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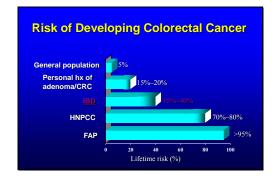
Goals

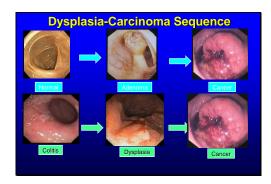
- Increased risk of colon cancer in IBD
- Importance of surveillance/technique
- Consider Chromoendoscopy
- Suggested Guidelines (evolving)
- Confirmed dysplasia = colectomy
 - -HGD/DALM
 - -LGD* controversial

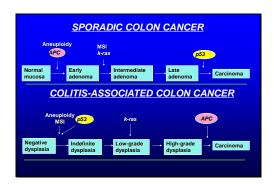
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The Enemy: Colorectal Cancer The risk of colorectal cancer in IBD is nearly 20 times higher than the general population

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Cancer and IBD

- Increased risk of colorectal cancer in UC^{1,2}

 0.5-1.0% per year after first decade of disease
- Risk is equivalent for UC and CD
 - Duration
 - Extent
- Cancers occur earlier in these patients
- Dysplasia in flat mucosa
- Risk not increased in patients with proctitis

¹Ransohoff. Gastroenterology 1988;94:1089 ²Eaden et al. Am J Gastro 2000;95:2710

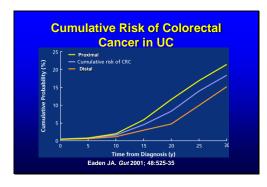
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Is the Risk This High?

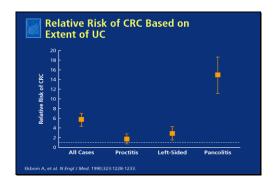
- 600 patients with extensive UC followed for 5932 person-years at St. Marks in London
- 30 CRCs detected (annual risk: 0.5% or 1/200)
- Cumulative probability of CRC was 2.5% at 20 years, 7.6% at 30 years and 10.8% at 40 years
- Linear regression suggested that CRC risk declined over the course of the study

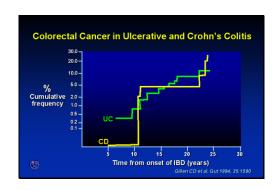
Retter MD, Standers BP, Williamon KH, Rumbles S, Schofield G, Katten MA, Williams CB, Price AB, Talbot IC, Fothes A. Thirty-year analysis of a colonoscopic surveillance program for neoplasis in alcerative colinic.

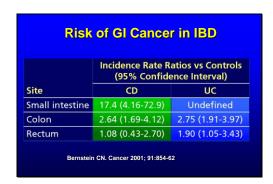
Gattmenterology 2006;18:1080-8.



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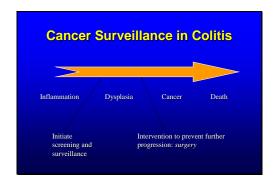


Cancer Risk Factors in IBD

- Extensive disease
 Higher risk: pancolitis
 Lower risk: proctosigm
- Disease duration
- Family history of colorectal cancer
- Primary sclerosing cholangitis
- Histologic Disease activity
- (severity of inflammation) Probable risk factors
 - Folate deficiency
- Poor compliance with medical therapy

Lewis et al. Gastroenterol Clin N Am 1999;28:459 Askling J, et al. Gastroenterology. 2001. Rutter, et al. Gastroenterology, 2004

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Dysplasia in IBD

- Unequivocal neoplastic epithelium confined to the gland in which it arose
- Marker of malignancy risk
- Present in 75-80% (close and distant) of patients with carcinomas
- Any portion of colon (parallels cancer)
- single, multifocal, diffuse
- Flat or elevated (DALM)

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Dysplasia Classification

- Negative for dysplasia
- Indefinite for dysplasia (probably negative, unknown and probably positive)
- Positive for low-grade dysplasia, high-grade dysplasia or invasive cancer
- Pathologists should no longer be grading dysplasia as mild, moderate or severe

Riddell RH, Goldman H, Ransohoff DF et al. Dysplasia in inflammatory bowel disease: standardized classification with provisional clinical applications. Hum Pathol. 1983;14:931-68.

