How to Navigate Sticky Neuroendocrine Issues

PRESENTED BY

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Raul Gonzalez reported no relevant financial relationships

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Grading of Neuroendocrine Neoplasms

- Based on mitotic count and Ki67 index (by IHC)
- Two survey questions sent out in January

NEN Grading: Counting Mitoses

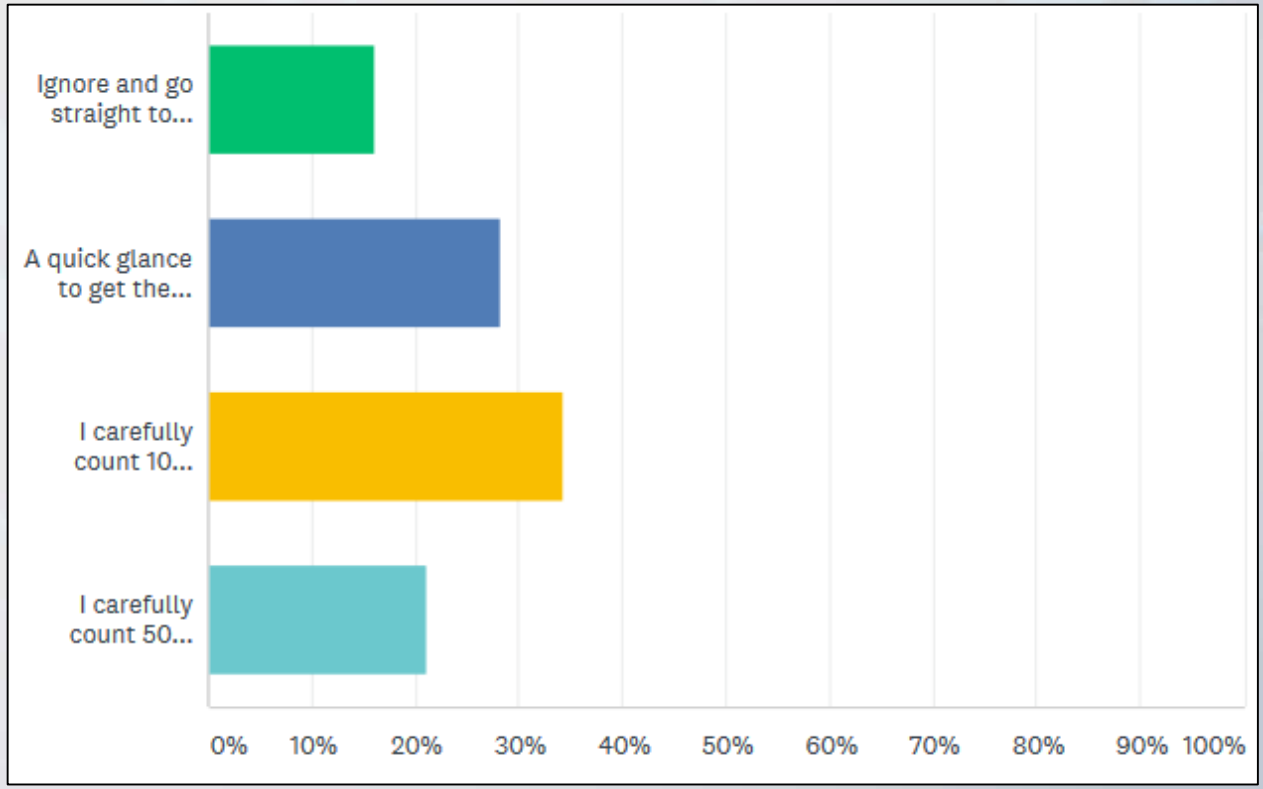
- How do you count mitoses when grading neuroendocrine neoplasms?

- A. Ignore and go straight to Ki67
- B. A quick glance to get the gestalt, then count if it seems high
- C. I carefully count 10 high-power fields (or 2 mm^2)
- D. I carefully count 50 high-power fields (or 10 mm^2), then average

NEN Grading: Counting Mitoses

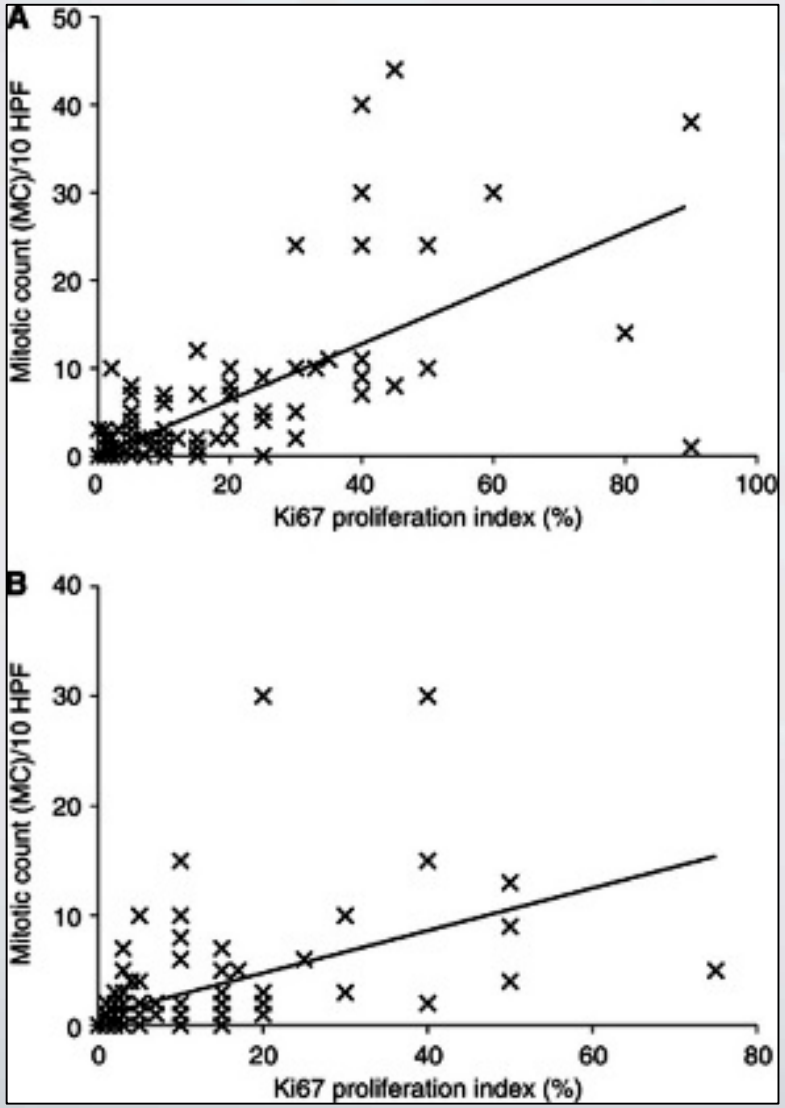
- How do you count mitoses when grading neuroendocrine neoplasms?

