

Graft Versus Host Disease: How You and I Diagnose it



VS



Joel K. Greenson, M.D.



Histopathologic Diagnosis of Chronic Graft-versus-Host Disease: National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: II. Pathology Working Group Report

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What is GVHD?

- To a Clinician it can be diarrhea, nausea, vomiting, skin rash, dry or itchy eyes, or jaundice
- To a Pathologist GVHD = Apoptosis, but Apoptosis does not = GVHD
- Infections, medications, bowel preparations and chemotherapy can all induce apoptosis identical to GVHD

What is Apoptosis?

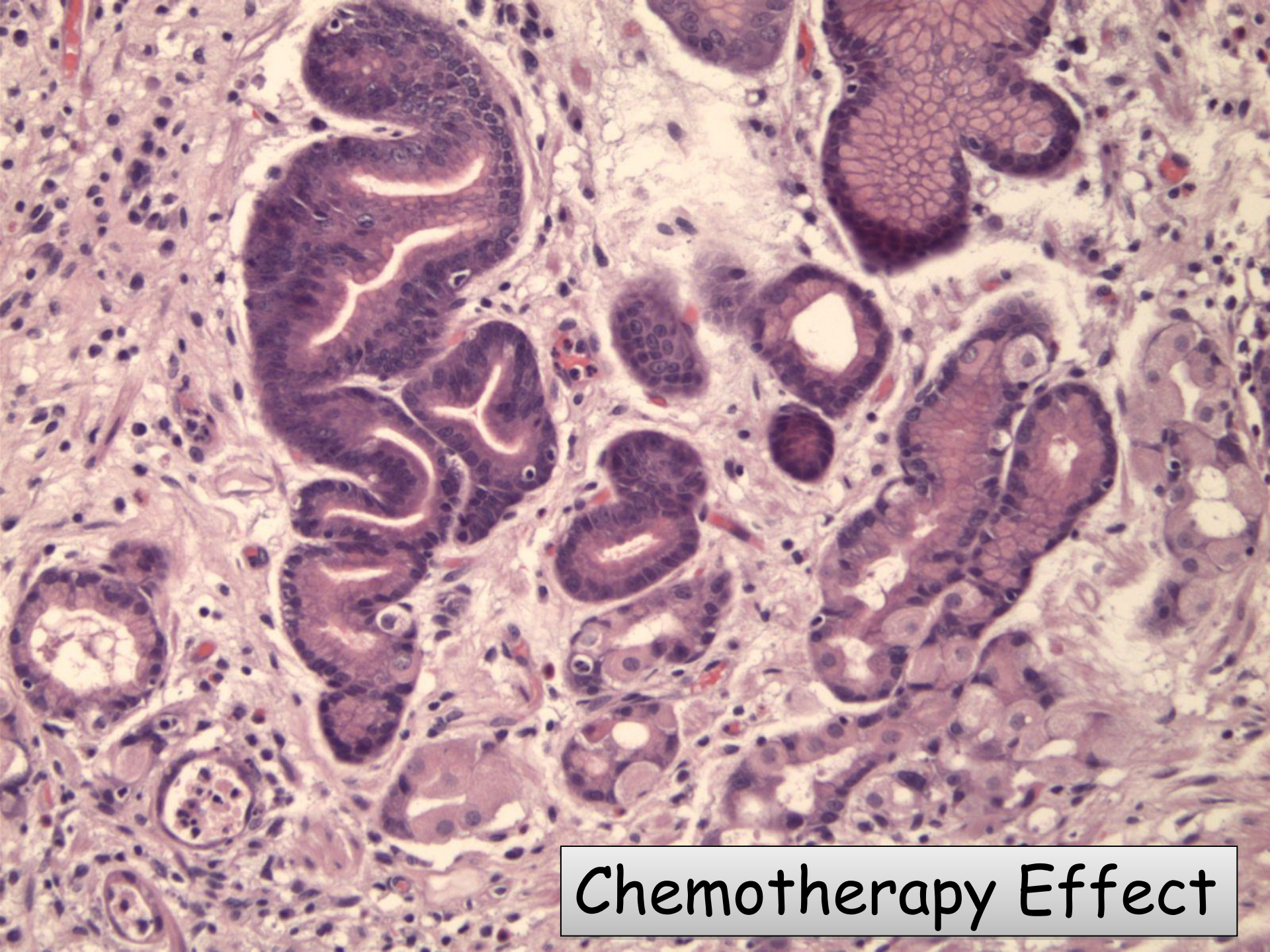
- According to Wikipedia it is the process of programmed cell death
 - 20-30 billion cells die via apoptosis every day (this is normal)
- The term is Greek for dropping off (like petals dropping off of a flower)
- A large number of complex pathways involving TNF, Fas, BAX, BCL-2 and numerous cytokines control apoptosis