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Limitations of Using Dysplasia as Endpoint

- Interobserver variation
 - Several studies demonstrated only moderate levels of agreement Agreement better for HGD/Negative than LGD/Indefinite

 - Confirm diagnosis by expert GI pathologist
- Scope when IBD quiescent
- Need for patient compliance with colonoscopy
- Dysplasia may be absent in 25-30% of colectomy specimens in patients with cancer

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Interobserver Variation in Diagnosis of Dysplasia

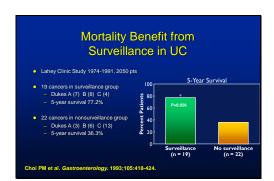
Degree of Dysplasia	% Agreement
High Grade	77
Low Grade	63
Indefinite	49
Negative	74

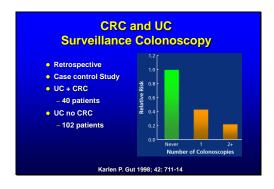
Ridell RH, et al. Dysplasia in inflammatory bowel disease: standardized ci provisional clinical applications. Human Pathology 1983;14:931-68.

Colonoscopic Surveillance for UC

- Can detect UC cancers at a curable stage for many patients¹
- Cancer mortality is reduced with surveillance²
 77% vs 37% 5 year survival
- At initial screening, 3% will have cancer and 11% will have dysplasia
- 1. Connell. Gastroenterology. 1994;107:934. 2. Choi PM et al. Gastroenterology. 1993;105:418.

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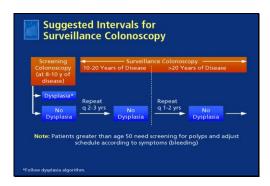


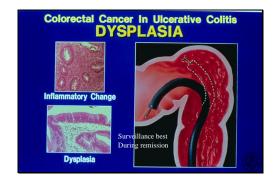
Surveillance in chronic UC My Guidelines • Colonoscopic surveillance

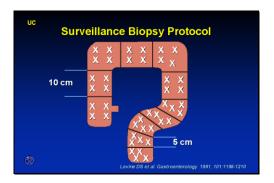
- - after 8-10 years of disease in patients with pan colitis
 - after 12-15 years in patients with left sided disease
- Q1-3 years
 - Consider FH, PSC, age, symptoms etc.
- After 20 years, annual colonoscopy
- NNT = 14 to prevent 1 cancer; 40 to prevent 1 death

Lashner. Gastrointestin Endos Clin N Am 2002;12:135 Provenzale. Gastroenterology 1995;109:1188

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Surveillance for Dysplasia in UC

- >32 biopsies are needed to exclude dysplasia with 90% confidence
- 4 quadrant biopsies every 10 cms
- Additional biopsies suspicious mucosal lesions
- Disease in remission at time of colonoscopy
- Surveillance is not perfect
- Prophylactic colectomy an option

Levin B. ASGE Clinical Update 2000;7:1313-6

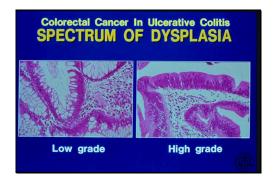
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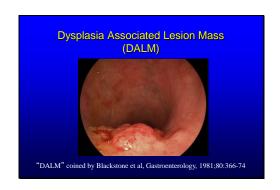
Surveying Surveillance: What are we (not) doing?

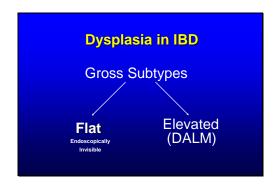
- 79% of physicians biopsy 2-4 sites
- 54% biopsy 5-9 sites
- 36% biopsy 10 or more sites
- Confusion about dysplasia, DALM

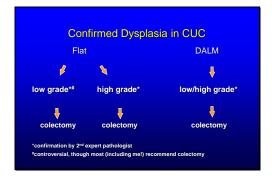
Bernstein et al., Am J Gastroenterol 90, 1999

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Colectomy for Dysplasia in UC

