



The Pathology Says What? GISTs, Carcinoids and Anorectal Squamous Malignancies

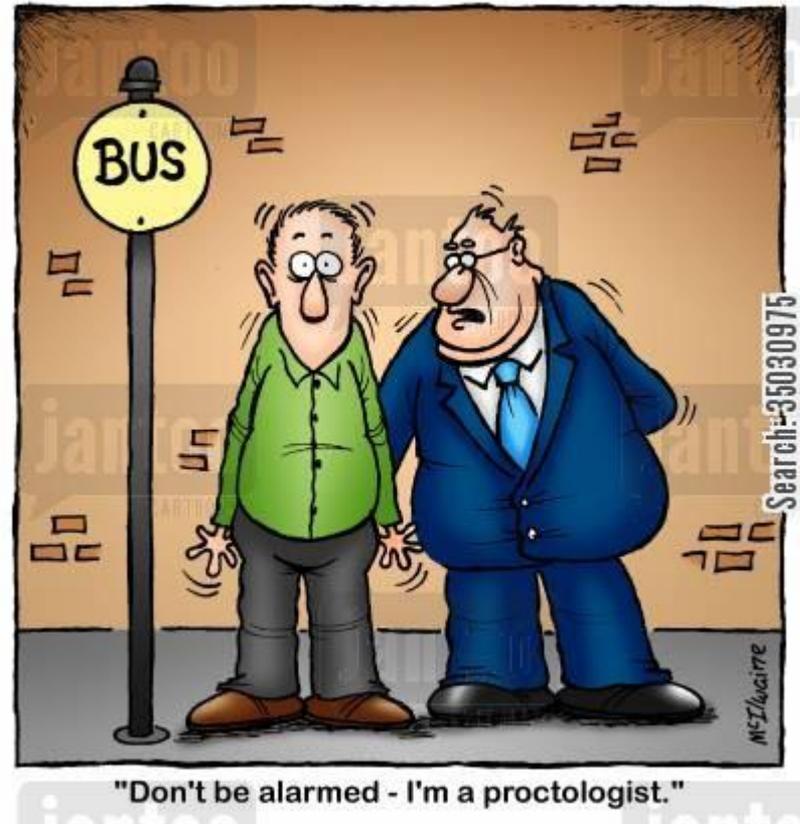
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Clinical Associate Professor



Conflict of Interests

- None Relevant
- Honoraria Received
 - 3M
 - Sanofi
 - Servier Pharmaceuticals
 - Medtronic
 - Takeda



Carcinoids, GISTs and Anal Canal Lesions

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- Carcinoids
 - Rectal Carcinoids
- Gastrointestinal Stromal Tumours (GISTs)
- Anorectal Squamous Cell Malignancies
 - HPV Associated lesions



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**“Don’t think of me as a Proctologist.
Think of me as Colon Tech Support.”**

