Endoscopic and Histological Grading in IBD

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ECCO

Inflammatory Bowel Diseases 2008

3rd Congress of ECCO – the European Crohn's and Colitis Organization

In collaboration with GETAID – Groupe d'Etude Thérapeutique des Affections Inflammatoires du Tube Digestif

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Cité – Centre de Congrés Lyon, France
February 28 – March 1, 2008

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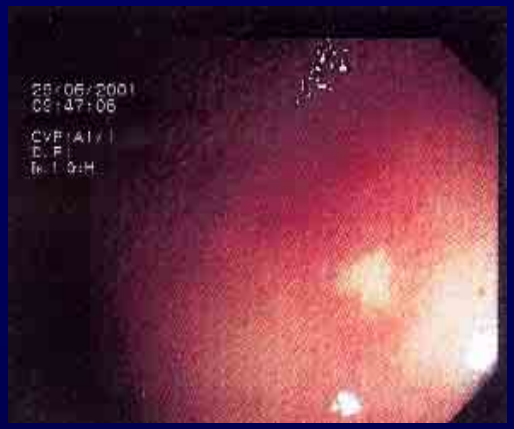
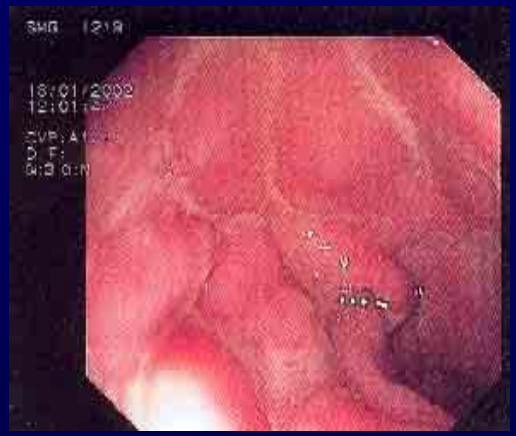
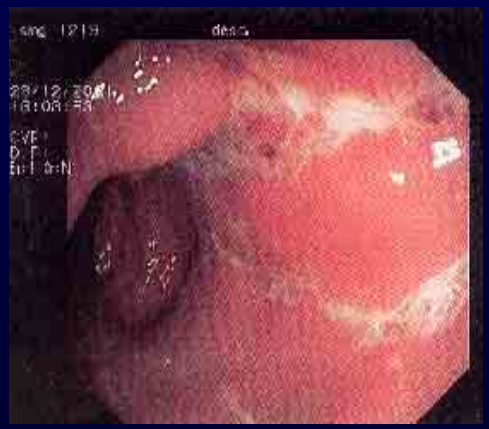
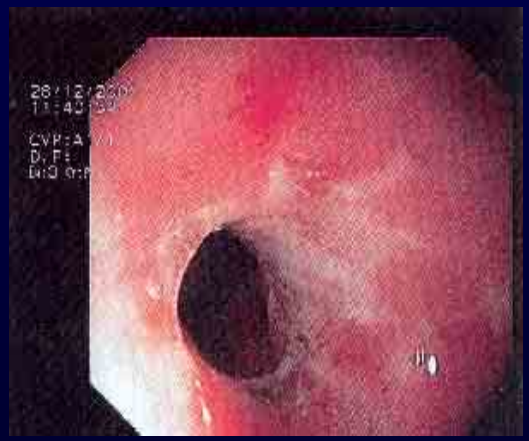
Typical Lesions in Active Crohn's Disease





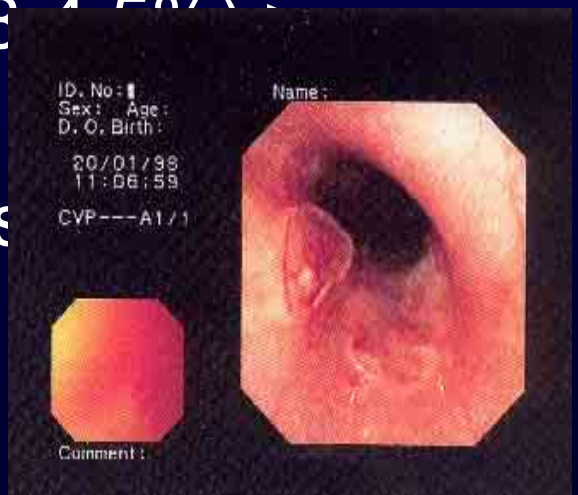
- Aphthous ulcerations
- Deep irregular ulcerations,
- 'punched-out' ulcers
- Longitudinal ulcerations
- Cobblestoning
- Discontinuous involvement (86%)
- Rectal sparing (25%)
- Luminal narrowing
- Fistulas





