

How to Approach Hirschsprung Disease

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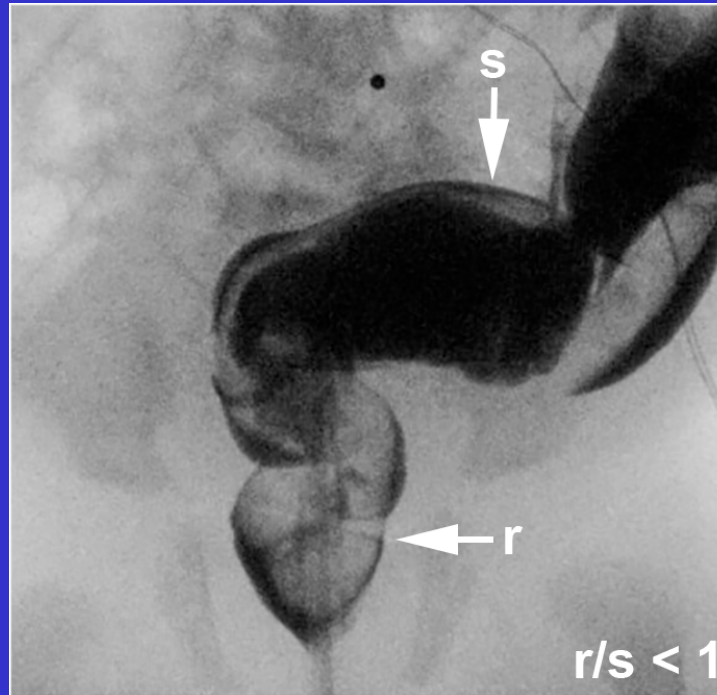
Objectives

1. Diagnosis (based on rectal biopsy)
2. Intra-operative consultation
3. Post-operative surgical pathology

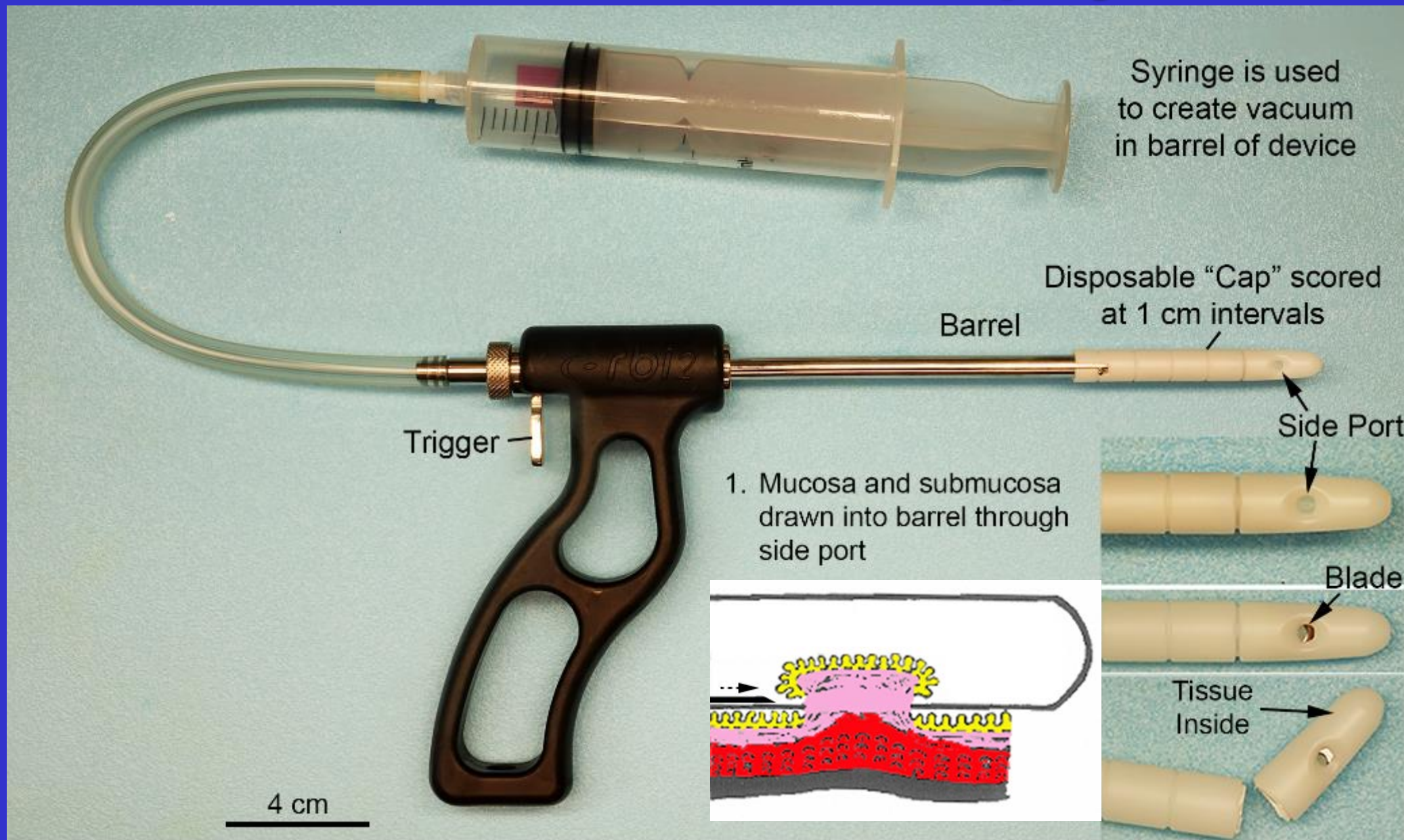
RECOMMENDATIONS

Clinical History

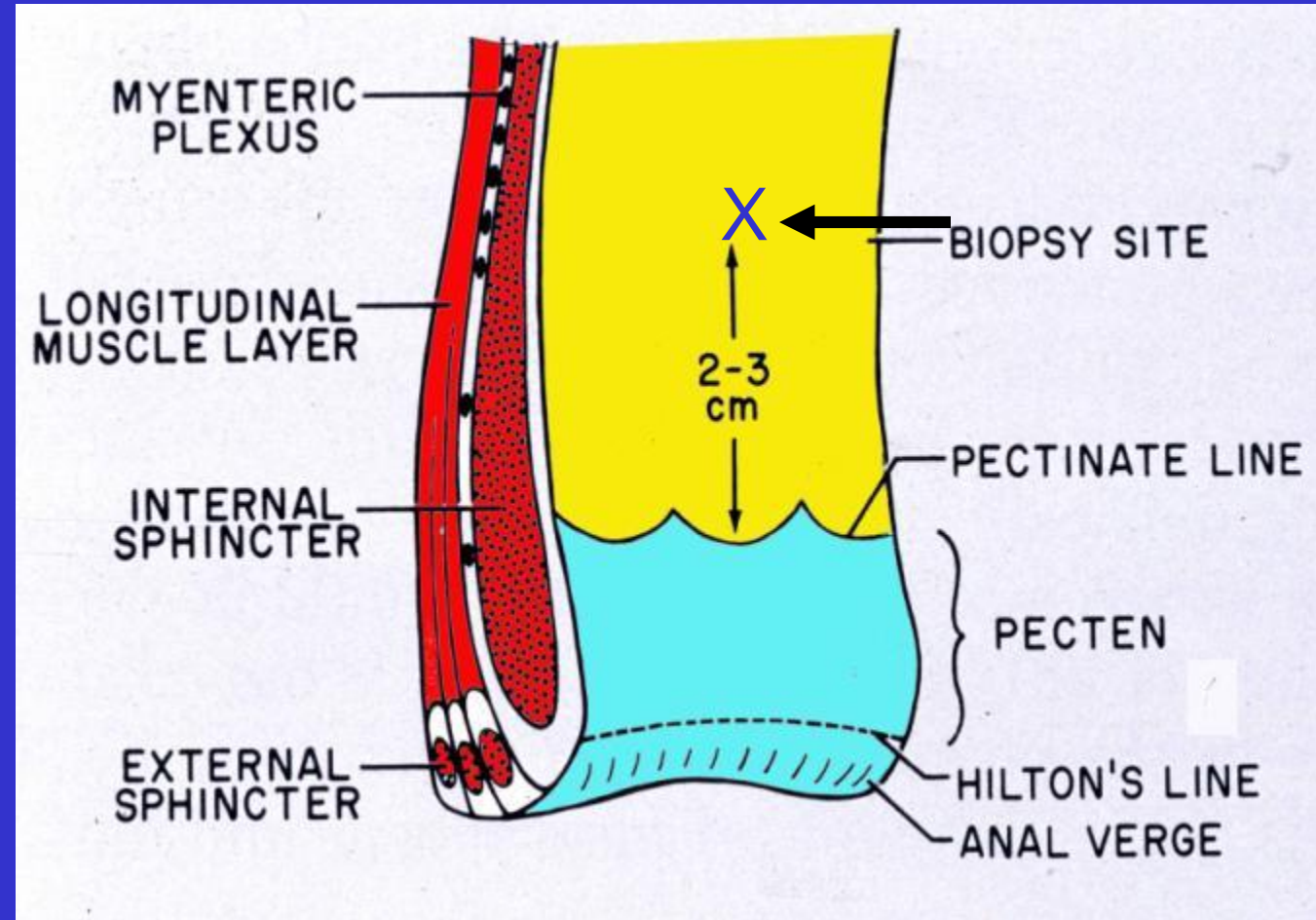
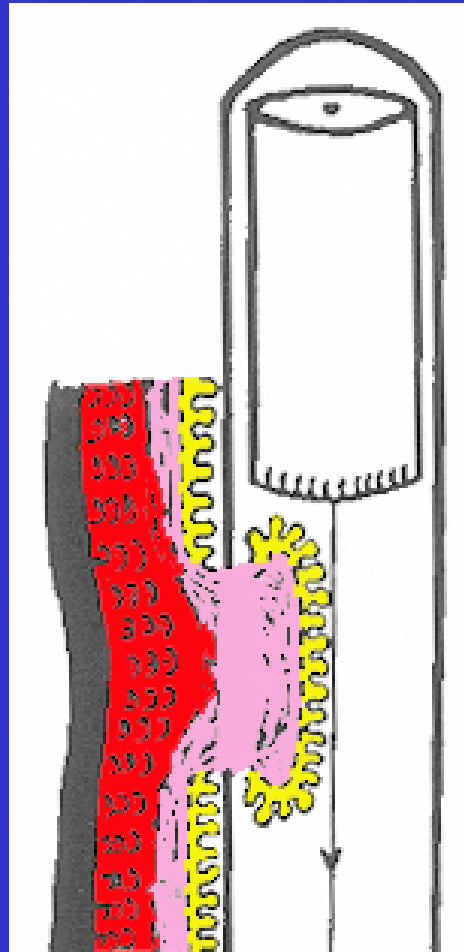
- 3 d old male
- Failed to pass meconium in the first 48h
- Abdominal distension and vomiting
- Barium enema shows dilated sigmoid and narrow rectum (recto-sigmoid ratio <1)