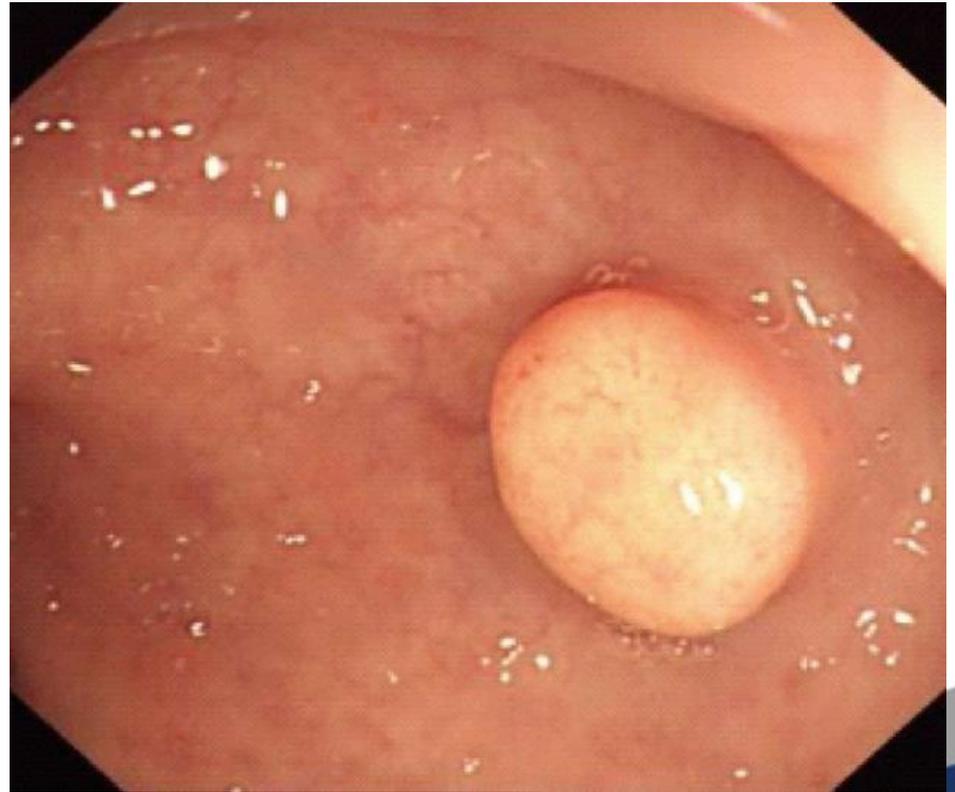


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Carcinoids

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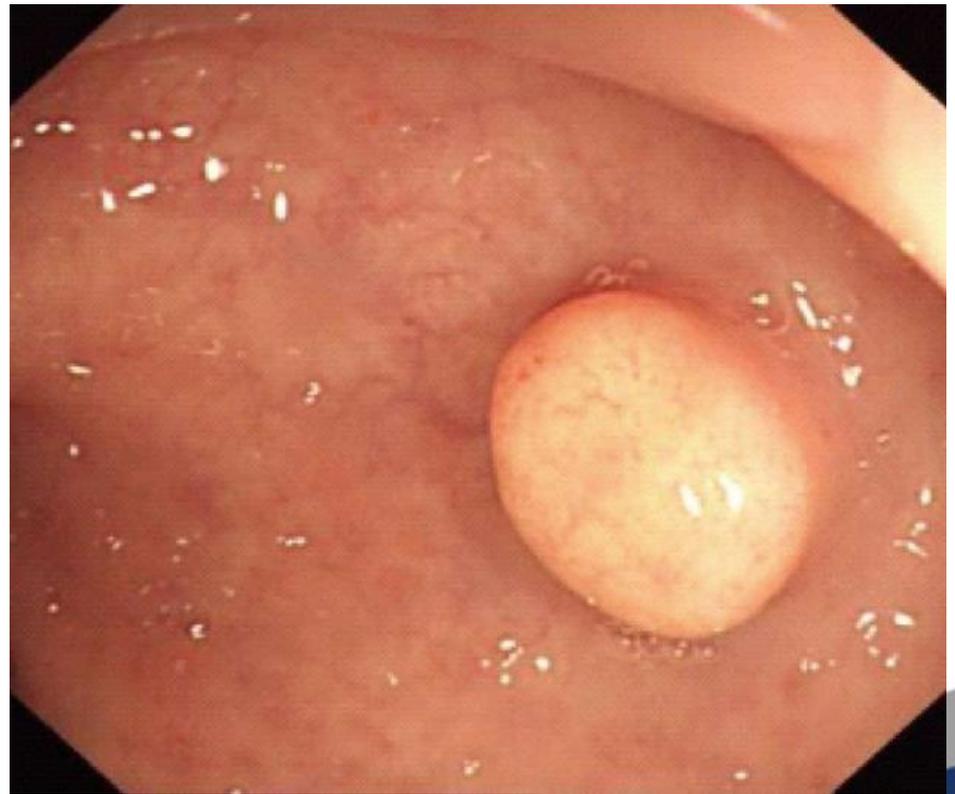
- 67 year old male
- FIT positive
– 110
- Normal colonoscopy, until just before withdrawal



Carcinoids

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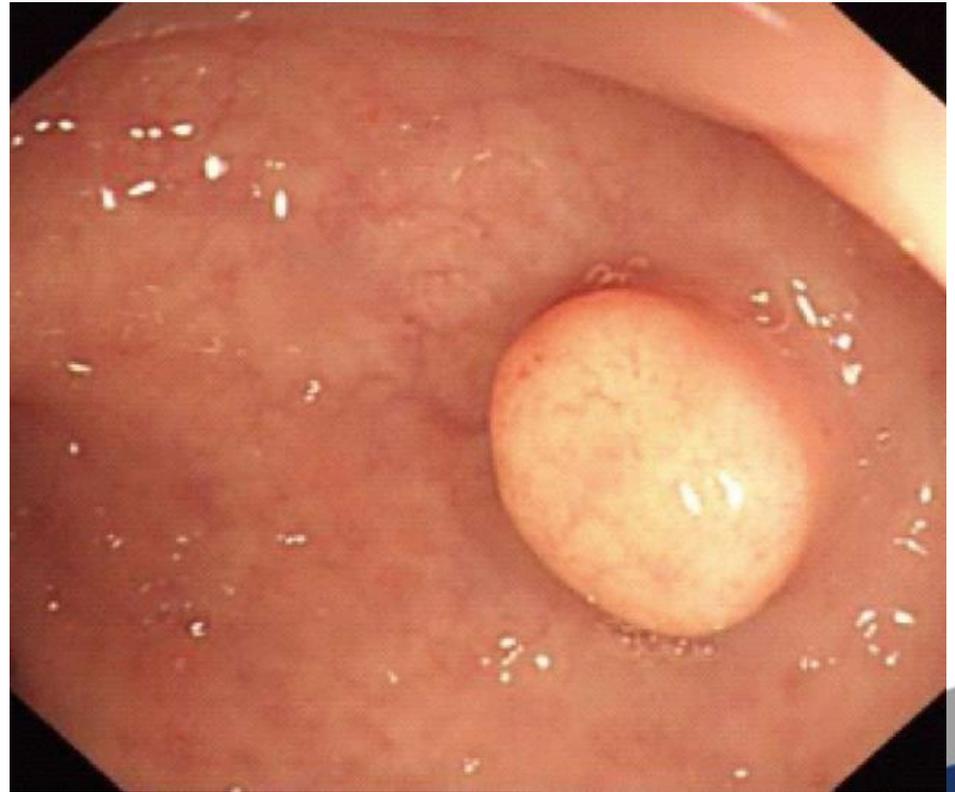
- Hard, nodular
- Normal appearing mucosa