- Low grade dysplasia
- → 20% cancer
- High grade dysplasia
- → 42% cancer
- DALM
 - → 43% cancer
- The finding of dysplasia of <u>any grade</u> should be confirmed by a pathologist with <u>special expertise</u> in gastrointestinal pathology
- Confirmed dysplasia = colectomy

Bernstein et al, Lancet 1994;334:71

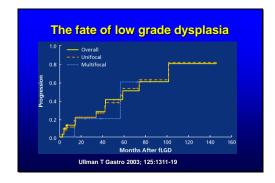
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The fate of low grade dysplasia

- Mt Sinai: 46pts → LGD on chart review
 - 7 cases of CRC
 - 4/17 (23.5%) had unexpected CRC at colectomy
 - 53% progression to advanced neoplasia at 5yr
 - 2 cancers at advanced stage despite surveillance
 - Unifocal LGD same risk as multifocal or recurrent LGD
- Confirmed LGD = Colectomy

Ullman, et al., Gastroenterology 2003;125:1311-1319

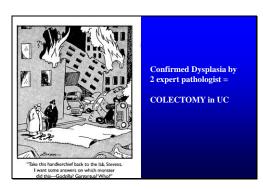
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Dysplasia Surveillance in UC: Recommended Actions

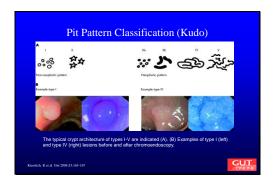
- Indefinite findings: increase surveillance
- Negative findings: survey according to duration and other RF
 - ->8 years: every 1-3 years
 - ->20 years: every year
- DALM, high grade, low grade: colectomy

Bernstein CN. J Gastrointest Surg. 1998;2:318-321.



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Study	Number of patients	Dye MB=methylene blue IC=Indigocarmine	Number of lesions	Difference (x-fold)
Kiesslich et al. (2003)	165	MB	42 (32 vs 10)	3.07
Huristone et al. (2004)	324	IC and magnification	93 (69 vs 24)	3.81
Rutter et al. (2004)	100	IC	7 (7 vs 0)	4.50
Kiesslich et al. (2007)	153	MB and Confocal Endomicroscopy	23 (19 vs 4)	4.75
Marion et al. (2008)	102	MB	20 (17 vs 9)	5.66

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Chromoendoscopy: Which Dye? Indigo carmine (0.1%-0.4%) Contrast stain neither reacts or is absorbed by the colonic mucosa Pools in mucosal grooves allowing better definition of small or flat tesions as well as alterations in mucosal architecture Can be washed off the mucosa Methylene blue Vital dye taken up by colonic mucosa within 1-2 minutes staining noninflamed mucosa but is poorly taken up by dysplastic tissue or inflamed mucosa No published studies comparing indigo carmine to methylene blue in patients with IBD

Chromoendoscopy in practice

- Single physician experience 2005-8/2012
- 184 scopes; 118pts, mean age 51.4 years

Chromo - IC (64 scopes) WLE (120 scopes)

38.8 minutes 20.5 minutes

42.0 bx (13 jars) 34.8 bx (10 jars)

157 polyps (2.45/scope) 87 polyps (0.725/scope)

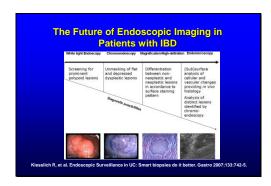
25/64 (39.1%) dys polyps (p<0.001)

*flat dysplasia on one random biopsy

Jatsukar N, Reinert S, Resnick M, Shah SA

IBD Advances, 2012, Hollywood, FL (earlier version at ACG, 2012)

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Goals

- Increased risk of colon cancer in IBD
- Importance of surveillance/technique
- Consider Chromoendoscopy
- Suggested Guidelines (evolving)
- Confirmed dysplasia* = colectomy
- YOU CAN HELP:
 - Is the pt due for colonoscopy
 - -# biopsies, careful technique, Chromo

Future

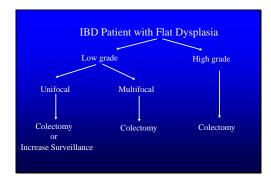
- Chromoendoscopy with only targeted biopsies; longer intervals in between scopes
 - -Random biopsies yield is very low
 - -Biopsies adds time and cost
- Stool DNA
- Blood tests to detect presence of dysplastic tissue in colon
- Chemoprevention: 5-ASA, Urso, Folic acid
 - -Future: ?

