

When to Incorporate Infectious Disease Stains?

Maria Westerhoff

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GIPS USCAP FORUM DISCUSSION

Goals for this Forum Topic – Discuss:

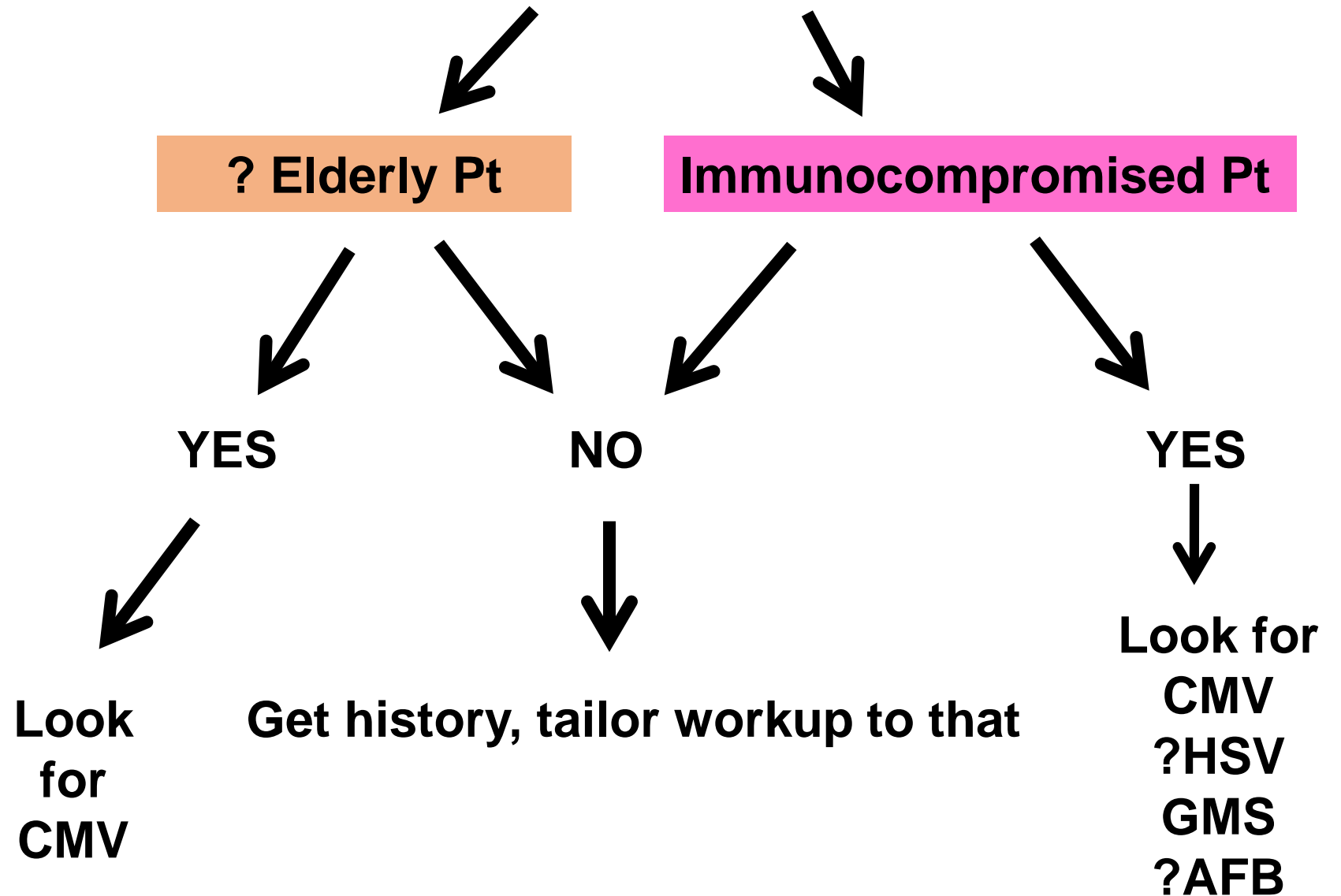
- **When do YOU incorporate infectious disease stains in routine practice?**
 - CMV and Colitis
 - Immunocompromised patient
 - Granulomas
 - **If we have time:**
 - When to incorporate infectious disease stains in unusual situations
- **All questionnaire results not mentioned during this session (due to time constraints), will be posted on GIPS website – see Nicole Panarelli to become a member to access all GIPS PPTs (npanarel@montefiore.org)**

Pattern of Tissue Injury

Clinical Setting

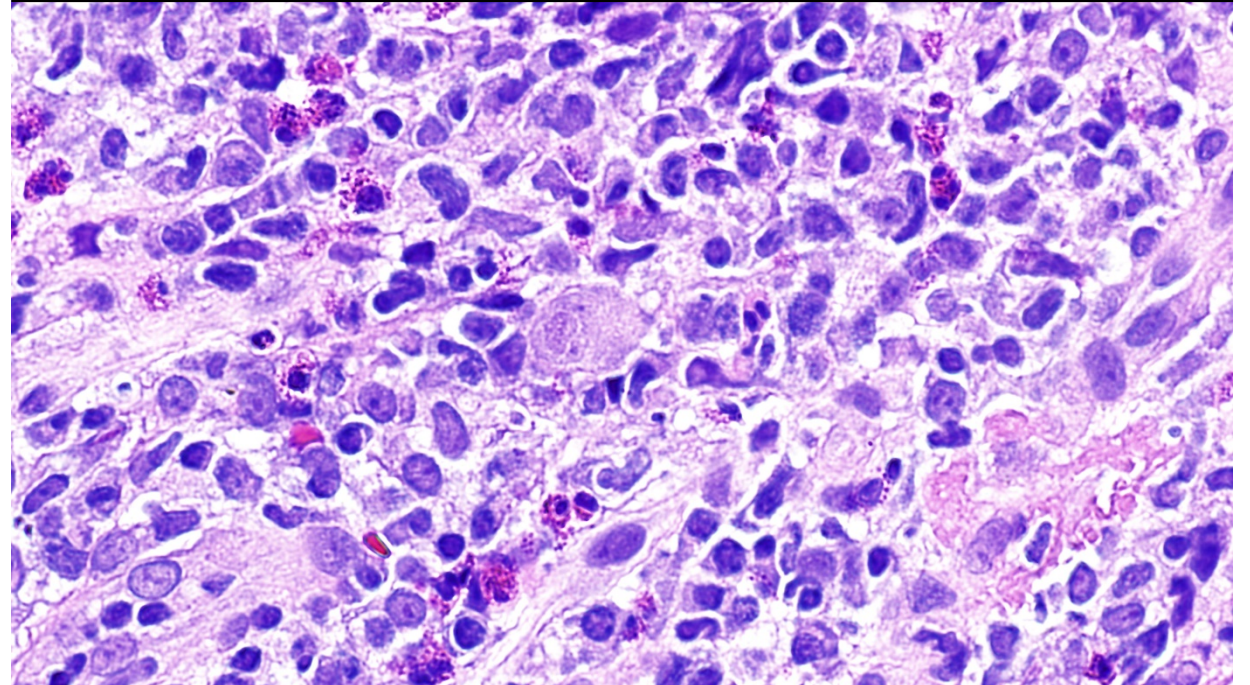
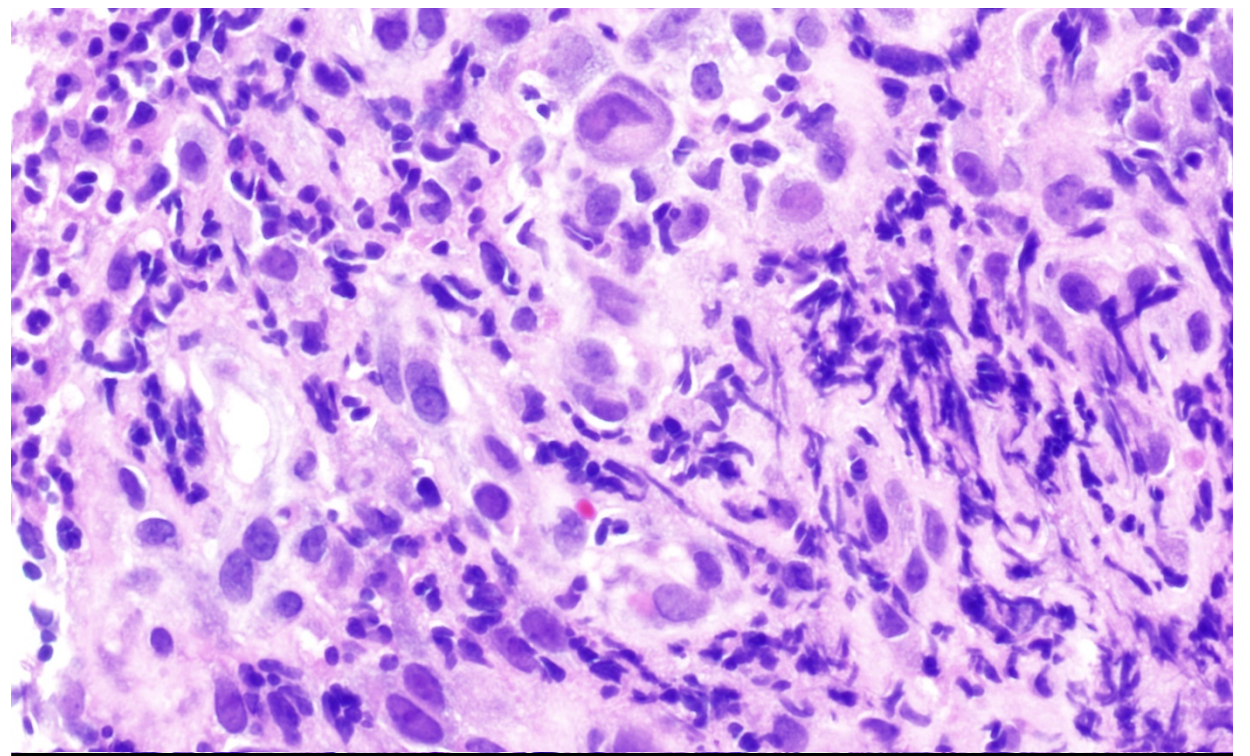
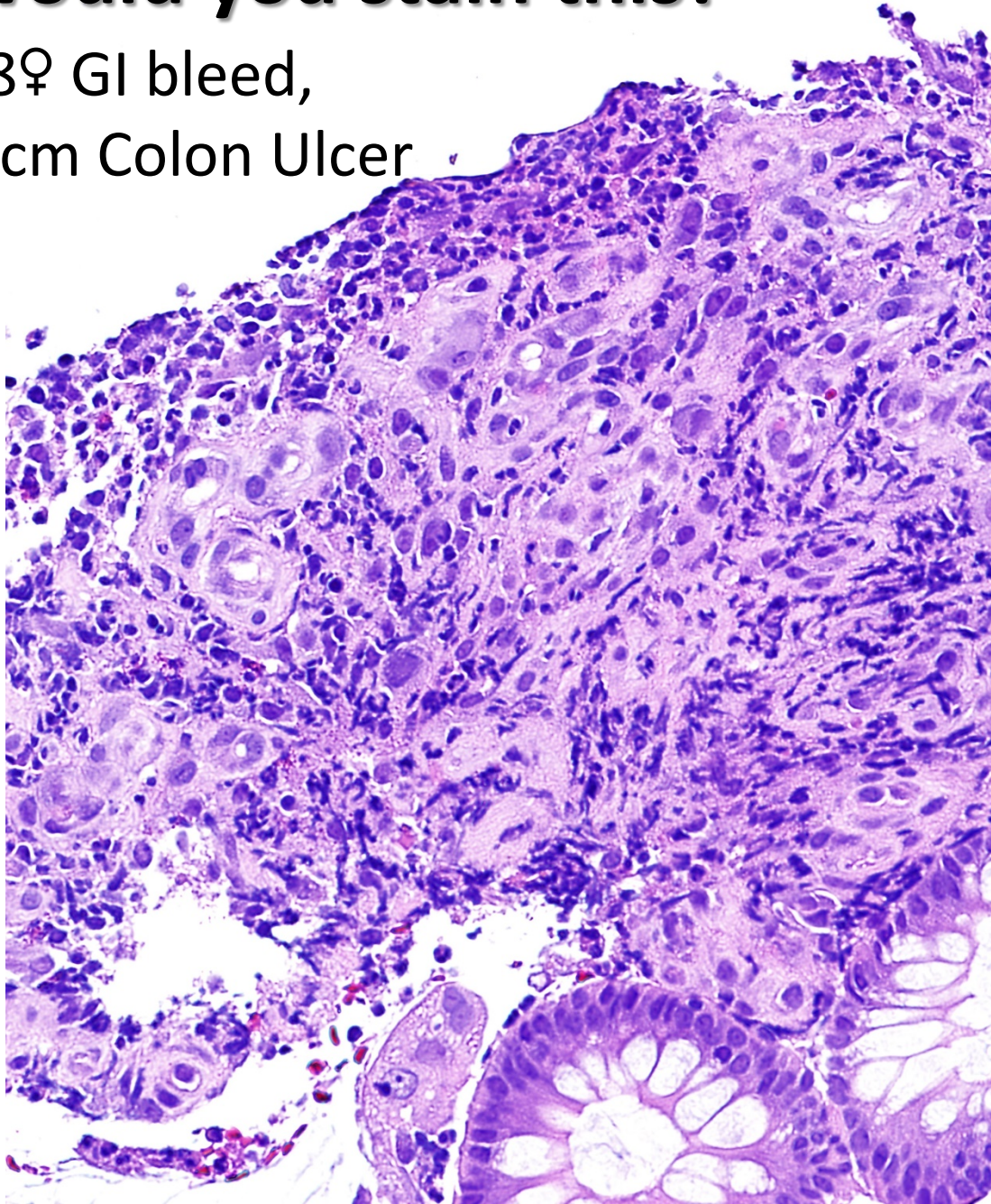
Ability/Comfort Level to Identify Infection without Stains

Big Unexplained Ulcer

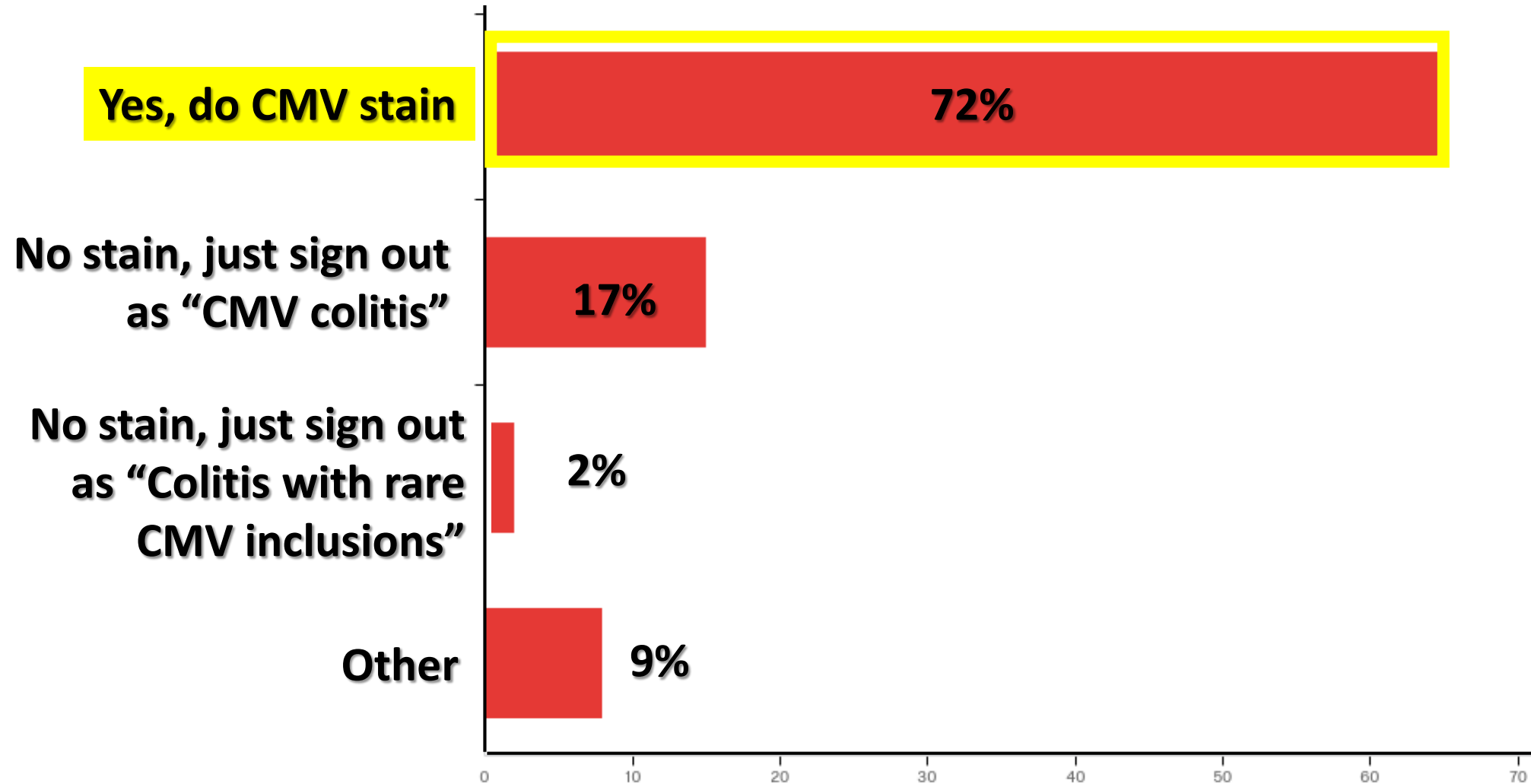


Would you stain this?