Carcinoids

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- Biopsy
 - 0.8 cm well differentiated carcinoid tumour



Carcinoids

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- Otto Lubarsch
 - First described in 1888
- Siegfried Oberndorfer
 - 1907: “*Karzinoid*”



Carcinoids

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- slow growing tumours of neuroectodermal origin
- Belong to the APUD system
- Originate from Kulchitsky cells in the crypts of Lieberkuhn



Carcinoids

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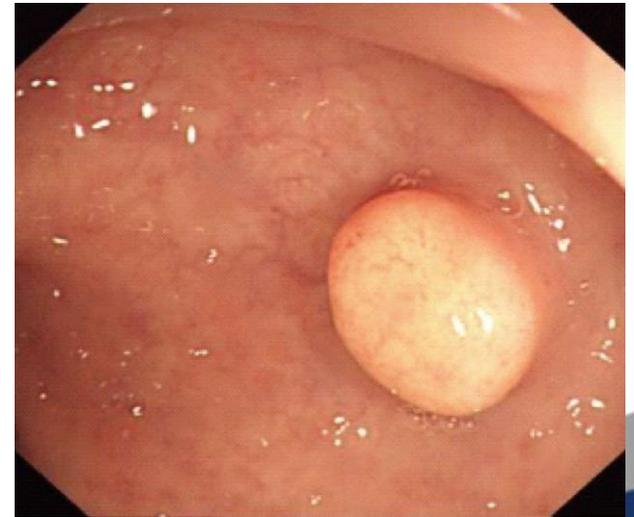
- Produce very different (> 30) amines and peptides
 - Serotonin
 - Chromogranin
 - Synaptophysin
 - Enolase
 - Other prostaglandins



Carcinoids

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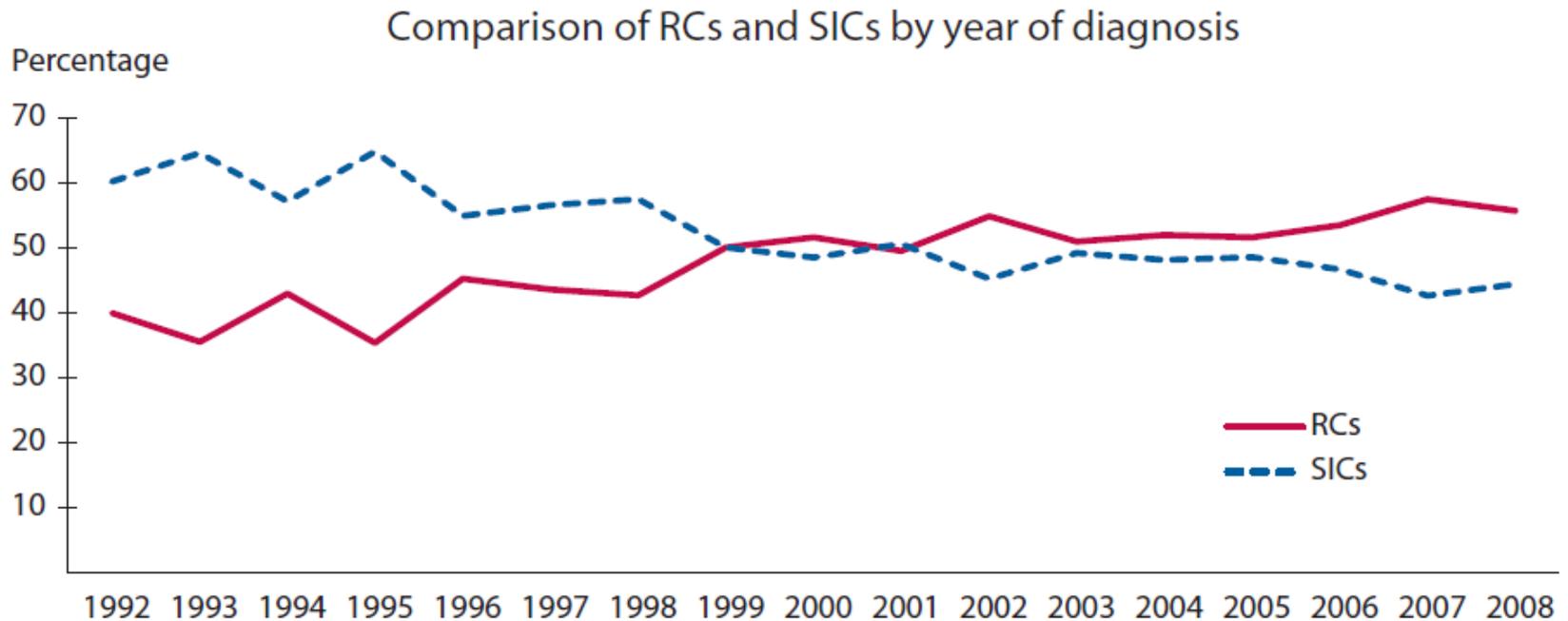
- 15% of all carcinoids occur in the rectum
 - Appendix, small bowel and bronchus