Typical lesions in Upper GI Crohn's Disease

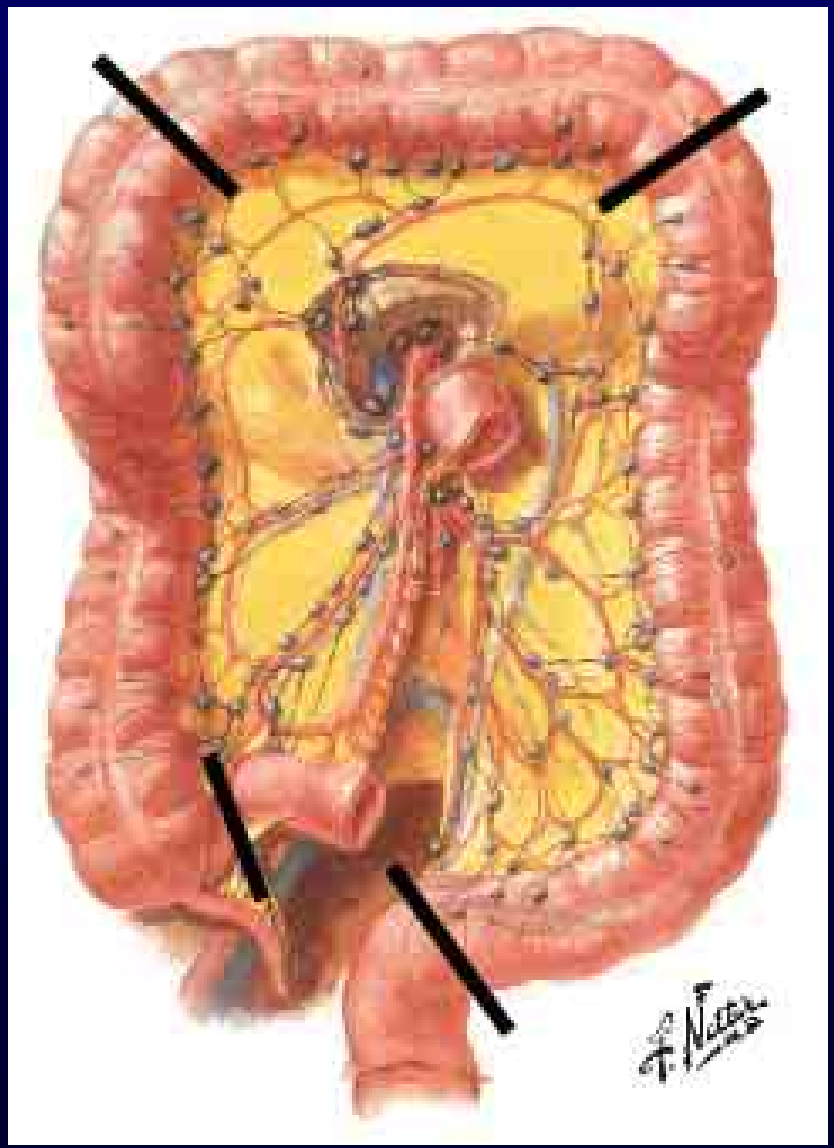
- Invariably accompanied by small bowel / colonic disease
- Prospective studies: 17 – 75 % (sympt and asympt)
- Retrospective studies: 0.5 – 13 %
- Oral (6-9%) > gastroduodenal (1.8
- oesophageal (1.8%)
- Oesophageal CD: aphthous ulcers
- ulcers, erosions, strictures



Measurement of Endoscopic Disease Activity in Crohn's Disease

- The Crohn's Disease Endoscopic Index of Severity (CDEIS)
- The Simple Endoscopic Index for Crohn's Disease (SES-CD)
- The Rutgeerts' score for postoperative recurrence