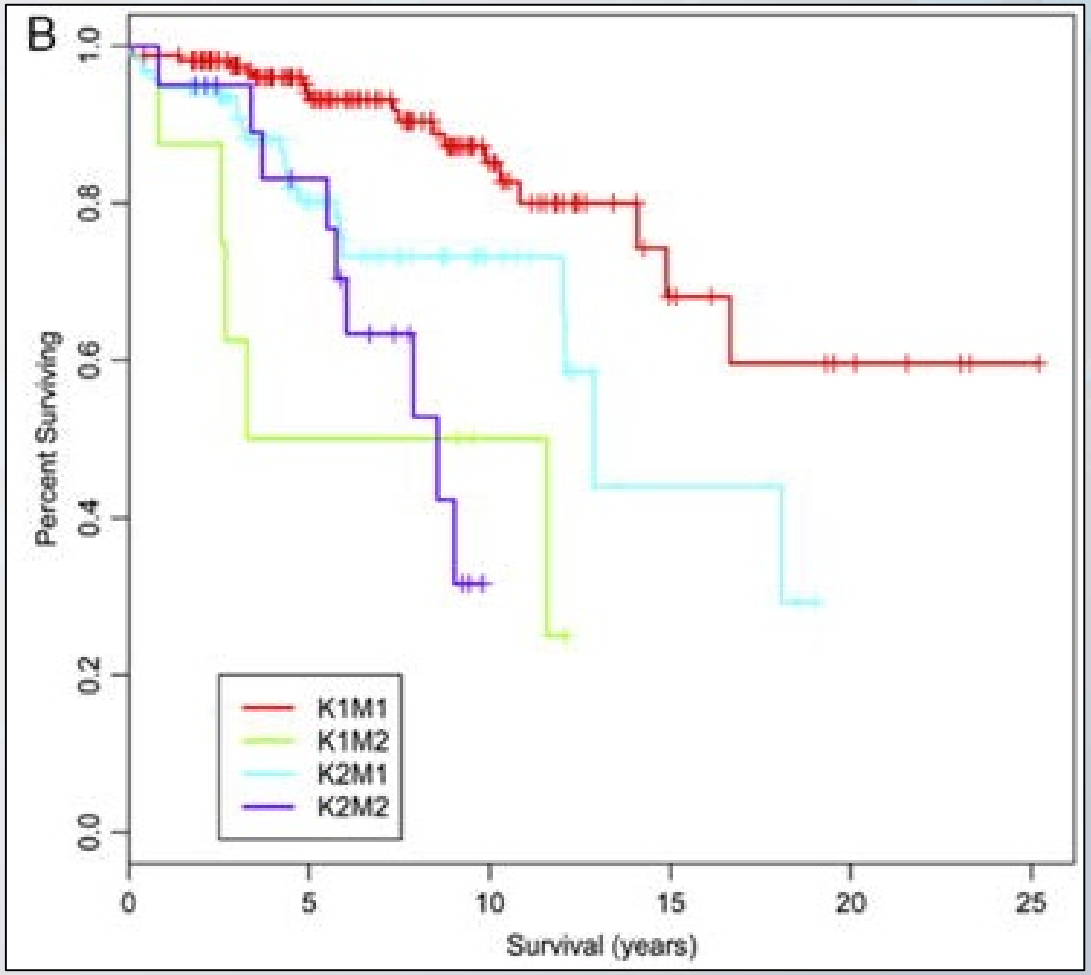
- A. Ignore and go straight to Ki67: 16
- B. A quick glance to get the gestalt, then count if it seems high: 28
- C. I carefully count 10 high-power fields (or 2 mm^2): 34
- D. I carefully count 50 high-power fields (or 10 mm^2), then average: 21
- WHO recommends choice D



NEN Grading: Counting Mitoses[1,2]

- If mitotic rate and Ki67 are discrepant, Ki67 is <u>usually</u> higher
- Best studied in pancreas





NEN Grading: The Key to Ki67

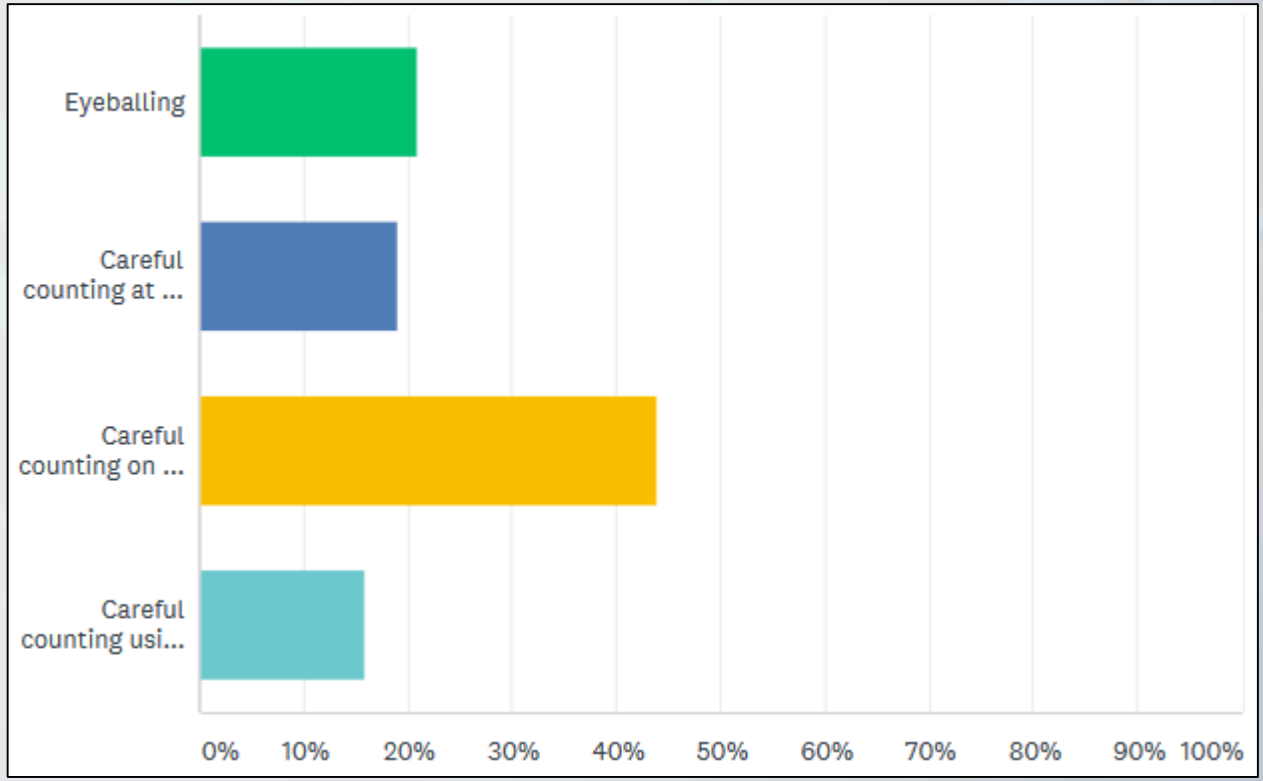
- How do you evaluate Ki67 when grading neuroendocrine neoplasms?