Carcinoids

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- Taghavi et al (DCR, 2013)
 - Rectal carcinoids are now more common than small bowel carcinoid



Carcinoids

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- Tichansky et al (DCR, 2002)
 - 13% risk of synchronous lesions
 - Colorectal Cancer most common
 - Small Bowel
 - Lung



Carcinoids

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- Majority of rectal carcinoids are picked up incidentally
- Symptoms are rare
 - Rectal bleeding
 - Minor change in bowel habits



Carcinoids

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- Carcinoid syndrome
 - RARE!
 - Flushing, diarrhea, abdominal pain
 - Only after metastatic disease to the liver, and in the setting of small bowel or lung carcinoids



Carcinoids

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- So, pathology is back? Now what?
- Complete Colonoscopy
- CT Chest, Abdomen, Pelvis
- Only in symptomatic patient or patient with high risk pathological features
 - Biochemical Tests
 - 14 h urine 5 HIAA
 - Somatostatin based CT PET



Carcinoids

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- What are high risk pathological features?
 - Size > 2 cm
 - Invasion of the muscularis propria
 - Lymphovascular invasion
 - Perineural invasion



Carcinoids

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< 1 cm

- Local excision

1-2 cm

- Low risk pathology features
- High risk pathology features

> 2 cm

- Radical resection

Gastrointestinal Stromal Tumours

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- 76 year old male
- FIT positive
 - 85
- Otherwise normal colonoscopy
- 1 cm lesion in low rectum



Gastrointestinal Stromal Tumours

- Most common mesenchymal neoplasm of the GI tract
- First described in 1983
- Arise from interstitial cells of Cajal or other mesenchymal stem cells

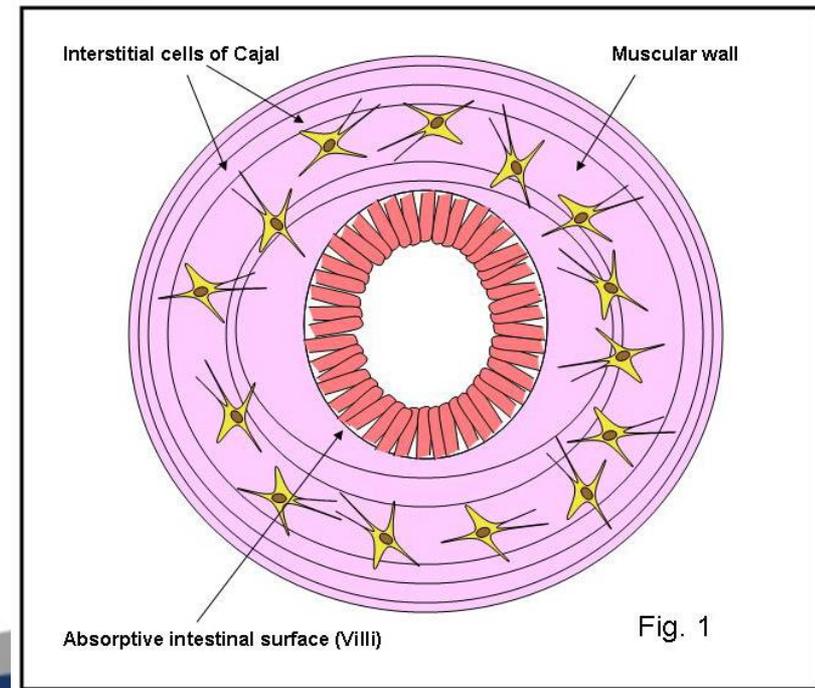
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The American Journal of Surgical Pathology
Volume 7 Number 6
September 1983

Michael T. Mazur, M.D.