Apoptosis

Mimics of GVHD

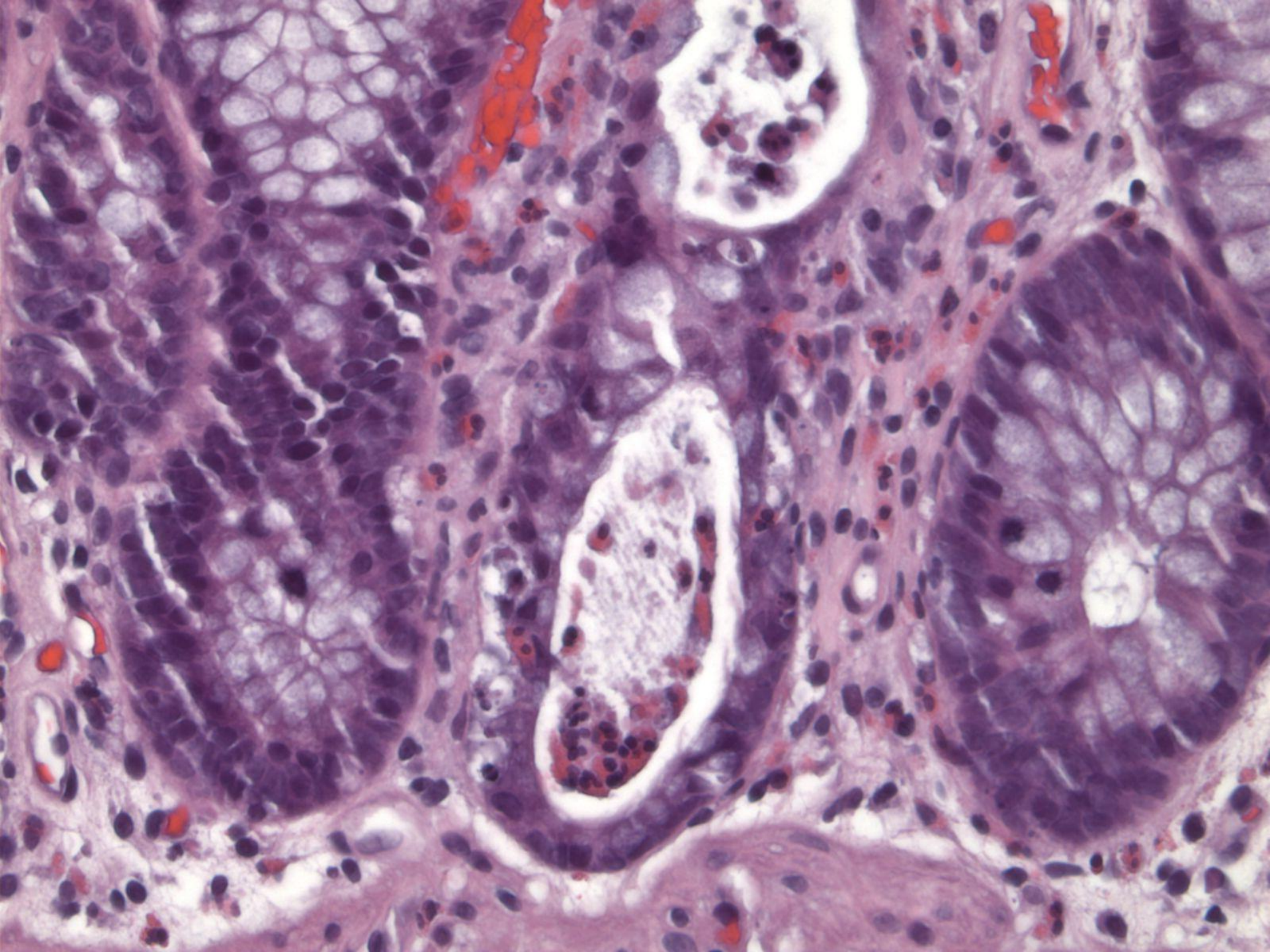
- Bowel Preparations
- Chemo/radiation therapy
 - Can't distinguish until day 21
- Drugs
 - Mycophenolate
 - NSAIDs
 - Proton Pump Inhibitors (PPI)
- Infections



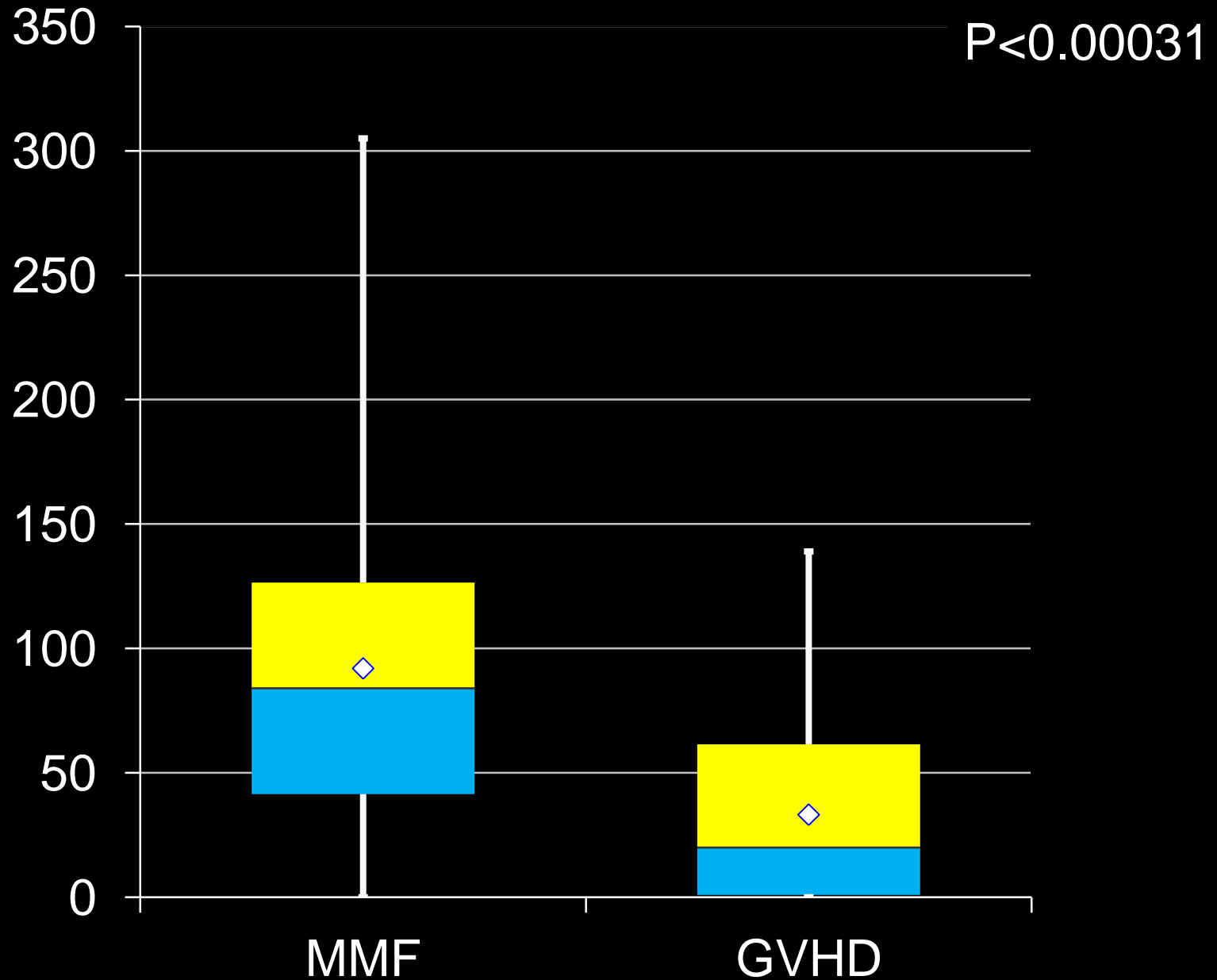
Chemotherapy Effect

Mycophenolate Mofetil (CellCept)