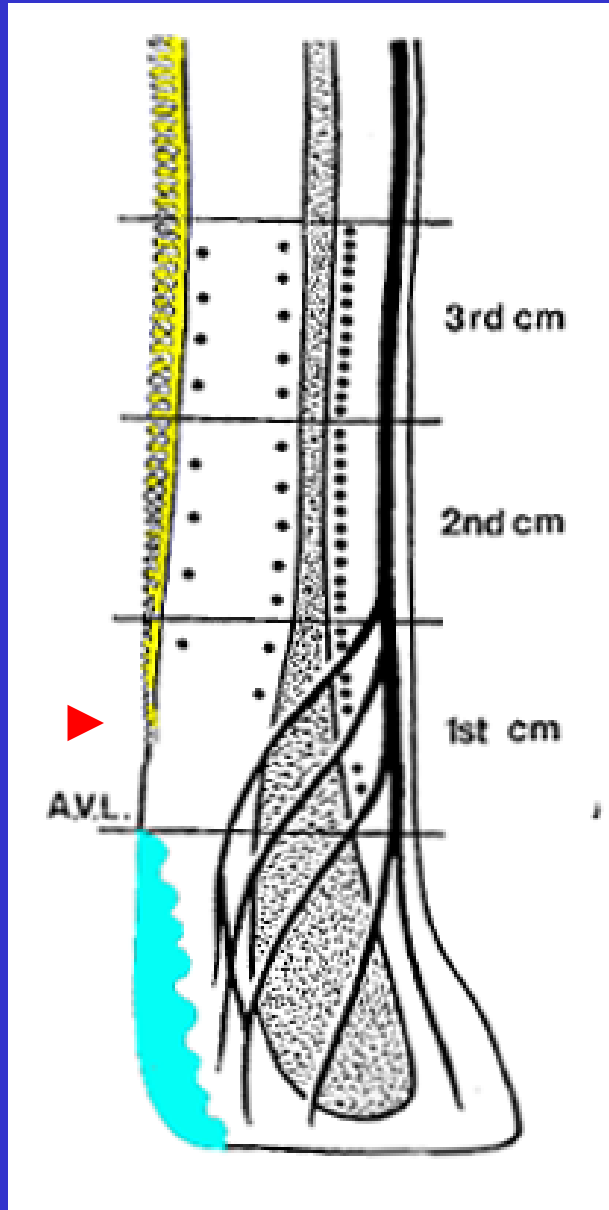
Suction Rectal Biopsy



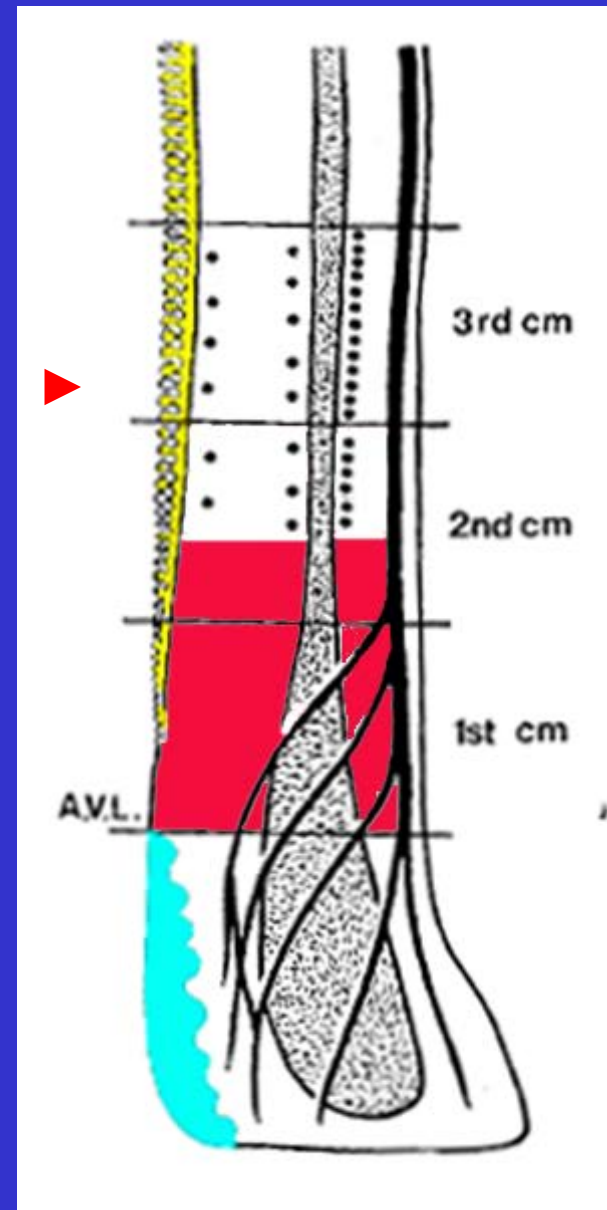
RECTAL BIOPSY-BASED DIAGNOSIS OF HIRSCHSPRUNG DISEASE



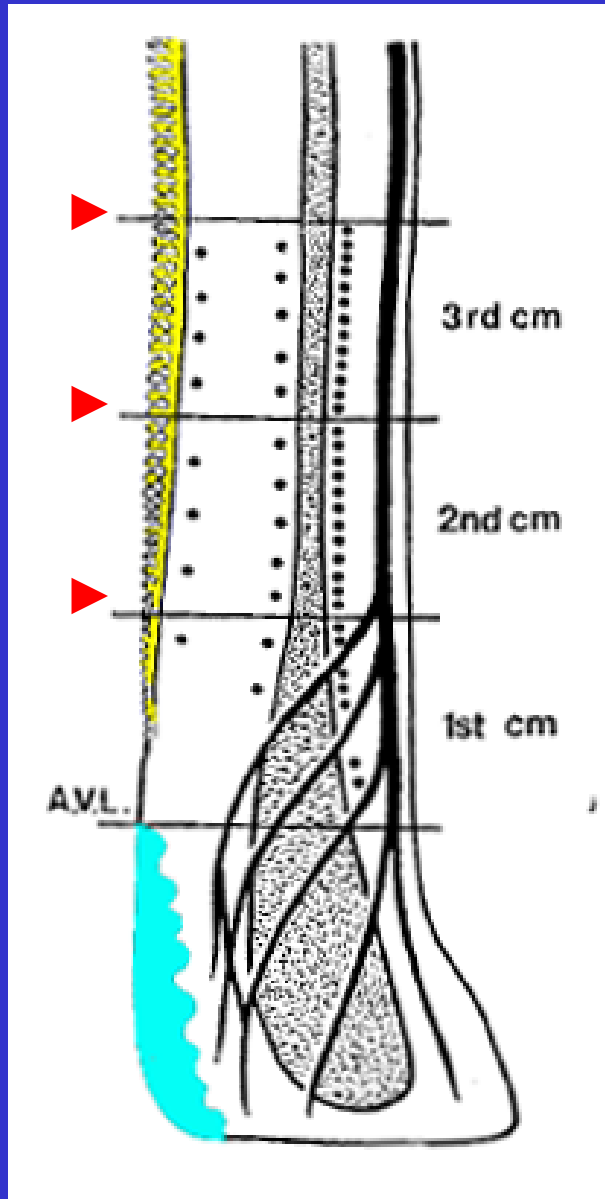
TOO LOW (False Positive)



TOO HIGH (False Negative)



Suction Biopsies from Multiple Levels



Less likely that all biopsies will lack sufficient submucosa

Fewer inadequate biopsies due to sampling of anal or transitional mucosa

Mapping data

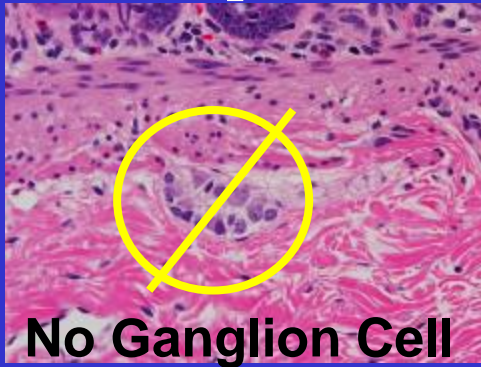
- "reposition" low biopsies
- very short-segment HSCR

R1: Advise surgeon to get biopsies from multiple levels in separate containers

IN MOST CASES H&E IS SUFFICIENT



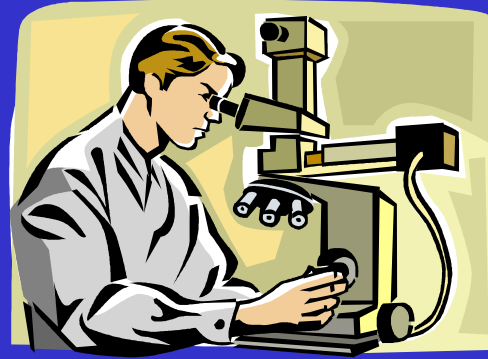
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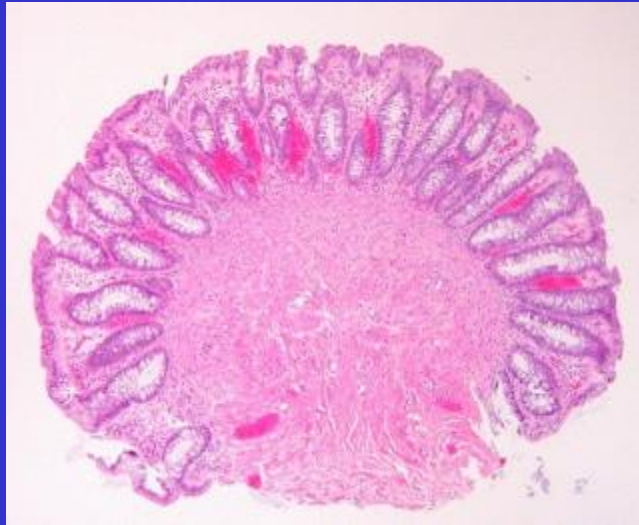
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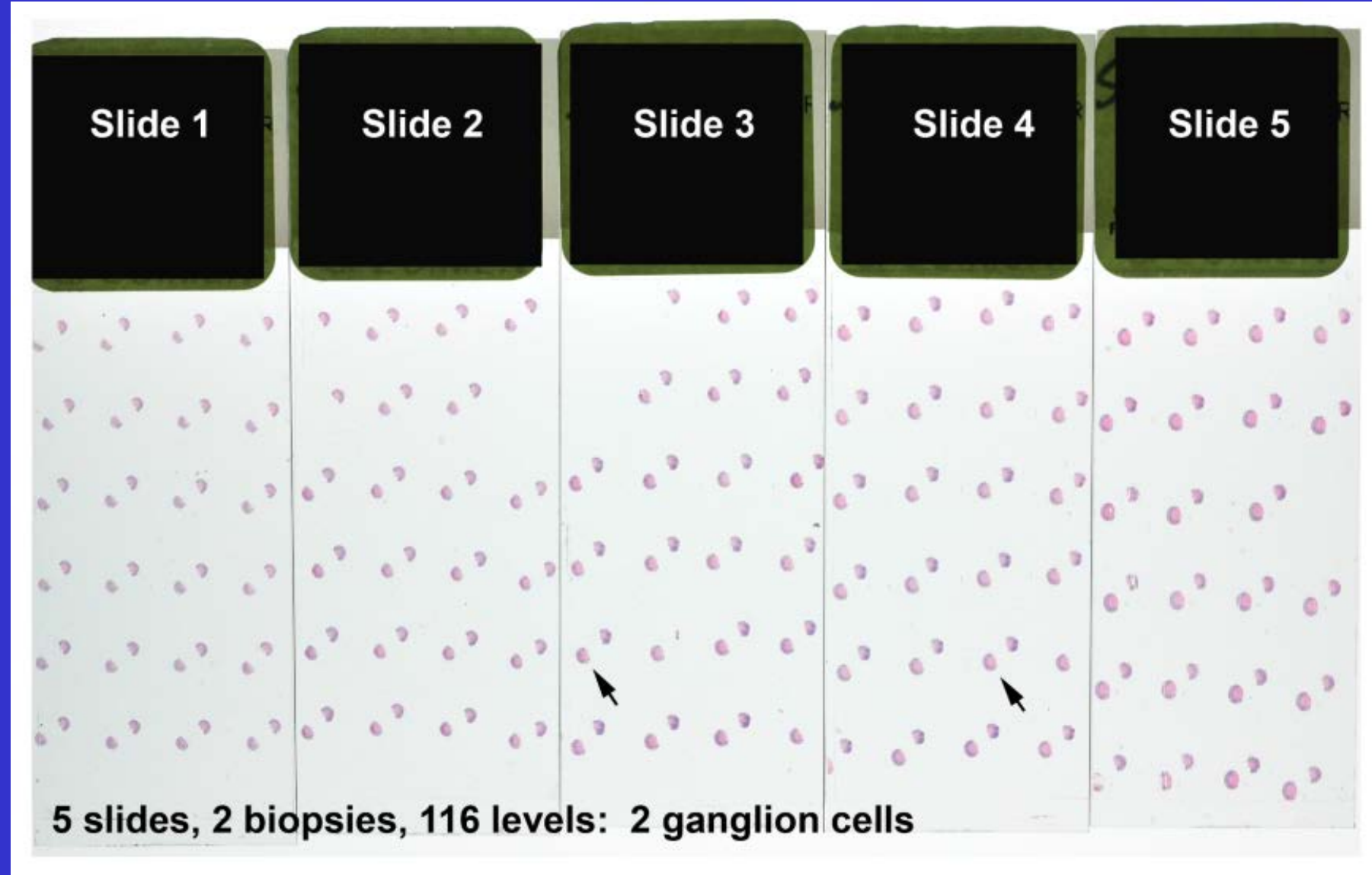
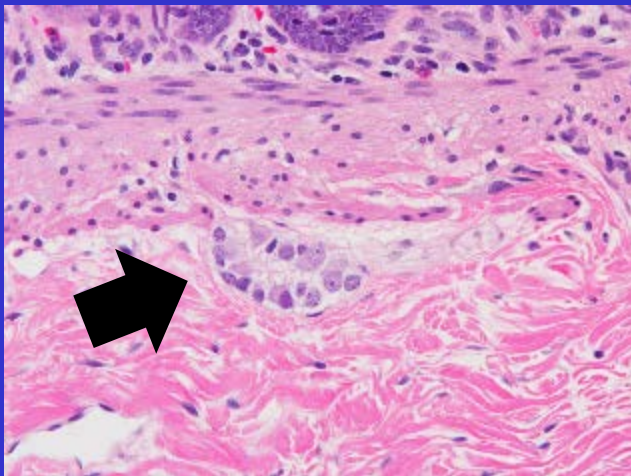
Experienced
Pathologist

= DIAGNOSIS

ADEQUACY

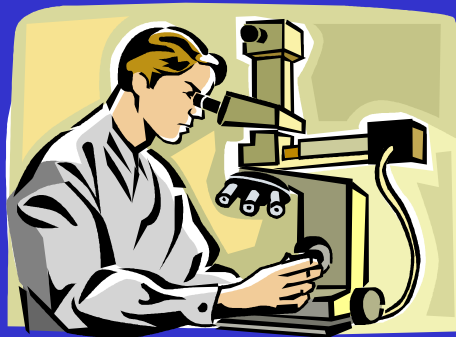
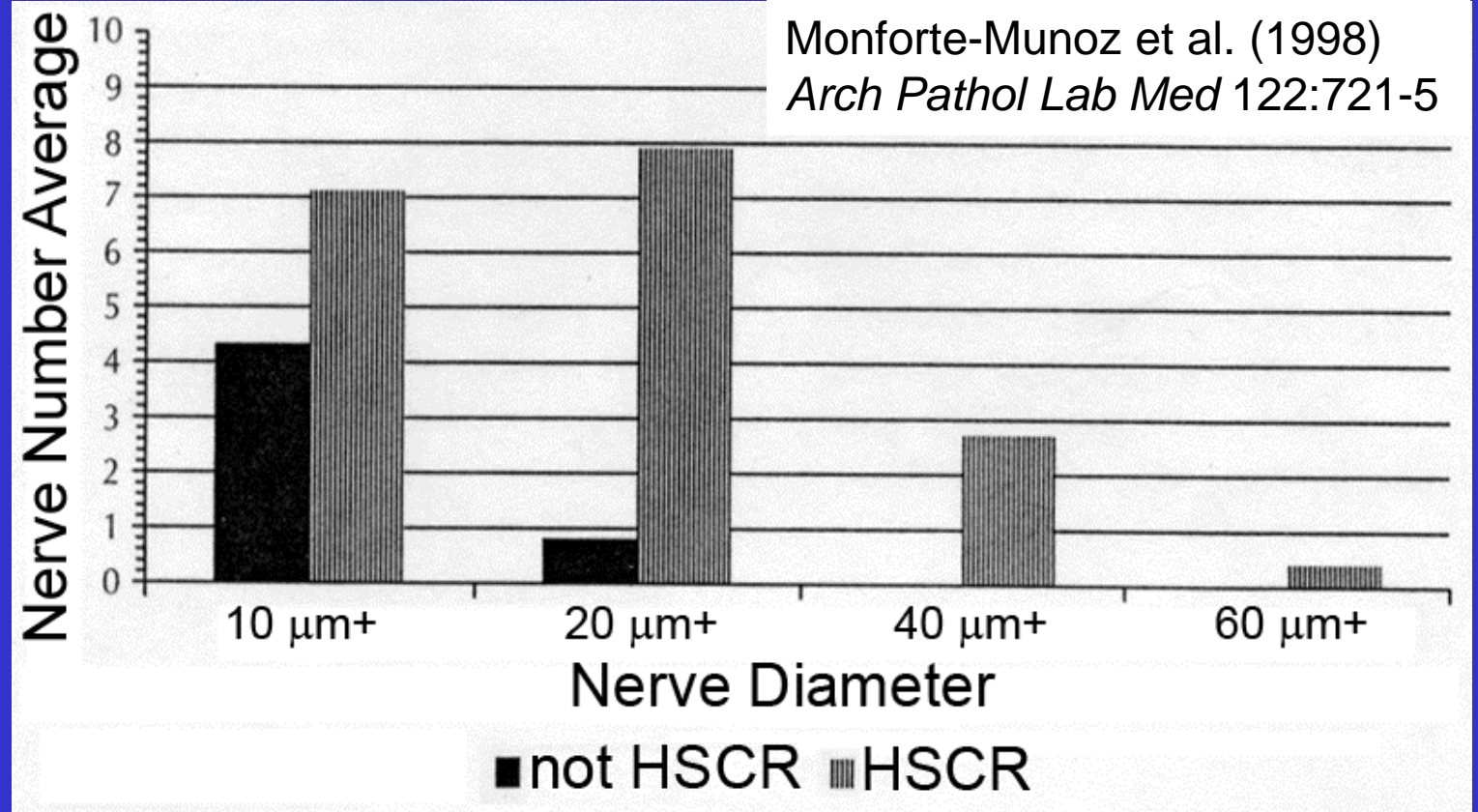
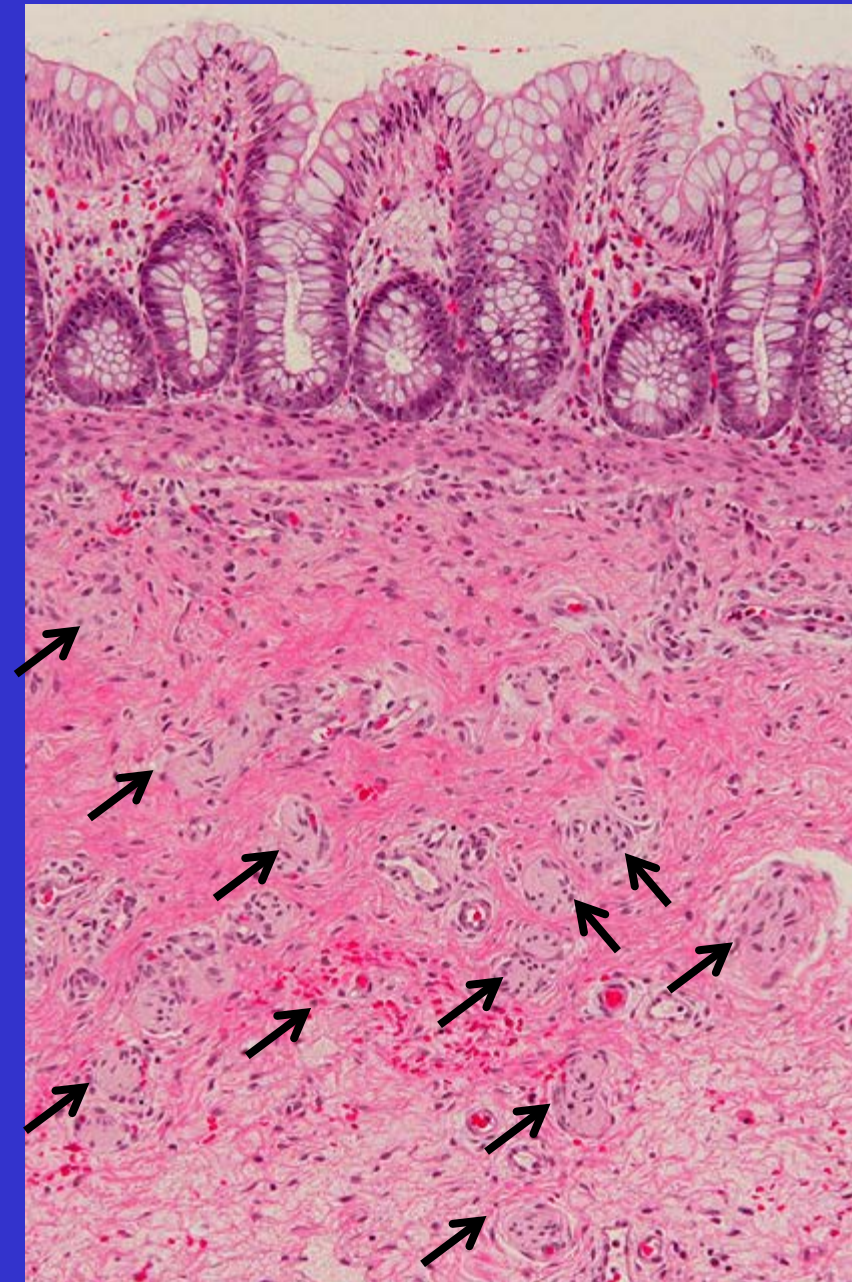