- A. Eyeballing
- B. Careful counting at the microscope
- C. Careful counting on a printed image
- D. Careful counting using a software program

NEN Grading: The Key to Ki67

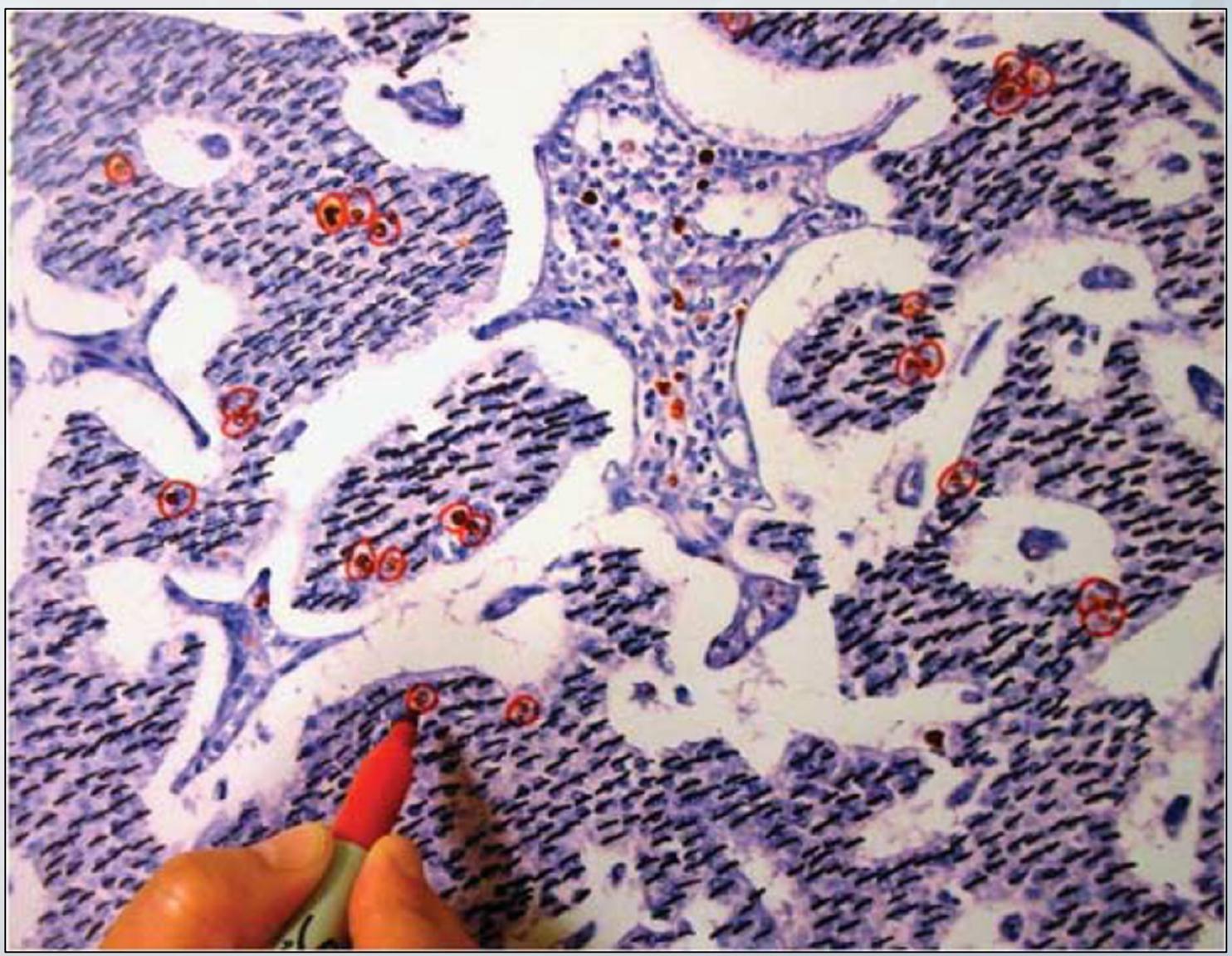
- How do you evaluate Ki67 when grading neuroendocrine neoplasms?

- A. Eyeballing: 21
- B. Careful counting at the microscope: 19
- C. Careful counting on a printed image: 44
- D. Careful counting using a software program: 16



NEN Grading: The Key to Ki67[3]

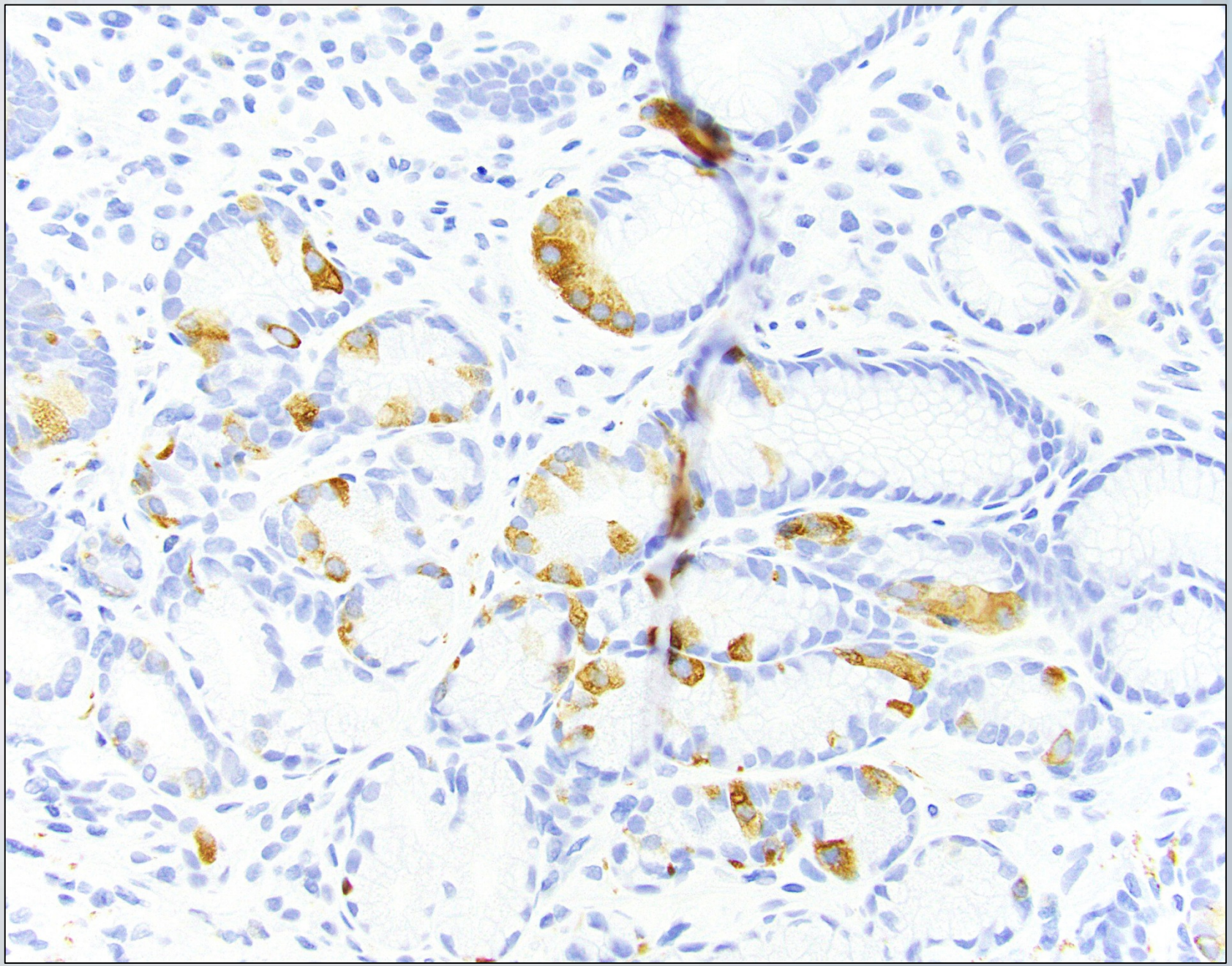
- Careful counting on a printed image seems to be the most reliable method
- Eyeballing is inaccurate and unreliable, but man it’s so easy
- Again, best studied in pancreas