- Immunosuppressive drug used primarily in organ transplantation
 - Now being tried for inflammatory/autoimmune diseases such as IBD, Arthritis, Myasthenia
 - Used to treat GVHD
- Has a pattern of colitis that resembles GVHD or ischemia.
- Stomach and small bowel can also be involved



Number of Eosinophils / 5 HPF



Histologic Features in Colon Biopsies Can Discriminate Mycophenolate From GVHD-induced Colitis

Kremena V. Star, MD, PhD, Vincent T. Ho, MD,† Helen H. Wang, MD,‡
and Robert D. Odze, MD, FRCPC**

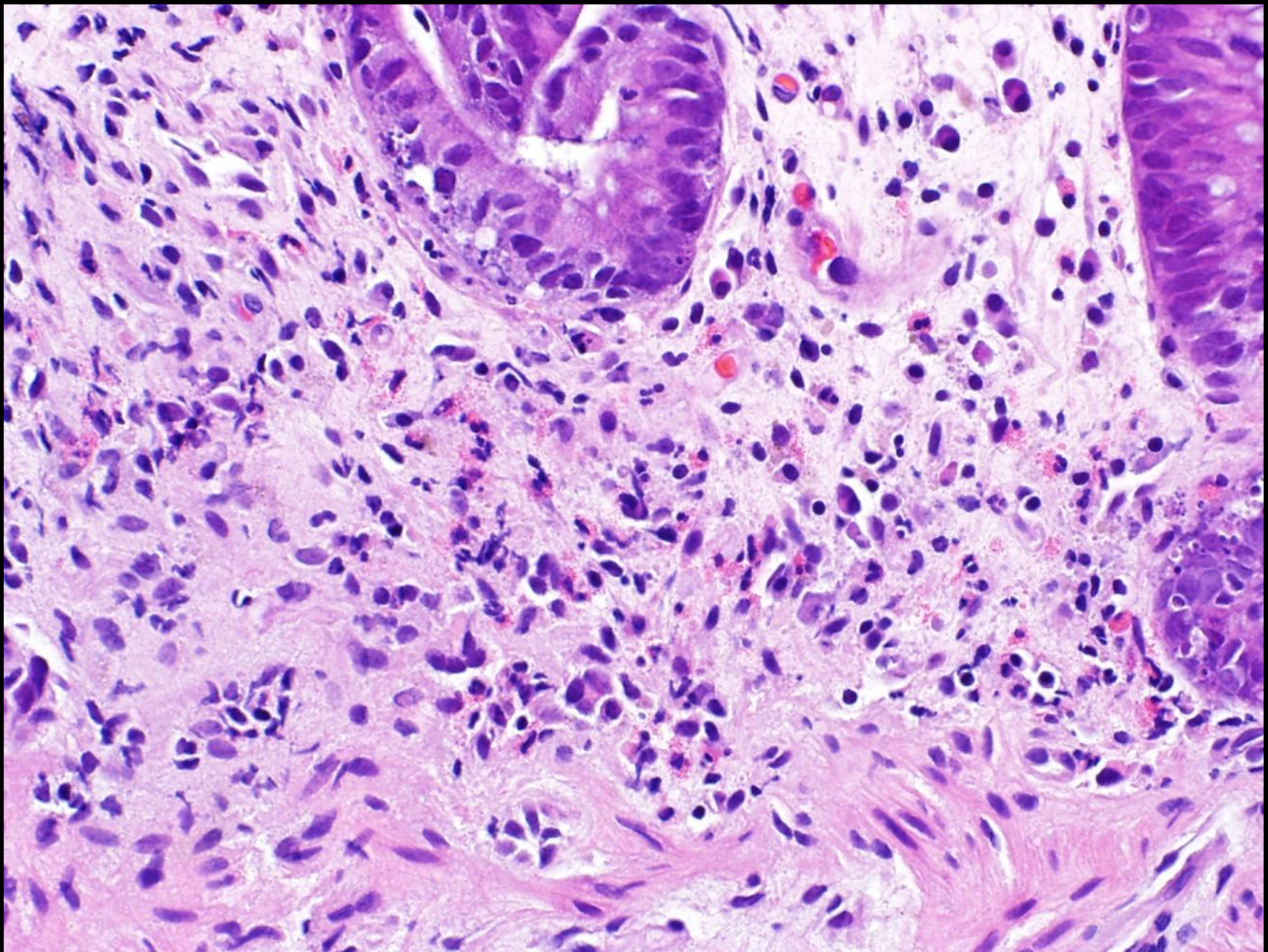
Abstract: Mycophenolate mofetil (MMF) is a T-cell inhibitor frequently used in the treatment of acute allograft rejection. MMF may cause colitis that clinically and histologically resembles graft-versus-host disease (GVHD). The aim of this study was to evaluate a wide range of histologic features that may help differentiate MMF from GVHD-induced colitis and to validate significant features on a cohort of bone marrow transplant patients who were also taking MMF as part of their immunosuppressive regimen and developed a diarrheal illness due to colitis. Routinely processed colonic biopsies from 17 patients with MMF colitis and 40 patients with GVHD-induced colitis

predictive values of 76%, 93%, 81%, and 90%, respectively, for identification of MMF colitis. On the basis of these data, we conclude that a variety of histologic features, in particular, eosinophils > 15 per 10 HPF, lack of endocrine cell aggregates in the lamina propria, and lack of apoptotic microabscesses, can be used by pathologists to help separate MMF from GVHD-induced colitis in routine clinical practice.

