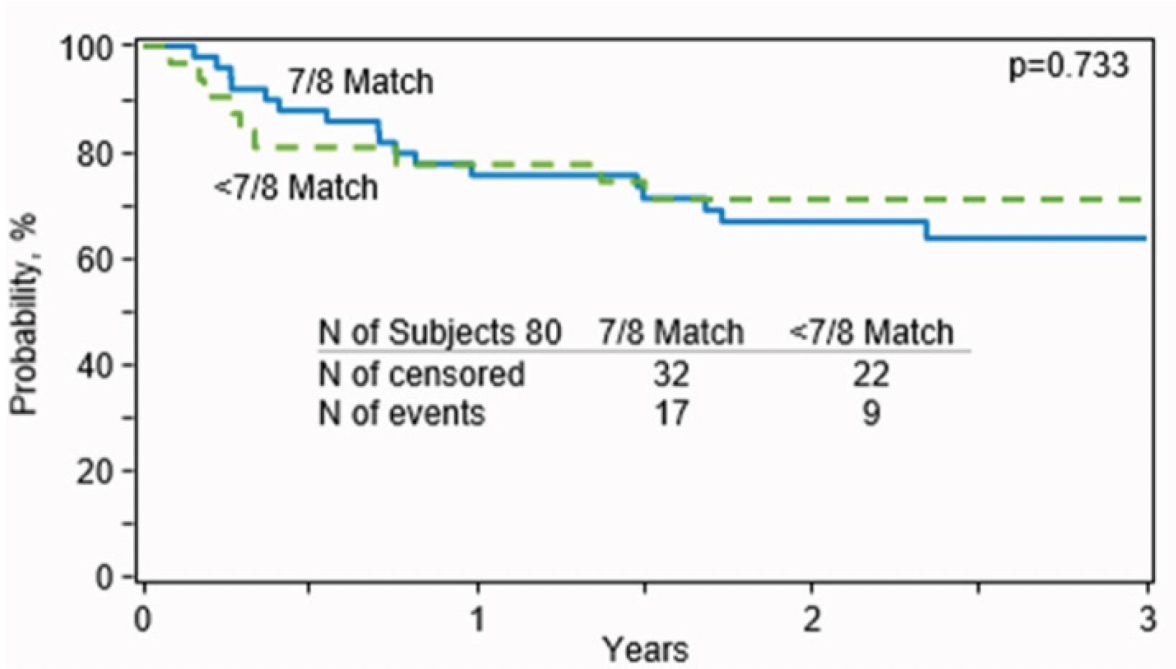
Post-transplant Cytoxan (PTCy) Makes HLA Match Less Important

PTCy: Matched (green) vs mismatch (blue)



Journal of Clinical Oncology
Volume 42, Number 28

PTCy: One mismatch vs more than one mismatch



Transplantation and Cellular Therapy (DOI: 10.1016/j.jtct.2022.12.017).

Acute GVHD of the Gut: Defining Characteristics

- An immune attack on the patient's body by donor cells
- Usually in the first 100 days
  - Usually, 2-7 weeks post-transplant
- Acute GVHD is not defined by the timing but by the symptoms
  - Red rash
  - Liver damage
  - Diarrhea
  - Persistent nausea and vomiting, loss of appetite, weight loss

Acute GVHD of the Gut: Incidence

- Risk of Acute GVHD is about 30-50%
  - Most cases are mild
- Moderate to severe Acute GVHD less than 10%
- Improvements over time in preventing severe Acute GVHD
  - 2000, about 20%
  - 2010, about 15%
  - 2021, about 6%

Chronic Graft versus Host Disease (GVHD)

- Typically occurs 4-12 months after transplant
- Symptoms:
  - Dry eyes
  - Dry mouth
  - Dry skin
  - Like an autoimmune disorder (Lupus, Sjögren's)
- Has improved over the last few years
  - 2015, about 35%
  - Currently, about 21%

How Do We Diagnose Acute GVHD?