3 mm



R2: Routinely cut lots of sections and have a low threshold for more levels

Hypertrophic Submucosal Nerves



Experience

R3: Pay careful attention to submucosal nerve calibers

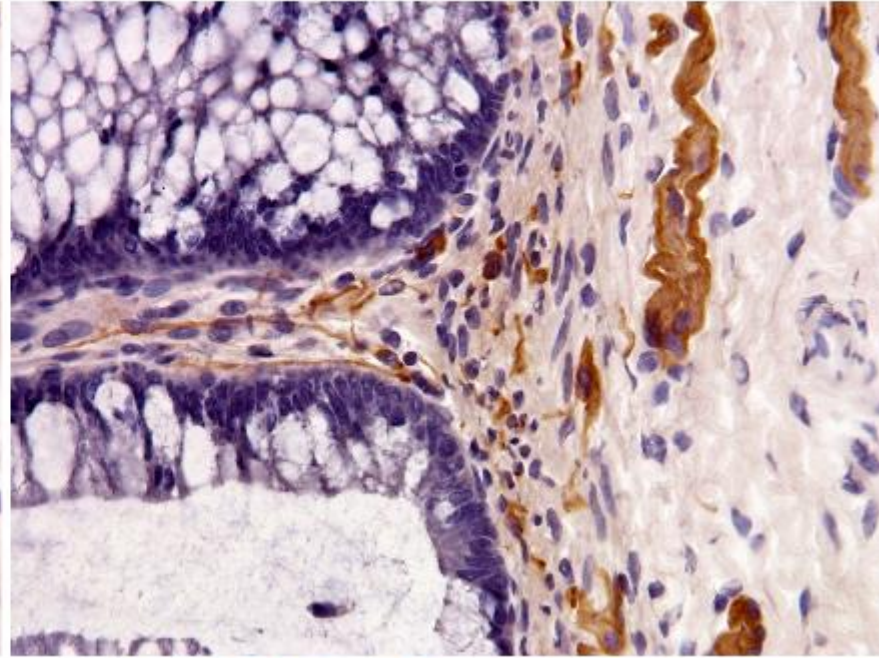
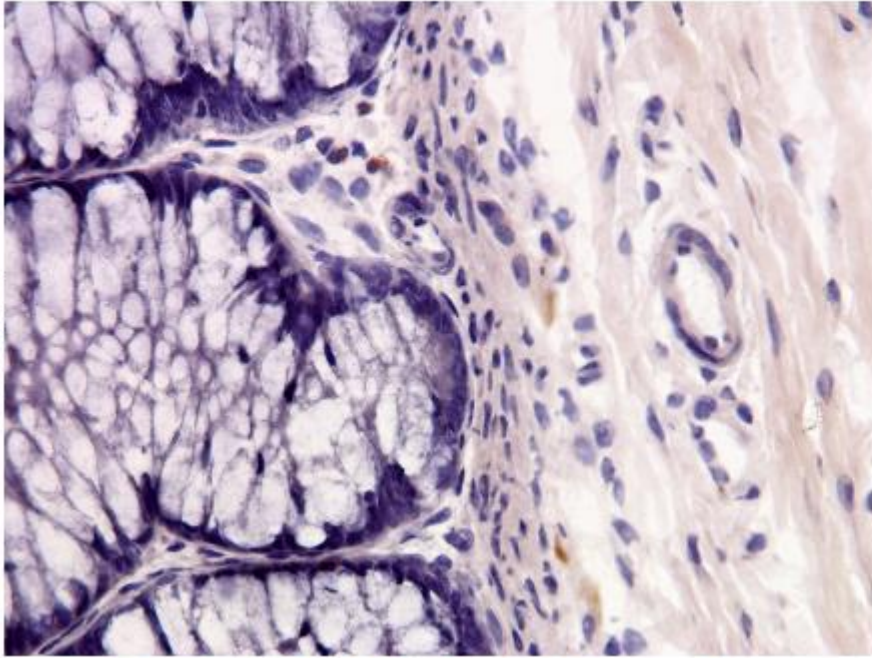
Ancillary Diagnostic Methods

- Experience varies (recognition of ganglion cells, especially immature cells, requires practice)
- Some biopsies have borderline adequacy
- Not all biopsies of aganglionic rectum contain hypertrophic nerves
- Histological quality varies
- Tissue sampling to exclude ganglion cells and large nerves is cumbersome and costly

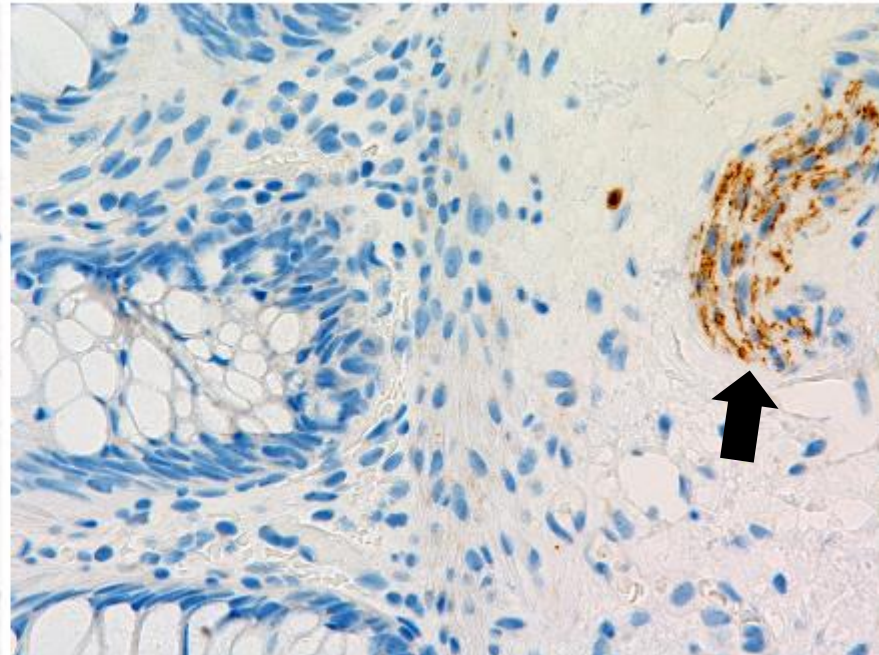
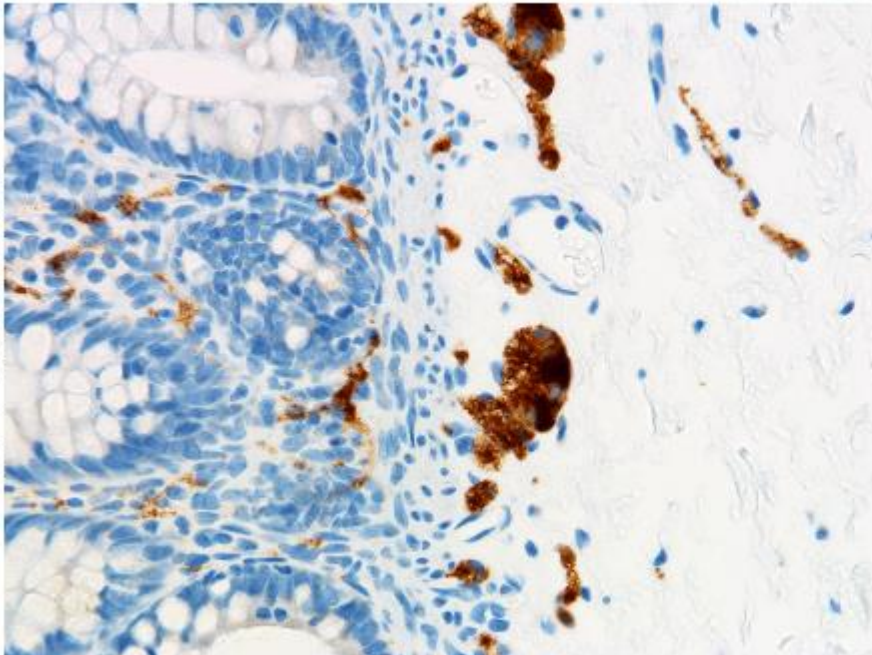
NORMAL

AGANGLIONIC

ACH E



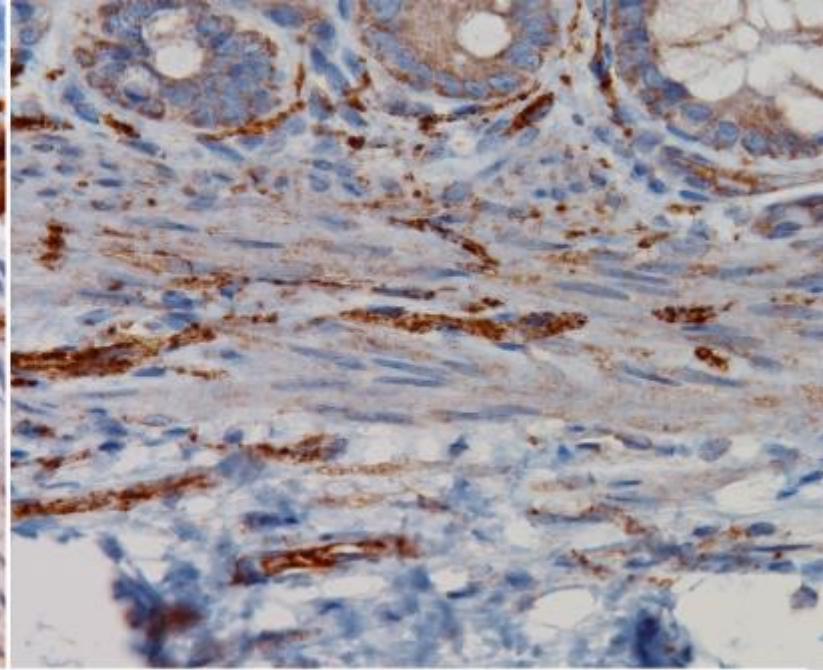
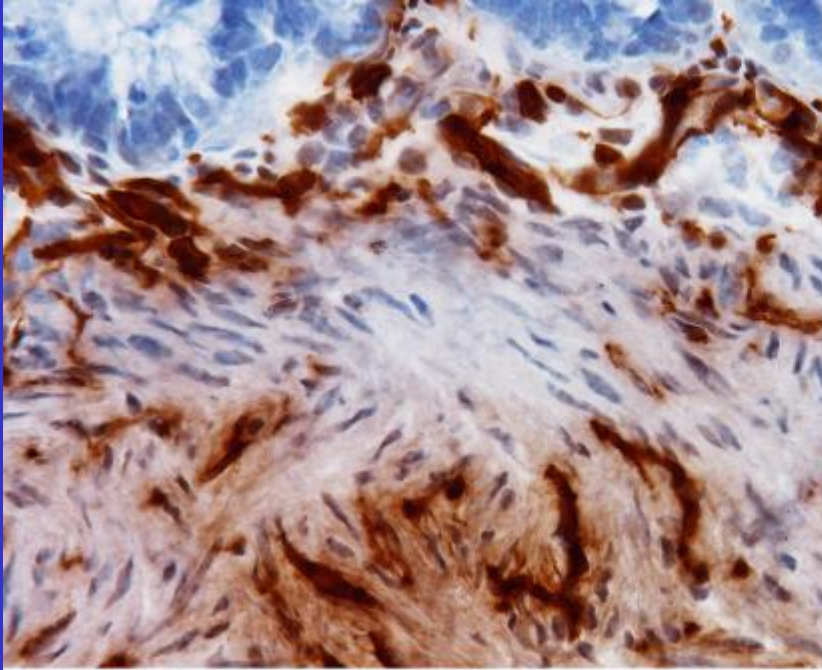
CALRETININ



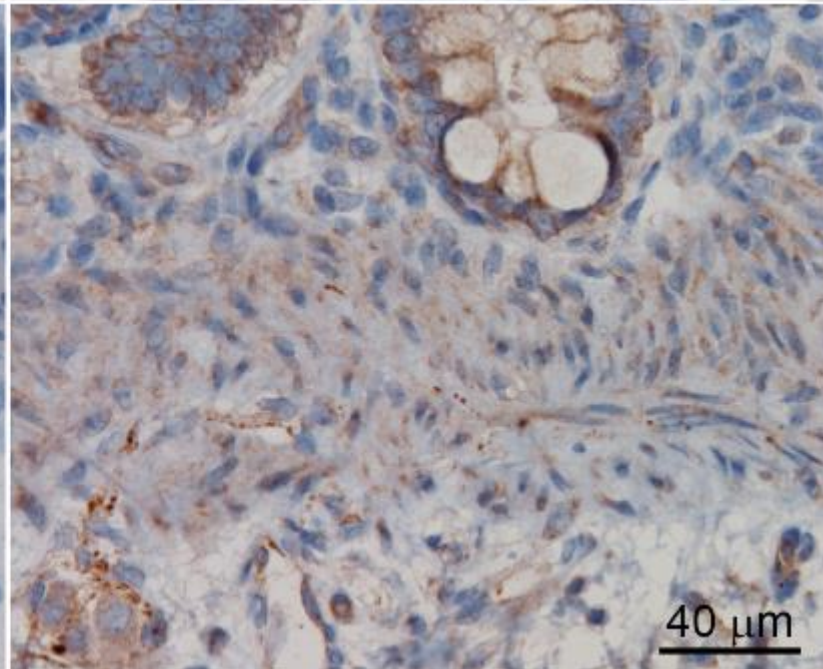
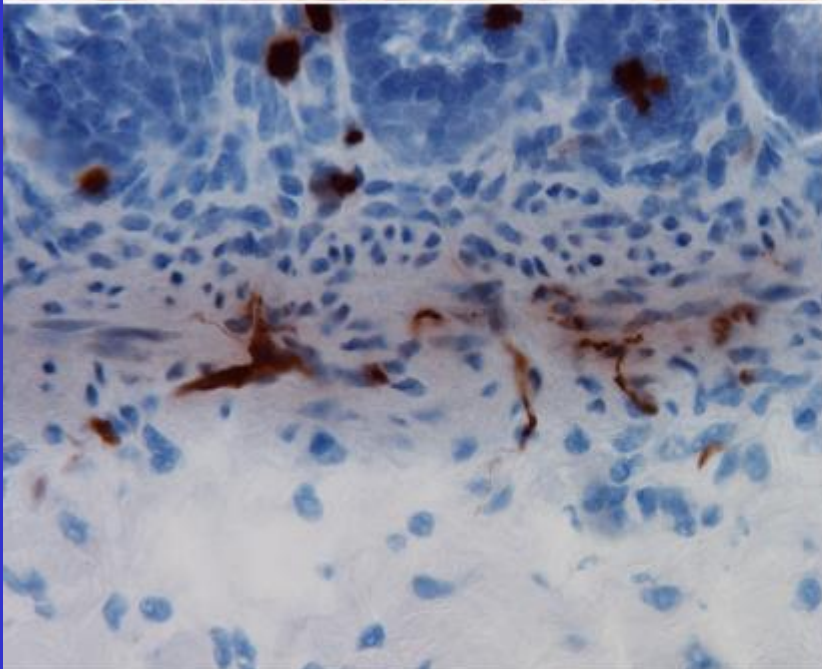
AChE (frozen)