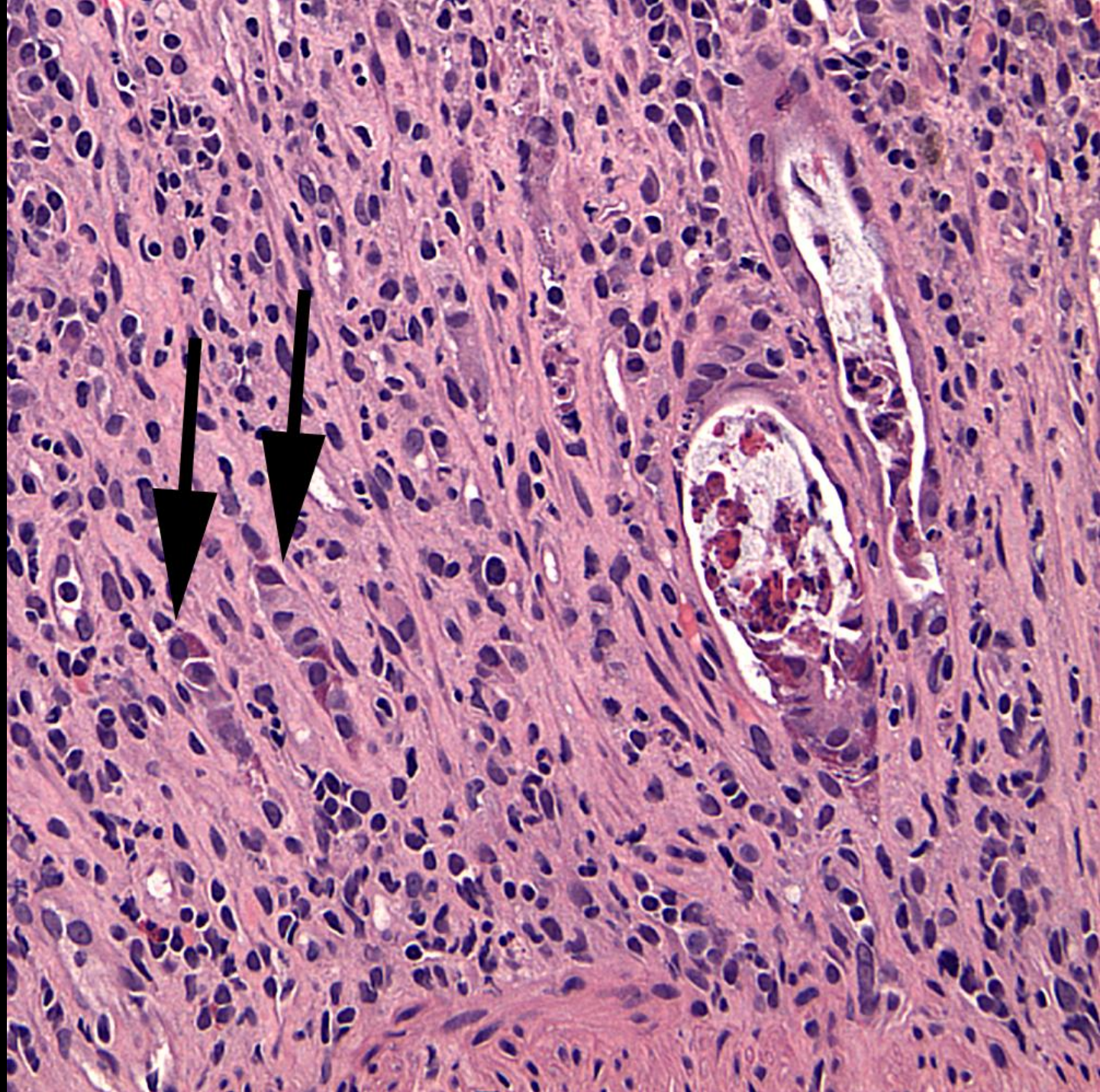
Key Words: graft-versus-host disease, drug-induced colitis, toxic colitis, eosinophils, apoptosis, differential diagnosis

(*Am J Surg Pathol* 2013;37:1319–1328)