88♀ GI bleed,
2 cm Colon Ulcer



GIPS MEMBERSHIP RESPONSES (n =99)



Cytomegalovirus (CMV) in gastrointestinal mucosal biopsies: should a pathologist perform CMV immunohistochemistry if the clinician requests it? ☆,☆☆

Gordana Juric-Sekhar MD, PhD, Melissa P. Upton MD,
Paul E. Swanson MD, Maria Westerhoff MD*

Department of Pathology, University of Washington, Seattle, WA, 98195 USA

- 449 clinical requests to rule out CMV: 37 positive for CMV (26 of those with IHC) (8.2% positive)
- 238 CMV analyses initiated by pathologist without clinical request: 15 positive for CMV (12 with IHC): (6.3% positive)
- Of those cases that were detected by IHC (n=38), **27 had overt viral inclusions on H&E (71%) on blinded retrospective review**
- **The 11 cases that did not show obvious inclusions:**
 - **8 were cases that had clinical request to r/o CMV (30% of cases with CMV IHC had no obvious inclusion)**
 - **3 without clinical request had severe tissue inflammatory reactions triggering the pathologist to order IHC for CMV (25% of cases with CMV IHC had no obvious inclusion)**

UW Study: Yield of CMV Evaluations depending on Clinical Request

Human Pathology (2017) 60, 11–15

CMV requested by Clinicians n = 449
8.2% +CMV

- 11 CMV detected without IHC
- 366 had IHC performed
 - 340 negative (93%!)
 - 26 positive- 8 did not have obvious inclusions on H&E

71% +CMV IHC had +Overt inclusions on H&E (n=27)

Sensitivity of H&E to detect CMV 79%

CMV IHC or H&E detection by pathologist without clinical request
n = 238
6.3% +CMV

- 3 CMV detected without IHC
- 235 had IHC performed
 - 223 negative (95%!)
 - 12 positive- 3 did not have obvious inclusions on H&E, but severe tissue inflammation triggered order for stain

Pattern of Tissue Injury

Clinical Setting

Ability/Comfort Level to Identify Infection without Stains

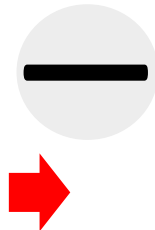
My Approach

- **If I see unequivocal CMV on H&E, I don't stain → Just diagnose as CMV**
 - 79% of CMV cases – visible inclusions
- **If I don't see inclusion but:**
 - Pattern of tissue injury [ulcer] + Concerning Clinical Setting + I am uneasy about H&E quality, etc → I stain it (~30% of the positive IHC did not have obvious inclusions)

ACG Guidelines on UC flares

What Does CMV Tissue + Mean Clinically? U of M Clinical Practices (2016-2019)

- 120/82,465 GI biopsies: “evaluate for CMV”
- 56 IBD, 27 GVHD, 30 solid organ tx
- 64% had serum CMV PCR



- 10/109 Treated despite
Neg CMV GI bx
- Average CMV PCR:
9665 I.U./mL

- Average serum CMV PCR
for 99/109 Untreated Neg
CMV GI bx:
112 I.U./mL



9.1% (n=11)
+CMV GI bx

- 10/11 Treated for CMV:
- Average CMV PCR:
4740 I.U./mL

- **CMV can cause tissue disease with discordantly low PCR serum levels**
- **Clinician will treat CMV if biopsy positive 91%**
- **Will treat even if biopsy is CMV neg: 9%**

What Does CMV Tissue + Mean Clinically? IBD - U of M Clinical Practices (2016-2019)

IBD

- 56/120 "evaluate for CMV"
- 0.067% of all GI biopsy requests
- 48% had serum CMV PCR

- 2/53 Treated despite Neg CMV GI bx
- CMV PCR of these 2:

0, 3369, I.U./mL

- Average serum CMV PCR for 51/53 Untreated Neg CMV GI bx:

30 I.U./mL

+

5.4% (n=3)
+CMV GI bx

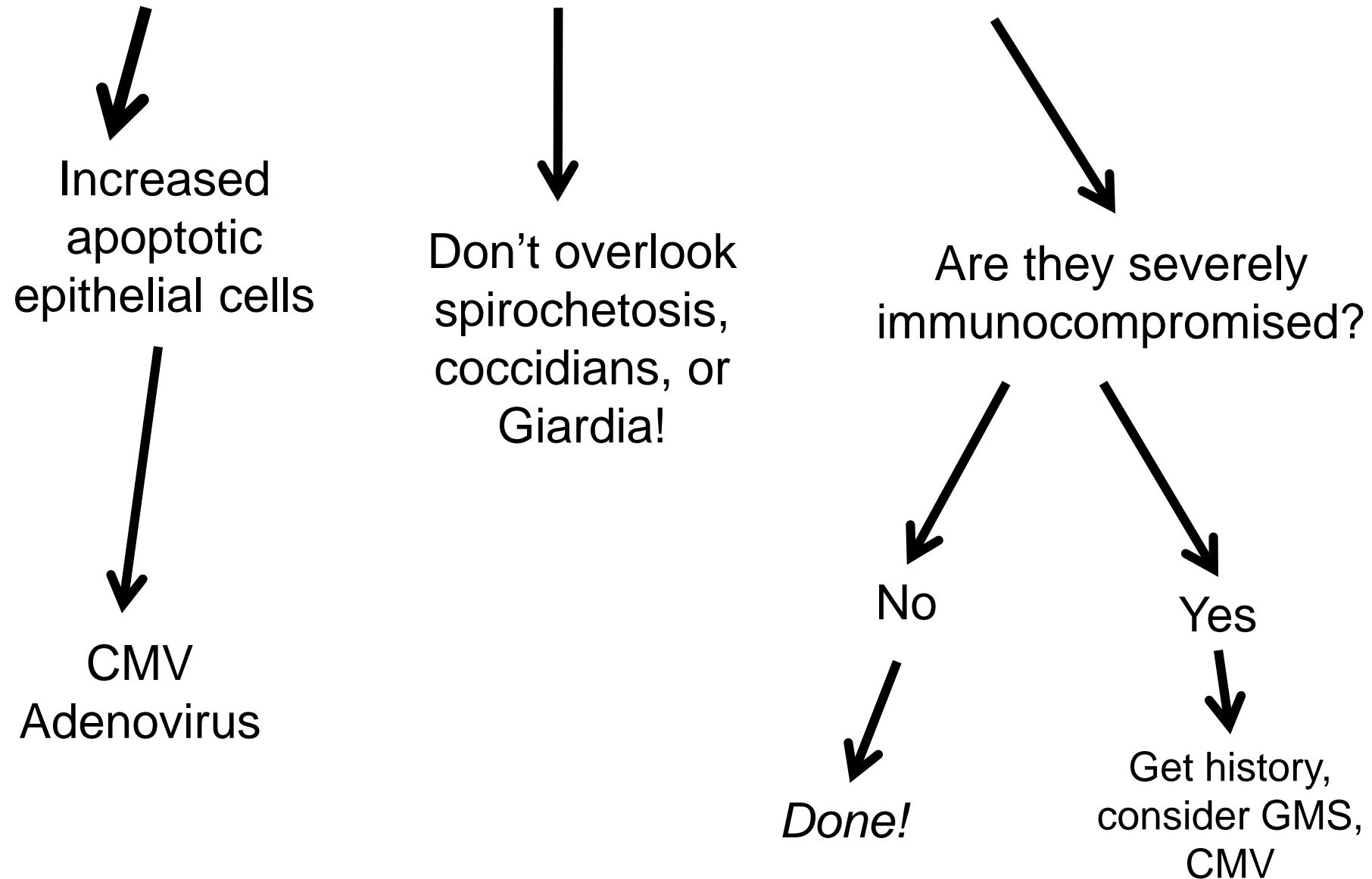
- 2/3 Treated for CMV:
- CMV PCR:

384, 6158, I.U./mL

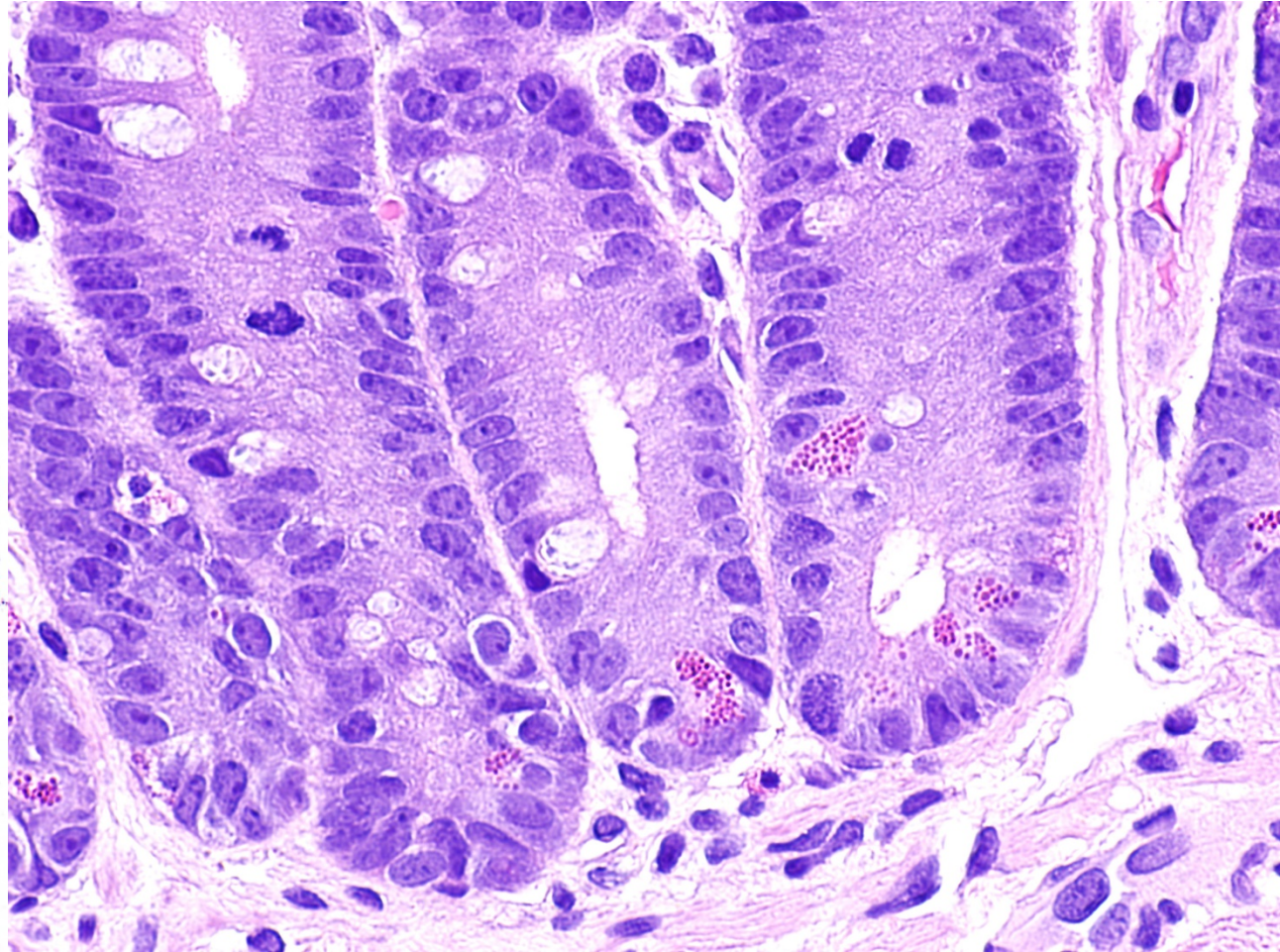
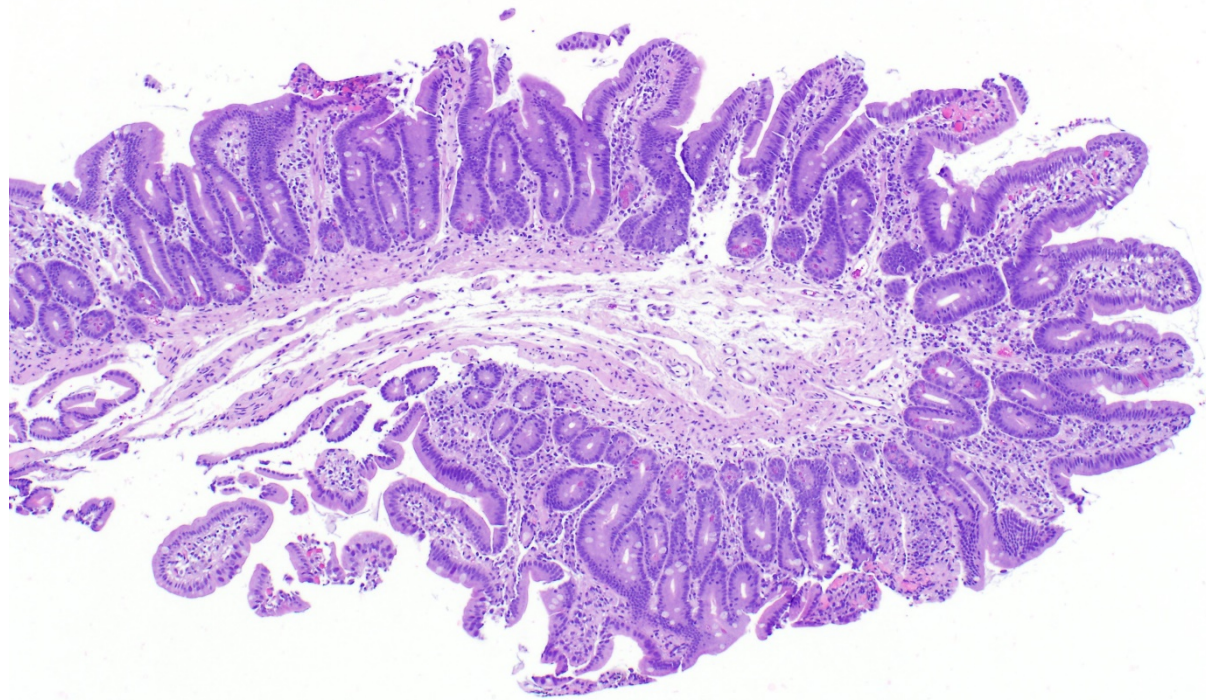
Indications for rule out CMV in IBD documented for 49:

- Flare (29)
- Flare while on Treatment or refractory to treatment (10)
- Severe endoscopic findings (4)
- Other: fevers chills, pain, hematochezia (6)