ChT (FFPE)

Aganglionic

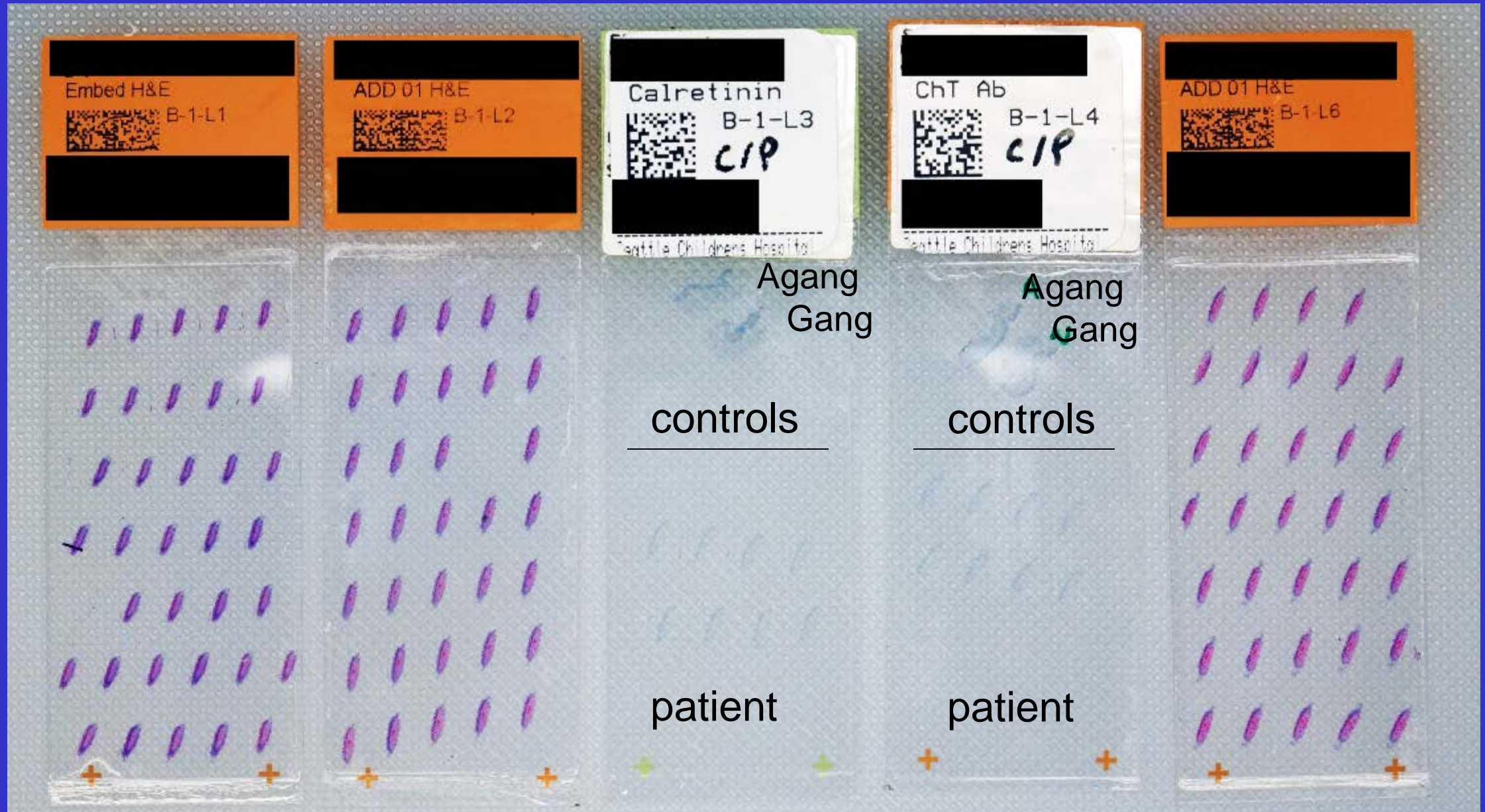


Ganglionic



Kapur et al
Pediatr Dev Pathol
2017; 20:308-20

RECOMMENDED APPROACH

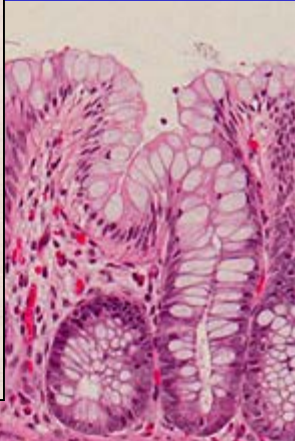


YOUR DIAGNOSIS?

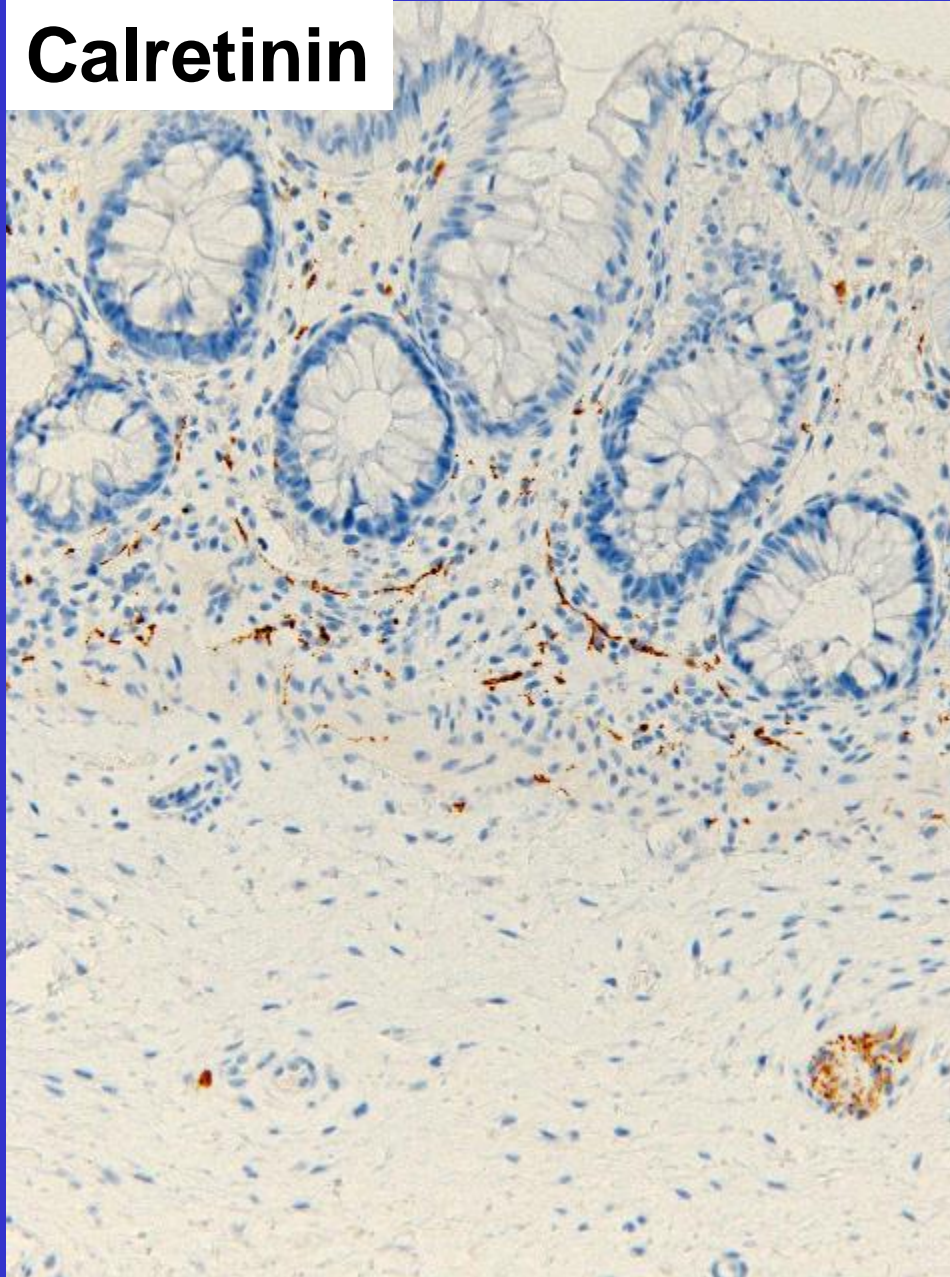
“2 cm”