H. Brent Clark, M.D., Ph.D.

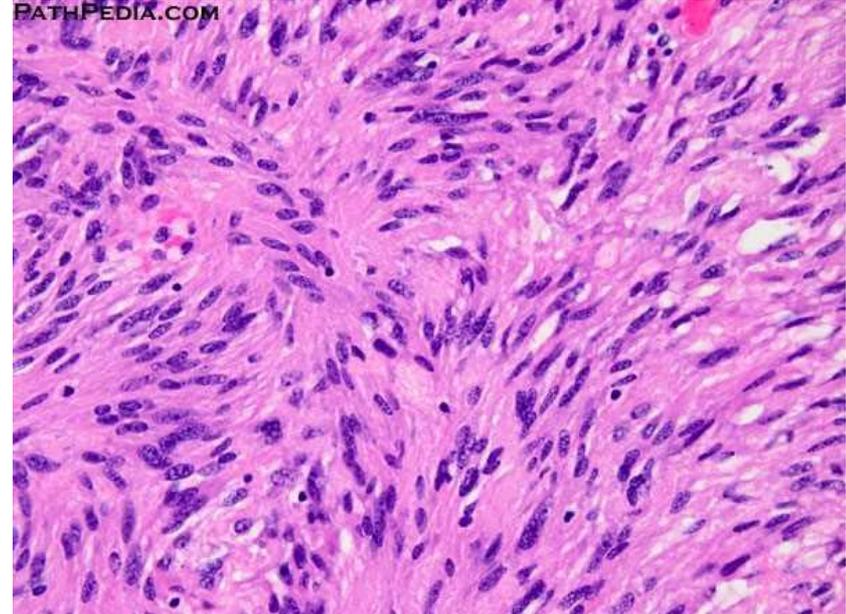
Gastric stromal tumors Reappraisal of histogenesis



Gastrointestinal Stromal Tumours

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- Spindle cells
- CKIT positive
- Prognostic Features
 - Size
 - Mitotic Rate



Gastrointestinal Stromal Tumours

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- Rectal GISTs are rare
- 10% of all GISTs
- Slow growing lesions
- Metastatic location
 - Liver, peritoneum



Gastrointestinal Stromal Tumours

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- Workup
 - Colonoscopy
 - ERUS
 - CT Abdomen/Pelvis
 - MRI Pelvis



Gastrointestinal Stromal Tumours

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- Resection is necessary for all GIST
- En bloc resection with 1 cm margin
 - Negative margin is key
- No large series are available
- Liu et al (JSO, 2014)
 - Positive resection margin was worse prognostic indicator for recurrence



Gastrointestinal Stromal Tumours

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Rectal GIST

Will it require an APR?

No

YES!

Local Excision

Low Anterior
Resection

Imatinib, then
reassess



Anorectal Squamous Cell Cancer

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- Uncommon malignancy (<2% of GI cancer)
- Almost always associated with HPV
- Risk factors
 - Prior Sexually Transmitted Disease
 - Anal Receptivity
 - Presence of anogenital warts
 - Presence of prior Anal intraepithelial neoplasia
 - Immunosuppression (Transplant/Steroids)
 - HIV positivity, with low CD4 count
 - Smoking



Anorectal Squamous Cell Cancer

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- Median Age is 60-65 years
 - Slightly more common in women
- > 1/3 of patients are asymptomatic
- 45% of patients may have painless rectal bleeding



Anorectal Squamous Cell Cancer

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- Ulcer or fissure with indurated margins
- Exophytic mass seen on anal spread
- MAY NEED EUA TO EXAMINE
- Sedated colonoscopy may be the only opportunity to assess



Anorectal Squamous Cell Cancer

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- Usual spread is to groin lymph nodes
 - Should be assessed on clinical exam
- CT Chest/Abd/Pelvis
- CT PET
 - Anal Canal Squamous Cell Cancer is very FDG avid



Anorectal Squamous Cell Cancer

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TABLE 12: TNM classification of anal canal tumors

Primary tumor (T)

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor \leq 2 cm in greatest dimension
T2	Tumor $>$ 2 cm but not $>$ 5 cm in greatest dimension
T3	Tumor $>$ 5 cm in greatest dimension
T4	Tumor of any size that invades adjacent organs (eg, vagina, bladder, urethra, bladder) ^a