Issue #1

- This chromogranin IHC is from a patient suspected to have atrophic gastritis. Would you consider this neuroendocrine hyperplasia?

- A. Yes
- B. No



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Poll: This chromogranin IHC is from a patient suspected to have atrophic gastritis. Would you consider this neuroendocrine hyperplasia?

Classifying Gastric NE Hyperplasia[4]

- Evaluation of ECL cells using synaptophysin or chromogranin IHC
- Linear hyperplasia: five or more cells lying inside the basement membrane of glands
  - Focal: at least five chains are present in one specimen
  - Diffuse: a mean of at least two chains per linear millimeter of mucosa
- Micronodular hyperplasia: Clusters of five or more endocrine cells, not exceeding in size the diameter of a gastric gland
  - Mean of at least one micronodule per linear millimeter of mucosa
- Adenomatoid hyperplasia: five or more micronodules, closely adherent
- Dysplasia: enlarging micronodule (more than 150 pm), fusing micronodules, microinvasive lesion, nodule with newly formed stroma

Issue #2

- You receive a small bowel resection specimen that contains multiple discrete NETs. Which do you perform Ki67 on?

- A. All of them
- B. Only the first one I see
- C. Only the largest one
- D. Only the most mitotically active one

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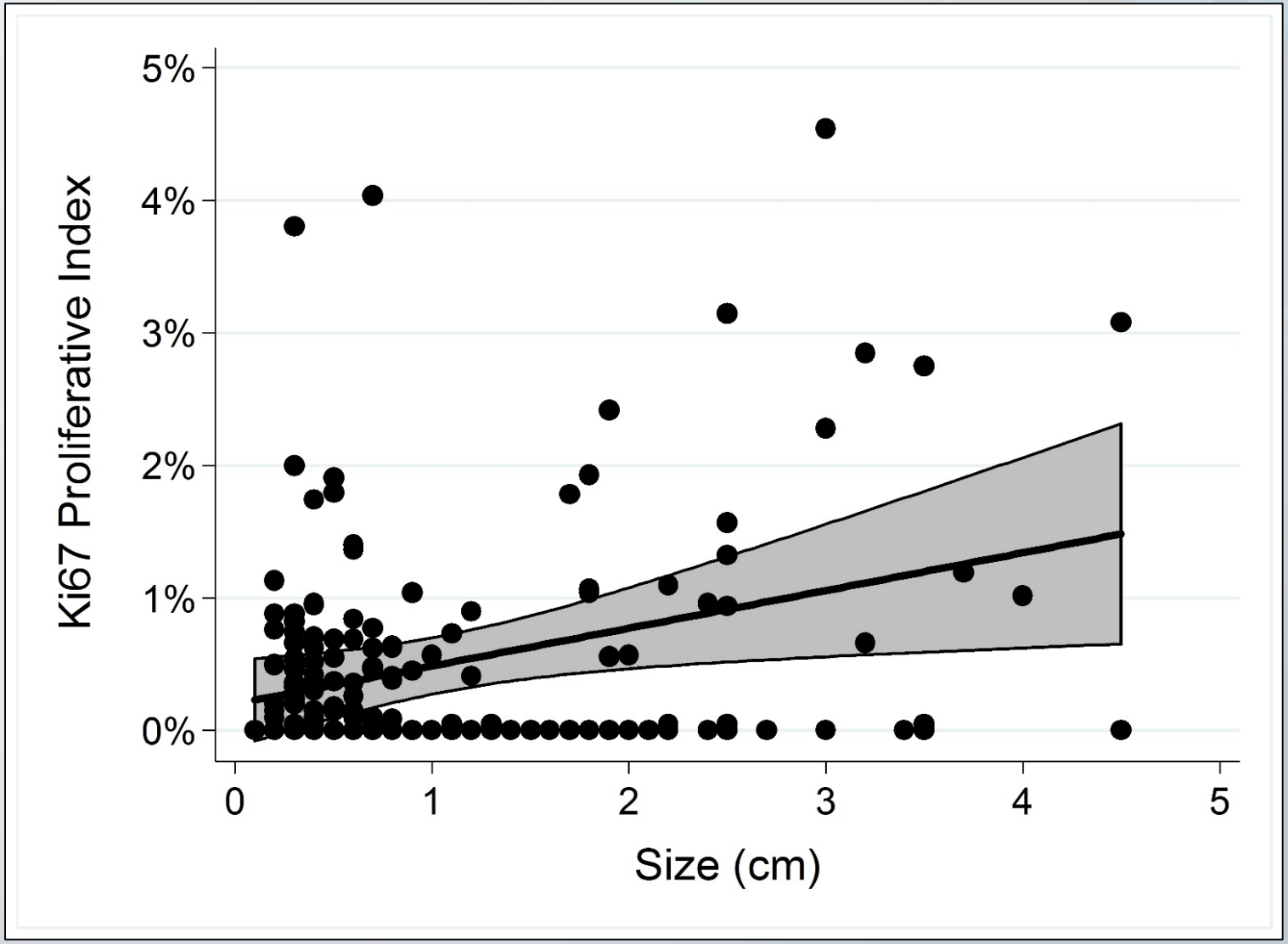
Poll: You receive a small bowel resection specimen that contains multiple discrete NETs. Which do you perform Ki67 on?