>15 eosinophils per 10 HPF = MMF

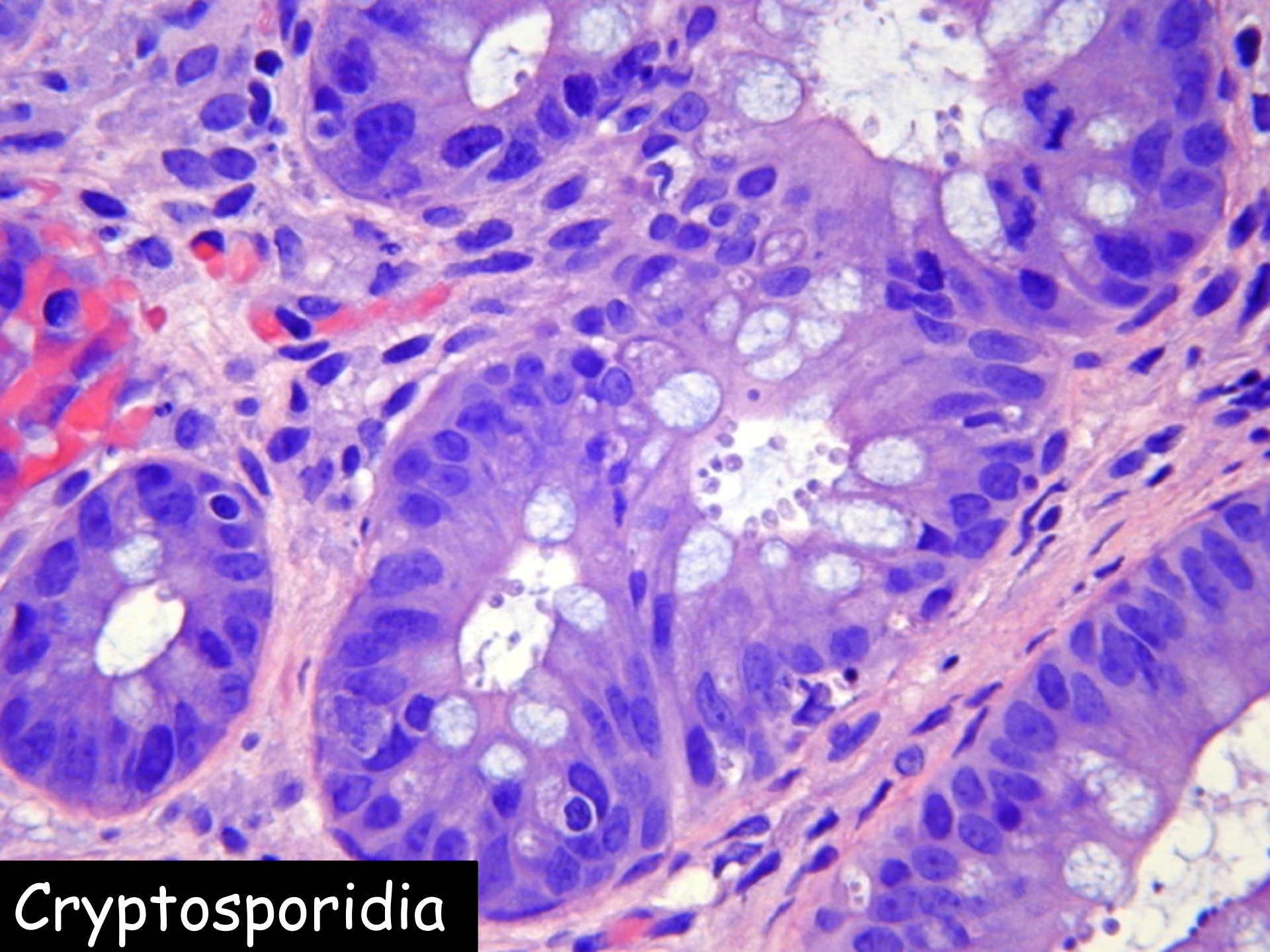


GVHD with numerous eosinophils

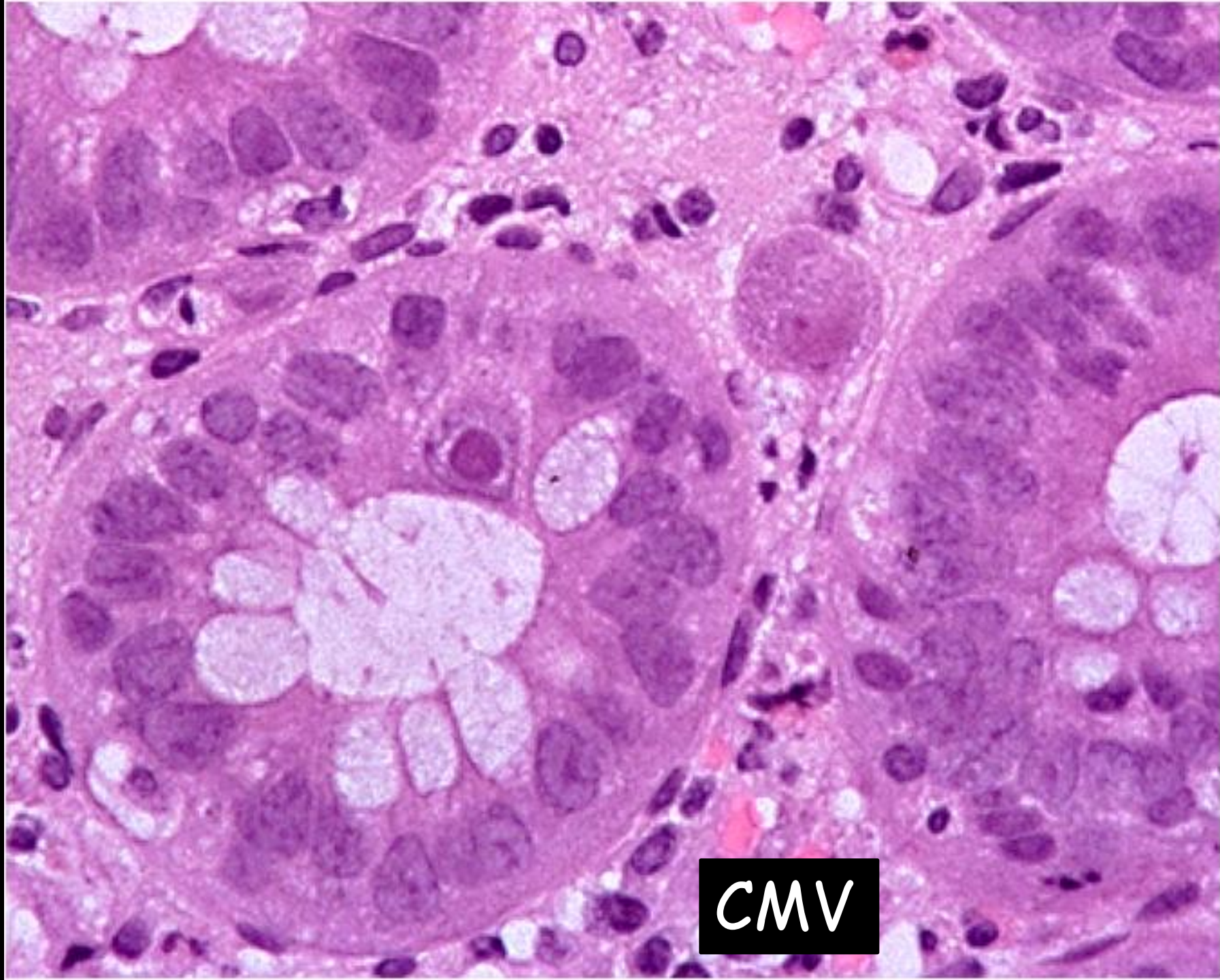


Infections and Apoptosis

- CMV
- Adenovirus
- HIV
- Cryptosporidia
- Bacteria?
 - Usually neutrophils/crypt abscess



Cryptosporidia



CMV

MS Art - Grading Rubric

Name: Adam R.

Project: Graffiti Lettering

1. Large, overlapping letters (3) 3 pts

* 2. Placement of Shadows (3) 1 pts

3. Use of Color (3) 3 pts

** 4. Craftsmanship (3) 2 pts

sub-total 9 pts

(adjusted +1 pts = 10 pts)

÷ weight of 1 = 10 total points

* Shadows need to be consistent,

** Erase guidelines,

(+1 pt. for staying late to finish)

Grade A-

Grading Scale for Art

12 points = **A+**

11 points = **A**

10 points = **A-**

9 points = **B+**

8 points = **B**

7 points = **B-**

6 points = **C+**

5 points = **C**

4 points = **C-**

3 points = **D+**

2 points = **D**

1 point = **D-**

0 points = **F**

Points may be adjusted for behavior, attitude and appropriate use of time.