Ileocolonic segments



CDEIS

	Rectum	Sigmoid and left colon	Transverse colon	Right colon	Ileum	Total
Deep ulcerations (12 if present, 0 if absent in the segment)	_____+	_____+	_____+	_____+	____+	Total 1+
Superficial ulcerations (6 if present, 0 if absent in the segment)	_____+	_____+	_____+	_____+	____+	Total 2+
Surface involved by disease (cm)	_____+	_____+	_____+	_____+	____+	Total 3+
Surface involved by ulcerations (cm)	_____+	_____+	_____+	_____+	____+	Total 4=
						Total A
	Number of segments totally or partially explored (1-5)					n
	Total A / n =					**Total B**
	If **ulcerated stenosis** is present anywhere add 3=					**C**
	If **non-ulcerated stenosis** is present anywhere add 3=					**D**
	TOTAL B + C + D = CDEIS					

CDEIS

Scores range from 0-44 (higher=more severe)

Mary JY et al. Gut 1989

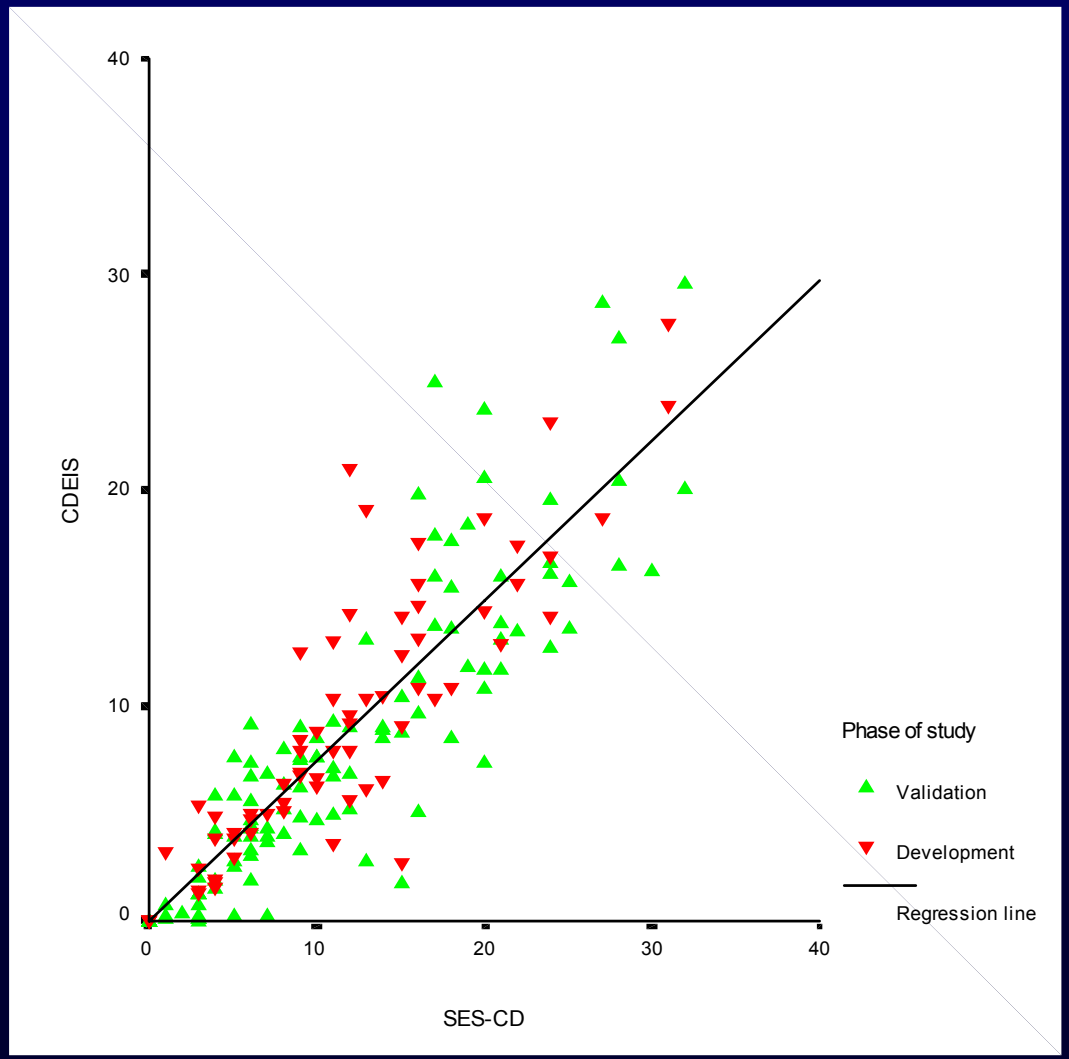
Simple endoscopy index : SES-CD

SEVERITY	0	1	2	3
Presence and size of ulcers	None	Aphtous <0.5 cm	Large, 0.5÷2 cm	>2 cm
Extent of ulcerated surface	0%	<10%	10-30%	>30%
Extent of affected surface	0%	<50%	50-75%	>75%
Presence and type of narrowings	None	Single, can be passed	Multiple, can be passed	Cannot be passed