Small Bowel NET Multifocality[5]

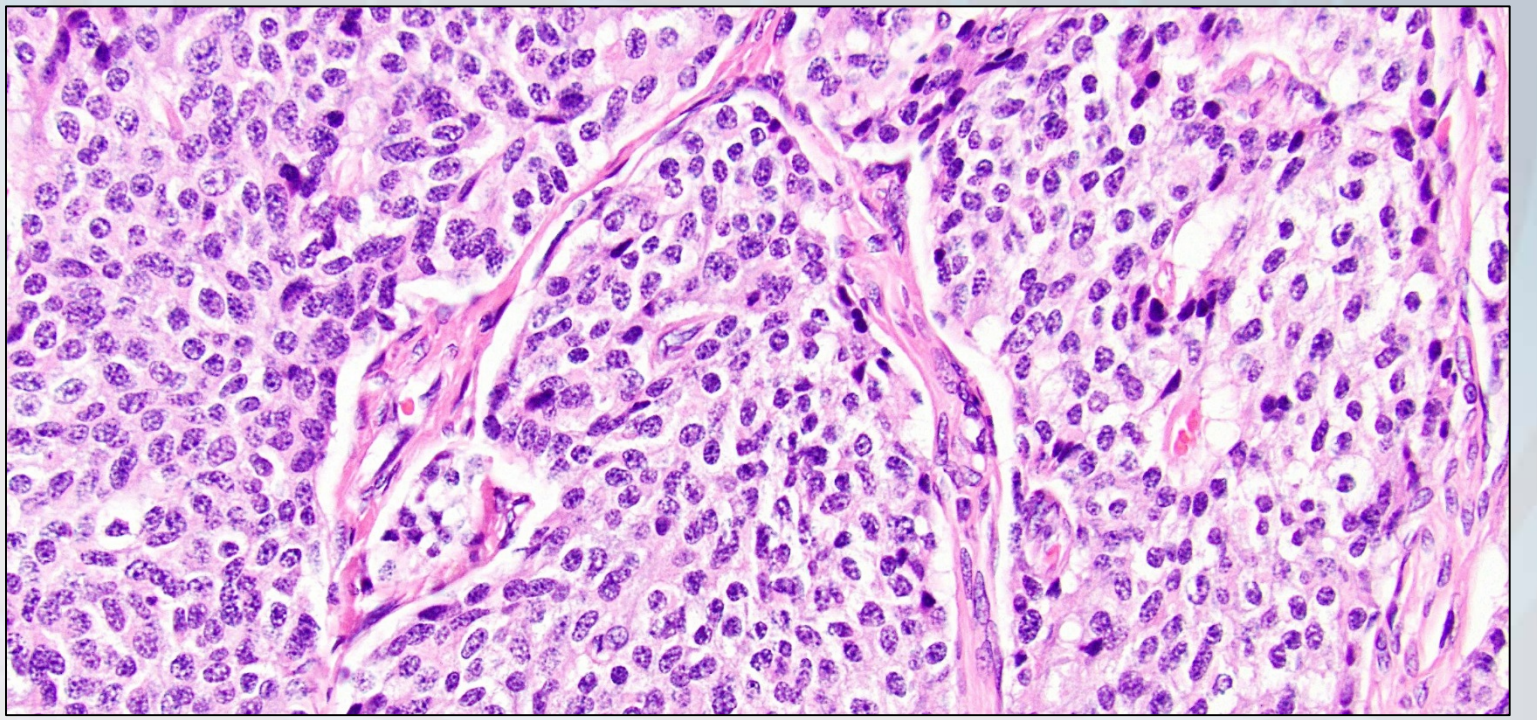
- Positive correlation between tumor size and Ki67 index (coefficient 0.28)
- Only staining the largest lesion for Ki67 should accurately grade almost all cases
- If one is more mitotically active, though, use that one!
- Primary focus vs. node?

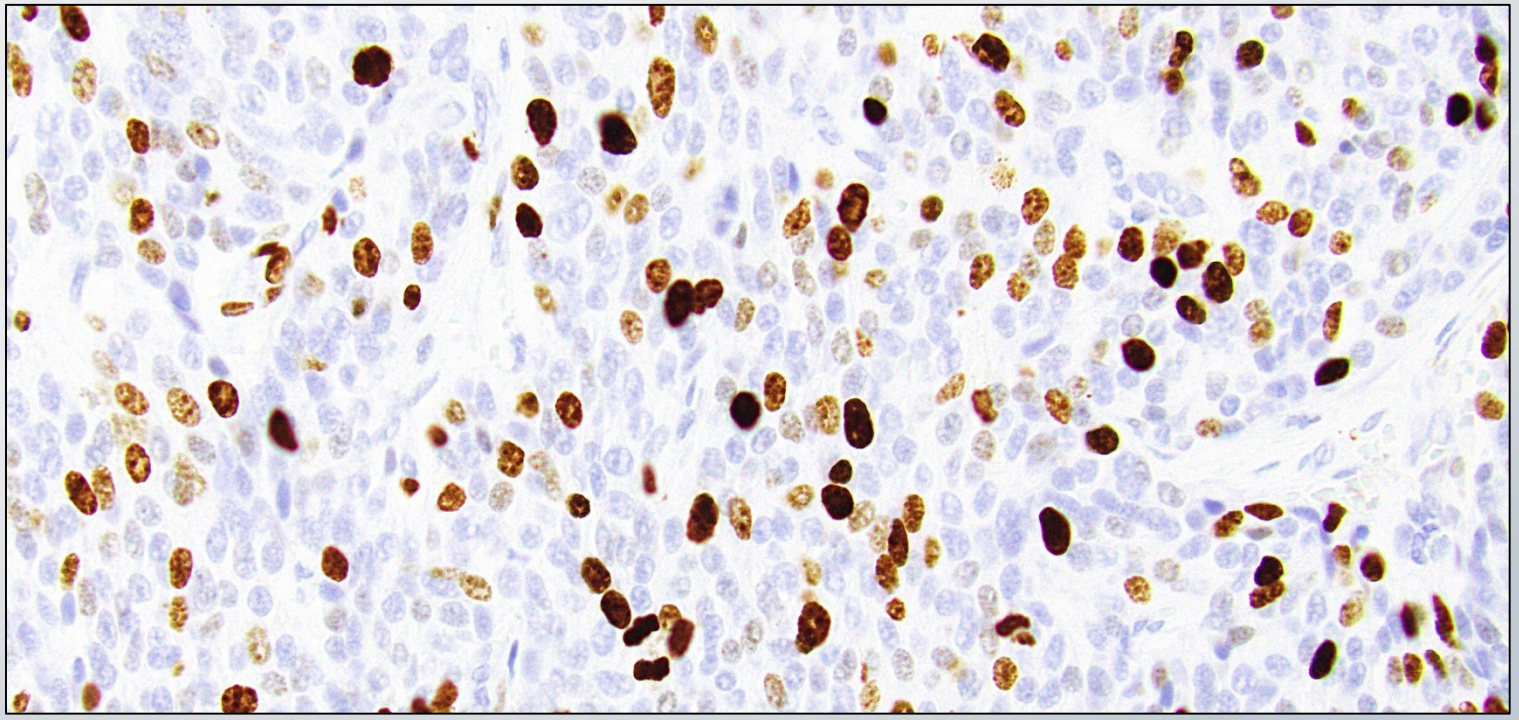


Issue #3

- Same small bowel resection. H&E and Ki67 to the right. What would you call this?