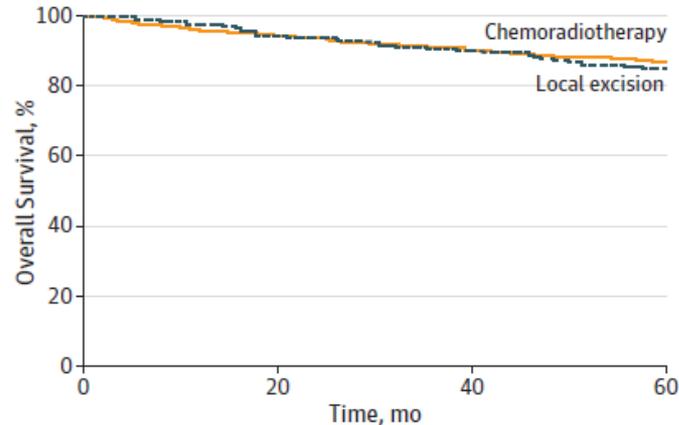


Anorectal Squamous Cell Cancer

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- < 2 cm in size
 - Can you excise it with clear margins?

Figure 3. Difference in Overall Survival by Treatment



No. at risk					
Chemoradiotherapy	1724	1513	1161	784	
Local excision	500	419	290	161	

$P = .93$ (log-rank test).

Chai et al. JAMA Surg. 2017



Anorectal Squamous Cell Cancer

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- All other tumours
 - Refer to BCCA for chemoRT
 - 45 Gray radiation over 5 weeks
 - Mitomycin, 5 FU



Anorectal Squamous Cell Cancer

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- Ben-Josef et al (JCO, 2010)
 - 20% local failure rate at 5 years, stabilizes out at 1 year
- Ongoing surveillance is important
- If residual disease at 6 months
 - APR becomes necessary
 - ~ 50% 5 year survival (Ghouti et al, DCR, 2005)



Anal Intraepithelial Neoplasia (AIN)

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- Dysplastic condition of the anal canal
- Premalignant stage of anal cancer
- Secondary to HPV infection
 - HIV status
 - Anal receptivity



Anal Intraepithelial Neoplasia (AIN)

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- Dysplastic condition of the anal canal

- Pre

- Seco

- H

- A

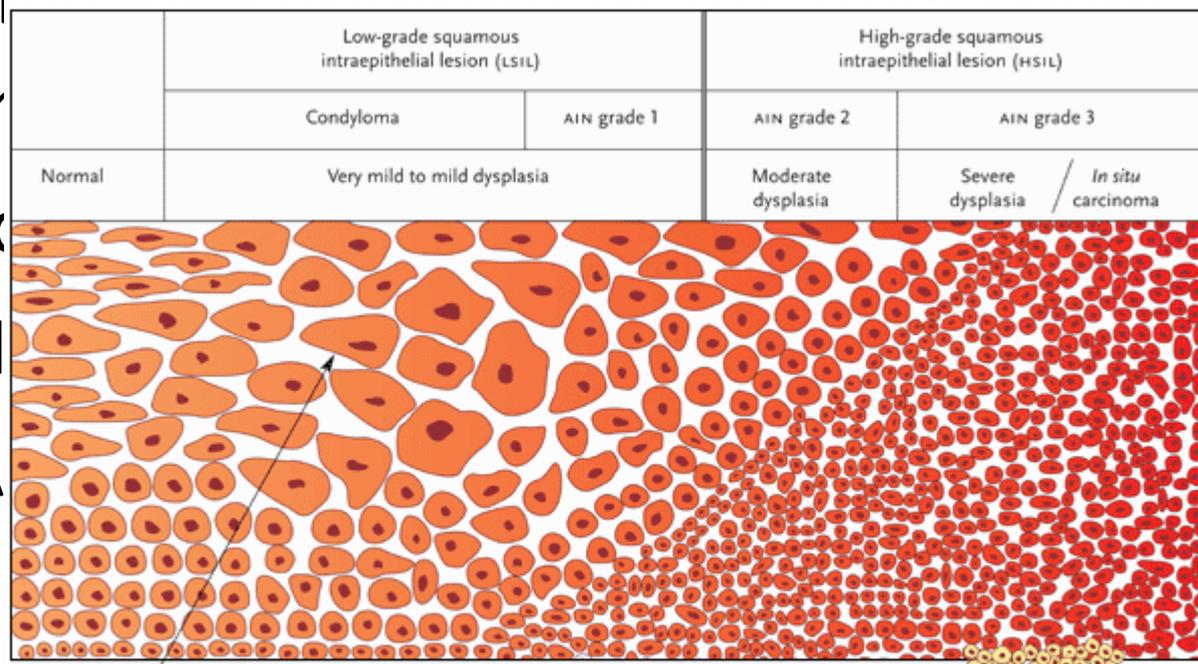


FIGURE 1. Schematic Representation of SIL
 As shown in this illustration, with increasing severity of SIL of the anus, the proportion of the epithelium replaced by immature cells with large nuclear-cytoplasmic ratios increases. Invasive cancer probably arises from one or more foci of high-grade SIL (HSIL), as depicted in the drawing by epithelial cells crossing the basement membrane below the region of HSIL.