Essentially Normal Bx in Immunocompromised Patient

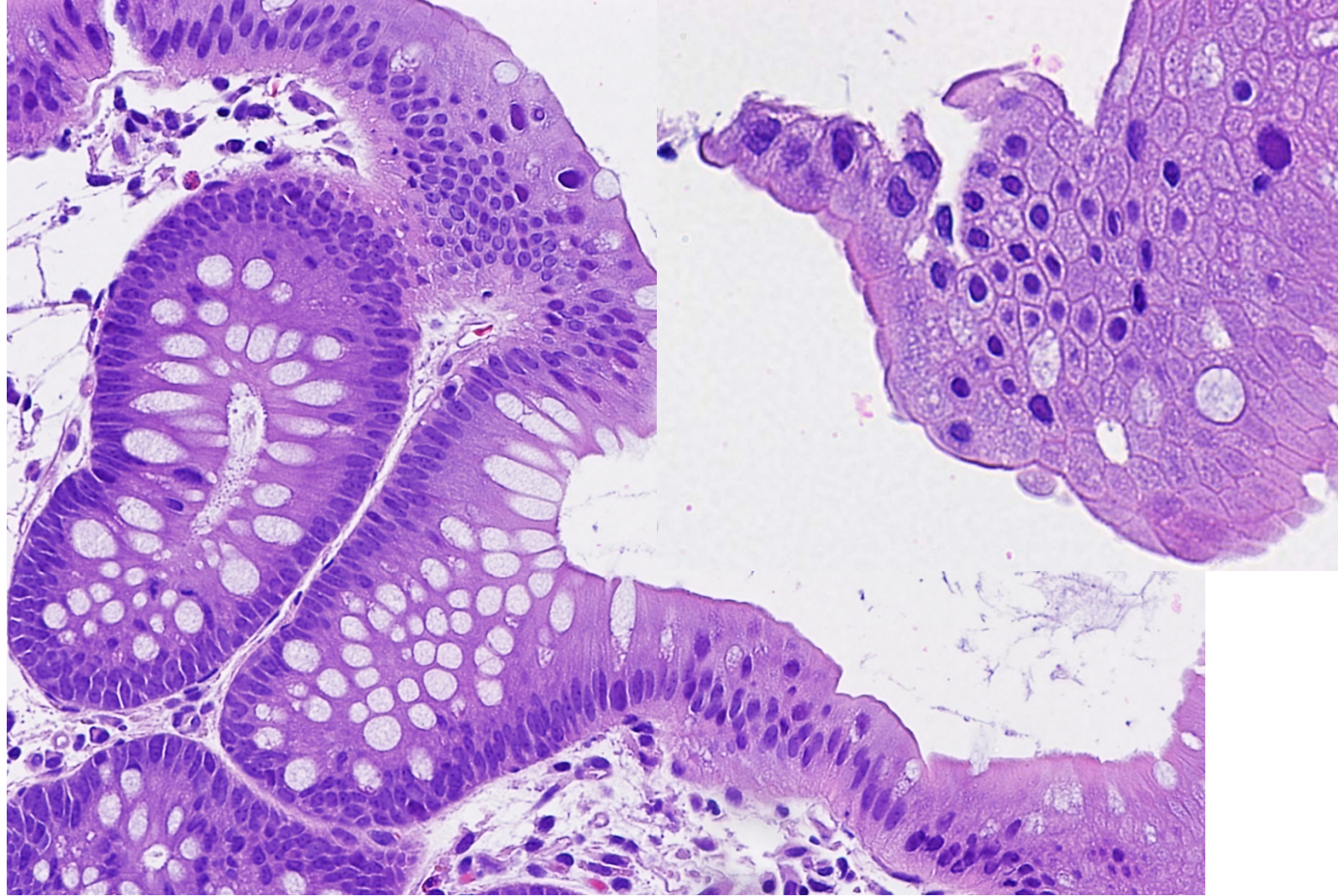
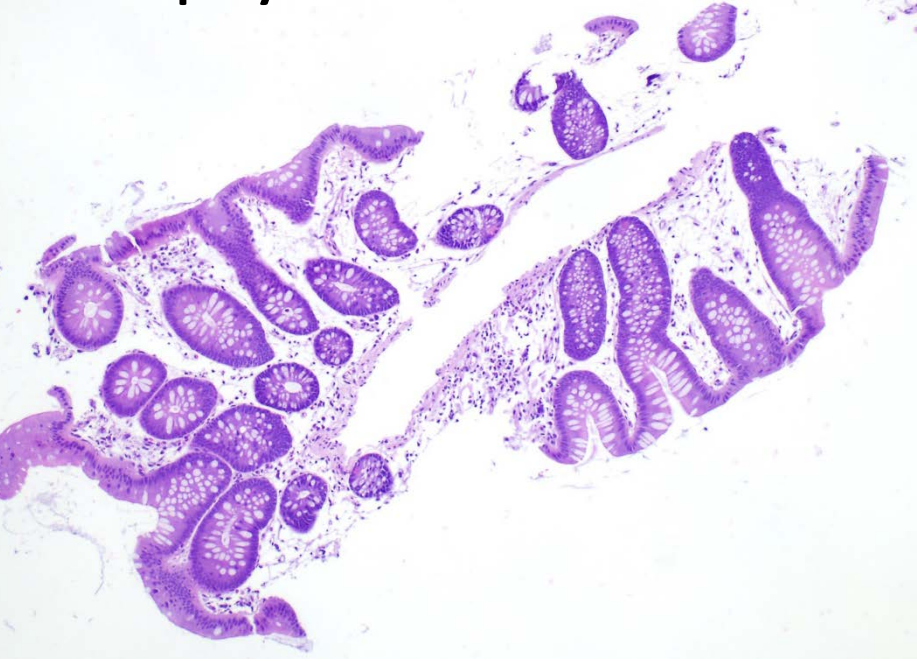


“Rule out GVHD”

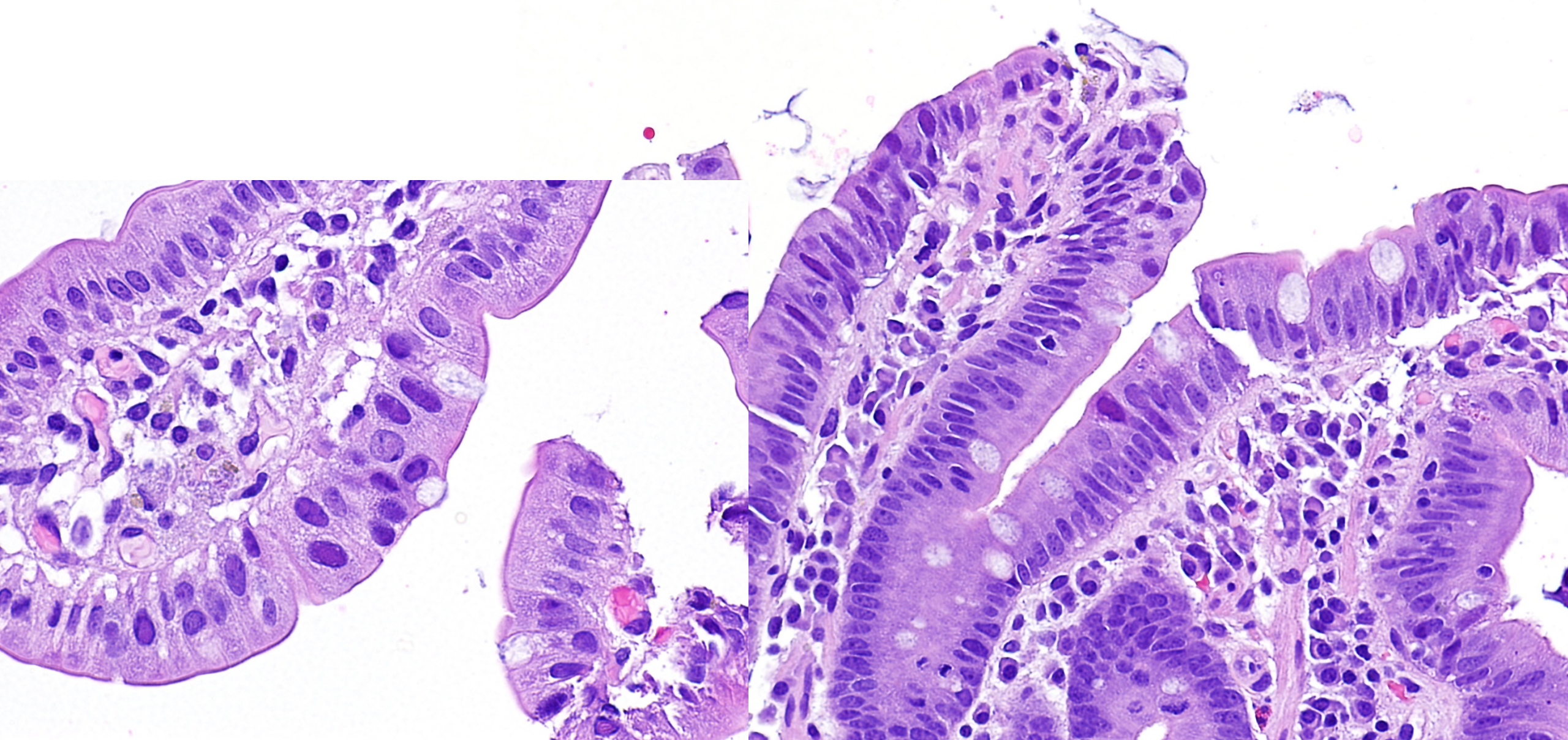


Would you stain this?

Biopsy for "Rule out GVHD"



“Rule out GVHD” case continued

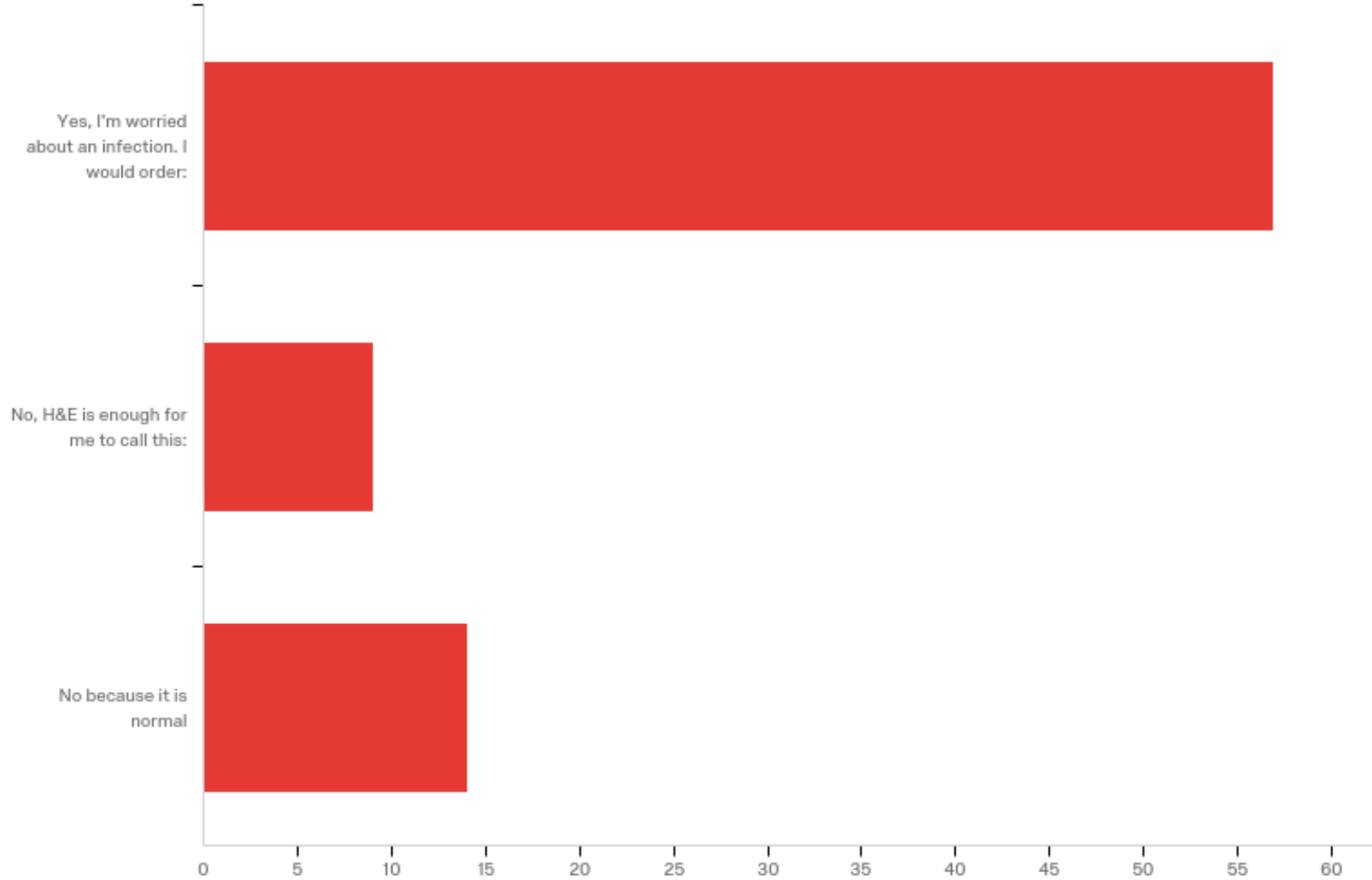


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Poll: High-grade squamous intraepithelial lesion