- A. NET, G1
- B. NET, G2
- C. NET, G3
- D. NEC





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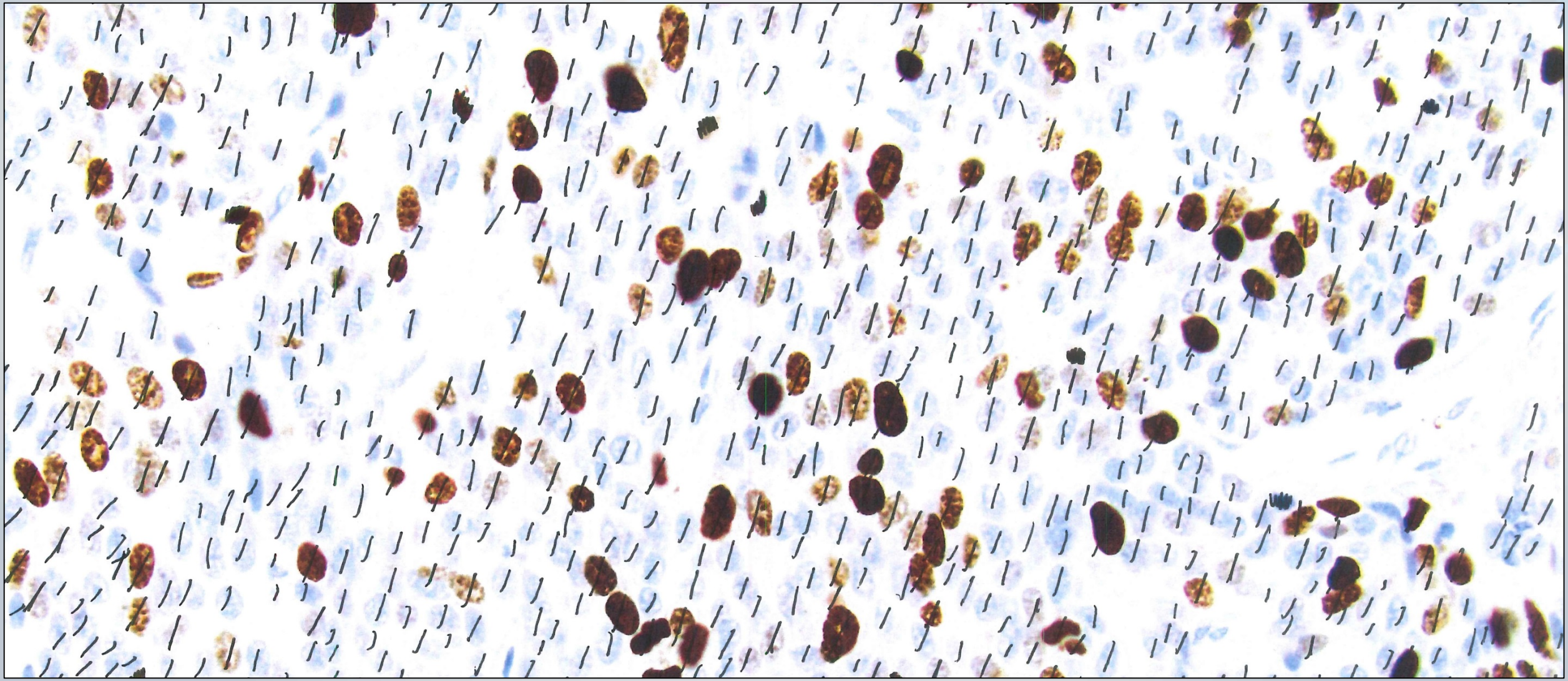
Poll: Same small bowel resection. H&E and Ki67 to the right. What would you call this?

Ki67: 28.7%



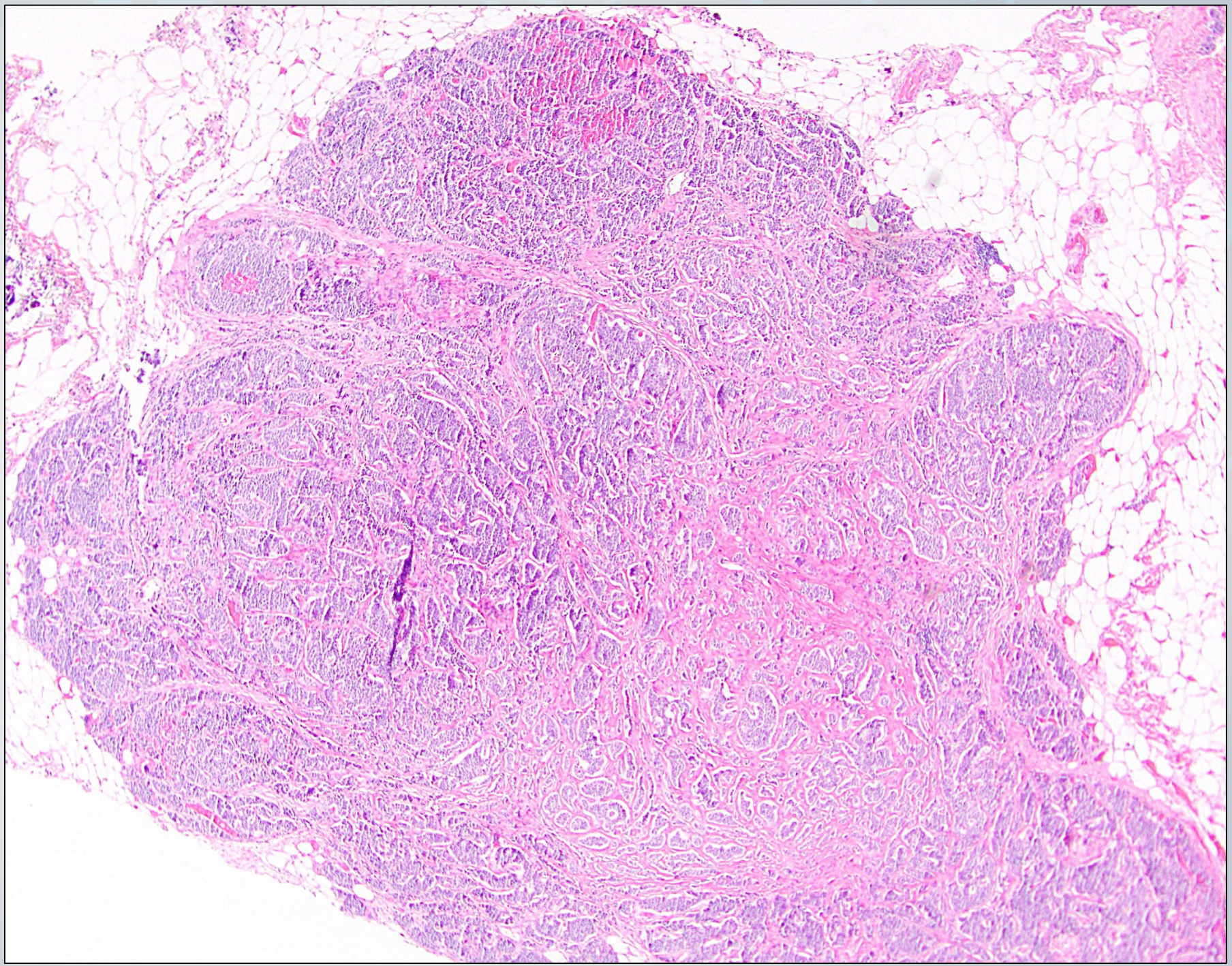
Digestive NENs: Naming & Grading (Says WHO)[6]