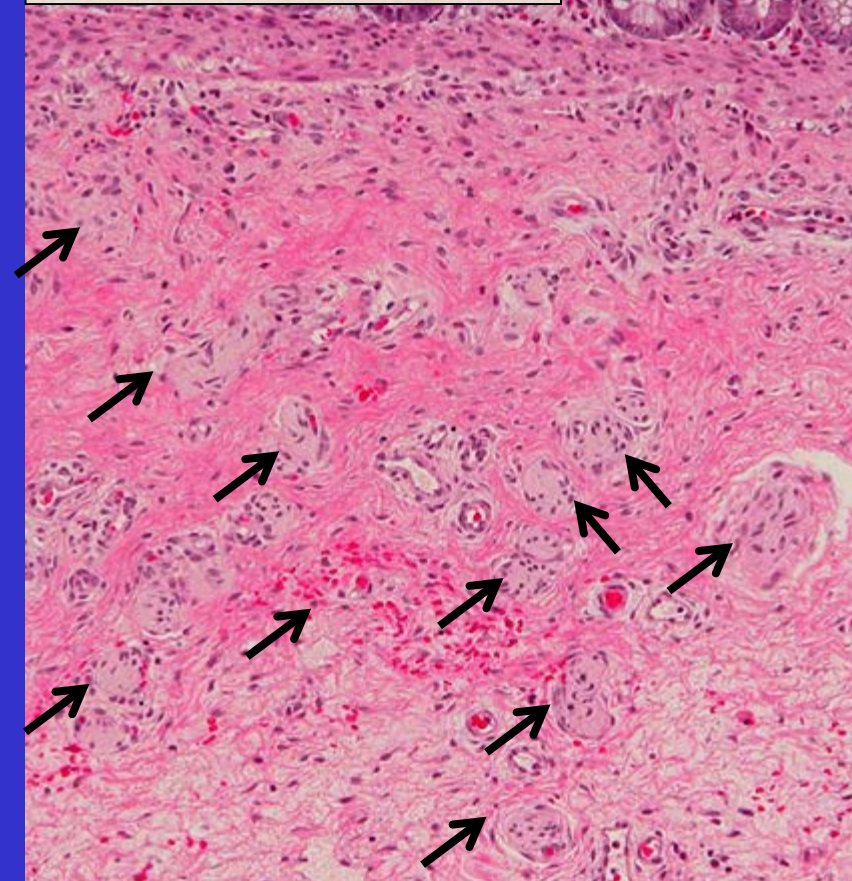
No ganglion cells



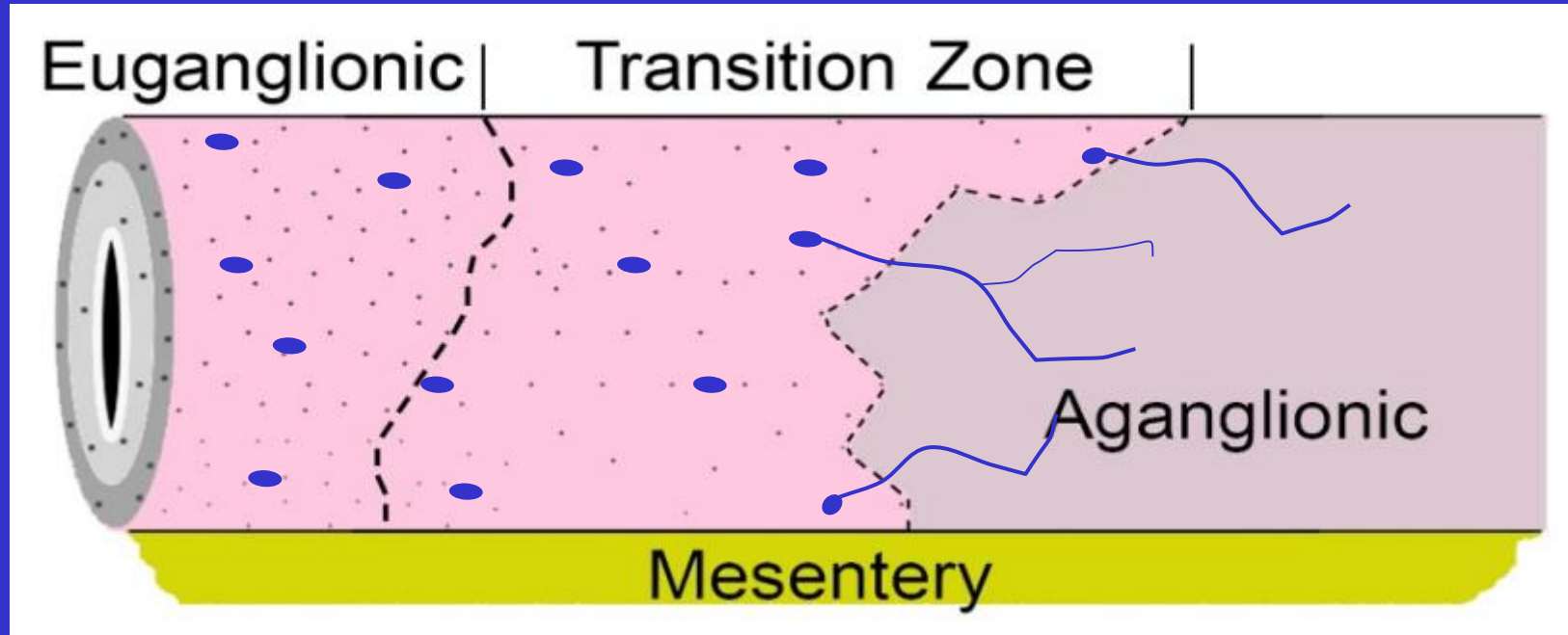
Calretinin



- A. Hirschsprung disease
- B. Not Hirschsprung disease
- C. Rebiopsy
- D. Other



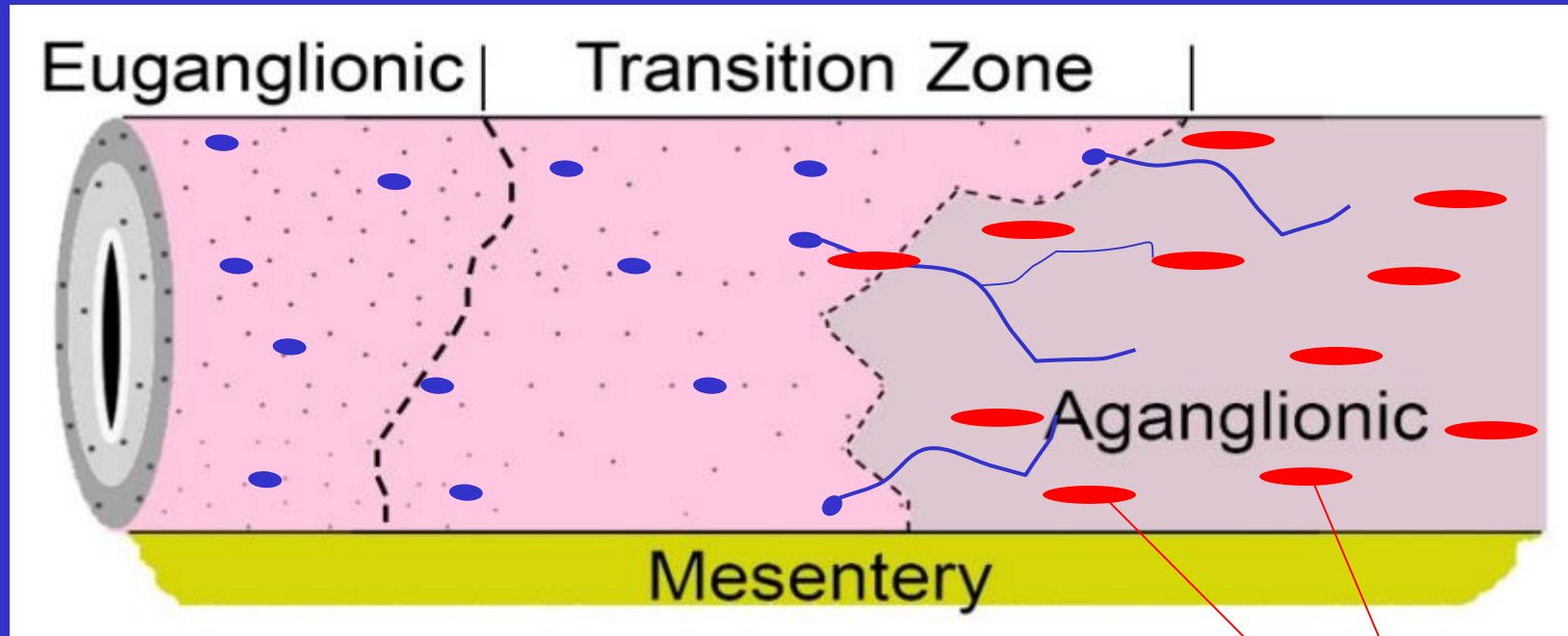
Intact Calretinin Innervation Aganglionic Rectal Biopsies



Calretinin-immunoreactive mucosal nerves are

- present in the proximal 1-to-2 cm of the aganglionic segment in HD
- may be present in aganglionic biopsies from the distal rectum of a patient with vssHD

Intact Calretinin Innervation Aganglionic Rectal Biopsies



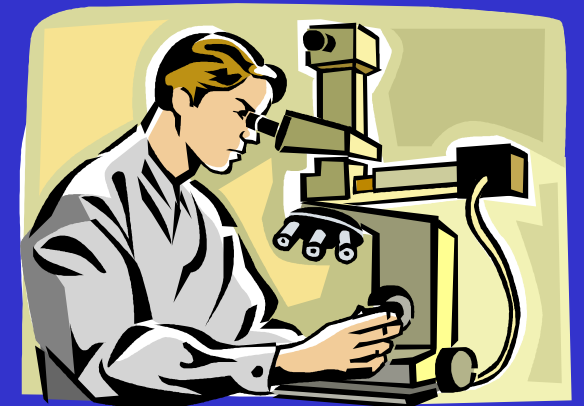
Hypertrophic
Nerves

R3: Pay careful
attention to
submucosal nerve
calibers!

Recommendations

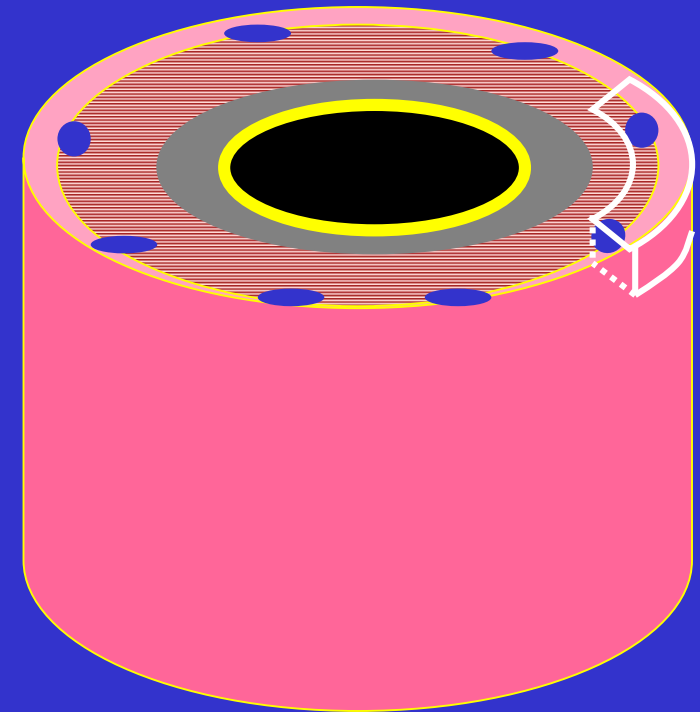
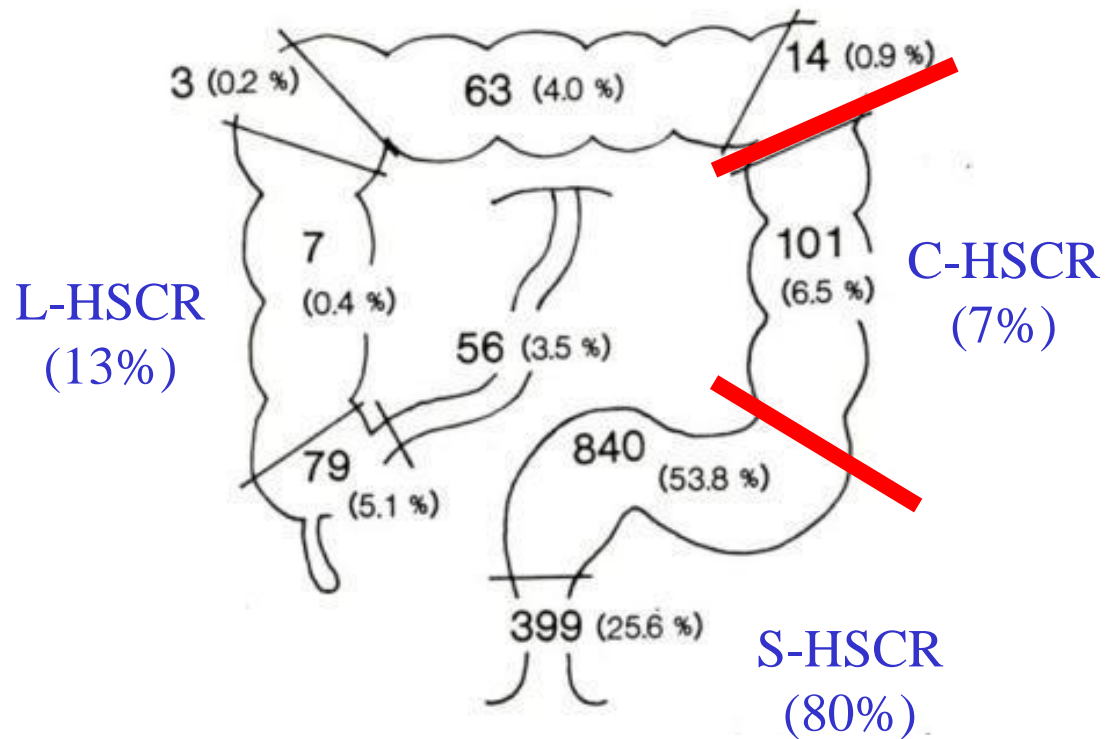
- Routinely obtain biopsies from more than one site
- Perform calretinin ihc on at least one biopsy from every patient
- Pay close attention to nerve hypertrophy, even if ganglion cells are present
- In some situations (e.g., vssHSCR), AChE histochemistry or ChT ihc may be particularly helpful
- Have low threshold for rebiopsy and/or full-thickness biopsy, especially in older patients