GIPS Membership Response

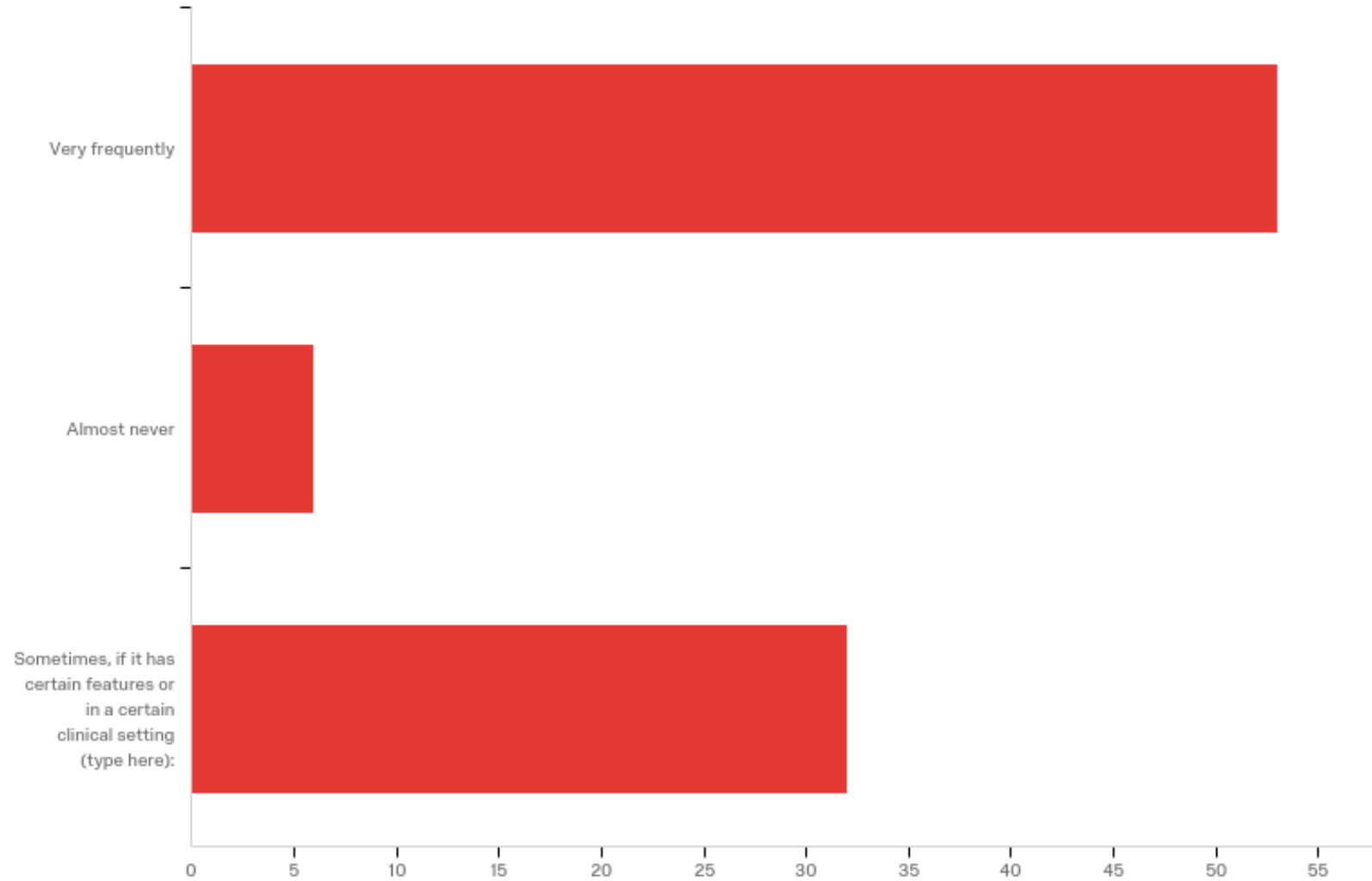


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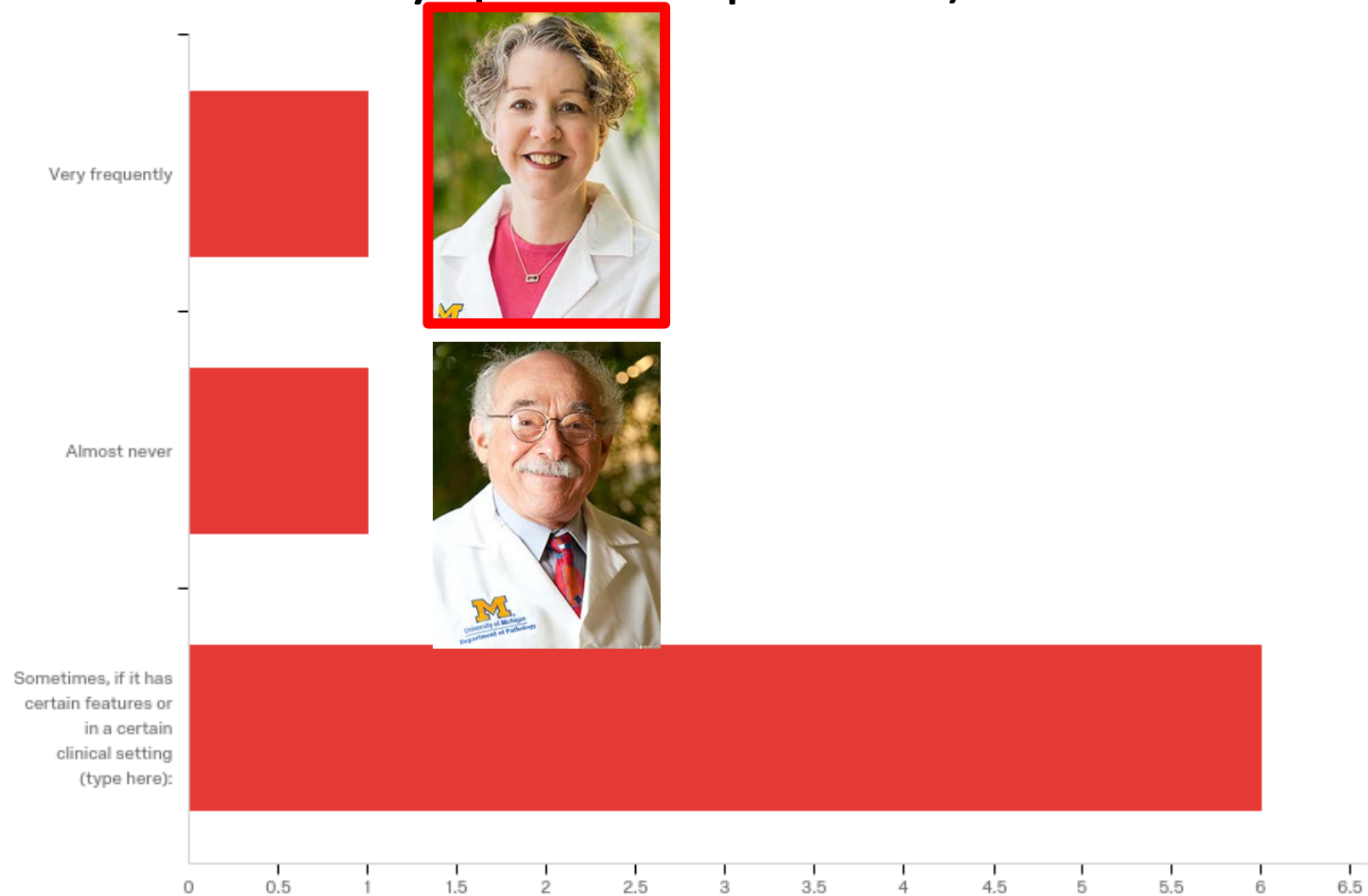
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Poll: If you see a granuloma on a GI biopsy, how often do you order special stains?

GIPS membership response

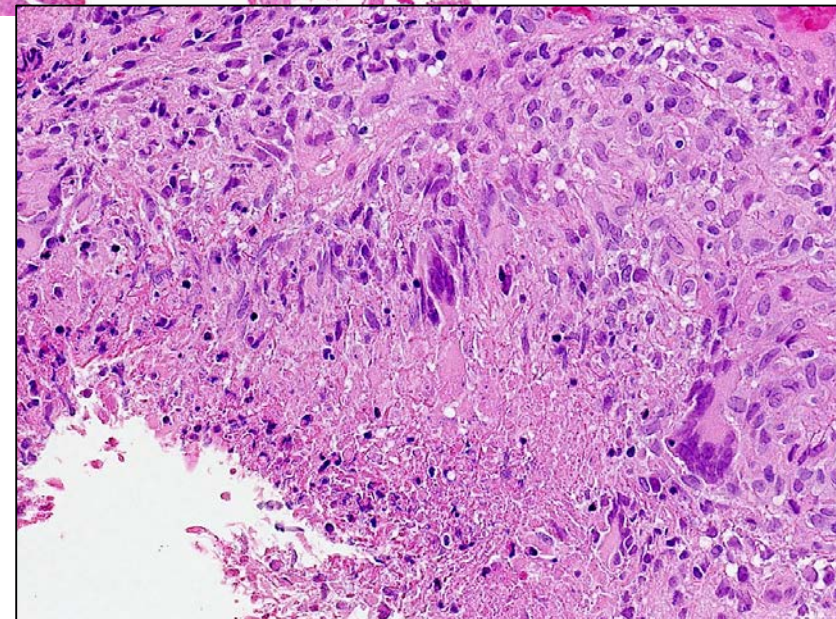
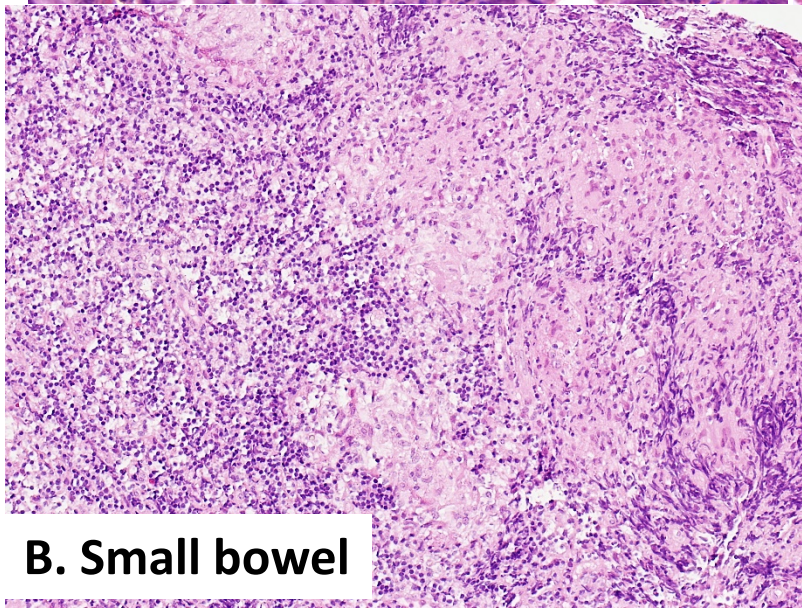
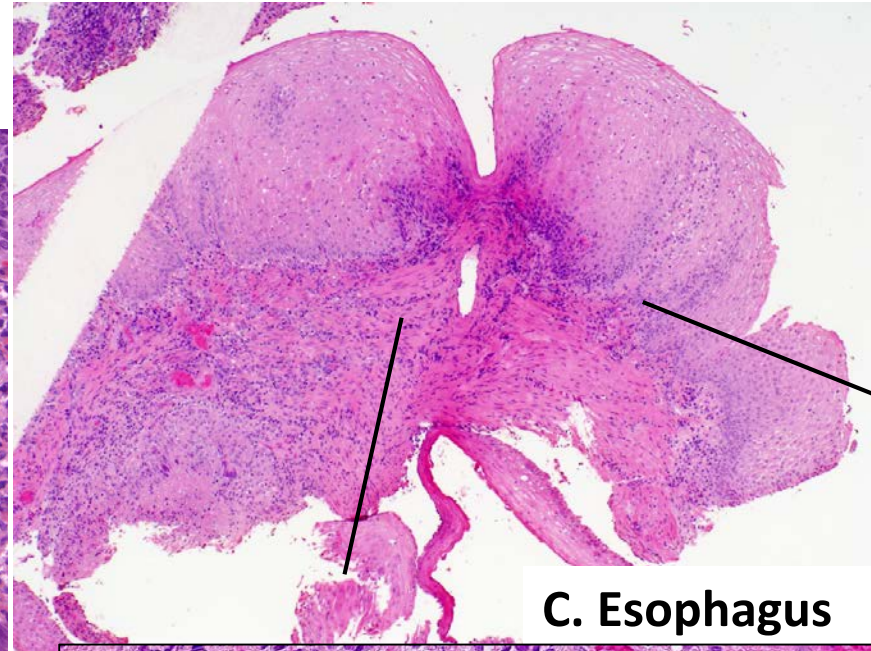
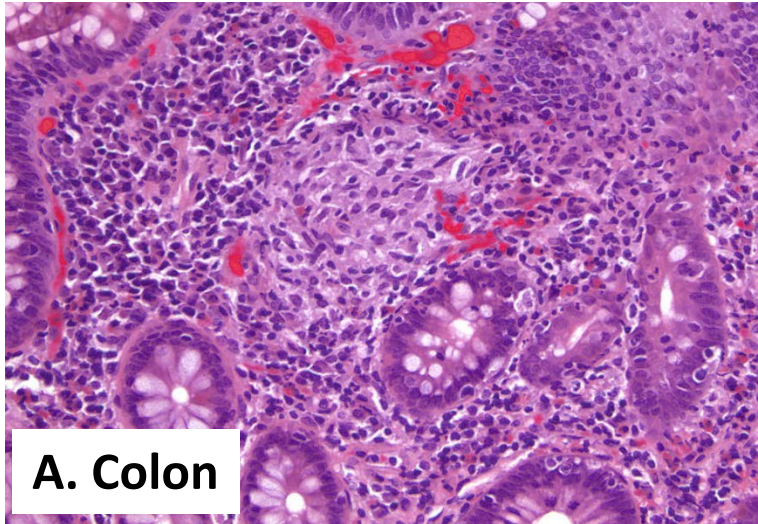


Spectrum of U of M response (with permission by participants)



ARS!!! Which Granuloma would you stain?

- A.
- B.
- C.
- D.