Histology	Mitotic rate (per 2 mm^2)	Ki67 index (at least 500 cells)	WHO grade
Well-differentiated neuroendocrine tumor	0-1	<3% (not 0-2%)	1 (low)
	2-20	3-20%	2 (intermediate)
	>20	>20%	3 (high)
Poorly differentiated neuroendocrine carcinoma	n/a (basically >20)	n/a (basically >20%)	n/a (not assigned a numerical grade; essentially all high-grade lesions)

Issue #4

- Same small bowel resection. You find this in the mesentery. Positive lymph node, or tumor deposit?

- A. Node
- B. Deposit



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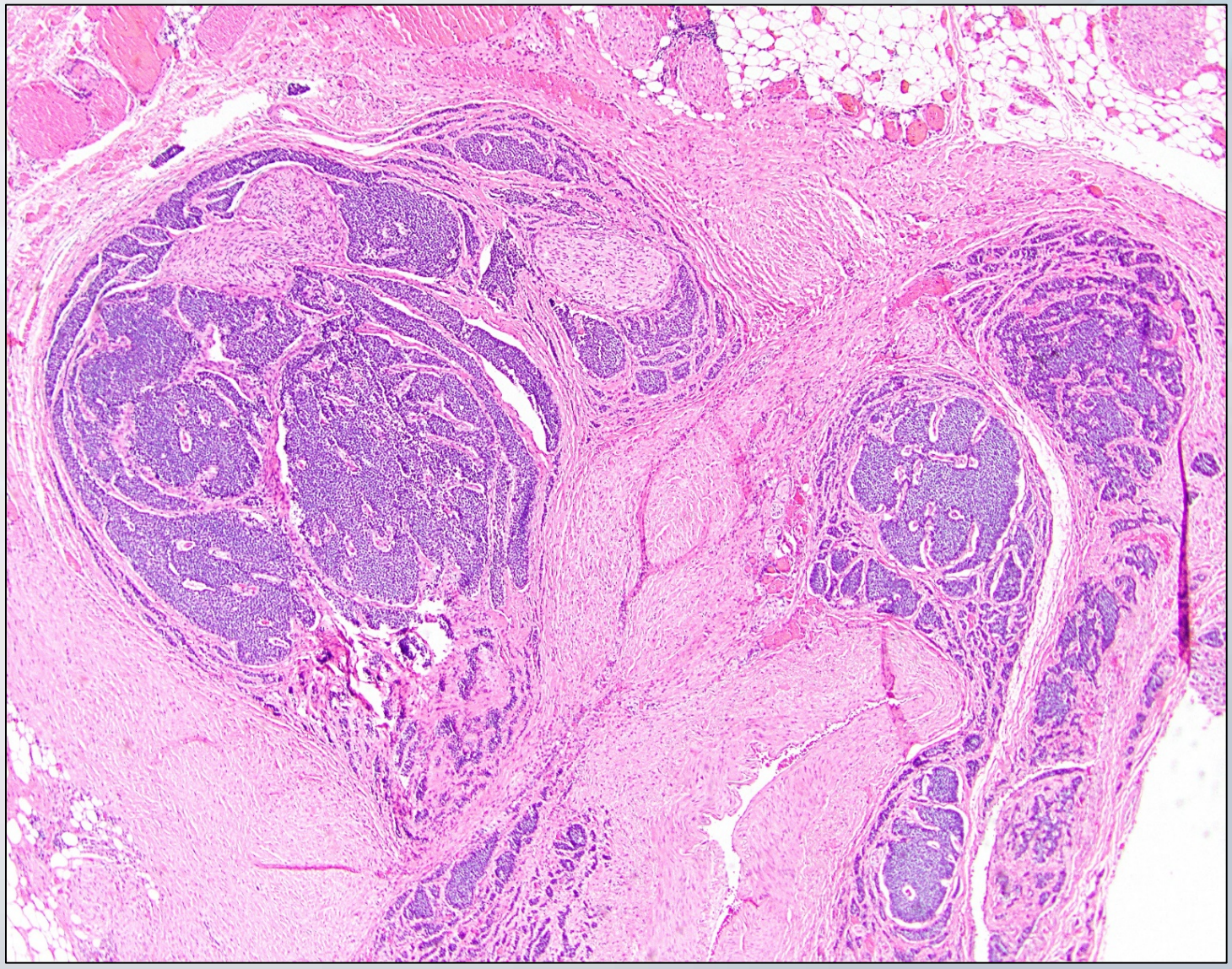
Poll: Same small bowel resection. You find this in the mesentery. Positive lymph node, or tumor deposit?

Small Bowel NET Tumor Deposits[7-9]

