Graft-versus-Host Disease: Gastrointestinal Tract and Liver

Celebrating a Second Chance at Life Survivorship Symposium

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NIH NIDDK

Graft-versus-Host Disease: Gastrointestinal Tract and Liver

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BMTinfonet.org 30 YEARS EMPOWERING PATIENTS
2023 SURVIVORSHIP SYMPOSIUM

Disclosures

- I am a gastroenterologist
- I assume most are post-transplant
- I love coffee
- I have none, I am your tax dollars

Problem

- Alone
- Overwhelmed
- Not understood
- You are the first patient I have seen with… Not meant to happen…
- And the time
- And the cost

Uncertainty

- Lets talk about it

Secret

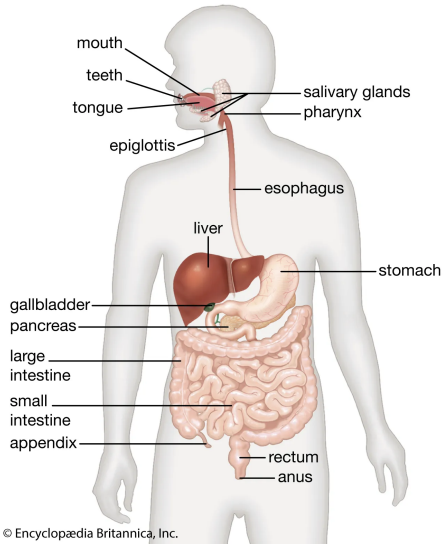
- I will deny I said this
- In some ways these organs are pretty dumb
- Hickam's dictum

- So it is even worse???

No! There are solutions

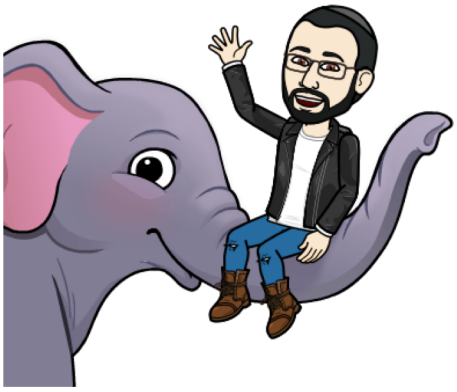
- Get involved, be proactive, it is not hopeless
- Educate
- BMT InfoNet
- Academic Centers
- NIH
- Clinical Trails
- Embrace and beware of Dr. Google

What is the geography?



https://www.britannica.com/science/gastrointestinal-tract#/media/1/15454/1087

What is the elephant in the room? GVHD



- New immune self does not recognize old self
- Good: Graft vs Tumor
- Bad: Graft vs Host

How often?

- GI GVHD: 13 to 50 to 74%
- Liver GVHD: 6 to 30 to 44%

Let's start

- Before
- During (~100 days)
- After

Before

- Pre-existing conditions
  - Often overlooked because of the urgency
- Liver: Metabolic syndrome, iron overload, chemo damage, viruses (HBV)
- GI: Less significant
- Risk stratify and prophylaxis
  - Calcineurin inhibitor: Cyclosporin or tacrolimus

What to do?

- Come in optimized!
- If you know, tell
- Don't smoke or drink
- Plant based diet
  - Microbiome
- Sometimes no choice

During (~100 days)

- Classic acute GVHD
- Inflammatory
- Company it keeps
  - Liver, gut, skin
- Overlap

What will I see or feel?

- **Gut**
  - Nausea/Vomiting
  - Diarrhea
  - Bleeding
  - Mucous
  - Not hungry at all
  - Feel full
- **Liver**
  - Nausea/Vomiting
  - Not hungry at all
  - Feel full
  - Yellow eyes
  - Dark urine
  - Light stool
  - Swollen stomach

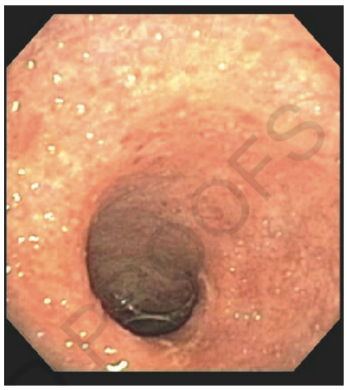
Have to ask: What else could it be?

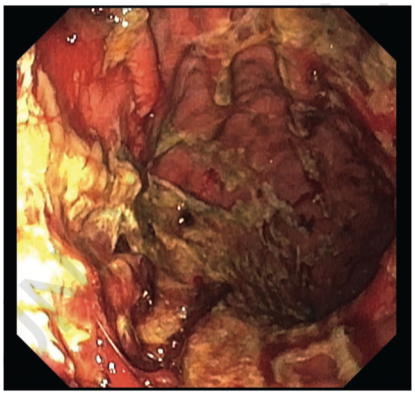
- **Gut**
  - Viruses
  - Bacteria
- **Liver**
  - Drug induced liver injury (dili)
    - livertox
  - Viruses
  - Cholangitis Lenta
  - Sinusoidal Obstructive Syndrome
  - Thrombotic microangiopathies

Investigate and think!