- GVHD is a clinical diagnosis, based on symptoms
  - Rash, usually a raised red rash
  - Diarrhea
  - Liver damage based on increased bilirubin
  - Persistent nausea and vomiting, weight loss, decreased appetite
- Biopsies are not required, but if possible:
  - Skin biopsy
  - Colon biopsy
  - Liver biopsy is not usually practical

Risk Factors for Acute GVHD of the Gut: Conditioning Chemotherapy and Radiation

- Intense chemotherapy +/- radiation before transplant damages the gut
  - Damaged cells in the gut release chemicals that stimulate the immune system to repair the damage, which is how the gut normally heals
- The new donor T cells try to heal the damaged gut cells, but aren't ready for the task
  - New donor T cells can't see the difference between the damaged cells and healthy cells

Other Risk Factors for Acute GVHD of the Gut

- HLA matching
  - Minor differences
- Infections
  - *Clostridioides difficile* (C diff)
- Gut microbiome

Grading the Severity of Acute GVHD of the Gut

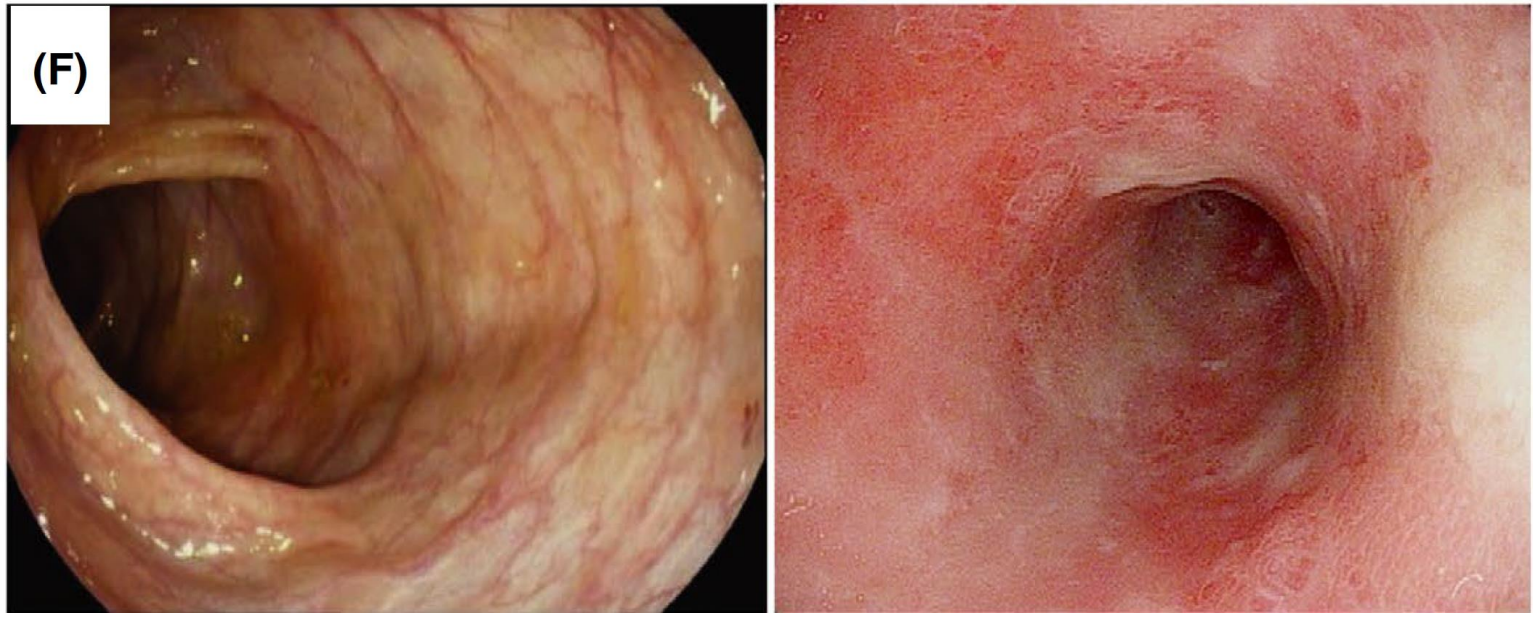
Stages of Gut Acute GVHD	Upper GI (Stomach)	Lower GI (Colon)
Stage	Upper GI (Stomach)	Lower GI (Colon)
0	No symptoms	Diarrhea < 500mL
1	Persistent Nausea	Diarrhea 500-1000mL
2	N/A	Diarrhea 1000-1500mL
3	N/A	Diarrhea > 1500mL
4	N/A	With severe abdominal pain