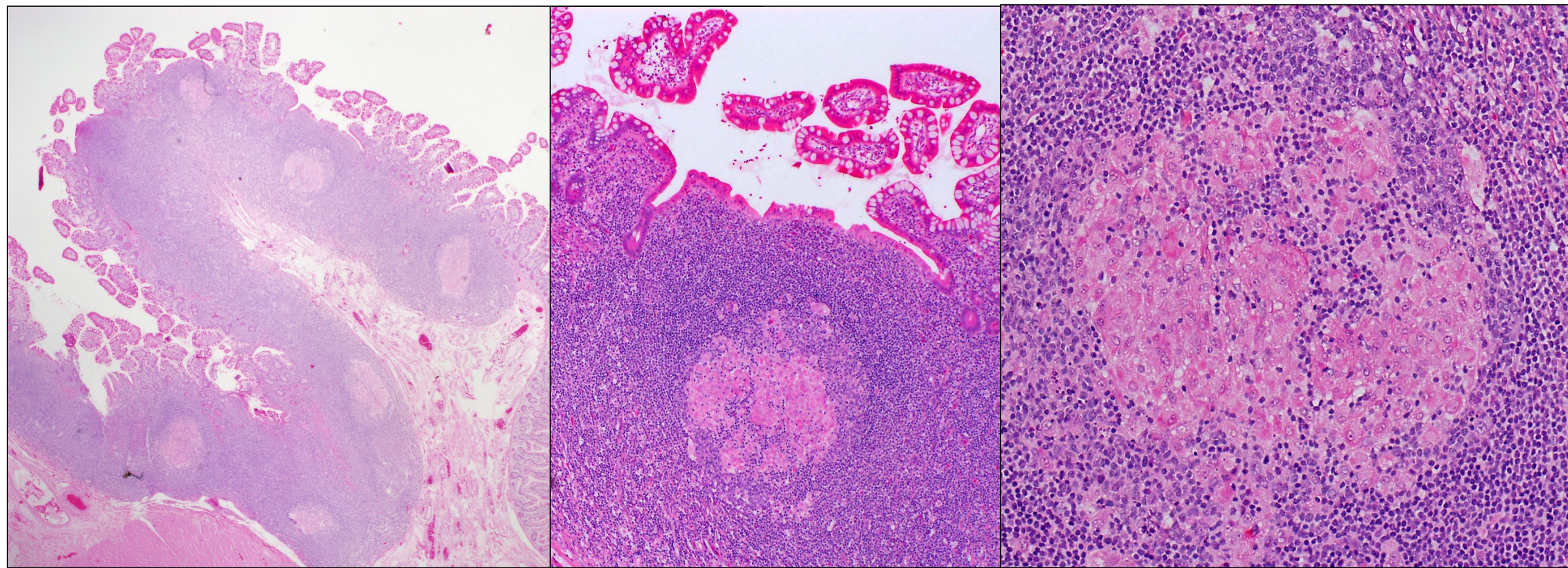


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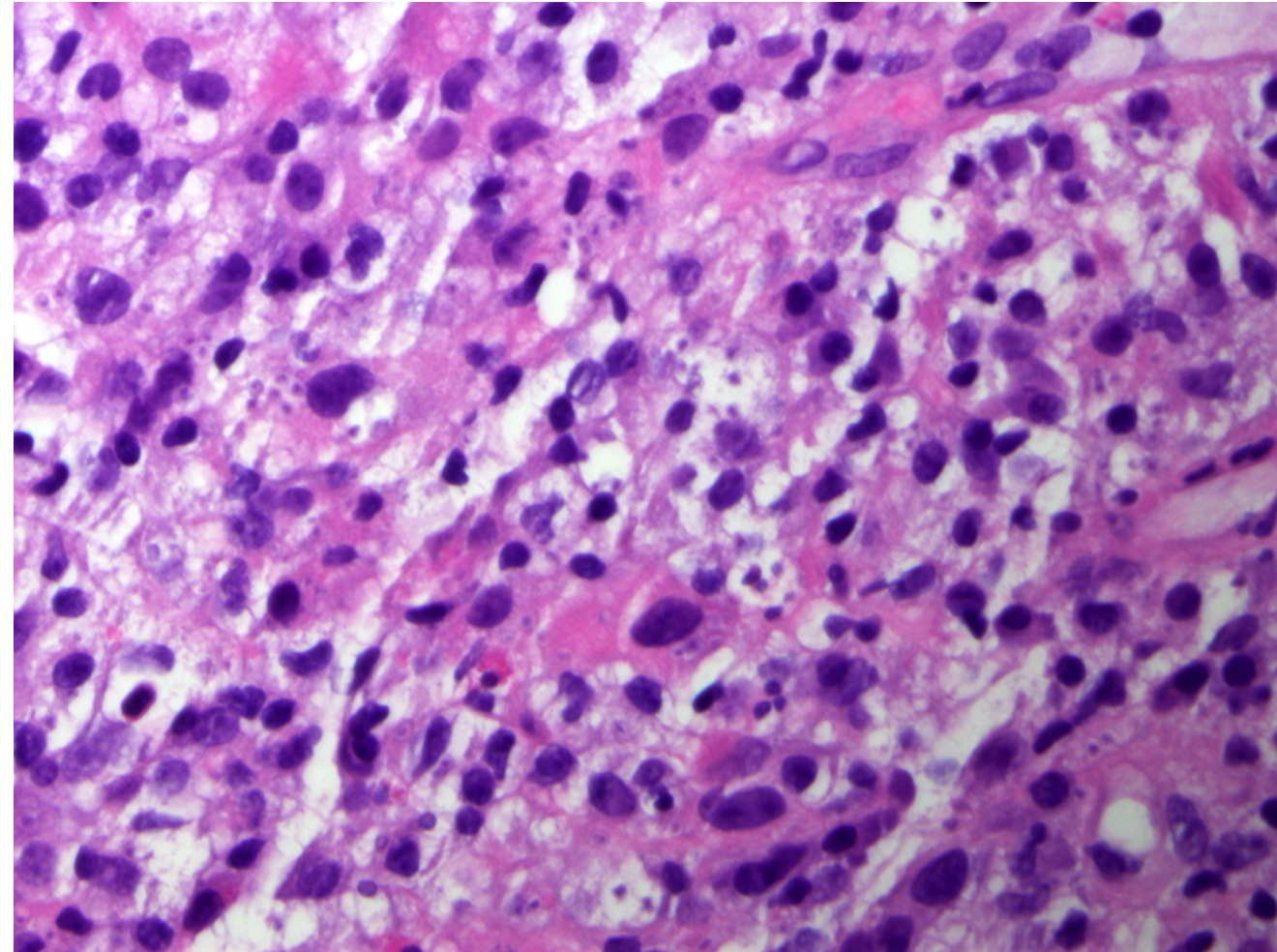
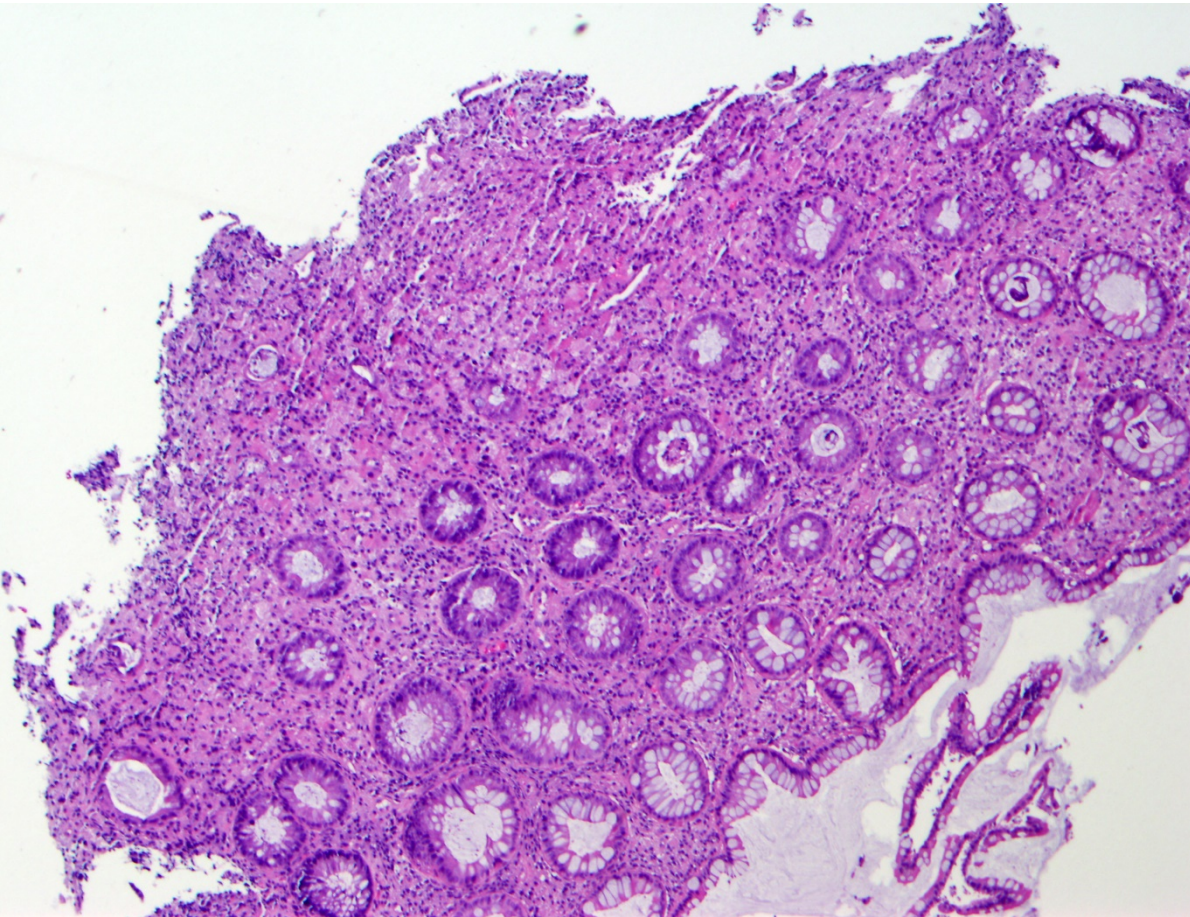
Poll: Which Granuloma would you stain?

Sometimes Non-necrotizing Granulomas Turn out to be Infectious



Case Courtesy of Dr. Laura Lamps: *Mycobacterium avium-intracellulare*

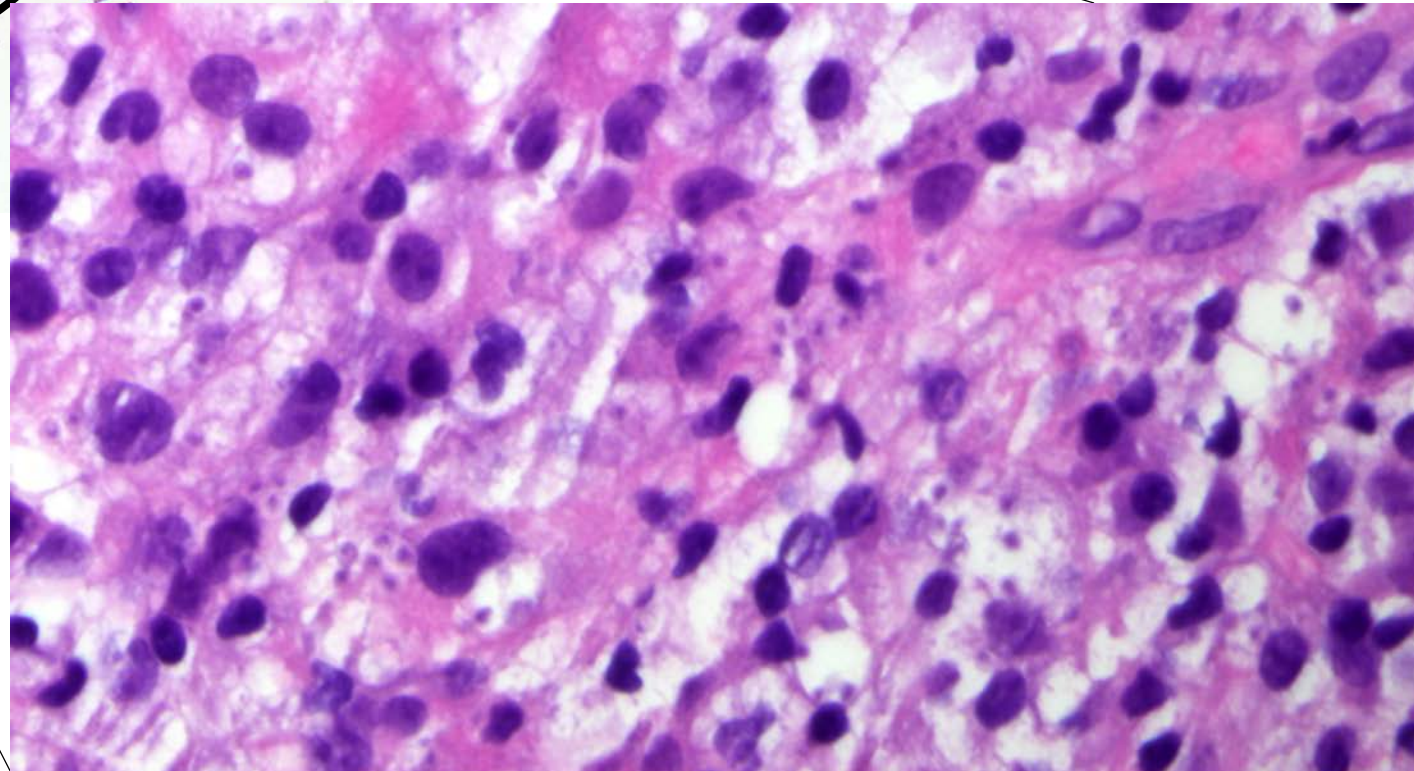
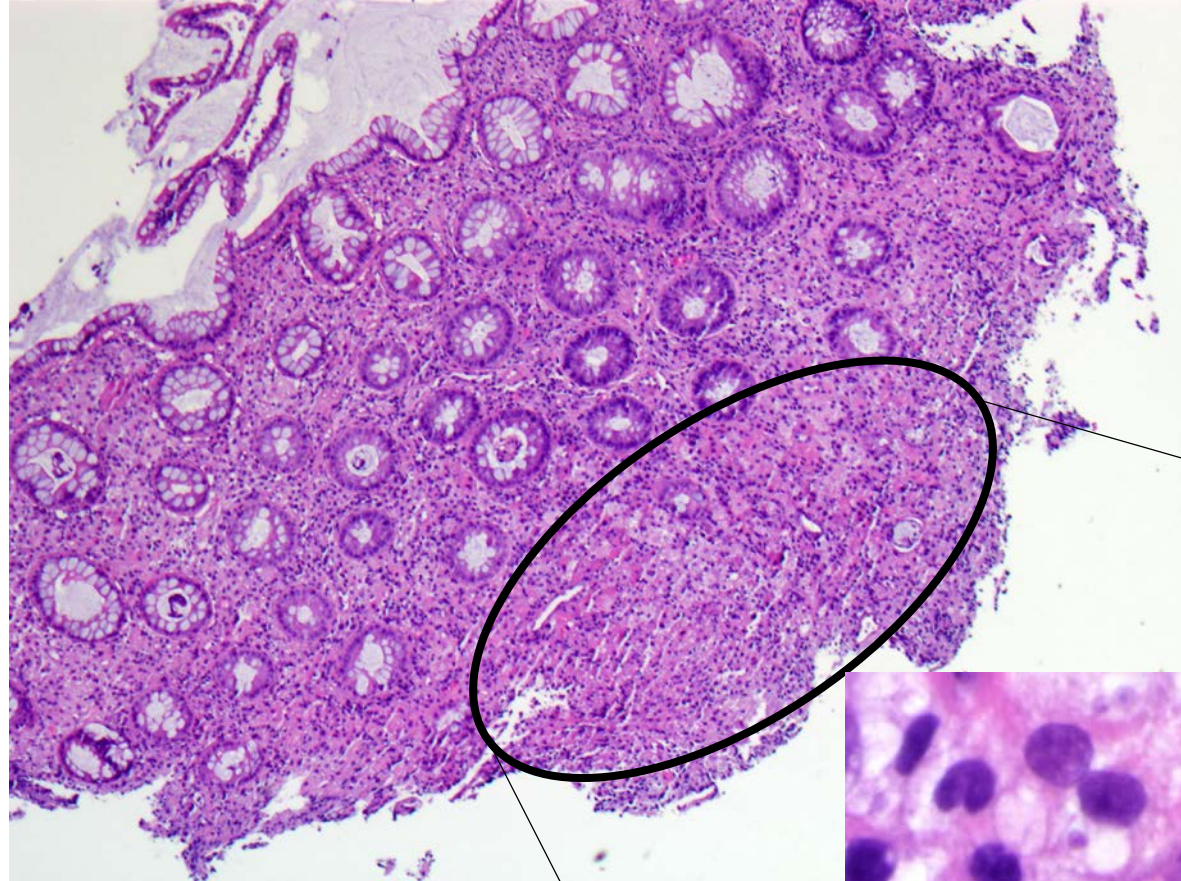
60 year old man carries a diagnosis of Crohn's disease. He is getting worse on treatment. The clinician sends original biopsy set for your review. Would you stain these biopsies? If so, what would you order?

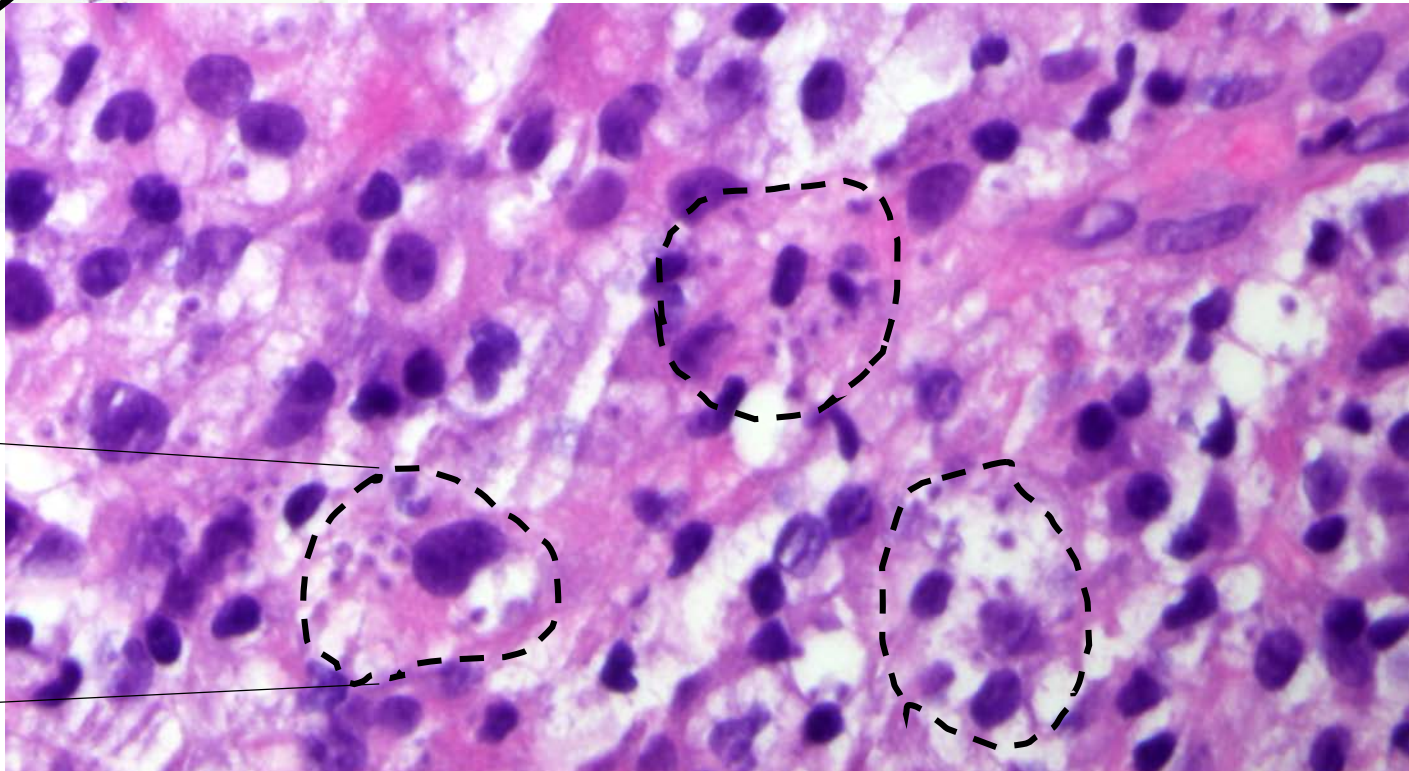
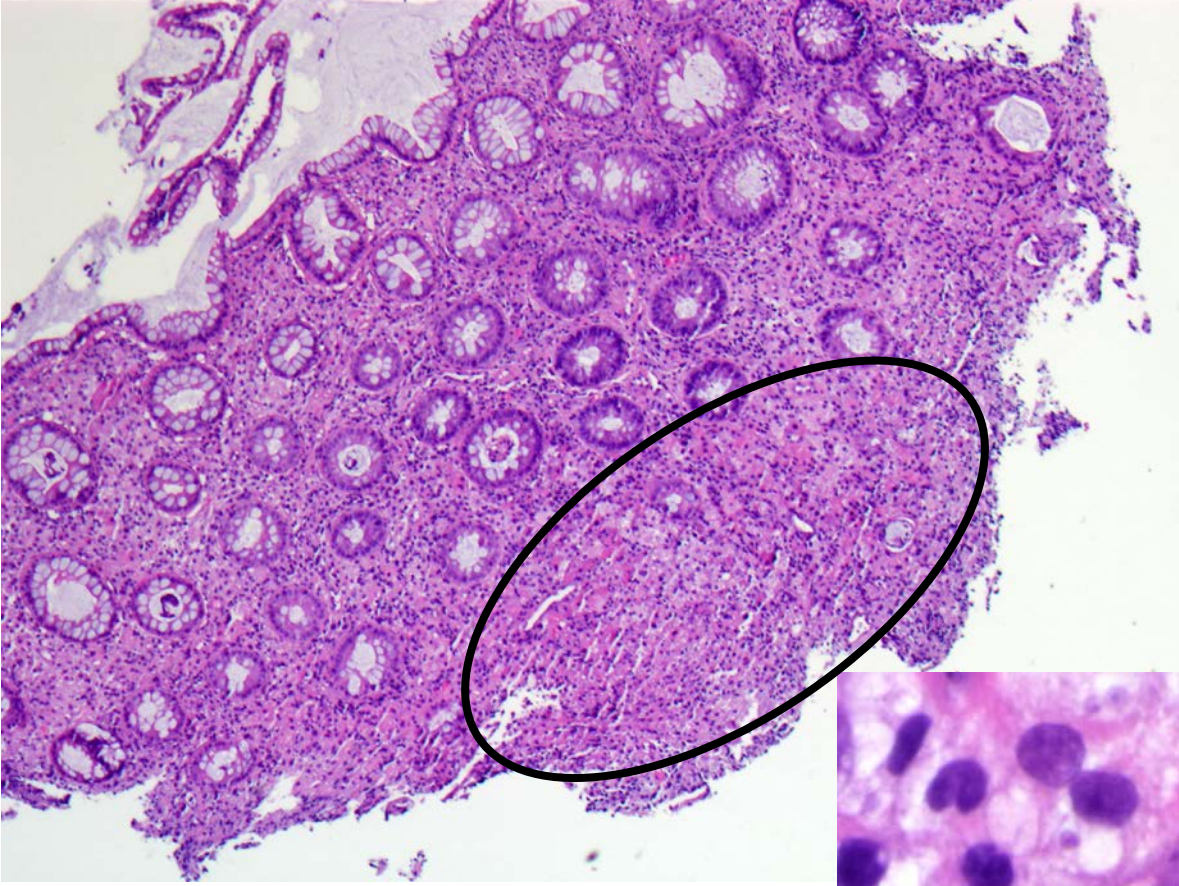