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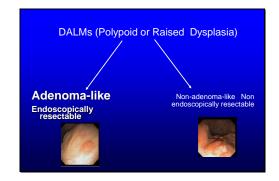
Should colectomy be performed for flat dysplasia?

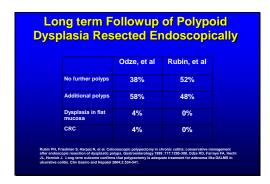
- Grade A: There is high certainty that colectomy for flat HGD treats undiagnosed synchronous cancer and prevents metachronous cancer.
- Grade Insufficient: The current evidence is insufficient to assess the balance of benefits and harms of colectomy for flat LGD.

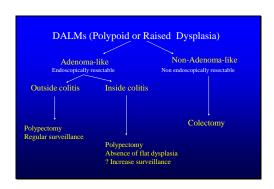
Farraye FA, Odze R, Eaden J, Hzkowitz S. Diagnosis and management of colorectal neoplasia in inflammator; bowel disease. Gastroenterology 2010; 138:746-774.



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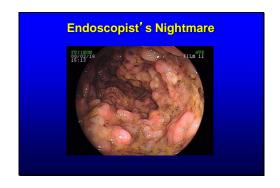








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Is there sufficient rationale for performing surveillance colonoscopy in patients with IBD?

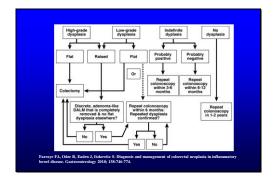
Grade B: There is moderate certainty that surveillance colonoscopy results in at least moderate reduction of CRC risk in patients with IBD.

- Despite the lack of randomized controlled trials, surveillance colonoscopy is recommended for patients with IBD at increased risk for developing CRC.
- Patients with extensive UC or CD of the colon are most likely to benefit from surveillance.

Farraye FA, Odze R, Eaden J, Itzkowitz S, Diagnosis and management of colorectal neoplasia in inflammatory bowel disease. Gastroenterology 2010; 138:746-774.

Slide 52	Surveillance Colonoscopy All patients should undergo a screening colonoscopy a maximum of 8 years after onset of symptoms Regardless of extent of disease at diagnosis Multiple biopsies to assess microscopic extent of inflammation Ulcerative proctitis or proctosigmoiditis are not considered at increased risk for IBD-related CRC Manage on the basis of average-risk recommendations Patients with extensive or left-sided colitis should begin surveillance within 1 to 2 years after the initial screening colonoscopy Firmy, TA Ode 10, Edua 1, old ACA smilled public scheme (as the diagnosts and amagement of relinent segment in inflammatory brent disease Contractivities 3105, 133-16-174.	
Slide 53	Surveillance Colonoscopy The optimal surveillance interval has not been clearly defined After 2 negative examinations survey every 1 to 3 years Representative biopsy specimens from each anatomic section of the colon should be obtained Minimum of 33 biopsy specimens be taken in pancolitis patients Chromoendoscopy with targeted biopsies is recommended as an alternative to random biopsies for endoscopists who have expertise with this technique Increased sensitivity for detecting dysplasia	
Slide 54	Surveillance Colonoscopy Patient with PSC Survey at time of diagnosis and then yearly Ideally, surveillance colonoscopy should be performed when the colonic disease is in remission More frequent surveillance examinations: History of CRC in first-degree relatives Ongoing active endoscopic or histologic inflammation Anatomic abnormalities such as a foreshortened colon, stricture Multiple inflammatory pseudopolyps Same recommendations for patients with Crohn's colitis who have	

Farraye FA, Odze RD, Eaden J, et al. AGA medical position statement on the diagraeoplasia in inflammatory bowel disease. Gastroenterology 2010; 138:746-774.



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