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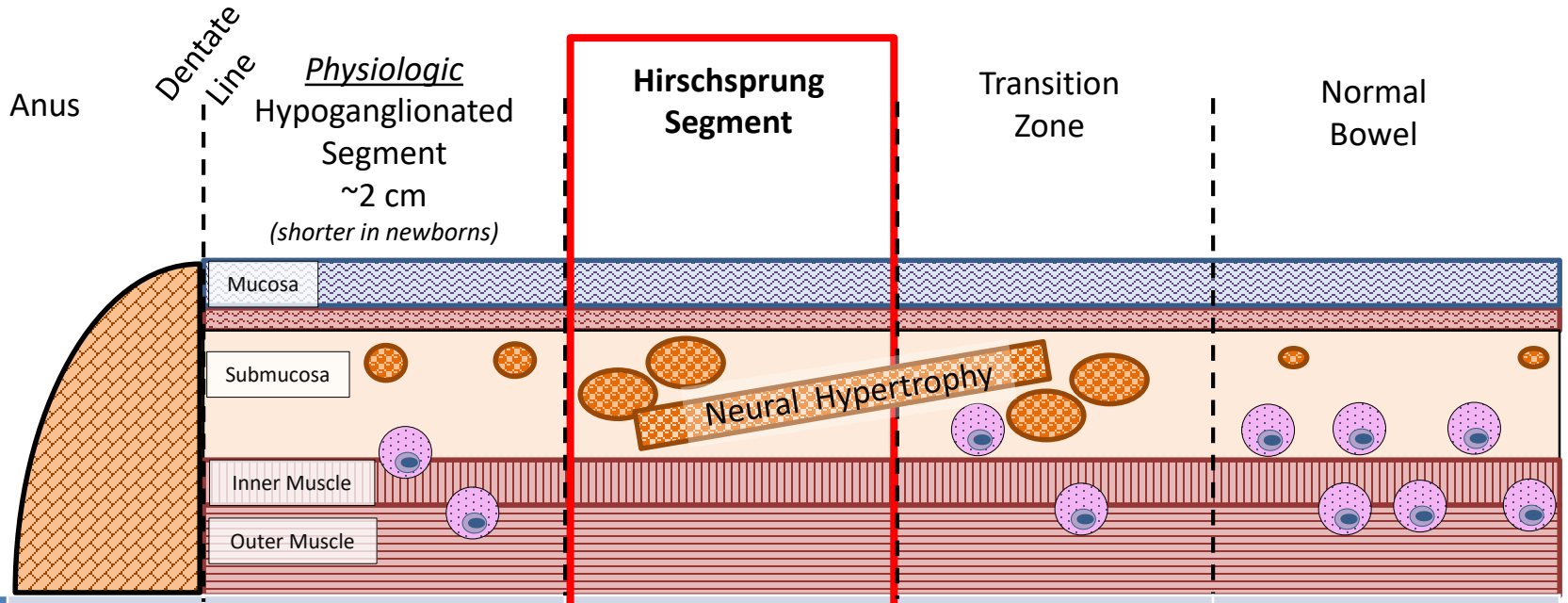
Hirschsprung Disease

- Congenital absence of ganglion cells in **both** nerve plexuses (Submucosal and Myenteric)
  → leads to poor peristalsis and obstruction → Proximal dilation with narrowed, spastic distal aganglionic segment
  → Failure to pass meconium, abdominal distention, constipation → can get enterocolitis
- Always impacts **distal**-most part of GI tract (farther for neural crest cells to travel to make ganglion cells)

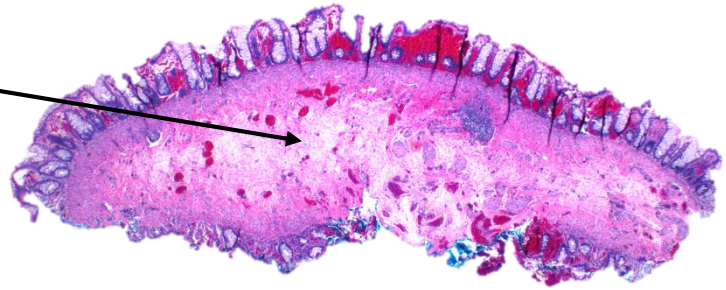


Ganglion Cells		Absent to Few	Absent	Present, but fewer	Present
Neural hypertrophy		Absent, but nerves may be more prominent	Present	Present	Absent
Nerve Twigs		Present	Absent	Present	Present
Mucosa	**Squamous**	Colorectal	Colorectal	Colorectal	Colorectal