Intraoperative Consultation



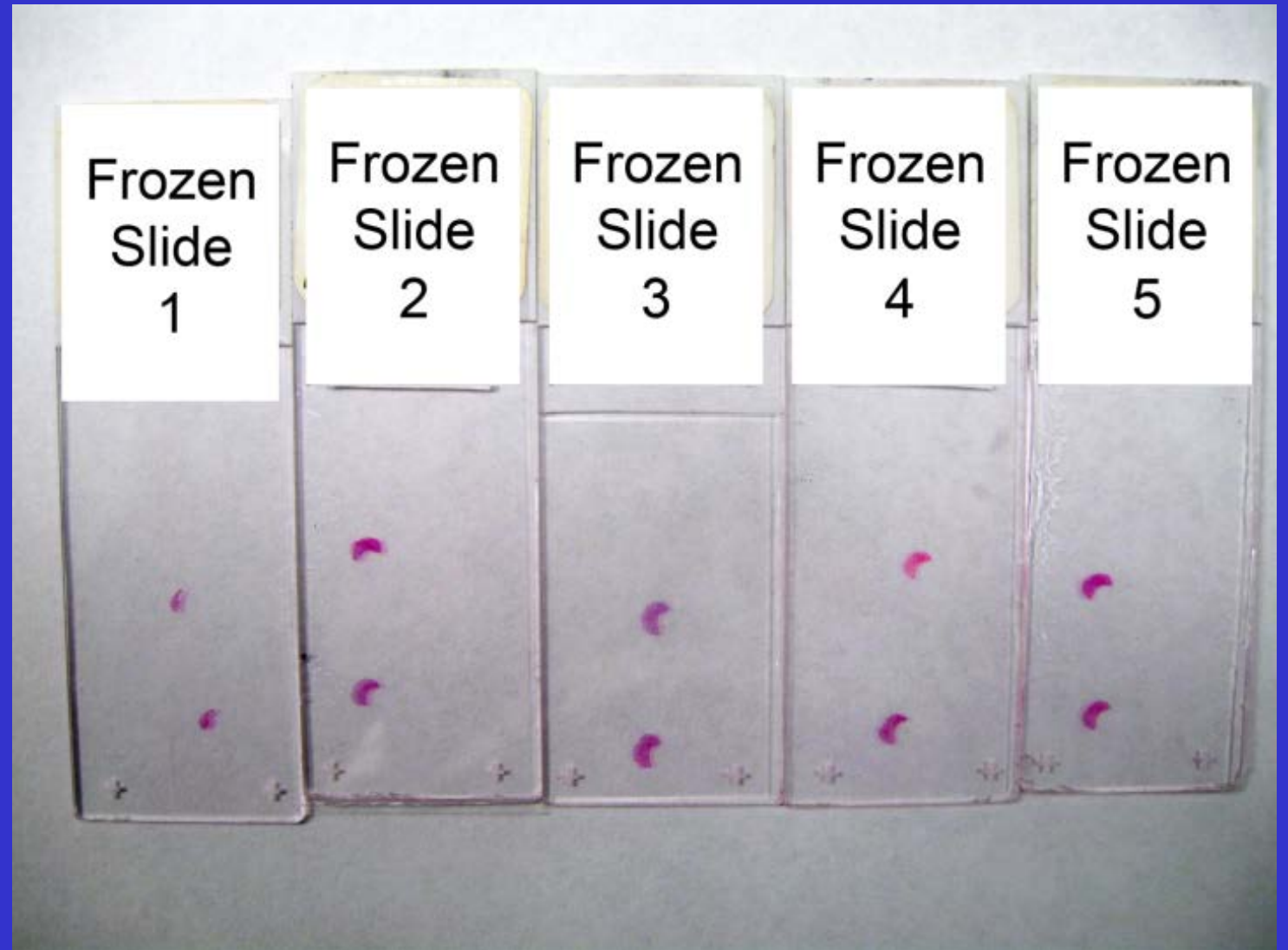
INTRAOPERATIVE LEVELLING BIOPSY

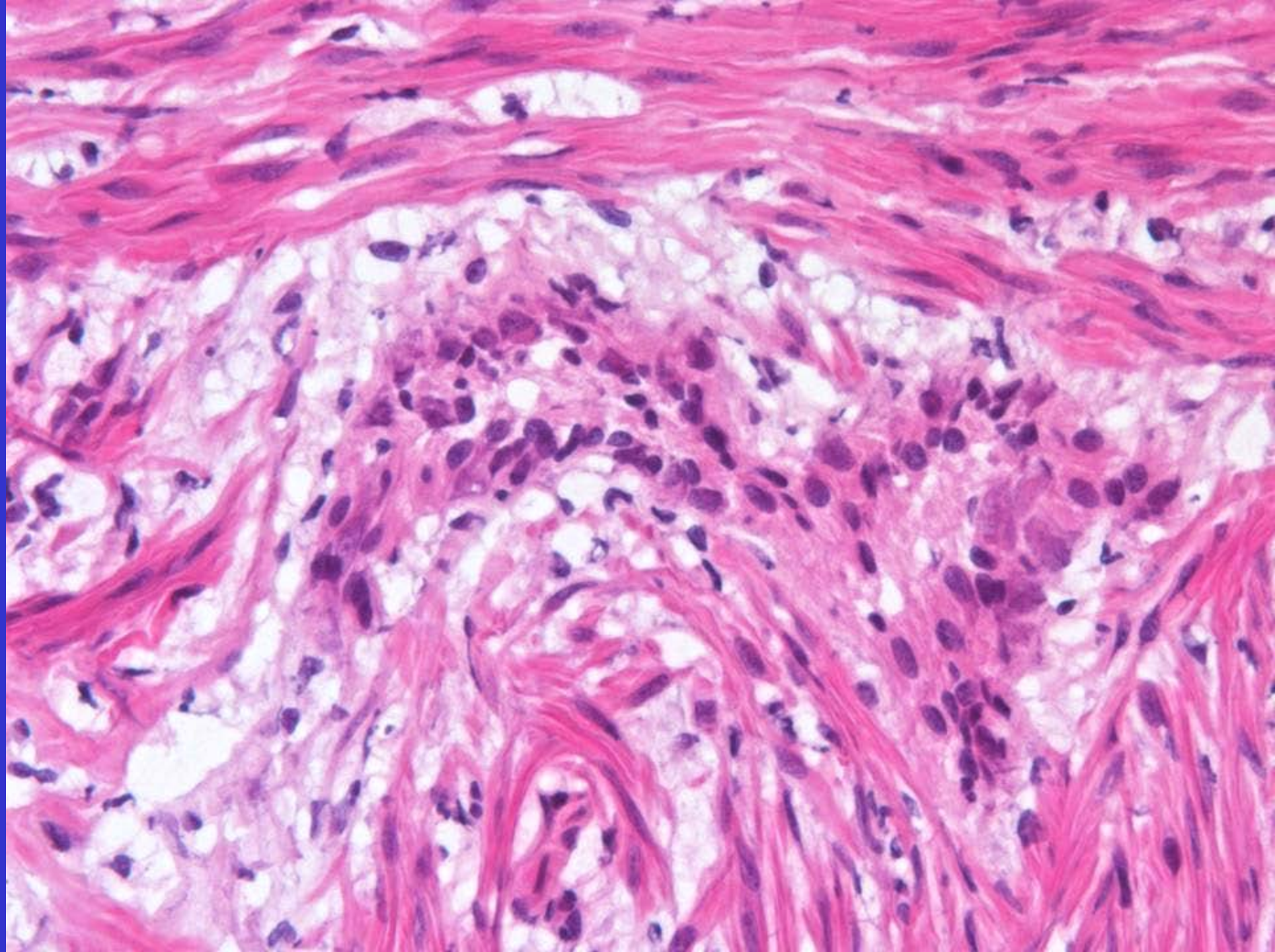
Finding Ganglionic Bowel

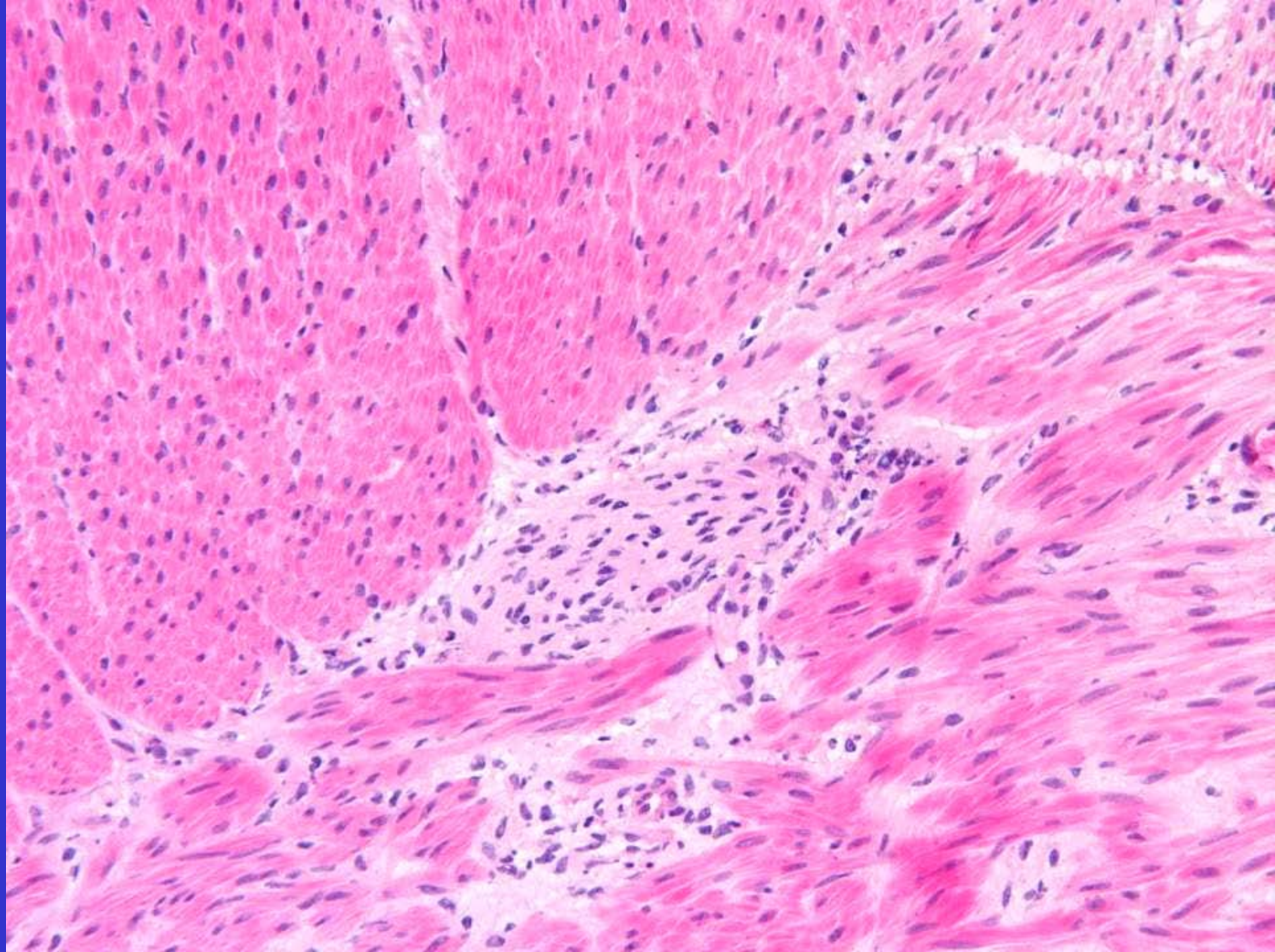


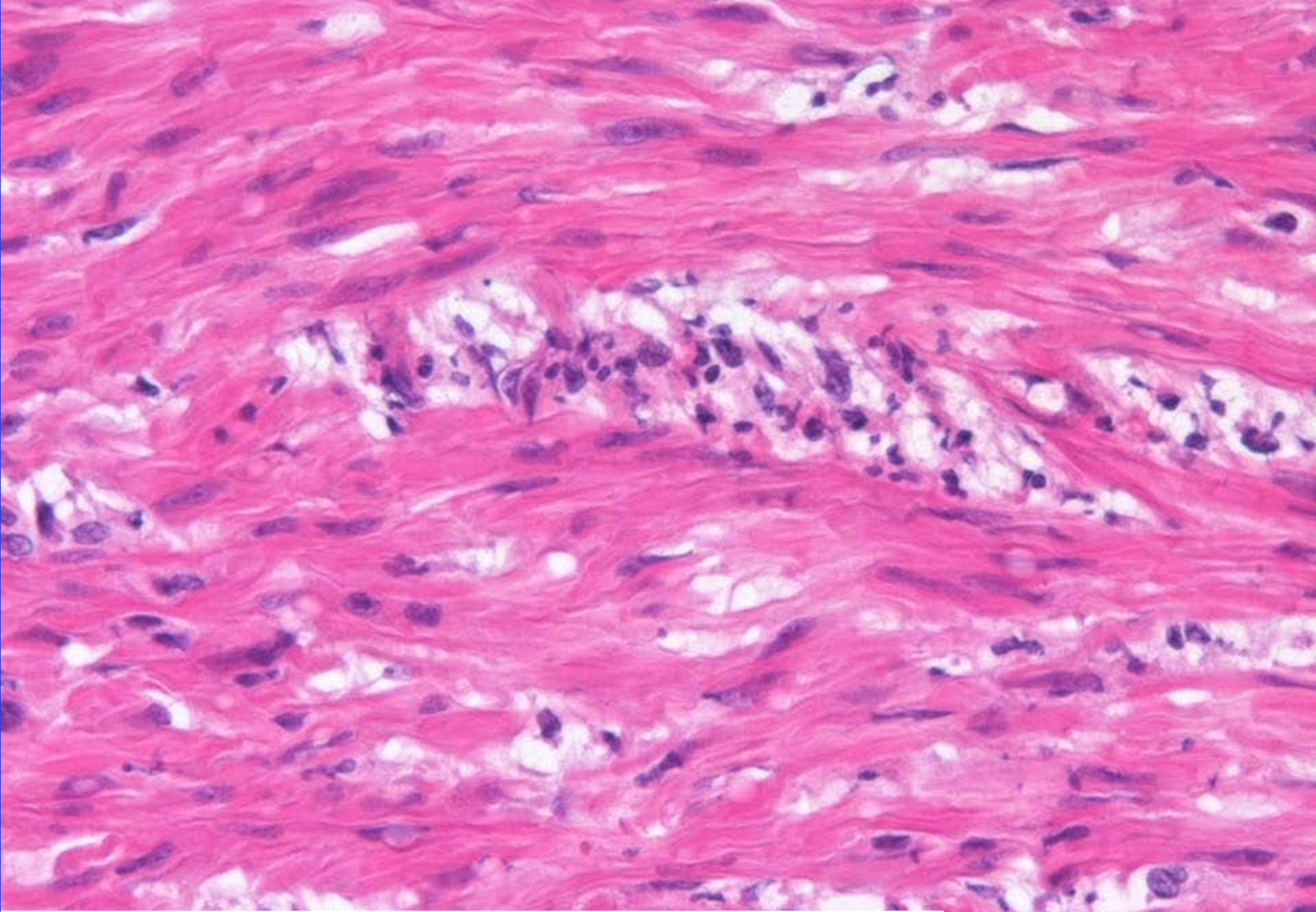
5-10 mm

HANDLING AND INTERPRETATION OF LEVELLING BIOPSY

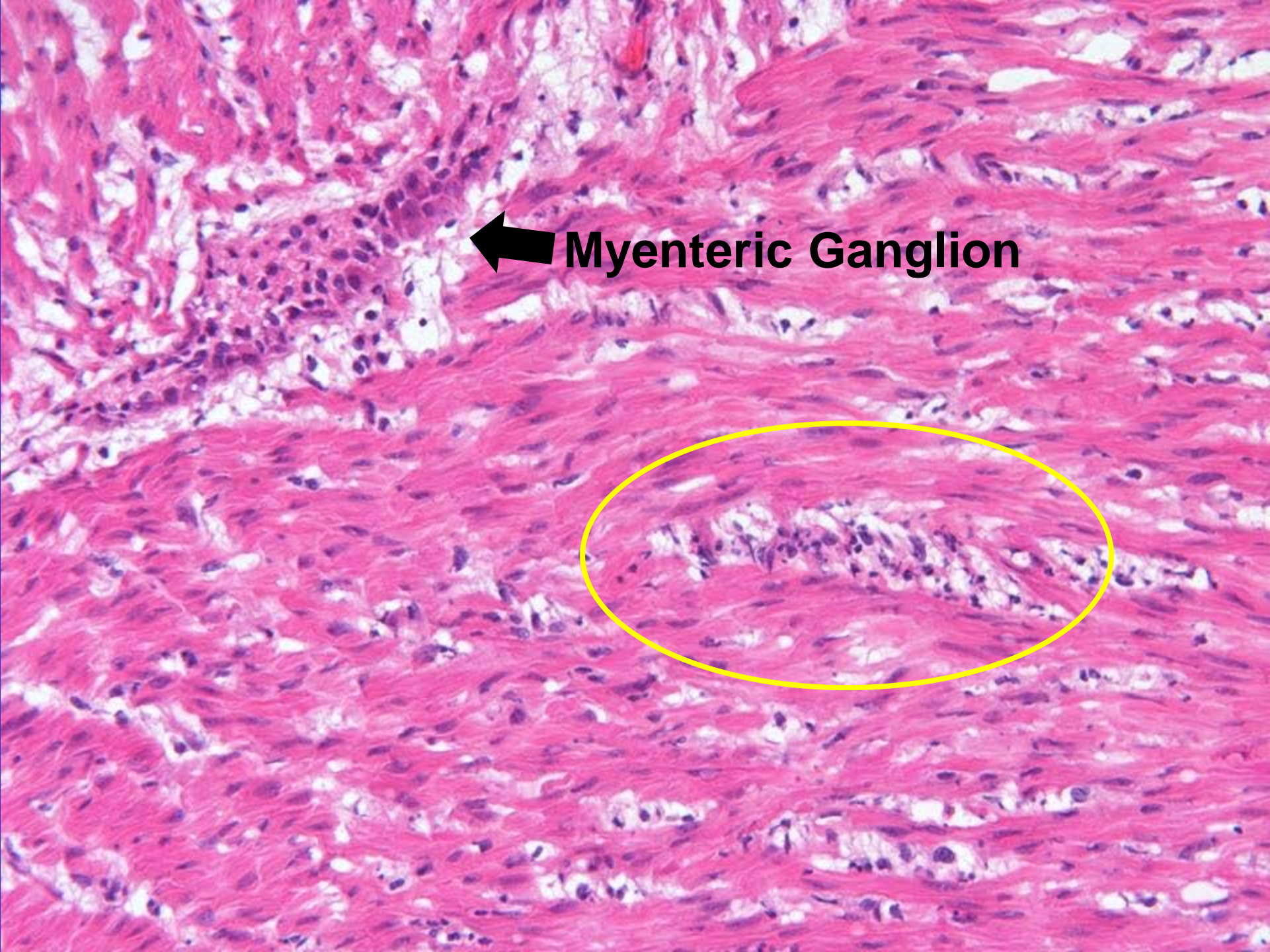




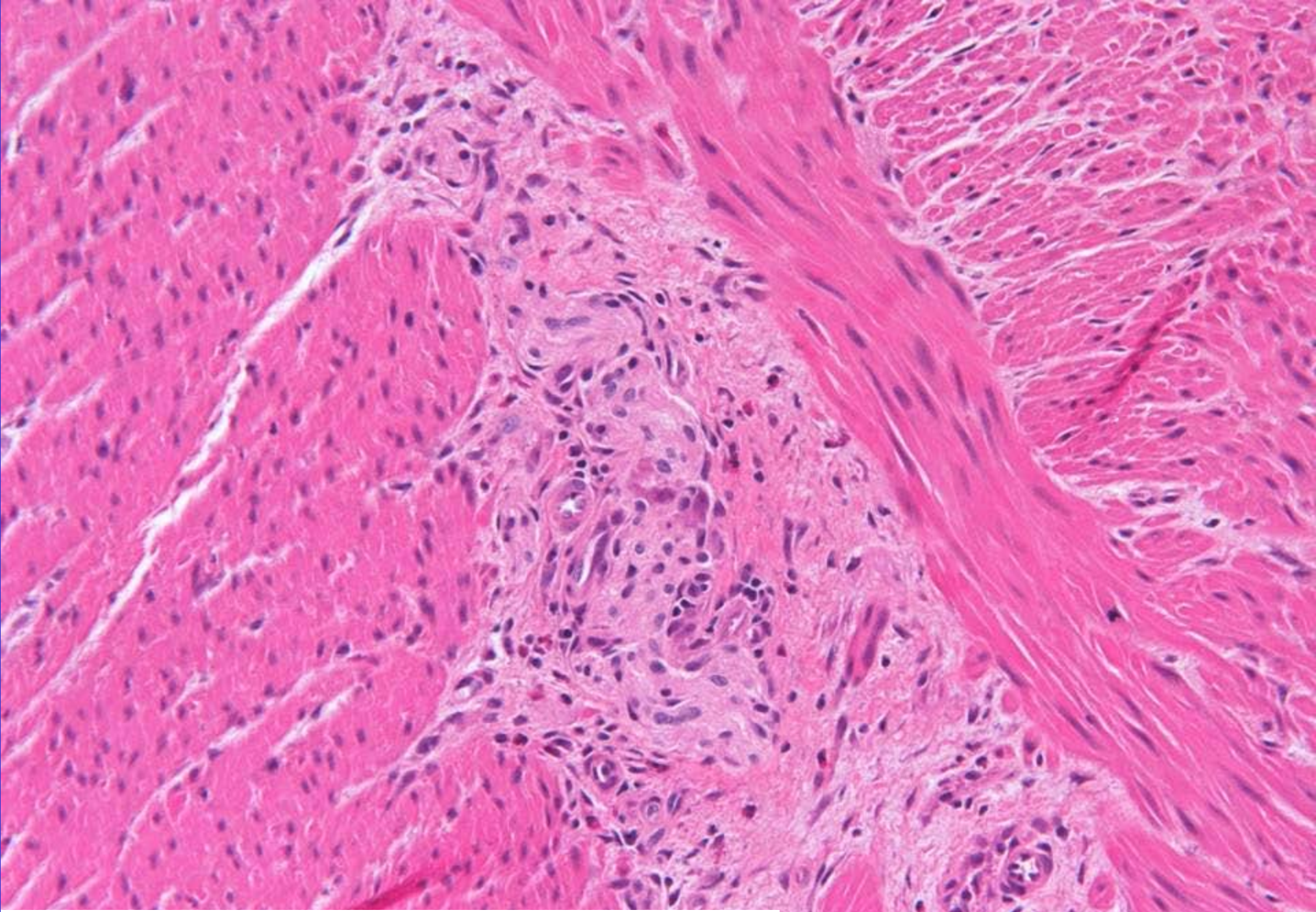




Orientation and location are important

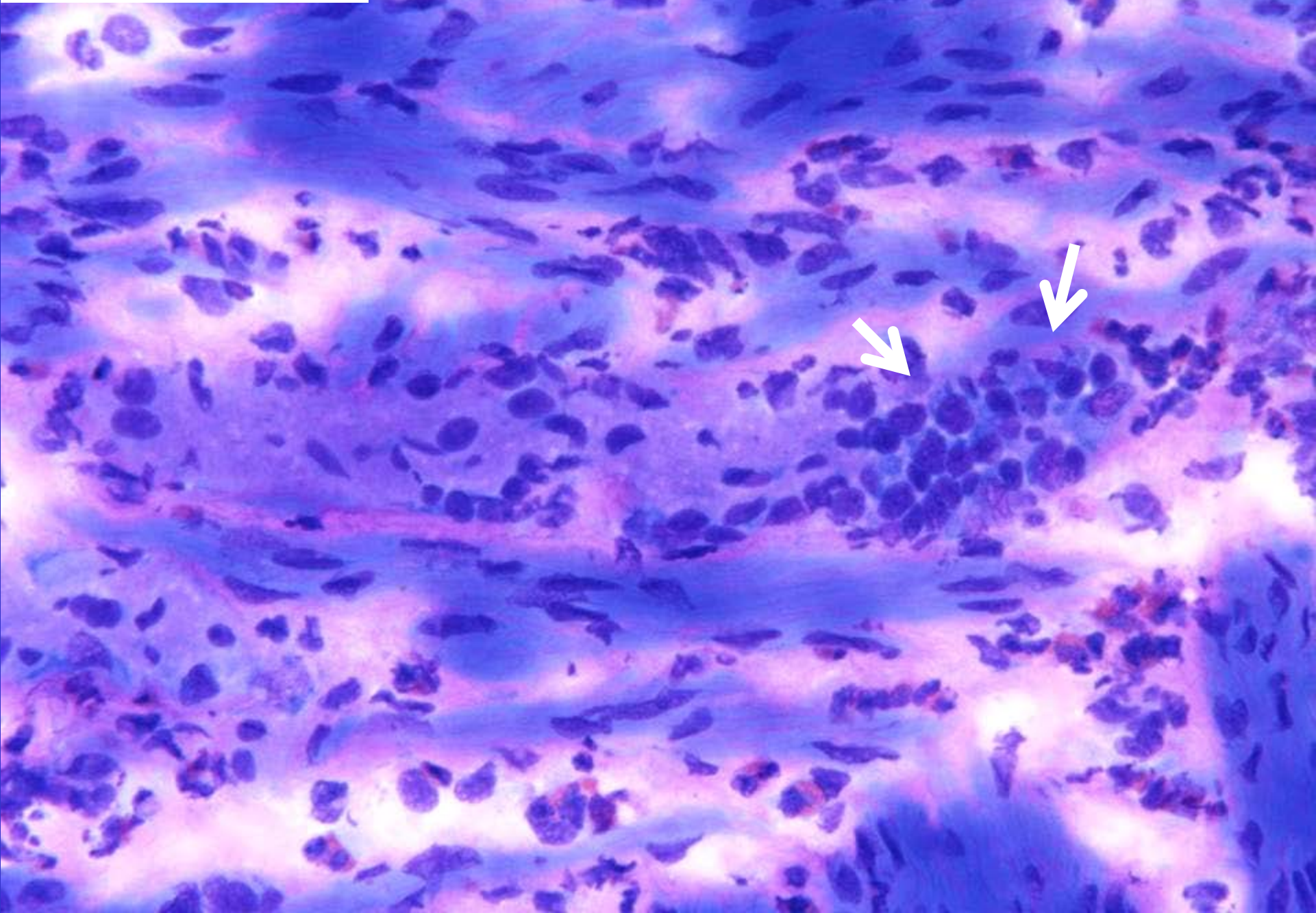


← **Myenteric Ganglion**



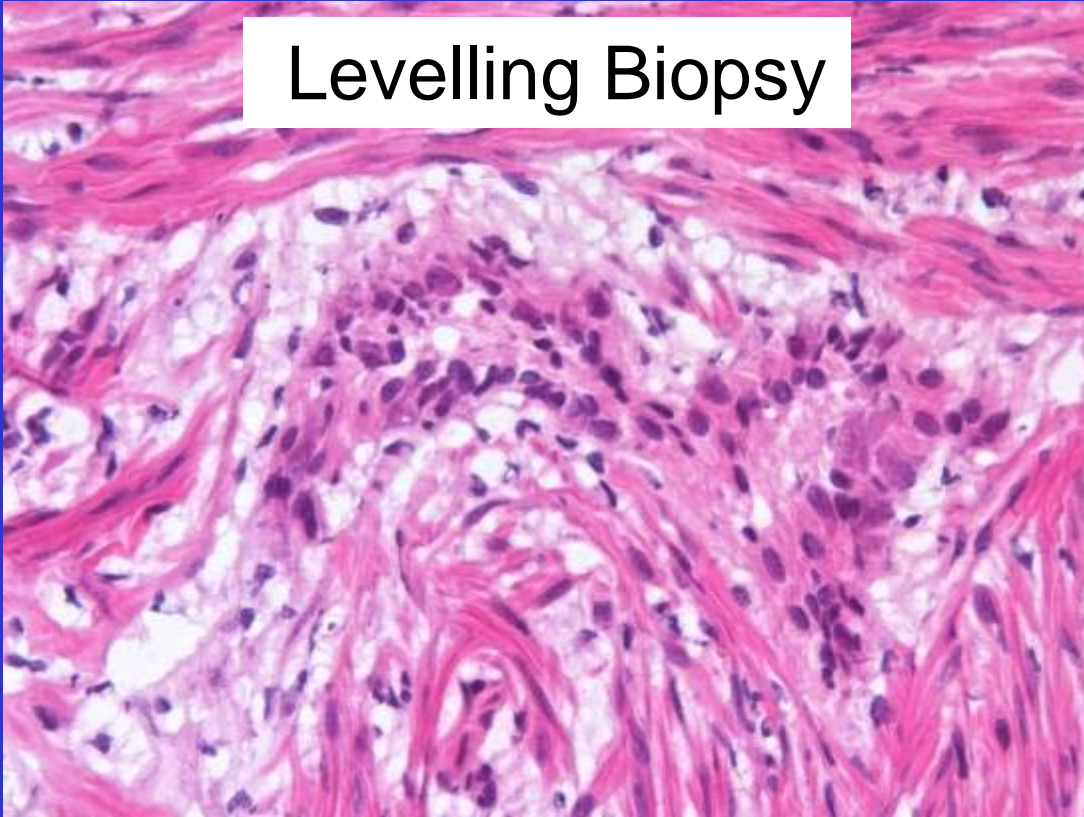
Set a high cytological threshold

Diff-Qwik Stain



What do you advise the surgeon?

Levelling Biopsy



Ganglion cells are present

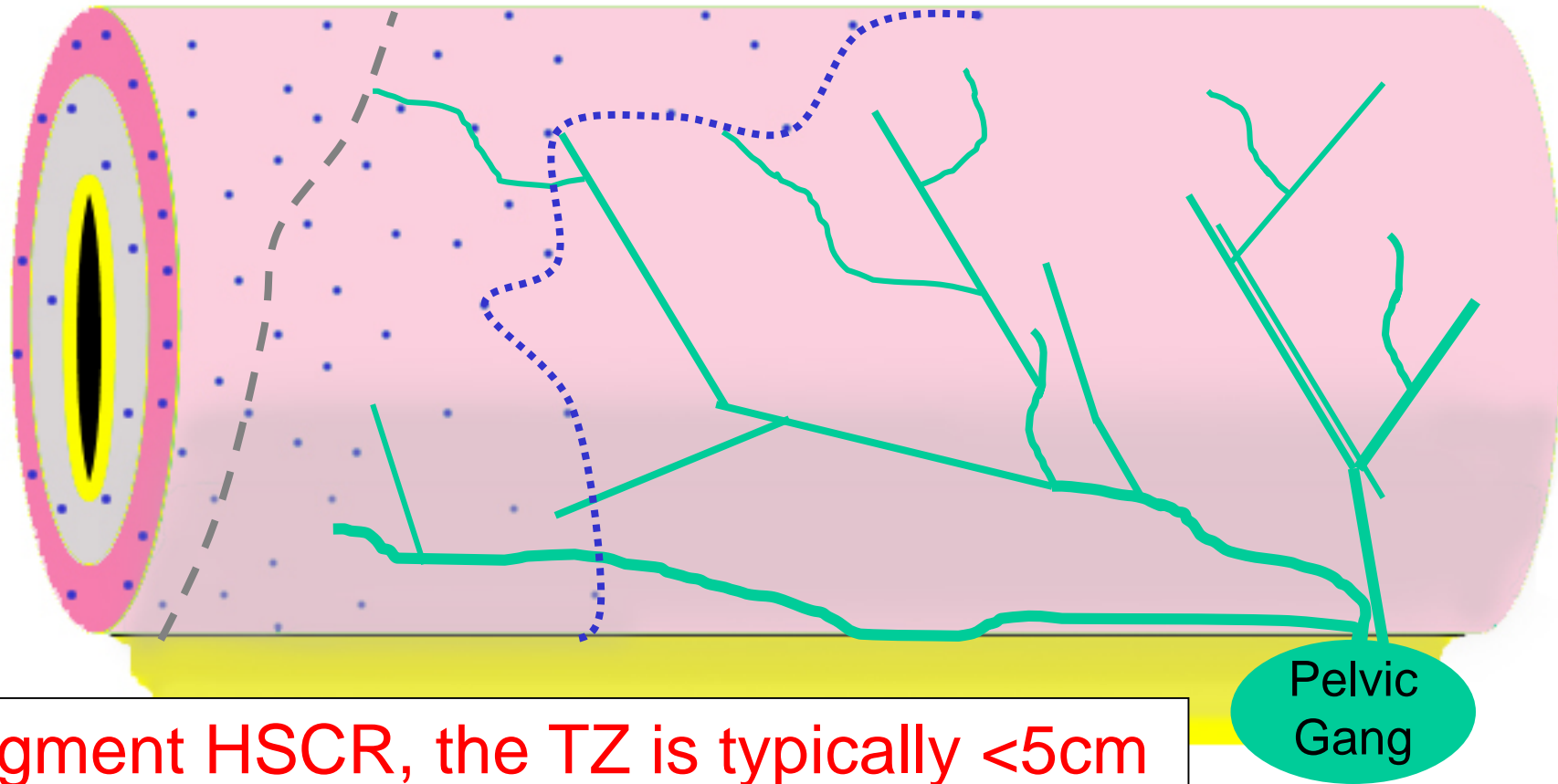