- **Gut**
  - History
  - Exam
  - Blood tests for infection
  - Stool tests for infection
  - **Endoscopy**
- **Liver**
  - Blood tests
    - Cholestatic (ALP/GGT/Bili)
    - Hepatitic (ALT/AST)
    - Exclude other causes
  - Imaging
    - Ultrasound to start
  - **Biopsy**

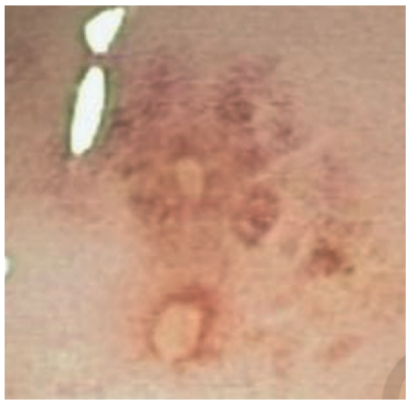
Endoscopy (see and sample!): GVHD





Bhattacharya S, et al. GI Complications of HSCT. Chapter 27.
In: Blood and Marrow Transplantation Long Term Management: Prevention and Complications, Second Edition. Savani, B, Tichelli, A, ed. Wiley-Blackwell, Hoboken, NJ. 2021.

Mimics!



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Now what?

- Team work makes the dream work
- Transplant, Infectious Disease, Gastroenterology, nutrition, nursing, PT/OT
- Diagnose before treating
- Treat early
- Define severity
  - Determines extent of treatment

Things to consider during treatment

- Monitoring
  - How does the patient look and feel
  - Stool volume
  - Blood work
  - Infections (prophylaxis)
  - Endoscopy
  - Other causes
  - Symptomatic treatment
  - Nutrition and activity

Treatment for GVHD

- To date, no consensus has been reached … for management of steroid-resistant … acute graft-versus-host disease. The choice of treatment has been guided largely … trial and error according to physician experience, ease of use, need for monitoring, risk of toxicity, and potential exacerbation of preexisting comorbidity.

  - Martin PJ, *Blood* (2020)

But! Treatment is effective

- Steroids are the initial mainstay
- Both oral and "first pass" drugs
- Examples are methylprednisolone and budesonide
  - Weeks then tapered over months
- Should see response within 7 days
- Worsening by 5 days is also considered significant
- If no response or worsening then steroid resistant or refractory

Beyond Steroids

- Ruxolitinib
- If no response then consider mycophenolate, etanercept, Pentostatin, Alpha-1 antitrypsin, sirolimus, and extracorporeal photopheresis
  - And others!
- Clinical trials

General thoughts

- Can be transient and never again
- For some lifelong
- It can recur
- Lifestyle modifications are so challenging
  - Things change over time
  - Aim for a heart healthy diet but limited by tolerance and illness
    - Would not aim for Burgers/Fries/Steaks/Beer/Spicey
  - Keep active as much as possible

After

- Classic Chronic GVHD
- Late acute GVHD
- Fibrotic
- More organs

- Overlap

What will I see or feel?

- **Gut**
  - Malabsorption (Pancreas)
  - Weight loss
  - Failure to Thrive
  - Difficulty swallowing
    - Strictures – can dilate
- **Liver**
  - Nausea/Vomiting
  - Not hungry at all
  - Feel full
  - Yellow eyes
  - Dark urine
  - Light stool
  - Swollen stomach

Have to ask: What else could it be?

- **Gut**
  - Viruses
  - Bacteria
- **Liver**
  - Drug induced liver injury (dili)
    - livertox
  - Viruses
  - Textbook…
  - Syndrome
  - Thrombotic microangiopathies

Investigate and think!

- **Gut**
  - Look at weight
  - Look at muscle mass
  - Think about frailty
  - Stool tests for pancreatic function
  - Blood tests for nutrition
- **Liver**
  - Blood tests
    - Cholestatic (ALP/GGT/Bili)
    - Hepatitic (ALT/AST)
    - Exclude other causes
  - Imaging
    - Ultrasound to start
  - Biopsy

Questions for your provider…(in a nice way…)

- What else could this be?
- Are there treatment alternatives?
- Why am I not responding?
- Am I on the safest, lowest dose medicine needed?
- What are the complications?
- Are we monitoring for them?