Biol Blood Marrow Transplant. 2016 January ;
22(1): 4–10. doi:10.1016

Normal Colon Compared to Colon with Acute GVHD

Normal Colon

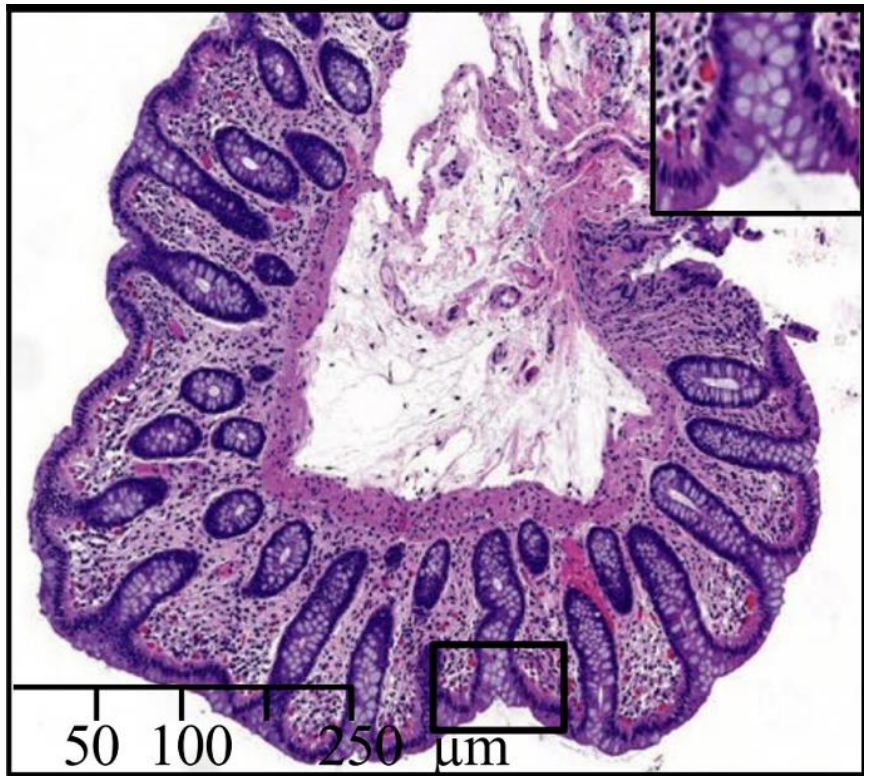
GvHD Colon



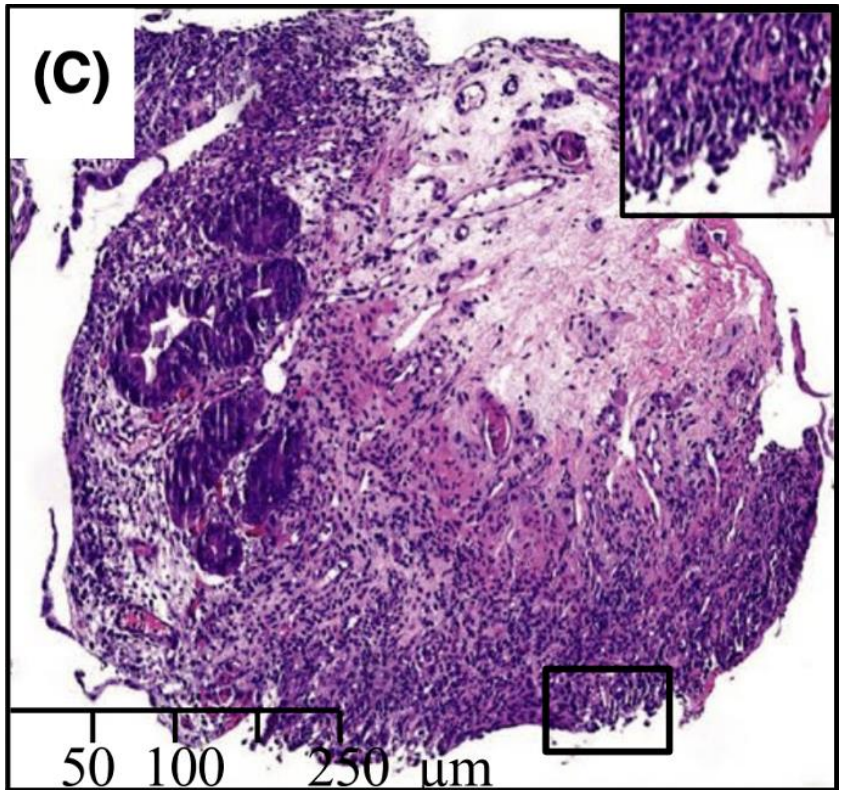
Am J Transplant. 2021;21:1878–1892.