GVHD Grading Scheme

GVHD GRADE

PATHOLOGY

I

SCATTERED
APOPTOSIS

II

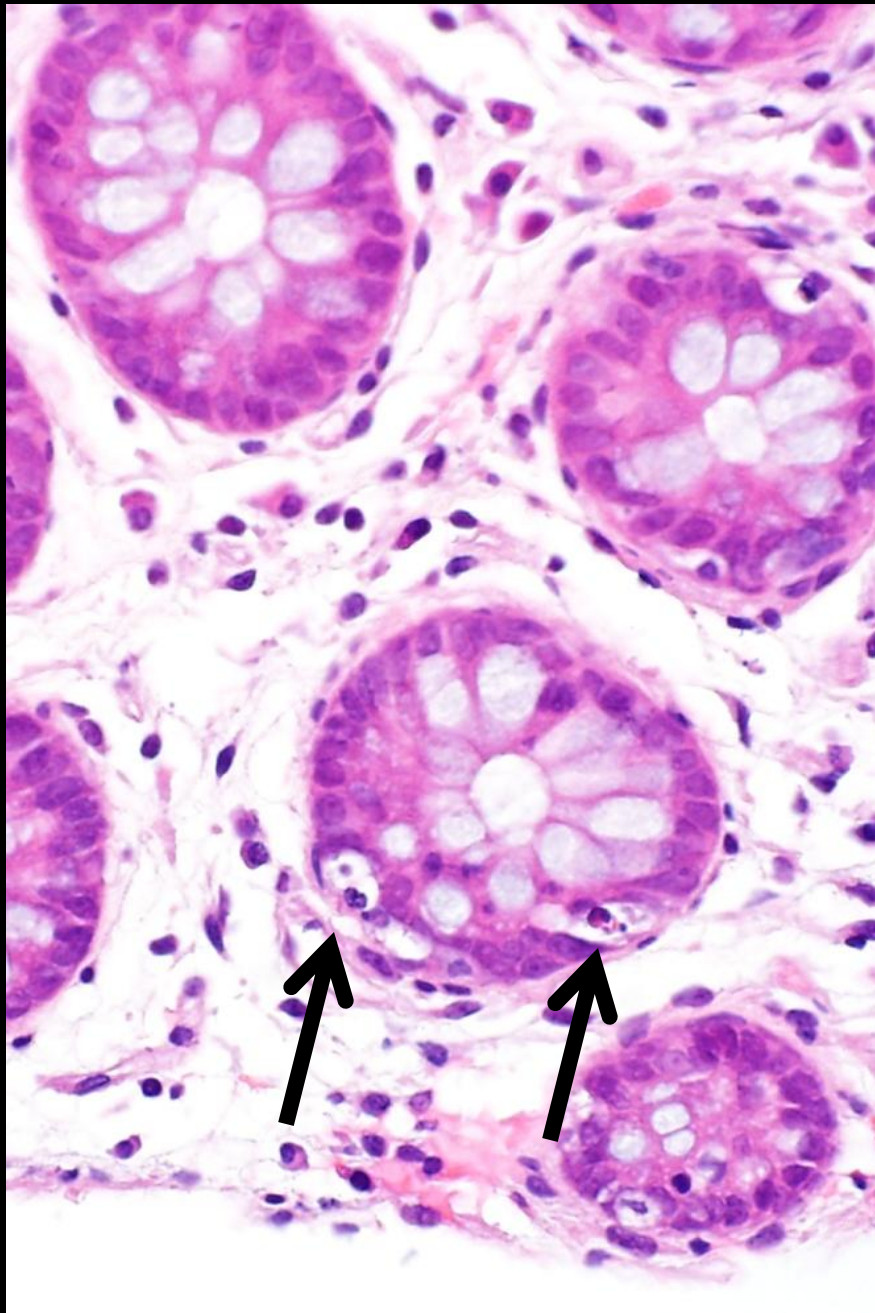
APOPTOSIS OF
COMPLETE CRYPT

III

LOSS OF CRYPTS

IV

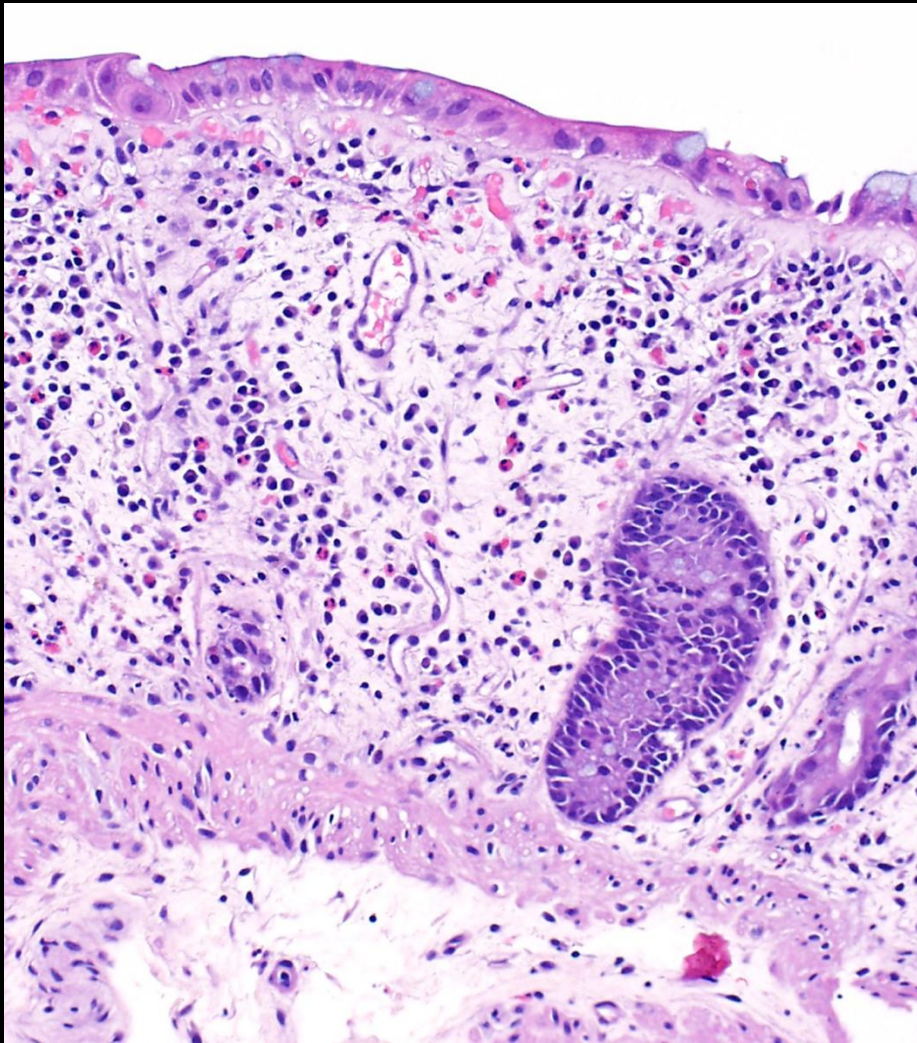
DENUDED MUCOSA



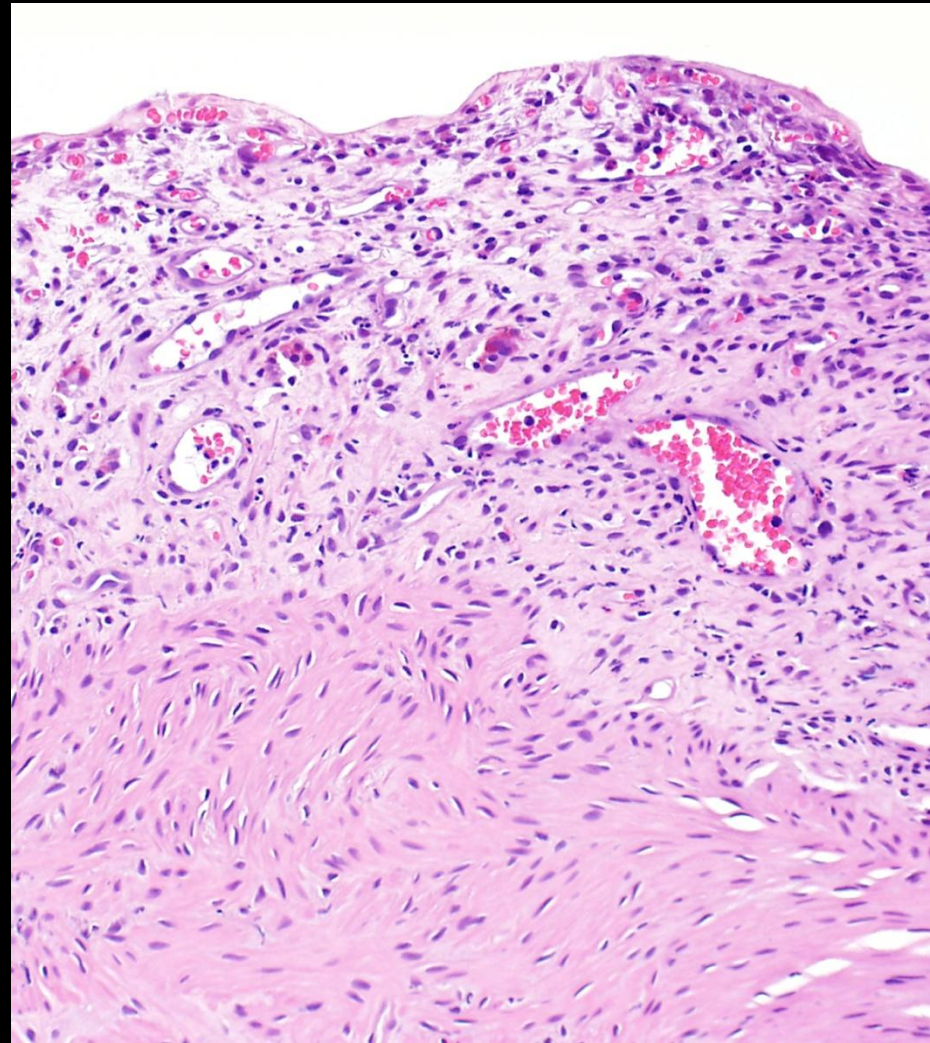