- A. Do an appendectomy to exclude a skip area
- B. Perform ileostomy or resection at this site
- C. Obtain seromuscular biopsy of more proximal bowel to confirm ganglion cells are present
- D. Other

TRANSITION ZONE

Submucosal Nerve Hypertrophy

Myenteric Hypoganglionosis

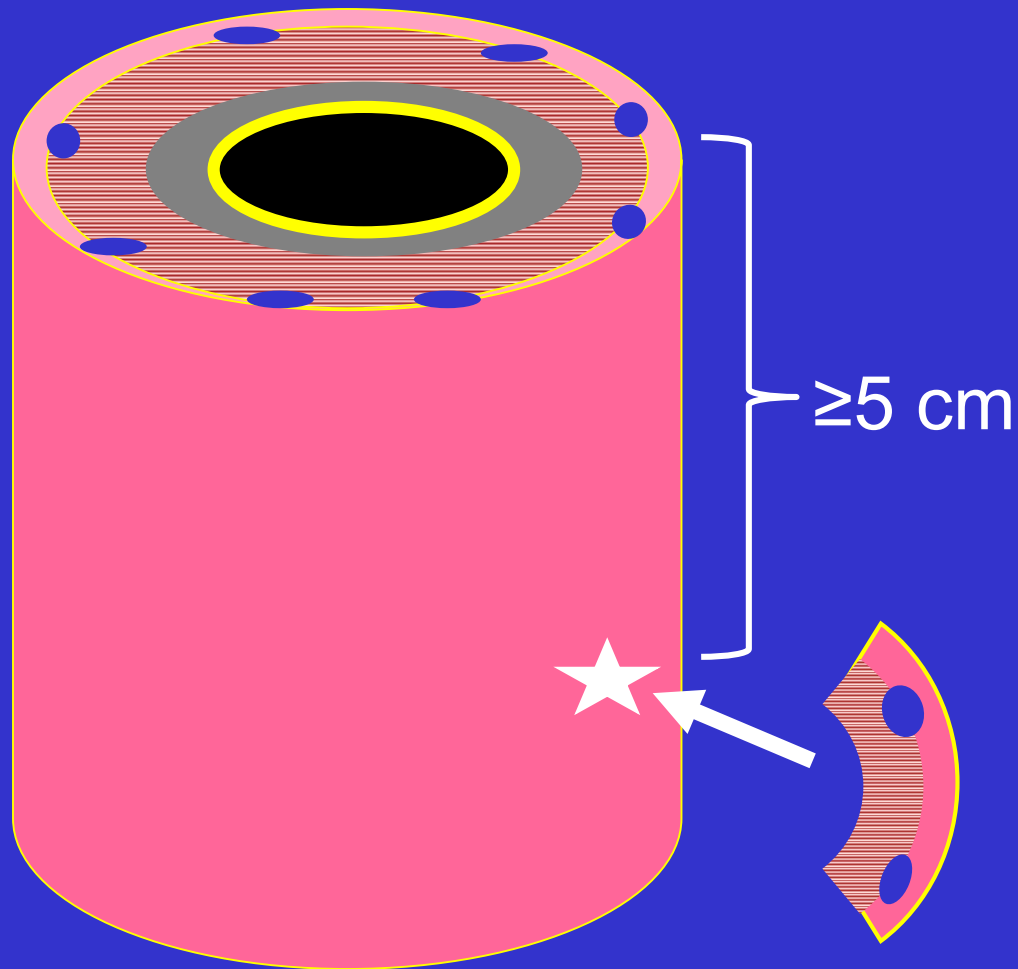
Partial Circumferential Aganglionosis



In short-segment HSCR, the TZ is typically <5cm

INTRAOPERATIVE HISTOPATHOLOGY

Excluding Transition Zone



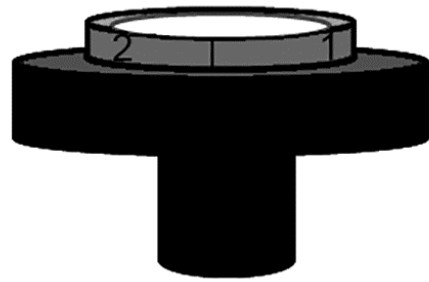
Find ganglion cells and make anastomosis at least 5 cm proximal to that point

Conduct frozen section examination of donut from proximal margin to assess circumferential distribution of ganglion cells and submucosal nerve hypertrophy