Biopsy Result of Normal Colon versus Acute GVHD

Healthy



Acute GVHD



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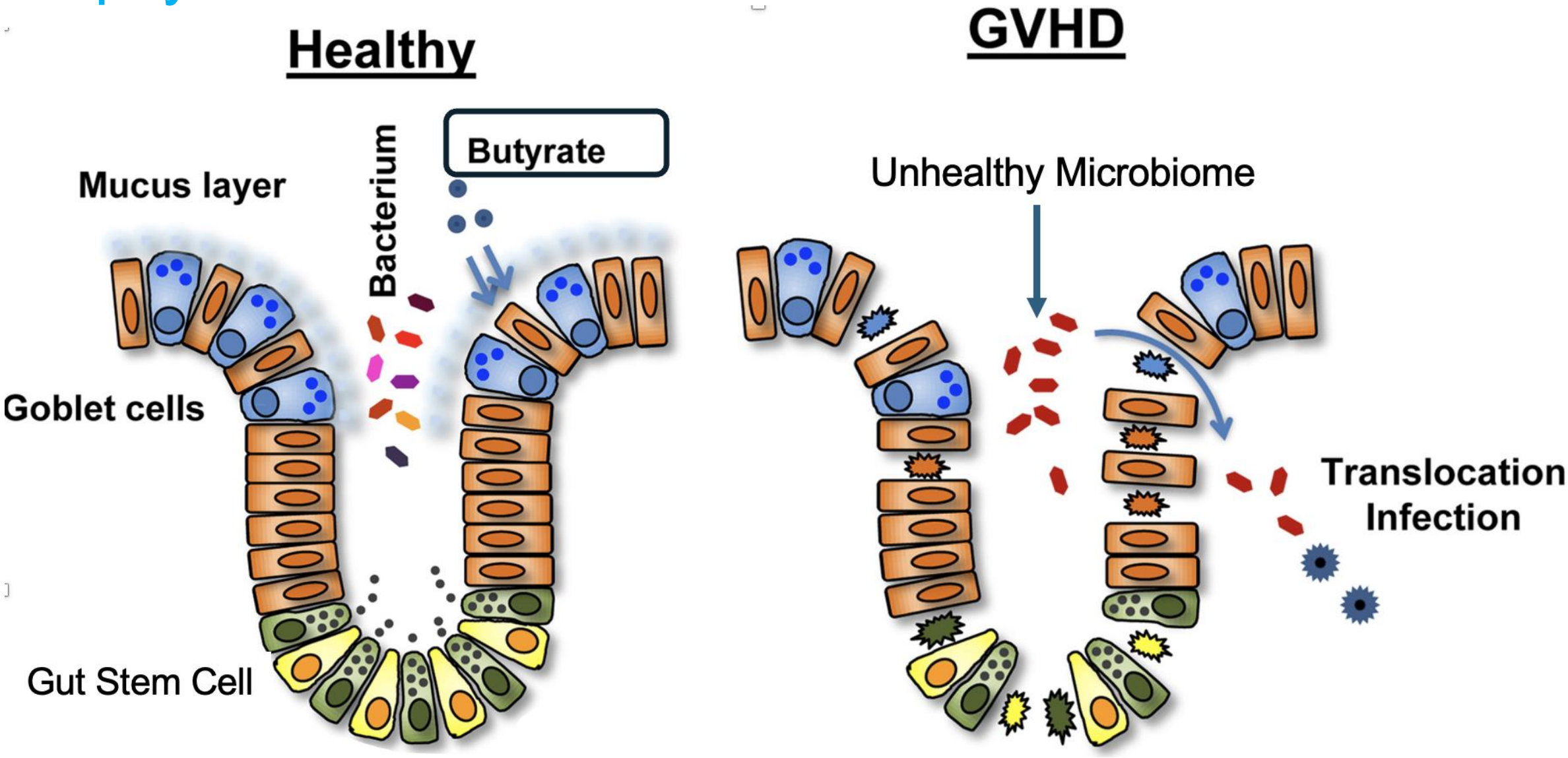