Grade I GVHD



Grade II GVHD



Grade III GVHD



Grade IV GVHD



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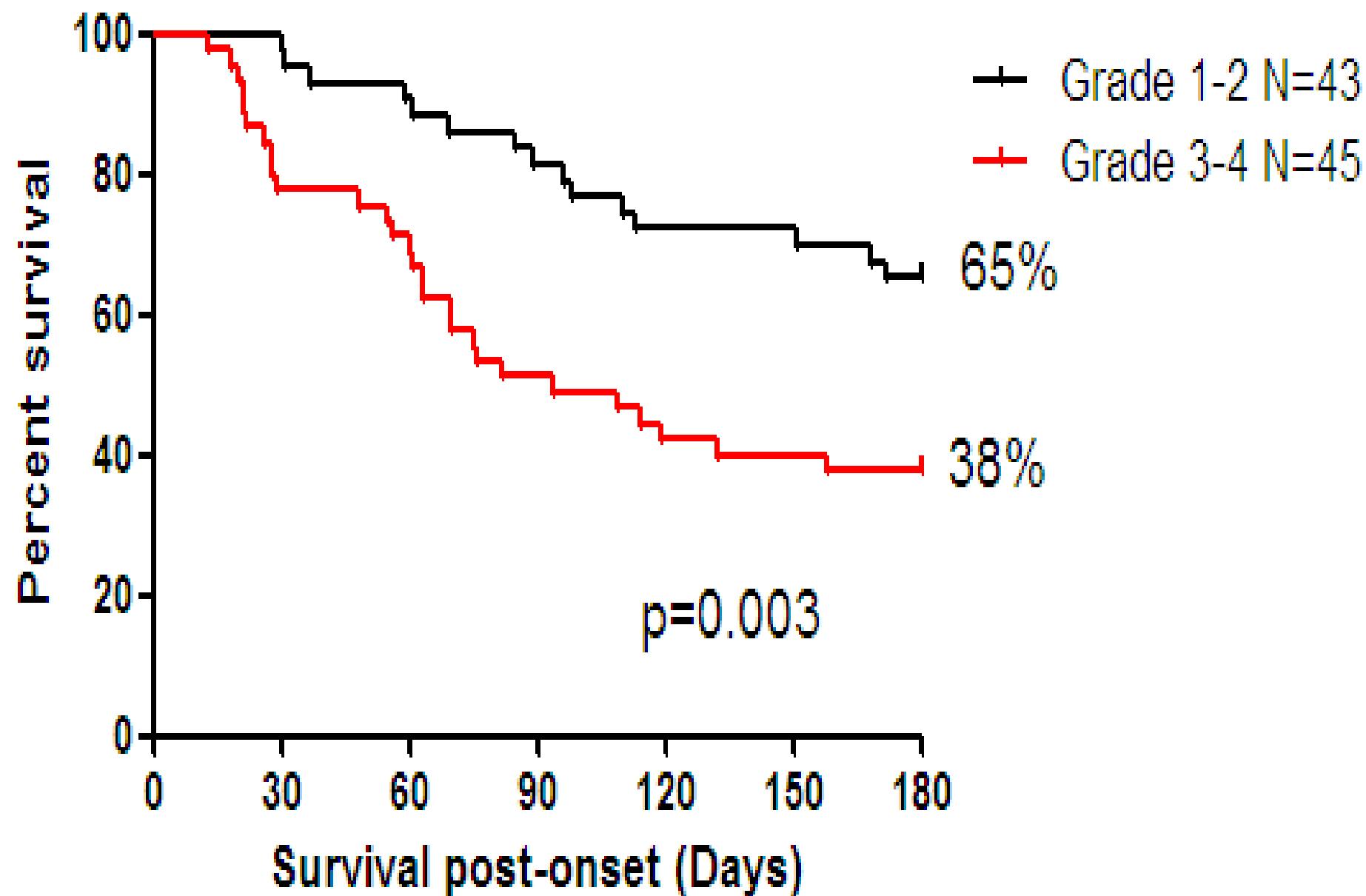
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Recommended sign out:

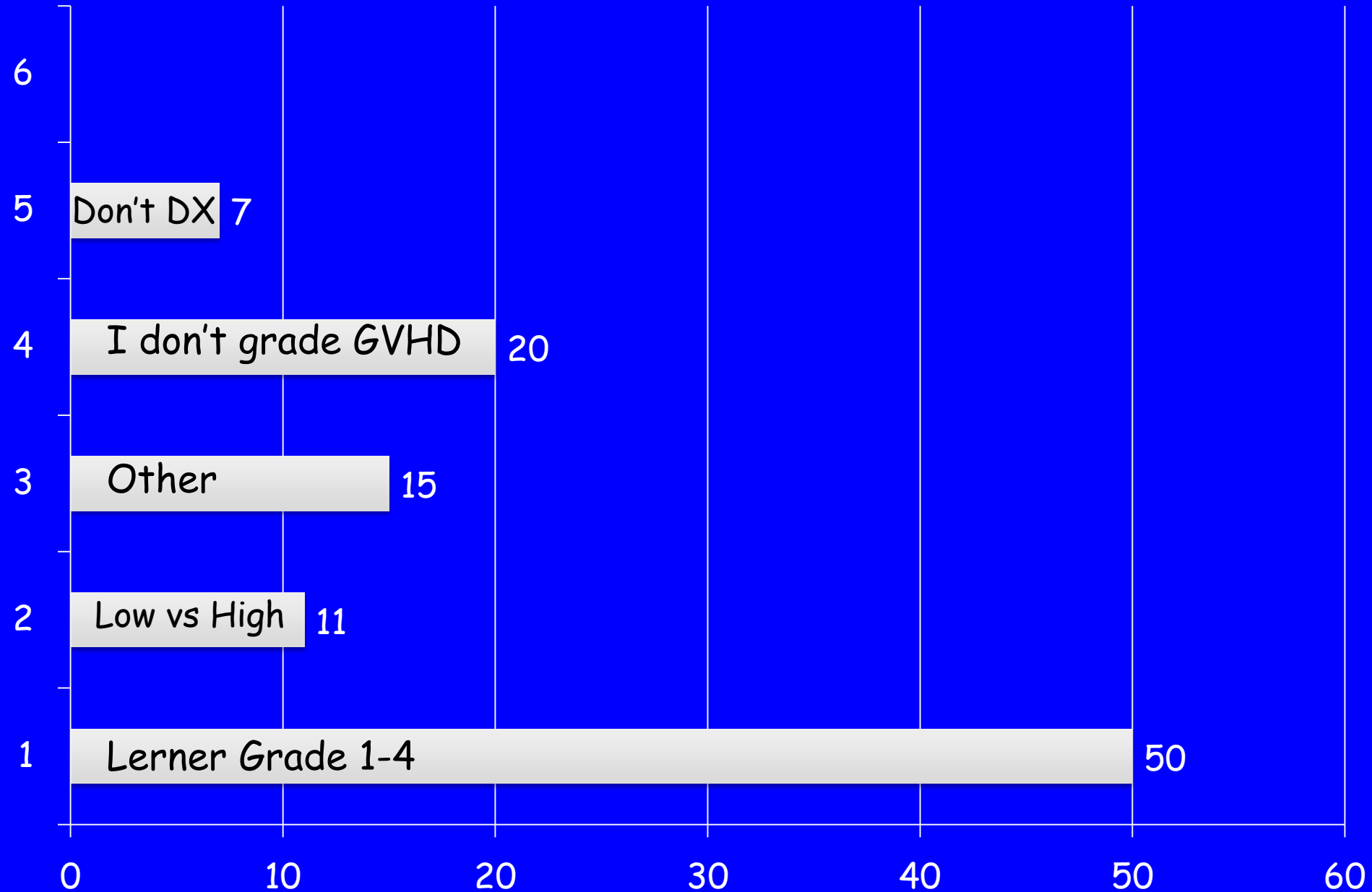
1. No GVHD
2. Possible GVHD
3. Consistent with GVHD
4. GVHD

WHO IS GIVING YOU THE GRADE

THE TEXTBOOK OR ME?



How do you grade GVHD?





Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org



Report

NIH Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: II. The 2014 Pathology Working Group Report



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Recommended sign out:

1. Negative for GVHD
2. Possible GVHD
3. Likely GVHD



Minimum Criteria for Grade 1 GVHD