Anal Intraepithelial Neoplasia (AIN)

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- Scholefield et al (BJS, 2005) & Watson et al (ANZ J Surg, 2006)
 - 50% of immunosuppressed patients progressed to cancer
 - 11% of all patients can progress to cancer without surveillance



Anal Intraepithelial Neoplasia (AIN)

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- So you saw a lesion on endoscopy, biopsy came back as AIN?
- Now what?
- Refer to Anal Dysplasia Clinic or your favourite General/Colorectal Surgeon



Anal Intraepithelial Neoplasia (AIN)

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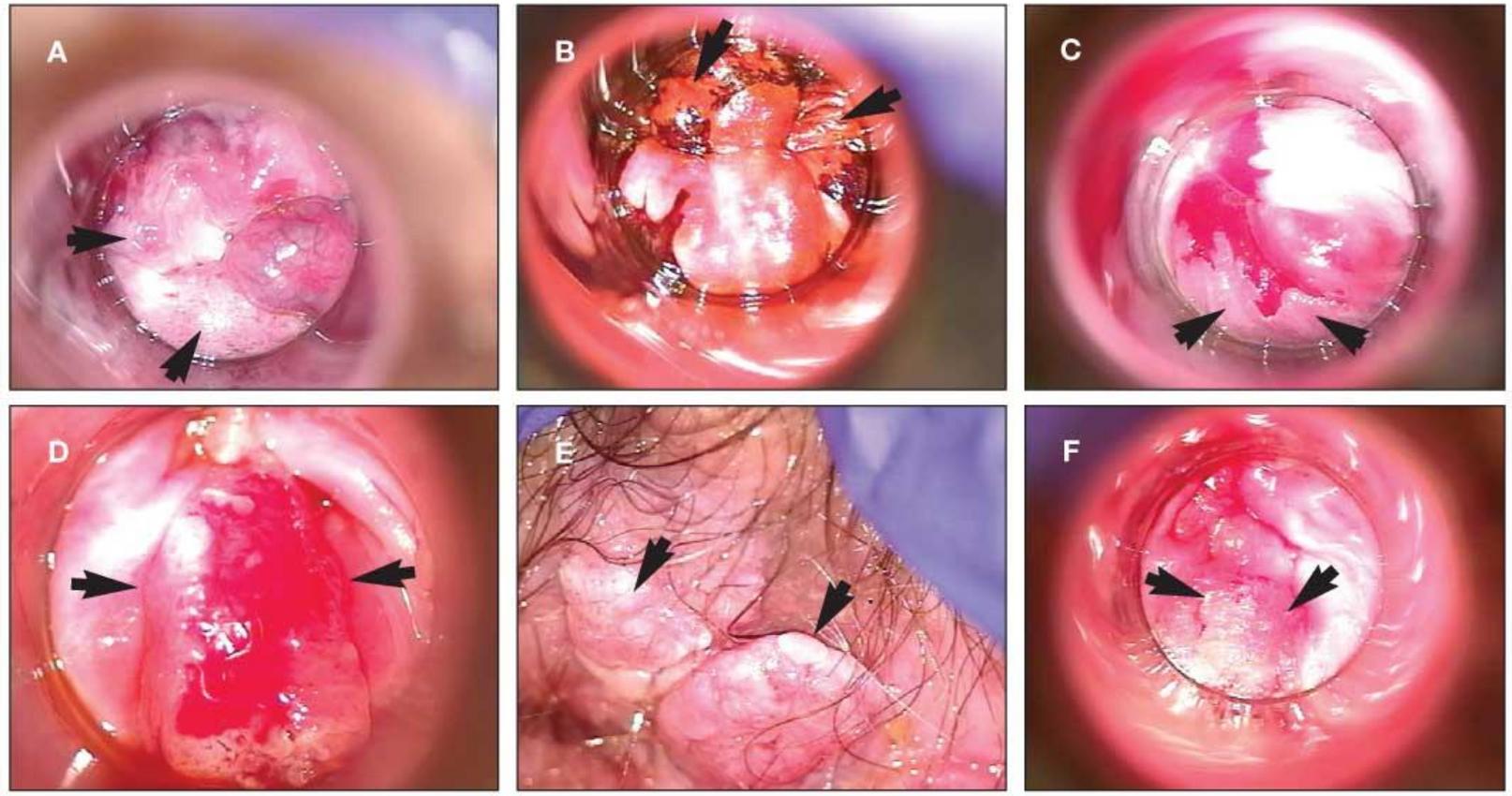
- Anal Dysplasia Clinic
 - Based out of St Pauls
 - Run by family physicians with extra training
 - Perform high resolution anoscopy
 - “Anal Pap Smear”