Managing Acute GVHD of the Gut

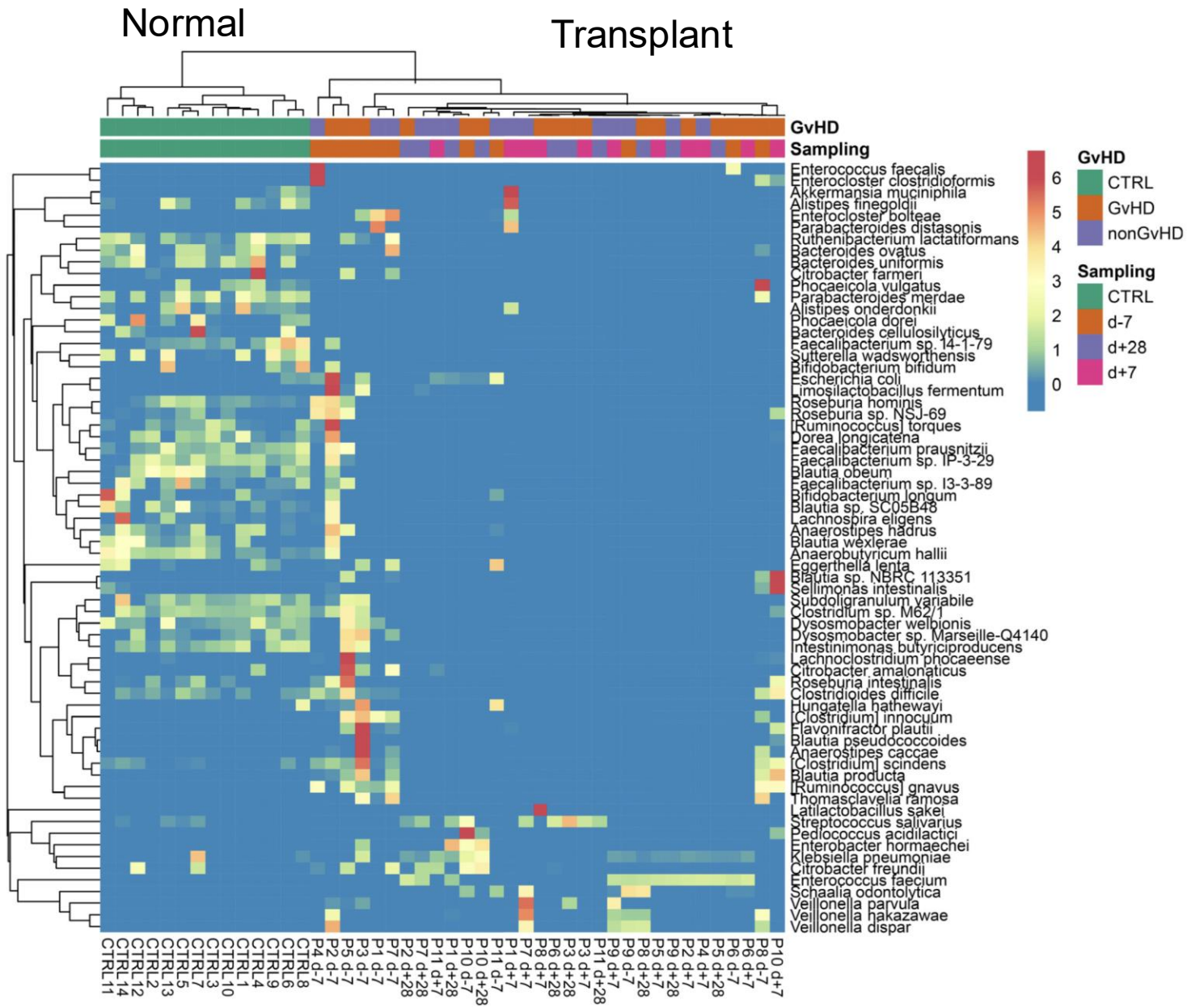
- Prevention
  - Pre-transplant considerations
  - GVHD prophylaxis
- Treatment
  - First line therapy
  - Second line therapy
- Supportive Care
- Options vary by grade

What is the Gut Microbiome?