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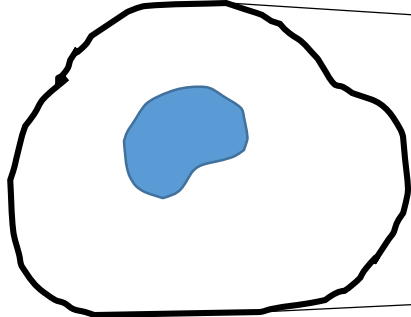
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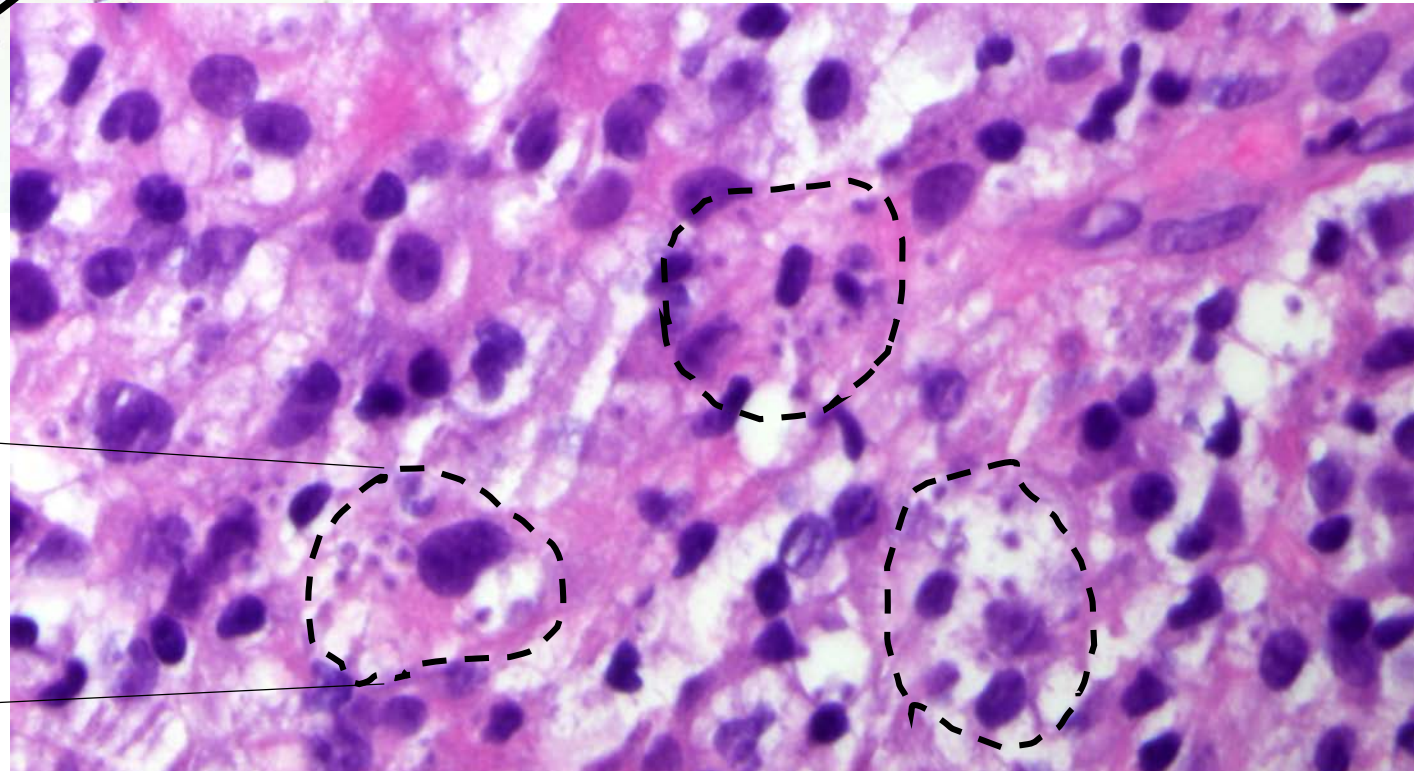
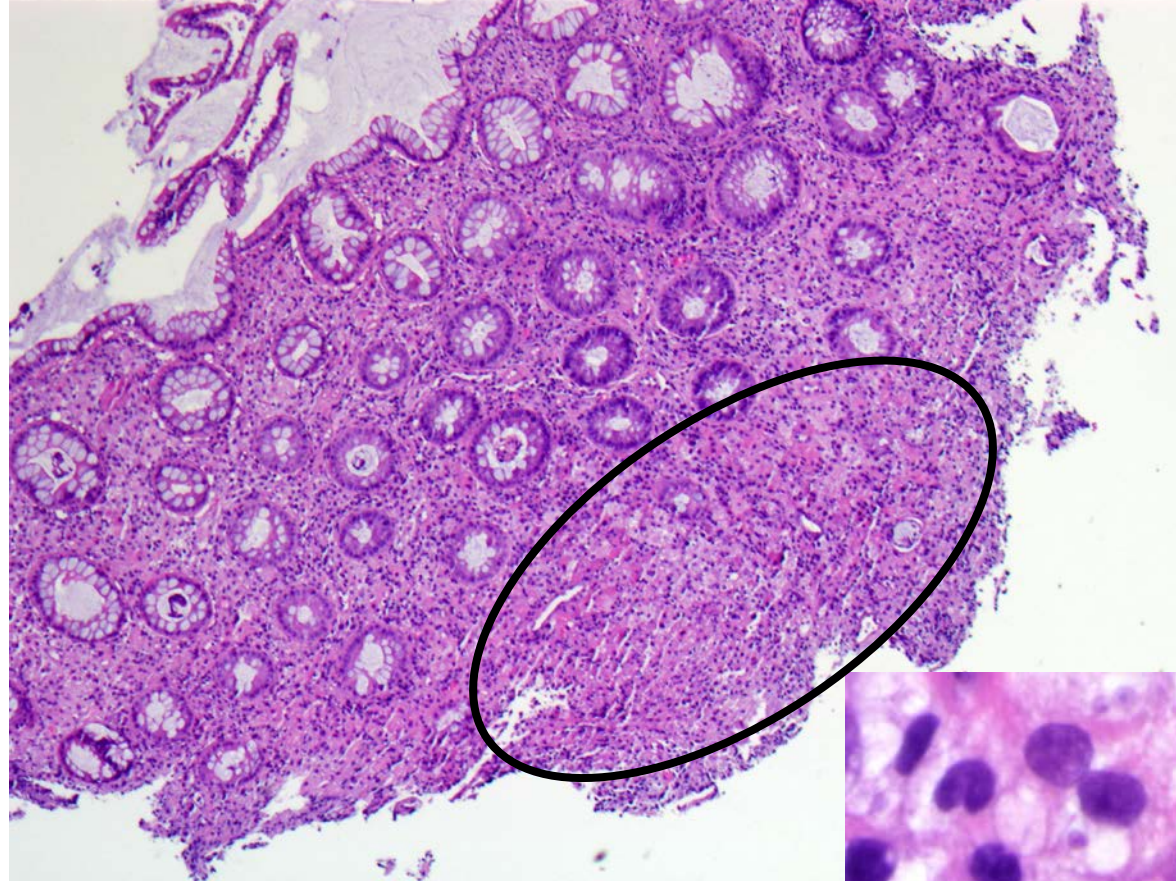
Poll: Would you stain these biopsies? If so, what would you order?



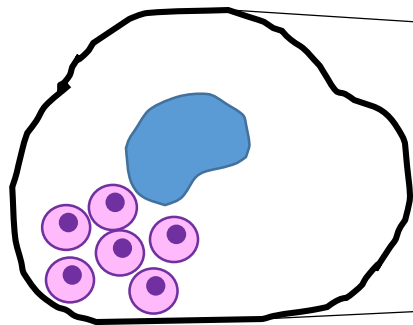


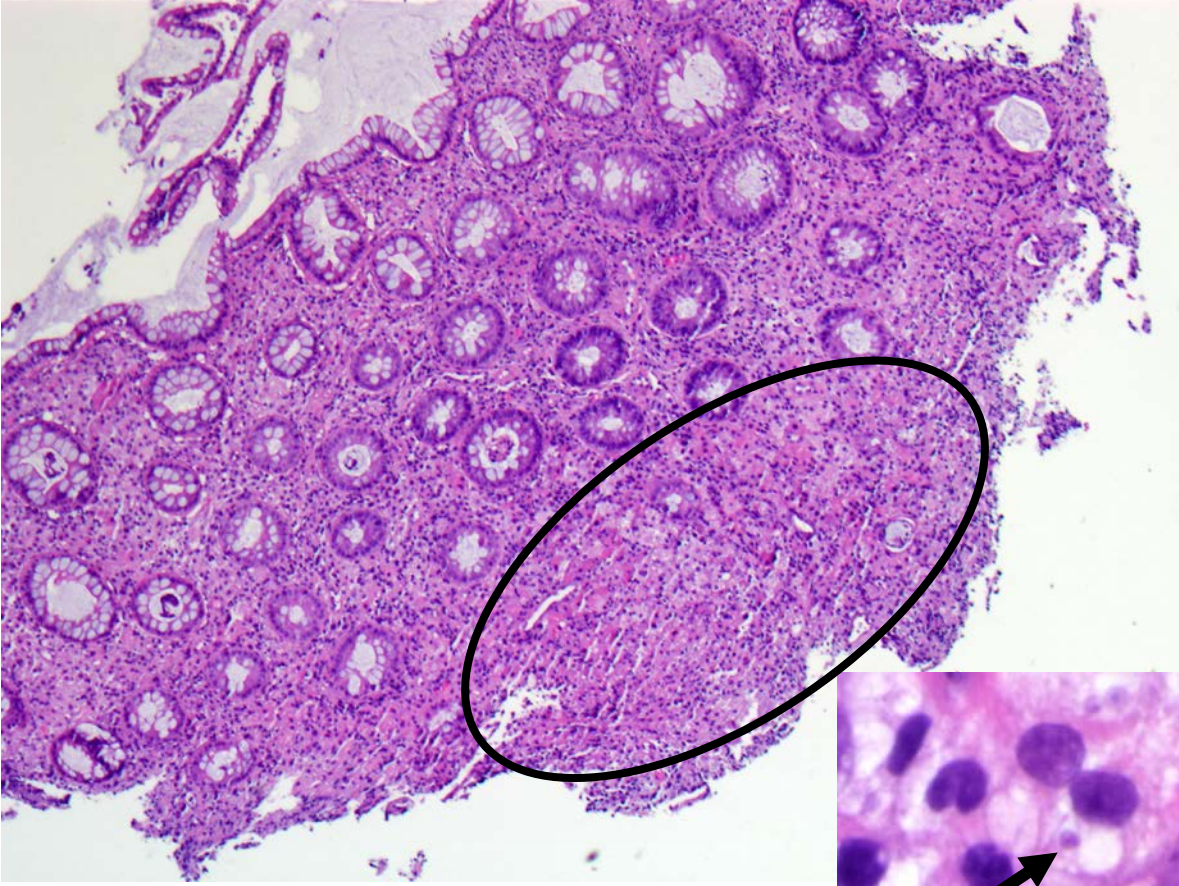
MACROPHAGE





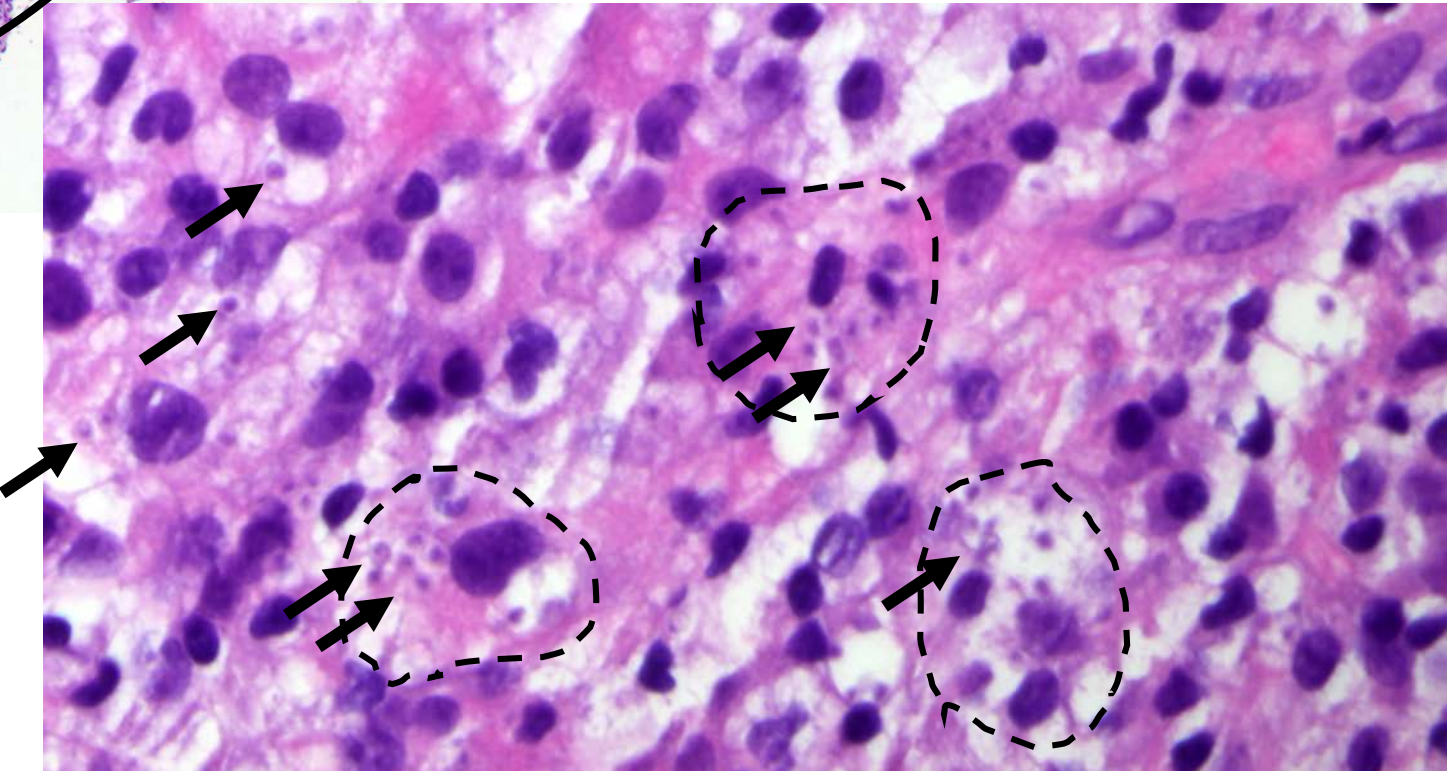
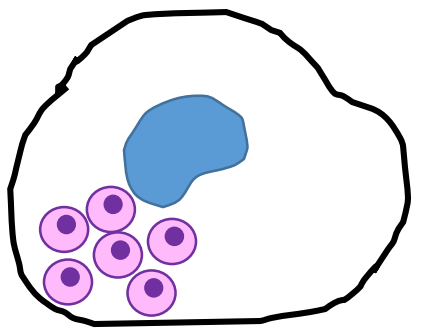
MACROPHAGE