- https://www.bmtinfonet.org/gvhd-directory

Example of persistence paying off

- 302 patients, 151 hepatic cGVHD based on NIH Consensus Criteria

	Biopsy	Biopsy no	Total

6 had only hepatic GVHD, 10 hepatic GVHD with either iron overload, nodular regenerative hyperplasia, or steatosis.

Yang, A et al Transplantation and Cellular Therapy 2022.

More thoughts…

- A systematic, meticulous approach will make the **correct** diagnosis
- Although we try to avoid it, sometimes an invasive procedure is the right choice
- And! Diagnosis is crucial because treatment **makes a difference**

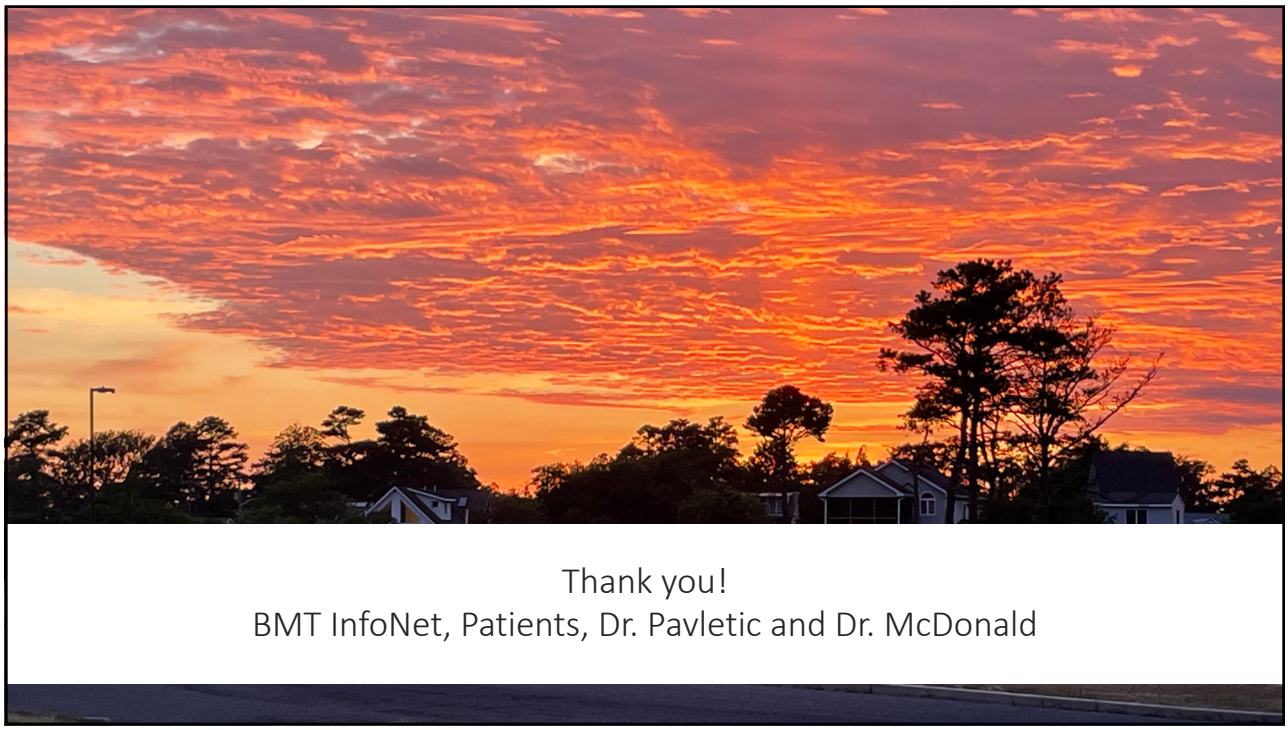
Imagine a future…

- No need for transplant
- Biomarkers
- Personalized treatment
- Induction of tolerance
- Microbiome
- HCV analogy

Build a team

- Family
- Friends
- Health care professionals
  - Open
  - Will learn with you
  - Available / accessible
  - Build trust
  - There in case of crisis
  - Center of excellence - caring
  - Even better if experience
  - Two tiered system of care – not always possible

Don’t forget to live!!!



Thank you!
BMT InfoNet, Patients, Dr. Pavletic and Dr. McDonald

QUESTIONS?

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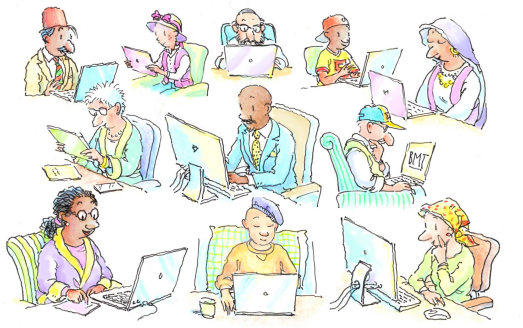
LET US KNOW HOW WE CAN HELP YOU



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