SES-CD

	Ileum	Right colon	Transverse colon	Left colon	Rectum	Total
Presence and size of ulcers (0-3)	___+	____+	____+	___+	___+	+
Extent of ulcerated surface (0-3)	___+	____+	____+	___+	___+	+
Extent of affected surface (0-3)	___+	____+	____+	___+	___+	+
Presence and type of narrowings (0-3)	___+	____+	____+	___+	___+	=
					RAW SUM OF VARIABLES	**Total**
					Number of affected segments	**n**
				Total - 1.4 x n =		**SES-CD**

Correlation between SES-CD and CDEIS (191 examinations)



Daperno et al, 2004

Clinical-endoscopic Correlations

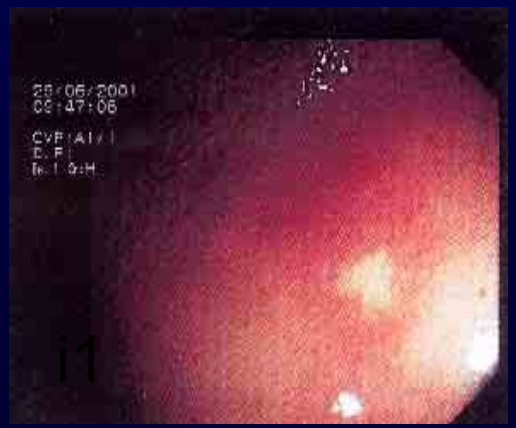
	SES-CD	CDEIS	GELS
CDAI	0.371 (p<0.0001)	0.321 (p=0.0003)	0.250 (p=0.005)
IBDQ	-0.231 (p=0.019)	-0.240 (p=0.015)	-0.203 (p=0.039)
CRP	**0.453** (p<0.0001)	0.422 (p<0.0001)	0.400 (p<0.0001)

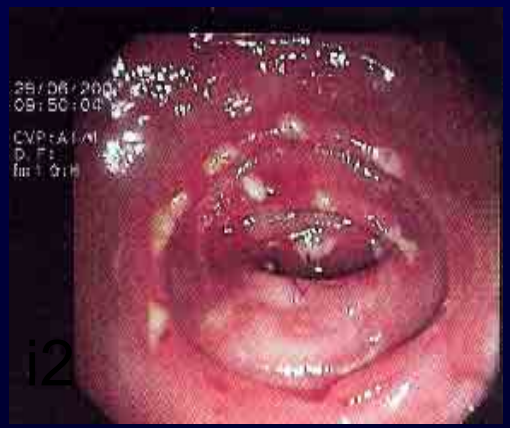
- Correlations to clinical variables were significant

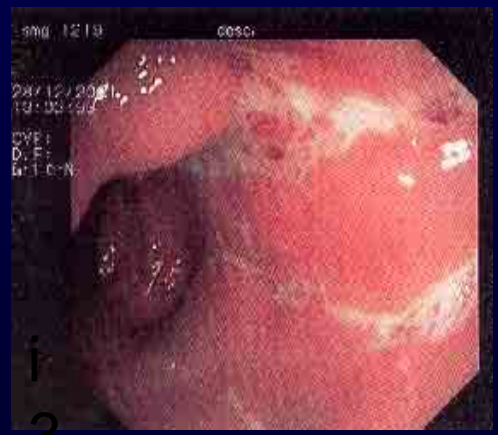
Daperno et al, GI Endoscopy 2004

Endoscopic Assessment following surgery : Rutgeerts' score

- Developed for lesions in the neoterminal ileum and at the ileocolonic anastomosis
- i0 – i4
- Correlates with clinical behavior in the future