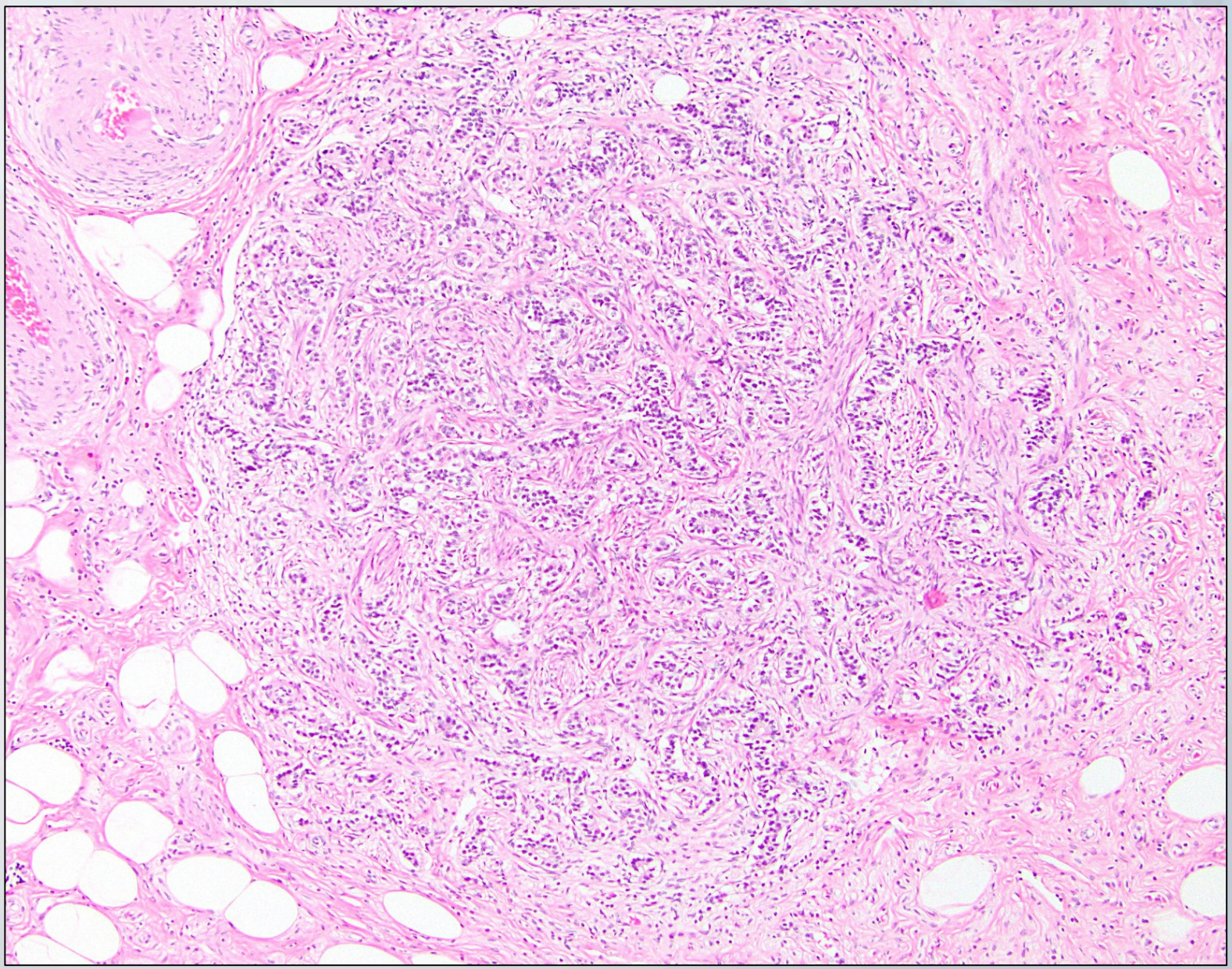
- Stronger predictor of poor patient outcome than nodal disease
  - pN2 per AJCC 8th edition (must be >2 cm)
- Usually many entrapped nerves and vessels
- Likely decent interobserver variability, as with colon



Issue #5

- You gross an appendix for “acute appendicitis.” You pay close attention to the tip section and find this 0.13 cm lesion. What do you do?

- A. Ignore it
- B. Write a short report
- C. Write a full synoptic
- E. Drop the slide on the floor and run over it with your chair



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Poll: You gross an appendix for “acute appendicitis.” You pay close attention to the tip section and find this 0.13 cm lesion. What do you do?

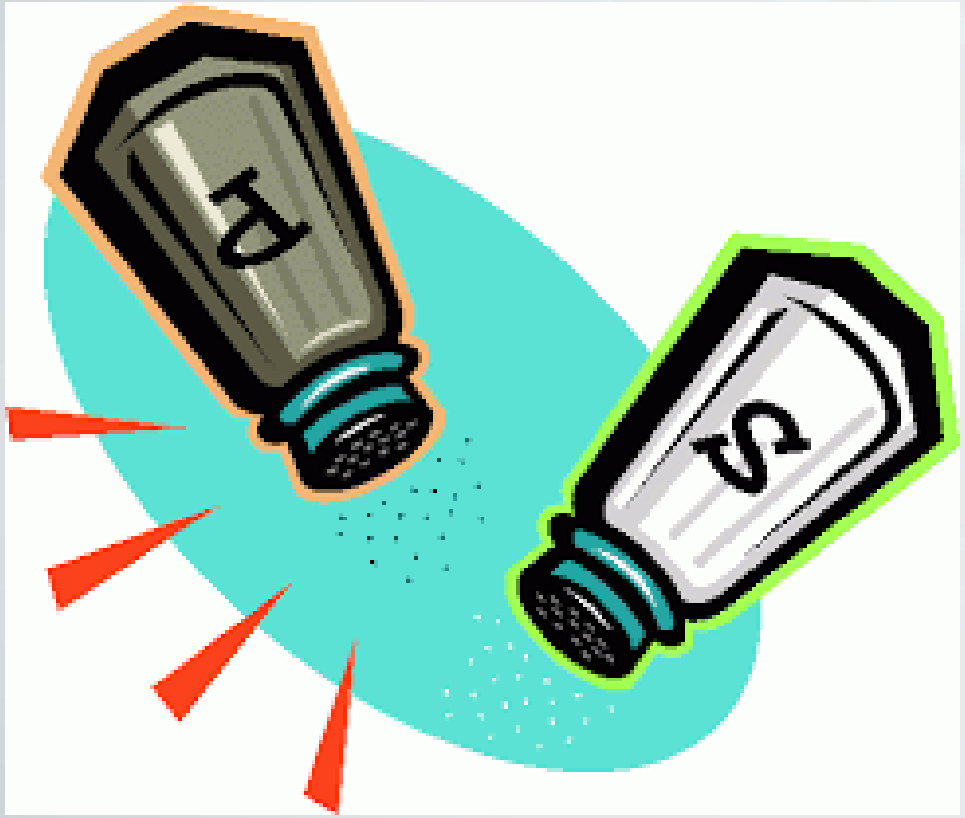
Significance of Incidental Appendix NETs[10-13]

- The vast majority do nothing
- Some metastasize to local nodes
  - Syracuse et al: Mesoappendix invasion
  - Groth et al: Size >2.0 cm
  - Brighi et al: Size >1.55 cm, G2 grade, lymphovascular invasion
  - Mehrvarz Sarshekeh et al: Size >1.0 cm (SEER data)
  - Noor et al: Size ≥1.0 cm (OR for 1.0 cm increase = 5.01)
- Anyone seen a case spread distantly (pM1)?
- We don’t do synoptics for pancreas microadenomas …

References (PMID)

1. 23579216
2. 24121170
3. 25412850
4. 3072229
5. 30326145
6. WHO 2019
7. 24457461
8. 27684993
9. 23902577
10. 464679
11. 21031414
12. 29995678
13. 29245922

Questions?



THANK YOU!