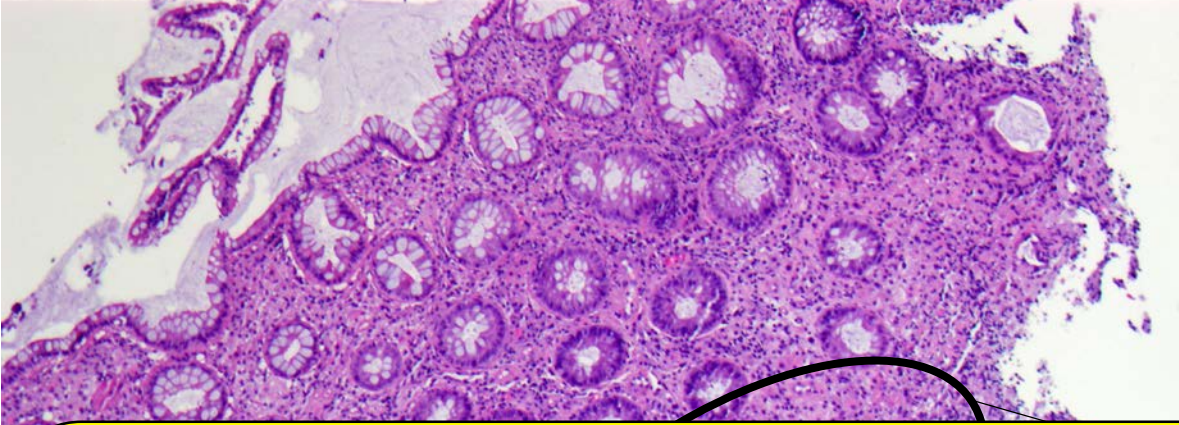




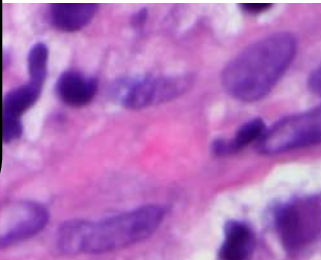
**Ovoid, 2-5 μm ,
intracellular
yeast forms**

MACROPHAGE

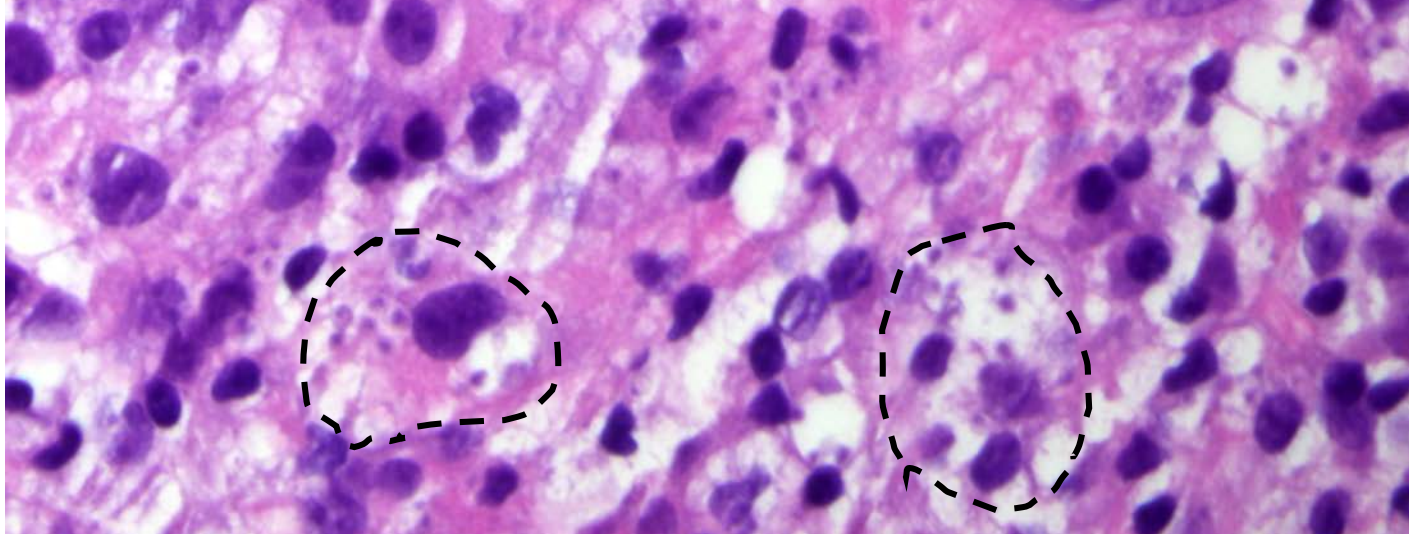
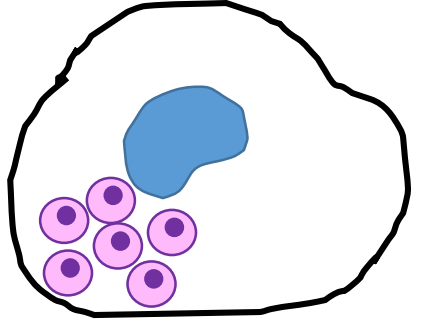
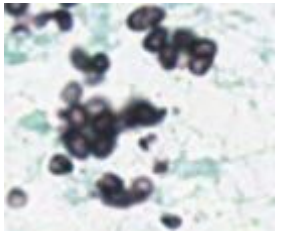




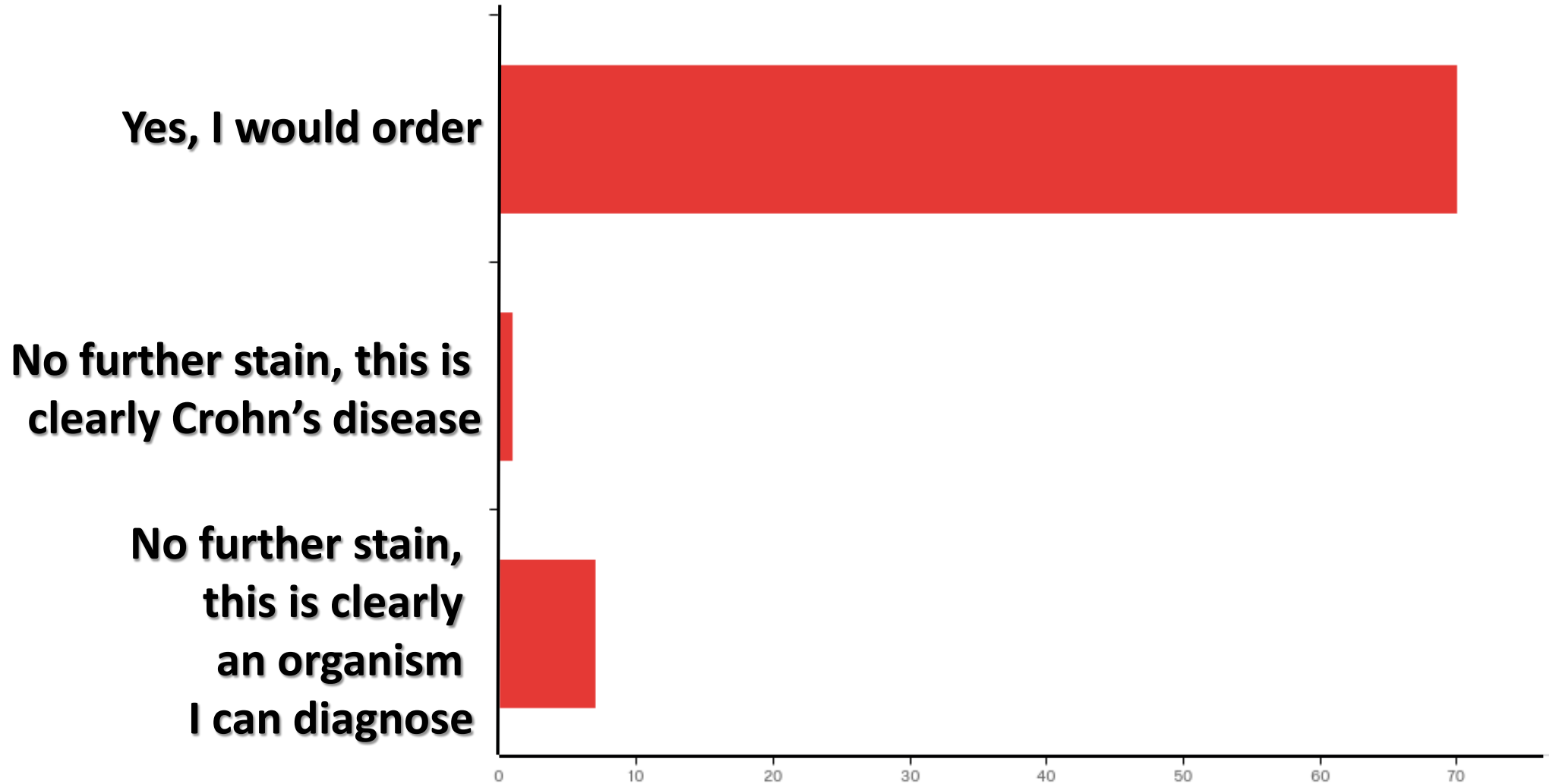
DIAGNOSIS: HISTOPLASMOSIS



MACROPHAGE



GIPS MEMBERSHIP RESPONSES (n =99)



LAMPS



Wrote the Seminal Paper on GI Histoplasmosis - GI Tract involved in 70-90% cases

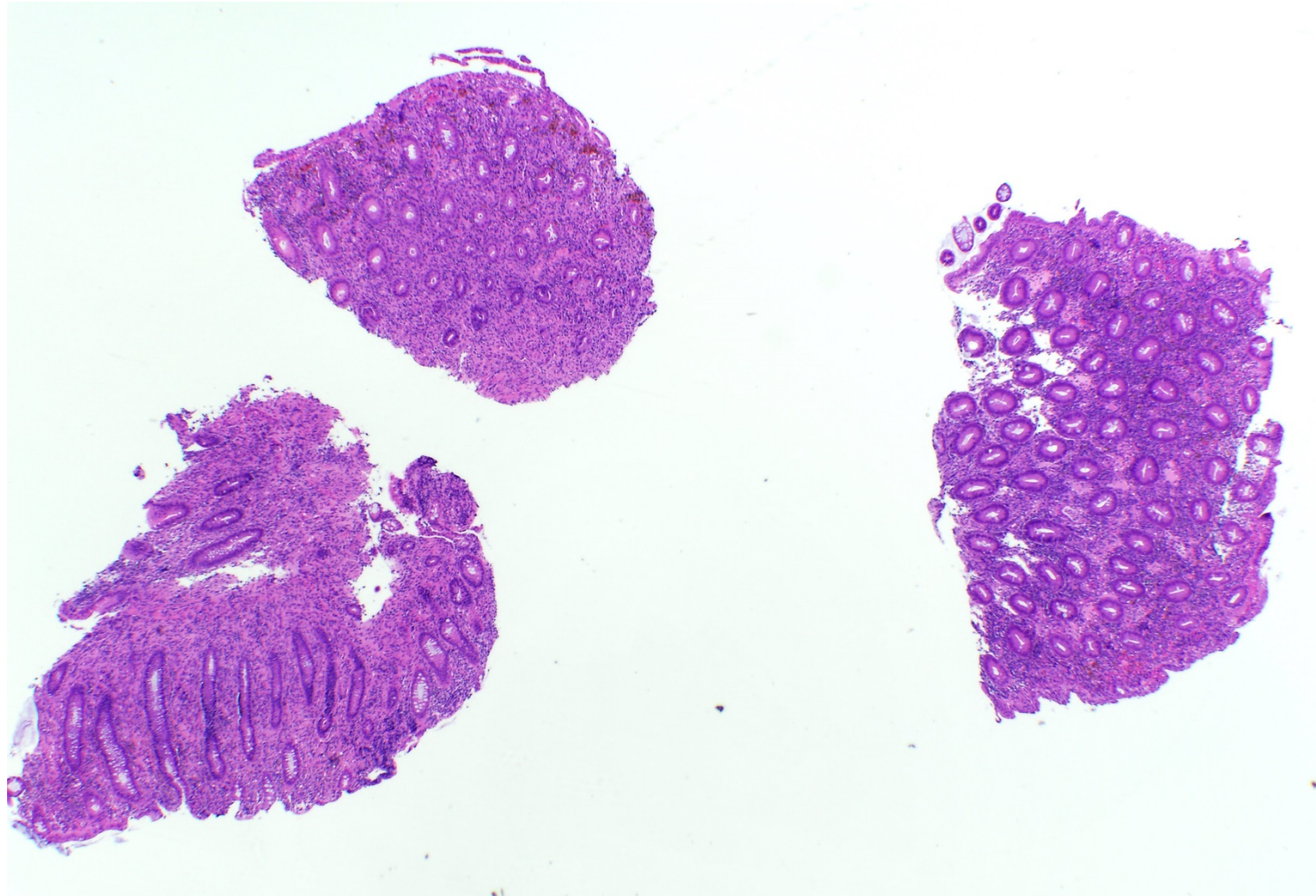
Am J Clin Pathol. 2000 Jan;113(1):64-72.

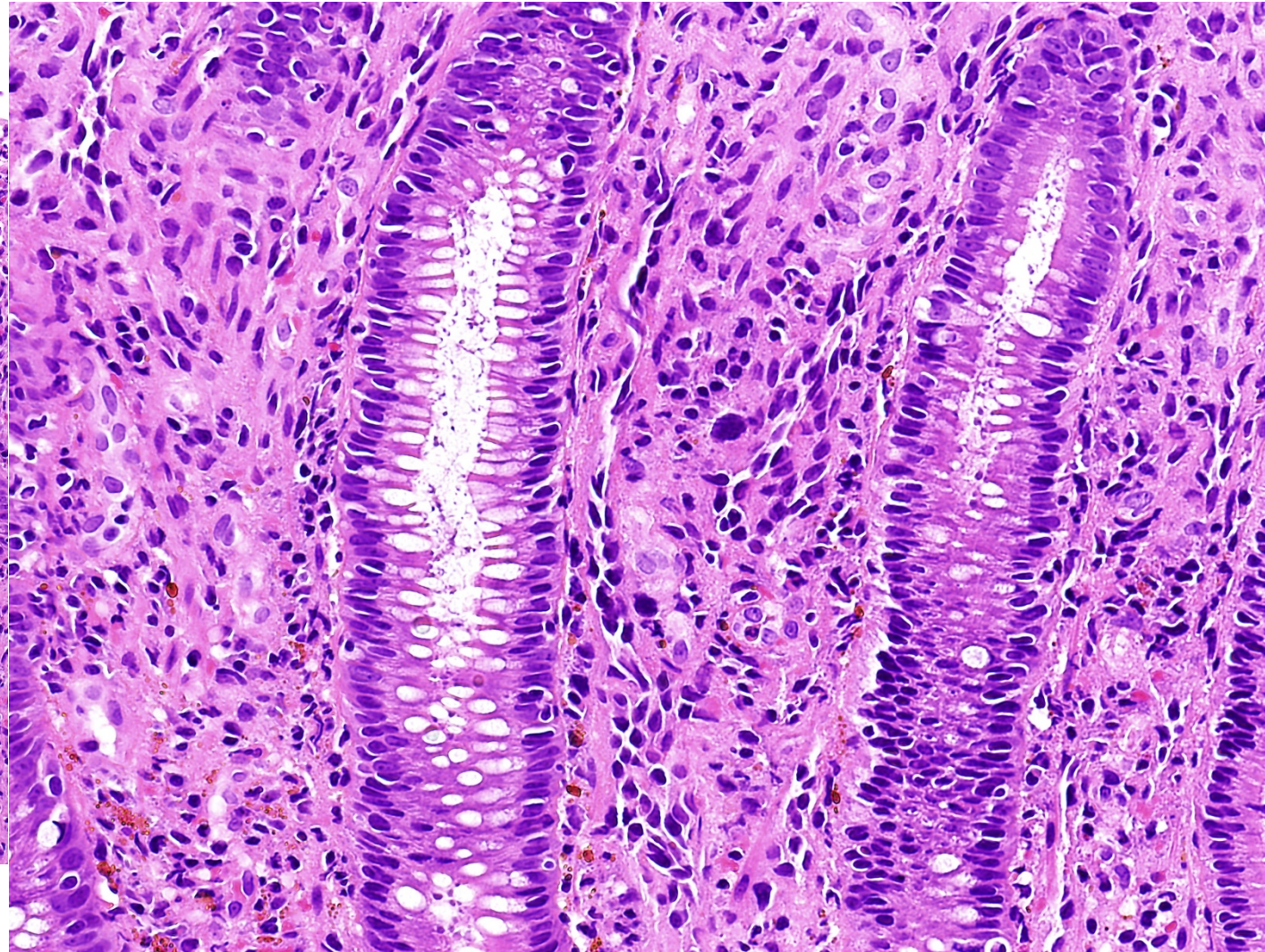
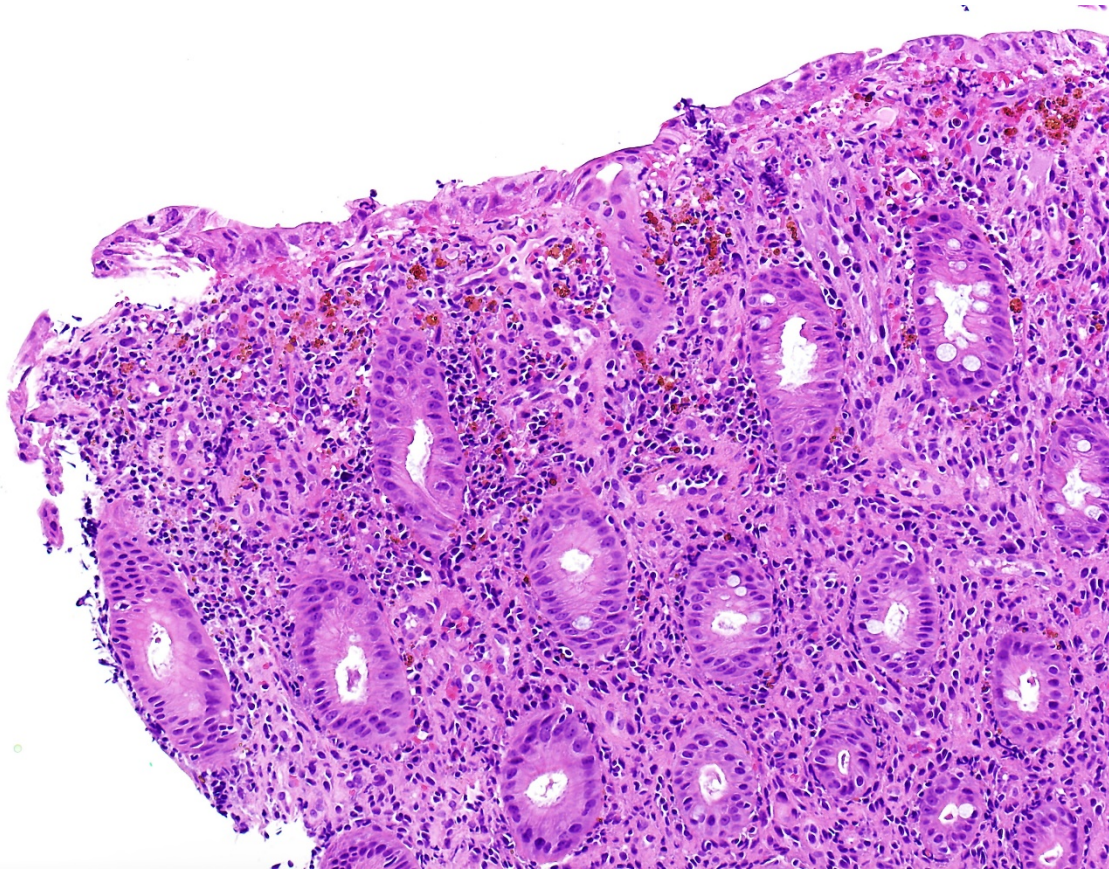
The Pathologic Spectrum of Gastrointestinal and Hepatic Histoplasmosis