Inadequate to confirm absence of ganglion cells as physiologically hypoganglionated

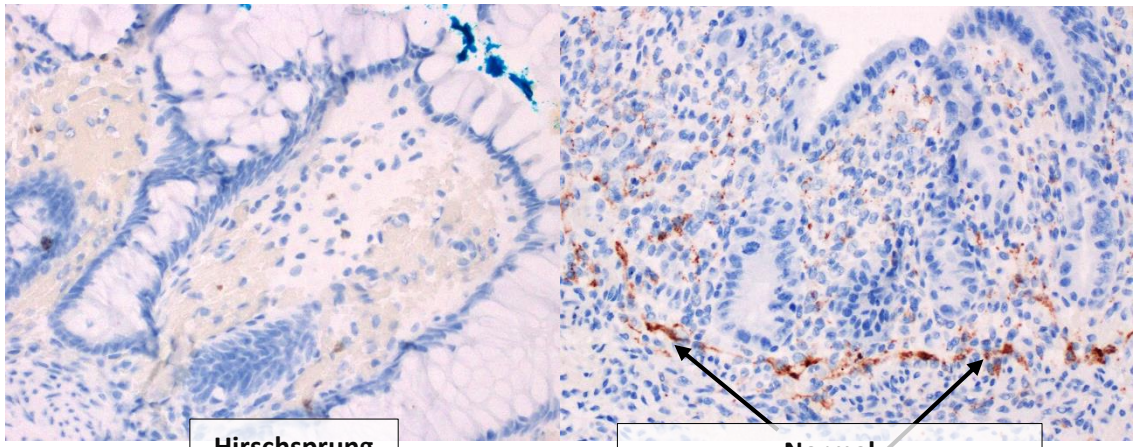
Suction Biopsy Protocol:

- Preoperative rectal suction biopsies are done to establish a diagnosis.
- Biopsies should be >3mm in diameter and at least 1/3 of the thickness should be submucosa.
- Should be >2 cm above dentate line to avoid physiologic area of fewer ganglion cells.
- Multiple serial sections are examined initially
  → If no ganglion cells, order additional sections (75 levels) and Calretinin IHC



Ancillary studies:

Calretinin:
Shows granular staining of small, intrinsic nerve twigs in mucosa and muscularis mucosae normally, which are absent in Hirschsprung. Also highlights ganglion cells and nerve bundles.



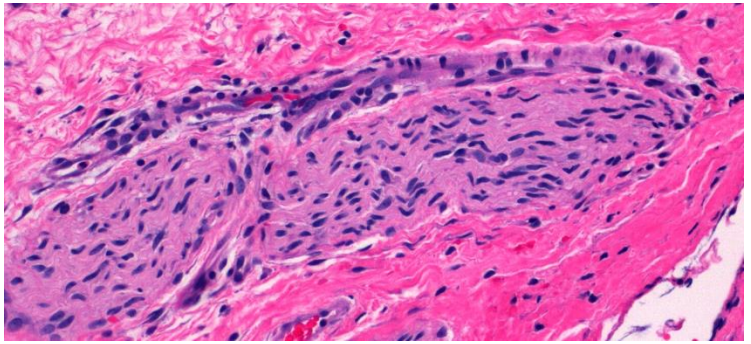
Hirschsprung (No Staining)

Normal (Excludes Hirschsprung Segment in that area—could still be transition zone)

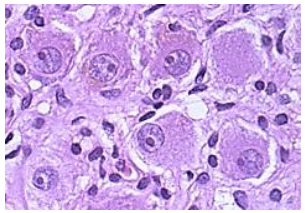
Neuronal markers:
(e.g., NSE, NeuN, and MAP-2) can be helpful in confirming the presence of ganglion cells

Definition of Neural Hypertrophy:

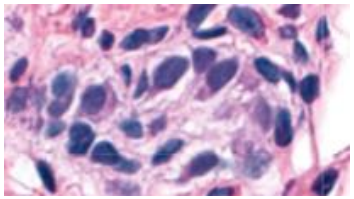
Submucosal nerves >40µm



Ganglion Cells



Mature/Adult



Immature/Infant

Often have less Nissl substance and higher N/C ratios