Anal Intraepithelial Neoplasia (AIN)

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Anal Dysplasia: Clinic



Anal Intraepithelial Neoplasia (AIN)

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- What should the surgeon do?
- Is there a mass or a lump?
- YES!
 - Then excise the lump
 - Ablate all abnormal tissue with cautery



Anal Intraepithelial Neoplasia (AIN)

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- What should the surgeon do?
- Is there a mass or a lump?
- NO!
 - Observe
 - Imiquimod (Aldara)
 - Expensive, burns
 - Topical 5U (free if prescribed by BCCA)
 - Burns



Conclusion

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- These diagnoses are rare, but can occur in a large screening program
- Carcinoids
 - Need complete endoscopic assessment
 - If small and good prognostic features, may only need local excision
 - Ask your pathologist for more information if needed



Conclusion

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- GISTs
 - Important to remove completely
 - Stage with ERUS and MRI
 - If major surgical procedure or unclear resectability, refer to Cancer Agency or local Colorectal Surgeon
 - Imatinib has changed the landscape completely



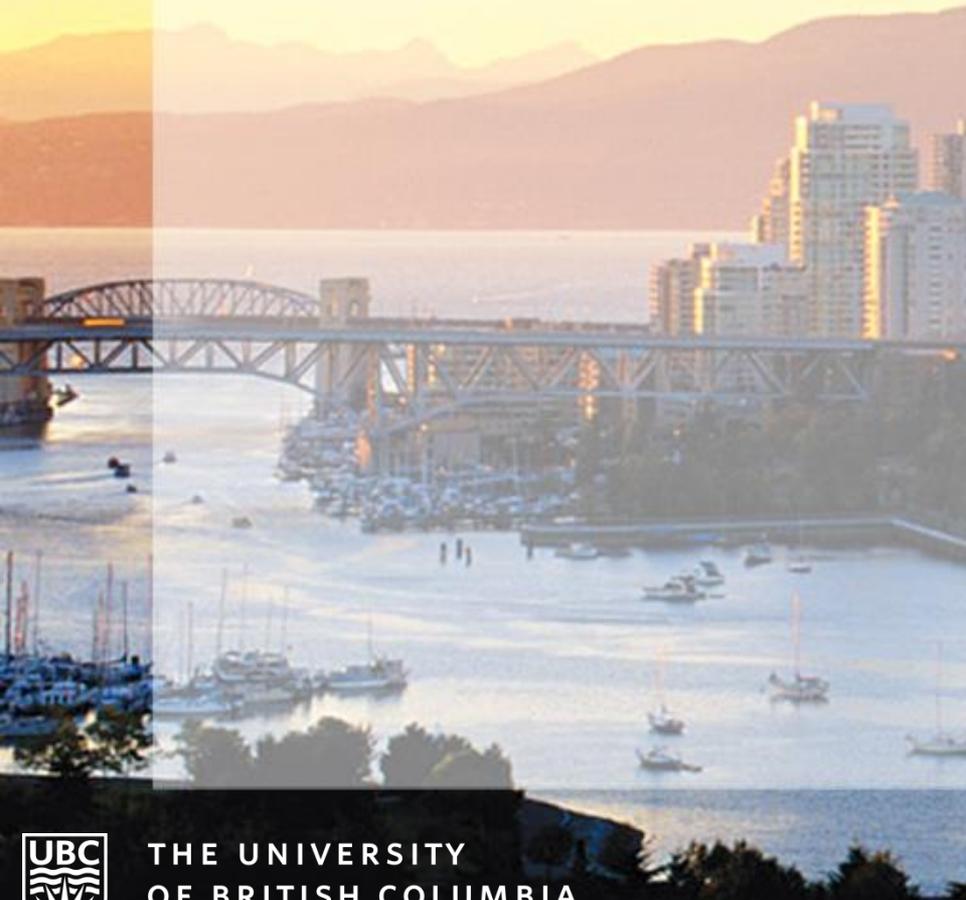
Conclusion

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- Squamous Cell Cancer
 - If small, local excision can be sufficient
 - If larger
 - CT + CT PET
 - Chemo RT based treatment
 - Watch closely for first year after treatment



Acknowledgements



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