*Laura W. Lamps, MD,¹ Claudia P. Molina, MD,² A. Brian West, MD,²
Rodger C. Haggitt, MD,³ and Margie A. Scott, MD¹*

Key Words: Fungus/fungal infection; Granuloma; Gastrointestinal infection; Hepatic infection; Immunocompromised; Histoplasmosis; Gastrointestinal histoplasmosis; Hepatic histoplasmosis; Inflammation

29 year old man with AIDS and colitis. Sample is from nodular rectal mucosa. Would you stain this for infectious organisms? What would you order?

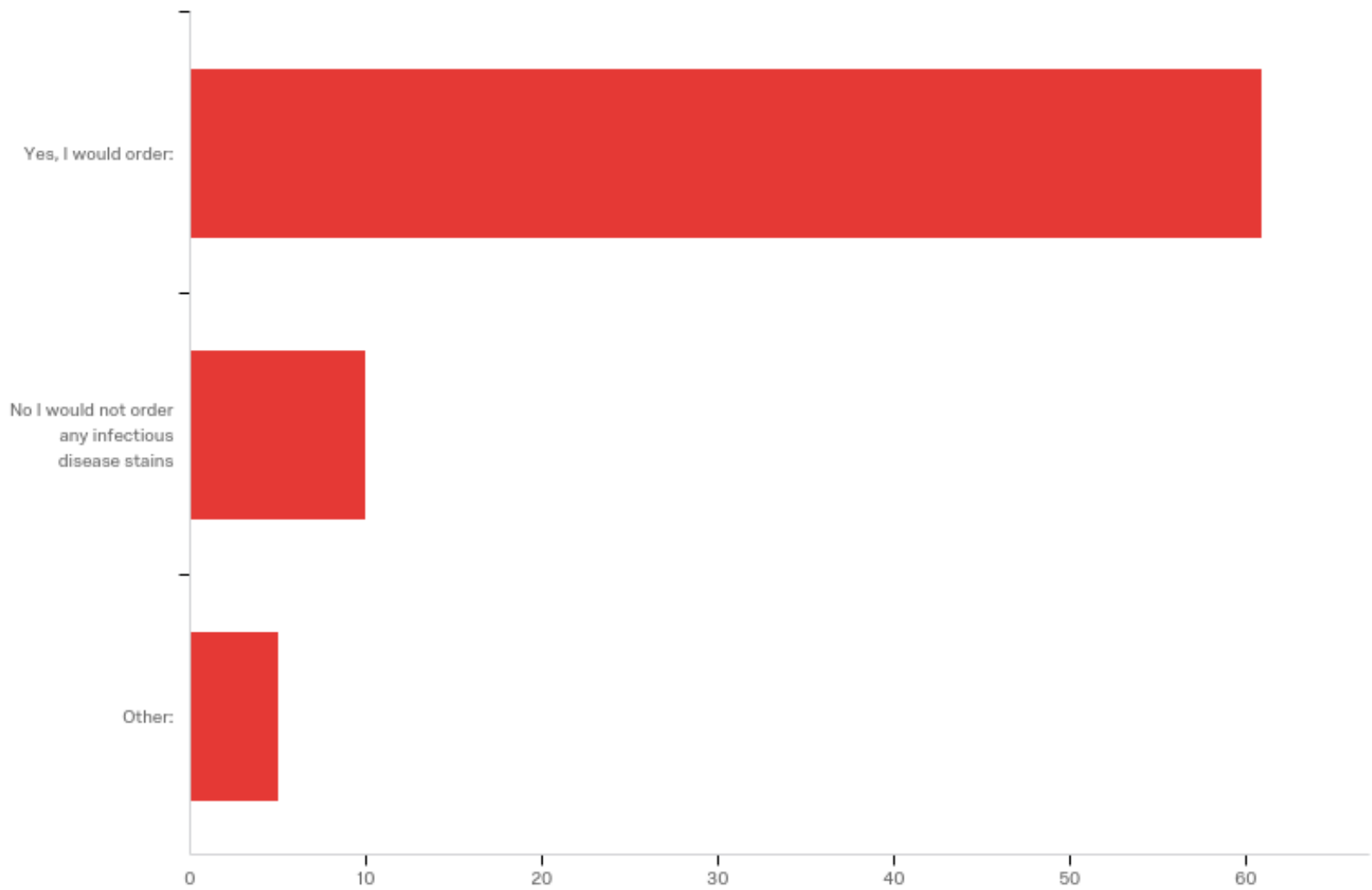


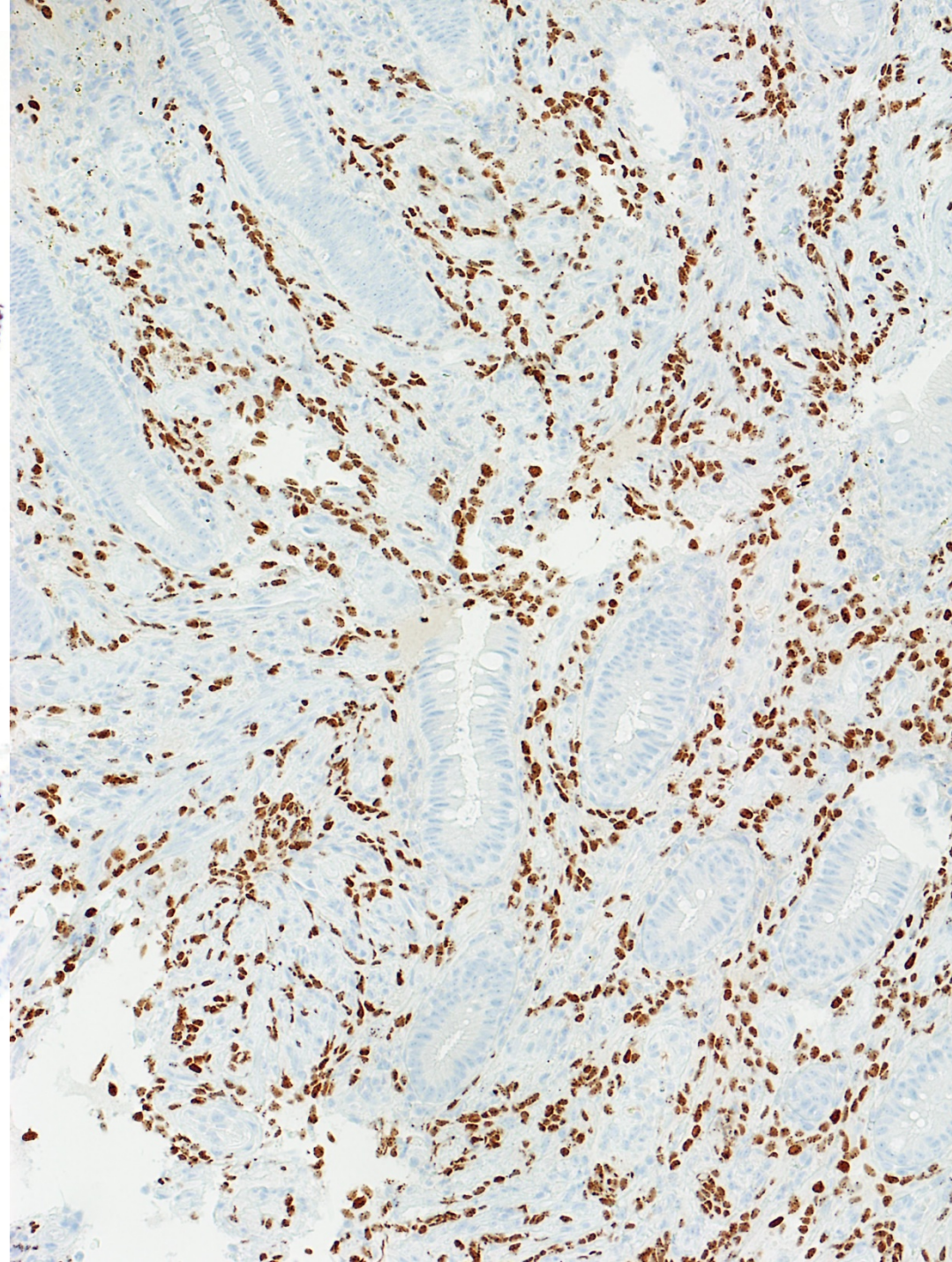
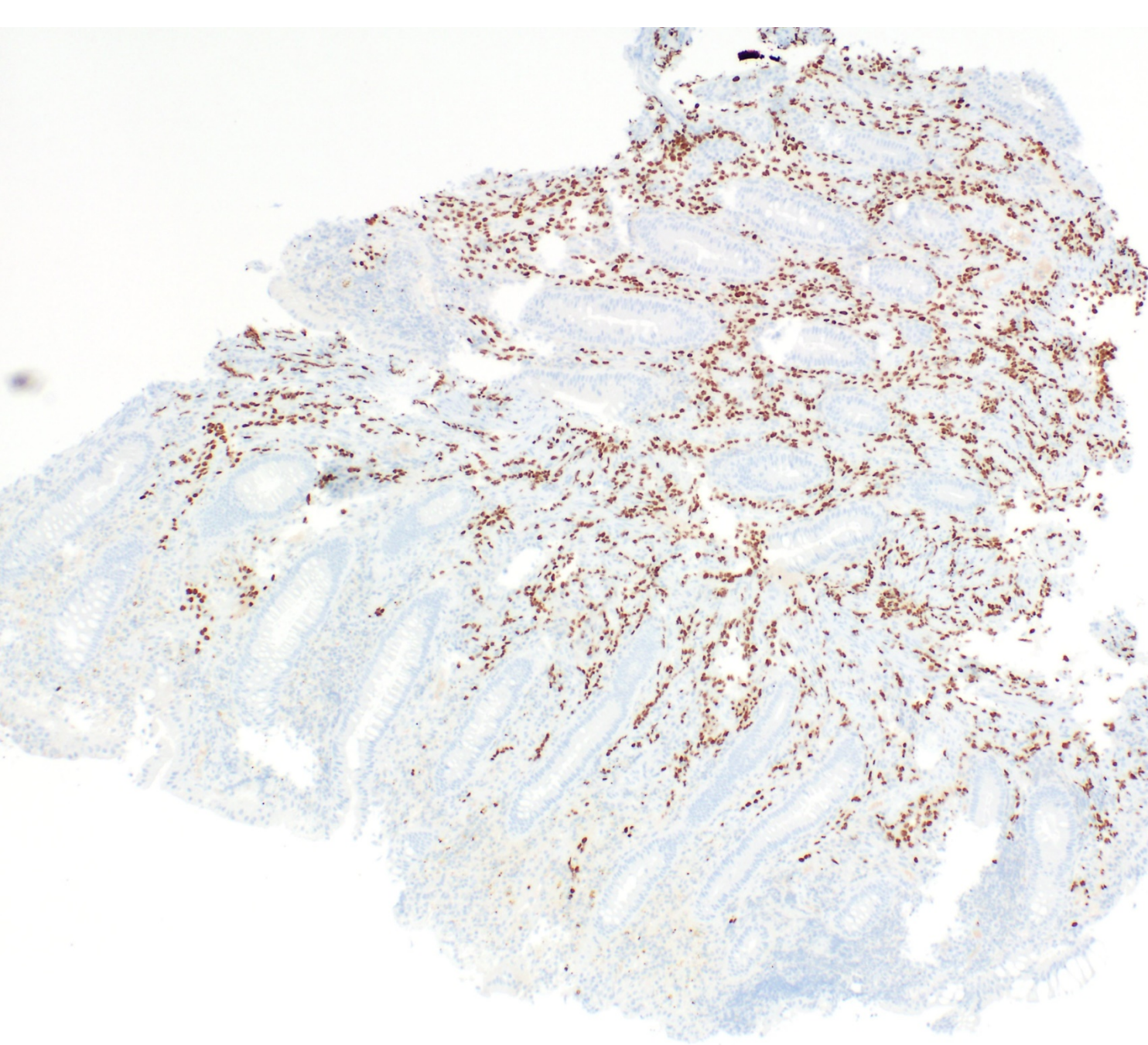


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Poll: Would you stain this for infectious organisms? What would you order?





What Influences Decision to Order Infectious Disease Stains?

**Pattern of
Tissue Injury**

+

Clinical Setting

+

**Ability (or Comfort
Level) to Identify
Infection Without
Stains**

What Influences Decision to Order Infectious Disease Stains?

**Pattern of
Tissue Injury**

+

Clinical Setting

+

**Ability (or Comfort
Level) to Identify
Infection Without
Stains**

- None (normal)
- Mild Inflammation
- Severe inflammation/
ulcer

What Influences Decision to Order Infectious Disease Stains?

**Pattern of
Tissue Injury**

+

Clinical Setting

+

**Ability (or Comfort
Level) to Identify
Infection Without
Stains**

- IBD
- Immunocompromised
(HIV, Bone marrow transplant)
- Clinician Requests
- Your pt population characteristics

What Influences Decision to Order Infectious Disease Stains?

**Pattern of
Tissue Injury**

+

Clinical Setting

+

Ability (or Comfort Level) to Identify Infection Without Stains

- How one was trained
- Fear of harming patient/
liability for missing infectious organism
- Heavy case load, not enough time to look carefully
- Quality of H&E

Conclusion

- When to incorporate infectious disease stain in everyday, common situation:
 - CMV and Colitis: Literature says you don't need IHC, but in practice, most people do it for the patient
 - “Rule out GVHD” cases: May have minimal to no inflammation, but still have infection
- When to incorporate infectious disease stain in unusual situation:
 - Histoplasmosis, HHV8 in Kaposi