- The gut microbiome is a diverse community of trillions of bacteria, viruses, and fungi that are essential for life
- Transplant patients have less diverse gut microbiomes due to
  - Chemotherapy
  - Antibiotics for the prevention and treatment of infections
  - Poor nutrition, limited diet at times

Preventing Acute GVHD:

Diverse Gut Microbiome Diversity is Better



Antibiotics **2023**, 12(12), 1667

How to Support the Gut Microbiome in Transplant Patients

- Probiotics and prebiotics
  - Probiotics are living bacteria that restore a healthy gut microbiome
  - Prebiotics are nutrients that are necessary for a healthy microbiome
- A species of bacteria in the gut called Blautia protects the gut lining
  - Increased Blautia species in the gut has been associated with less acute GVHD
  - Blautia produces butyrate for gut health and mucus production

Ways to Increase the Blautia Species in Your Gut

- Increase your intake of fiber, particularly fermentable fiber, e.g.
  - Whole grains
  - Legumes (e.g. dried beans, lentils, and peanuts)
  - Vegetables
  - Prebiotic foods such as garlic, onions, and leeks
- Resistant potato starch is high-in-butyrate prebiotic
  - e.g. Bob's Red Mill potato starch
  - Check with your doctor if you have irritable bowel syndrome

Other Ways to Support the Gut Microbiome in Transplant Patients

- Antibiotic stewardship
- Diverse diet with lots of plants
- Improve sleep and exercise routines
- Fecal Transplant
  - The best way to restore the gut microbiome, but it has potential risks

Acute GVHD Prevention

- Post-transplant cytoxan, tacrolimus, Cellcept®
  - current standard treatment
- Graft manipulation
  - T cell depletion
- Abatacept
  - FDA approved with limited scope for now

Acute GVHD Prevention, cont'd

- Ruxolitinib
  - already approved for treatment
  - early studies are promising and have very low chronic GVHD
- Vedolizumab
  - excellent data and likely awaiting FDA approval
  - approved for ulcerative colitis
- Clinical trials

Acute GVHD Treatment

- High-dose steroids
- Ruxolitinib (Jakafi®)
- Extracorporeal Photopheresis
- Budesonide
  - oral steroids that coat the gut and are not absorbed
- Mesenchymal stem cells (MSC)
  - slows down the donor T cell response
- Clinical Trials

Acute GVHD Treatment Side Effects

- High-dose steroids
  - Infection, diabetes, muscle weakness, cataracts, bone damage
- Ruxolitinib (Jakafi®)
  - Low blood counts, infection
- Extracorporeal Photopheresis
  - Accessing a port
- Mesenchymal stem cells (MSC)
  - Possible mild infusion reaction
- Clinical Trials

Acute GVHD Supportive Care

- Nutrition
  - Prefer oral nutrition, but can be challenging with 2 liters of diarrhea a day
  - For healing, the gut needs rest
  - If not able to tolerate oral nutrition, may need IV nutrition
- Infection
  - People with acute GVHD are at very high risk for infection
  - Anti-viral, anti-bacterial, and anti-fungal medications are available for the prevention of infection
  - Monitor weekly for infection

Acute GVHD Supportive Care, cont'd

- Physical Therapy
- Mental health issues with long hospital stays
- Inpatient rehab after discharge is often necessary
- Monitor for Chronic GVHD
  - Acute GVHD increases the risk for Chronic GVHD

Summary

- Allogeneic stem cell transplant remains the only curative option for many blood cancers, but comes with risks
- Acute GVHD can cause rash, diarrhea, and liver damage
- Acute GVHD risk is influenced by may factors
  - Donor, the most important factor is **age < 32**
  - Choice of chemotherapy
  - Choice of GVHD prevention – **Post-transplant cytoxan**

Summary, cont'd

- Treatment for Acute GVHD is improving
  - **Jakafi** first approved medication for the treatment of Acute GVHD 2019
  - Mesenchymal stem cells also improved
  - Ongoing clinical trials offer new hope in the prevention and treatment of Acute GVHD

Thank you

- BMT InfoNet
- Patients and their families

Questions?

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Let Us Know How We Can Help You

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