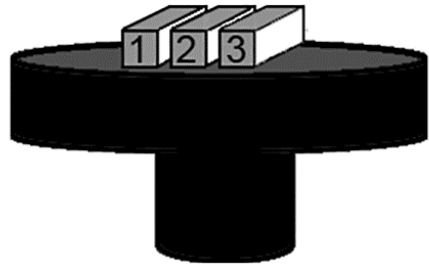
INTRAOPERATIVE HISTOPATHOLOGY

Excluding Transition Zone

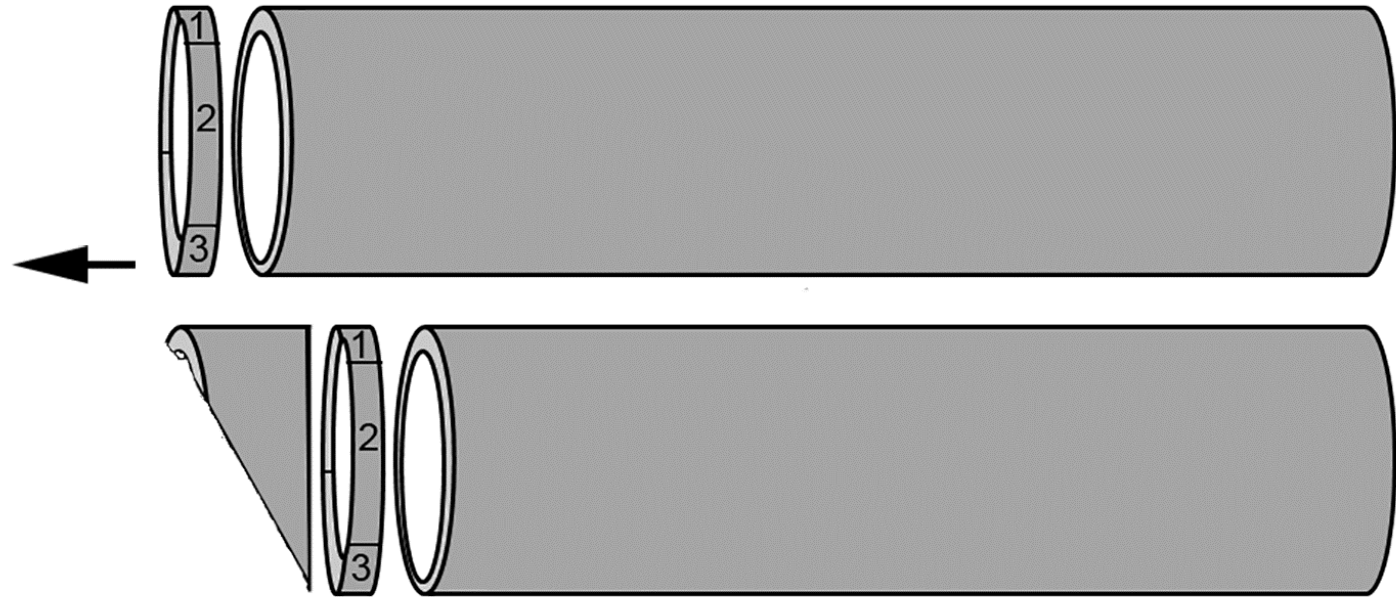
TRANSVERSE
FROZEN SECTION
OF PROXIMAL
MARGIN



or

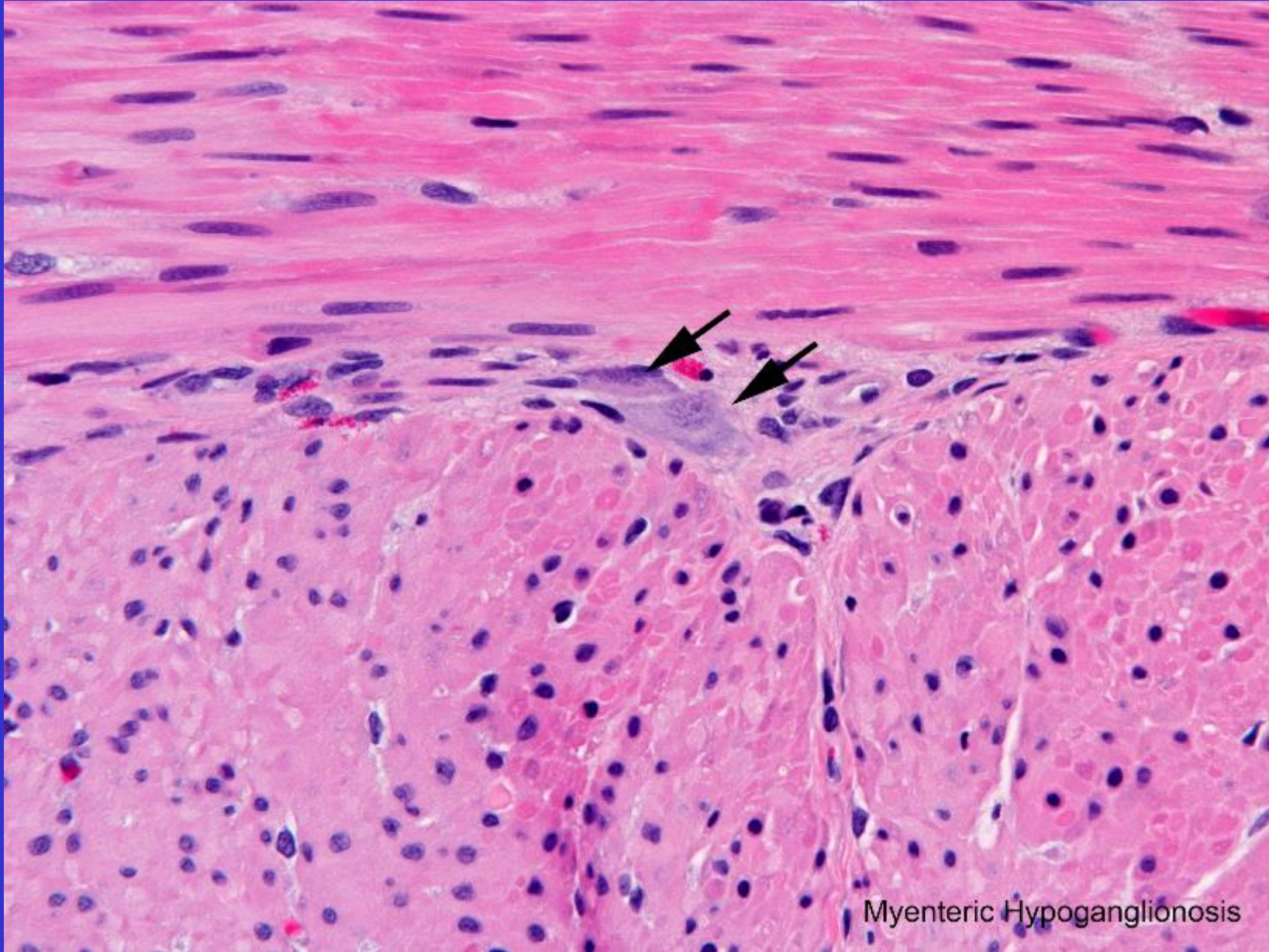


Submit remainder
for FFPE histology

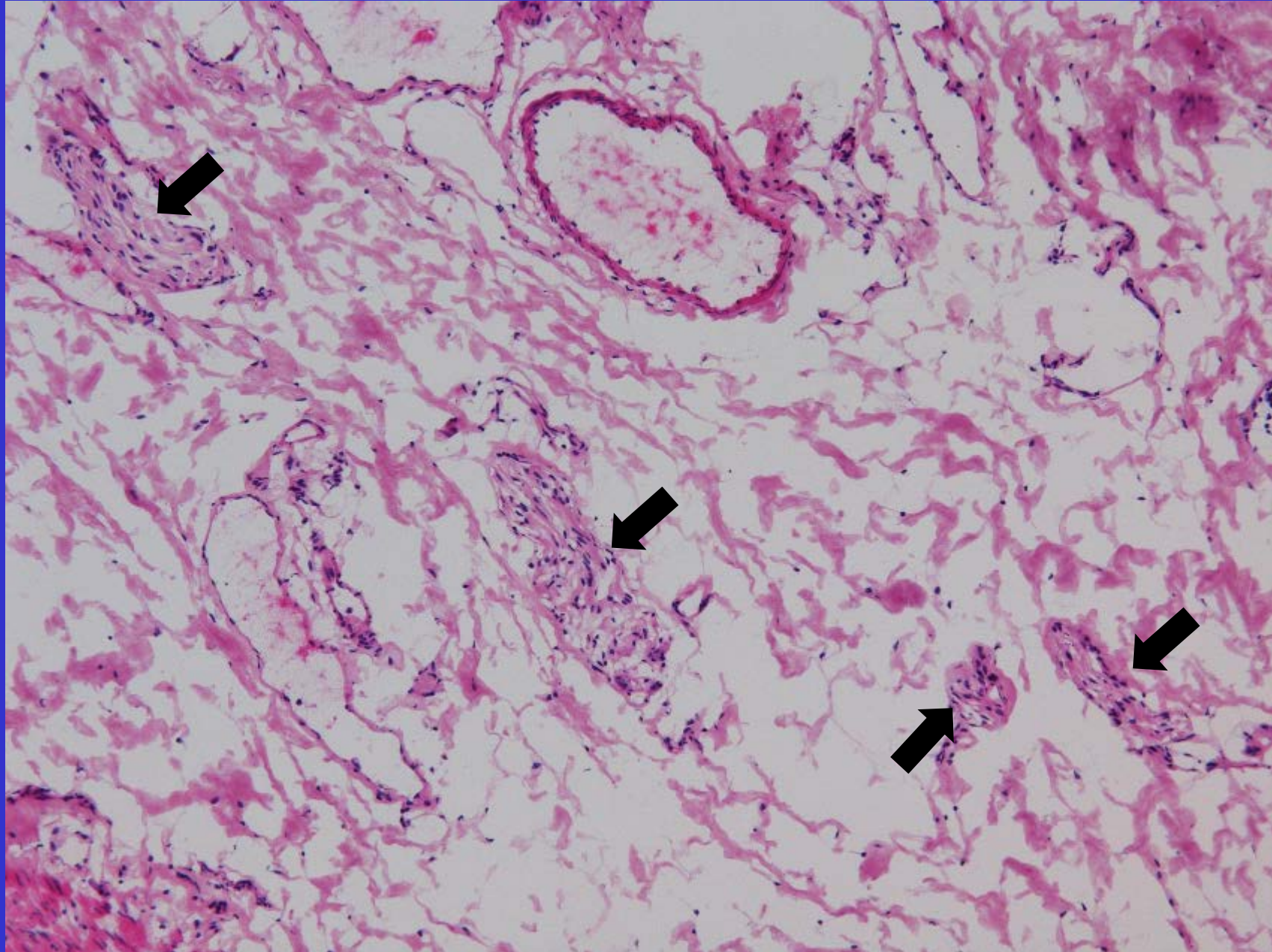


Exclude Features of Transition Zone:
Partial Circumferential Aganglionosis
Myenteric Hypoganglionosis
Submucosal Nerve Hypertrophy

MYENTERIC HYPOGANGLIONOSIS



SUBMUCOSAL NERVE HYPERTROPHY



≥ 2 submucosal nerves per high power field with diameters $\geq 40 \mu\text{m}$



Coe et al. 2012

3-STEP APPROACH

1. Levelling biopsy to find ganglion cells (identify a site oral to the aganglionic segment)
2. Surgeon should perform resection at least 5 cm proximal to levelling biopsy with ganglion cells
3. Frozen section of proximal margin to exclude features of transition zone

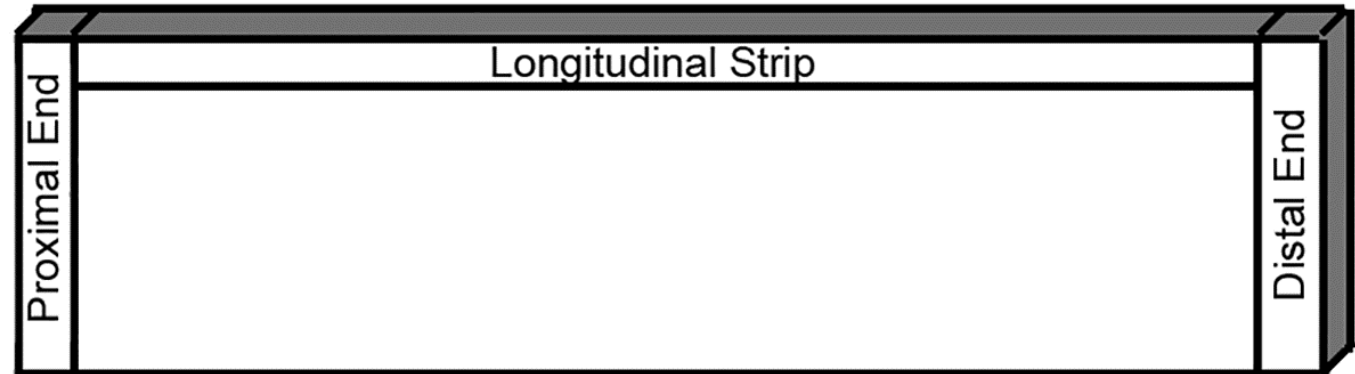
(Repeat 2 and 3 as needed)

HANDLING THE RESECTION SPECIMEN

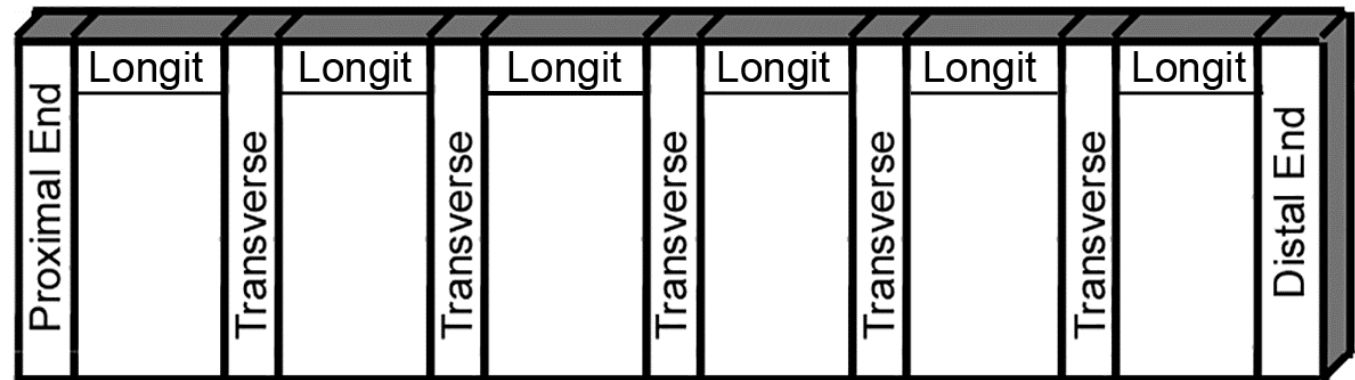
Open lengthwise to evaluate mucosa
Consider overnight fixation of flat specimen
improve orientation of histologic sections

Minimal goals are to

1. Confirm distal aganglionosis
2. Exclude features of transition zone at proximal margin
3. Document the length of the aganglionic segment



or



SYNOPTIC REPORTING

Journal of Pediatric Surgery 54 (2019) 2017–2023



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Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jped surg



Guidelines for synoptic reporting of surgery and pathology in Hirschsprung disease[☆]



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On behalf of the American Pediatric Surgical Association Hirschsprung Disease Interest Group

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YOUR HIRSCHSPRUNG DISEASE DESTINATION

REACH is a non-profit organization committed to improving the lives of children and families affected by Hirschsprung Disease by increasing awareness, promoting education, connecting families and supporting various research around the world.