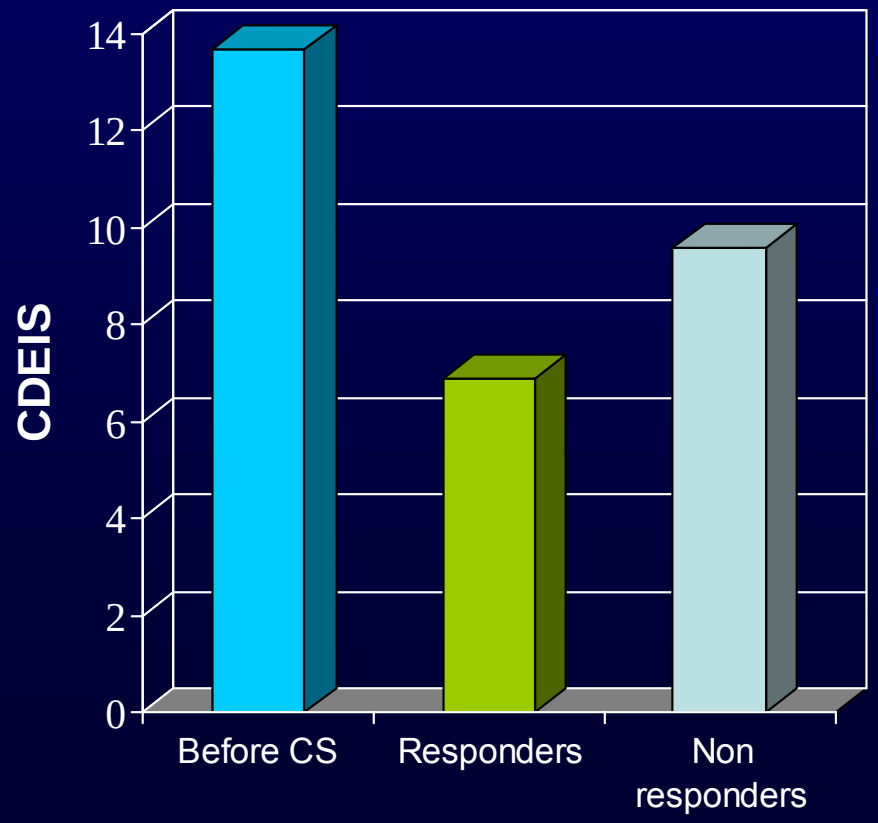


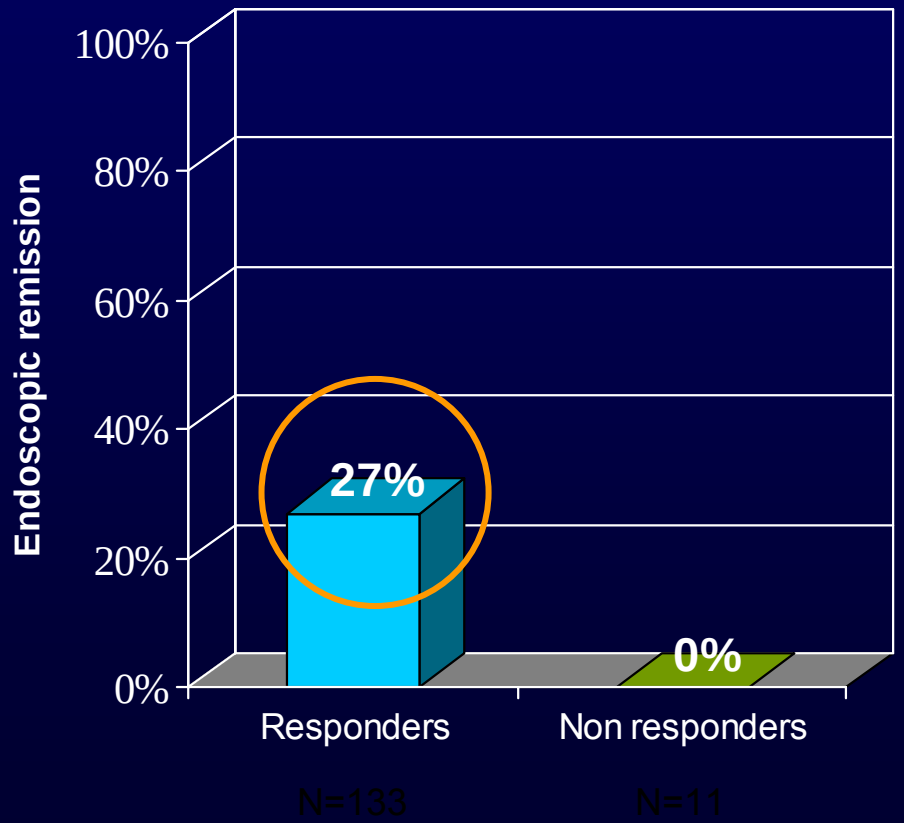




Rutgeerts P et al. Gastroenterology 1990

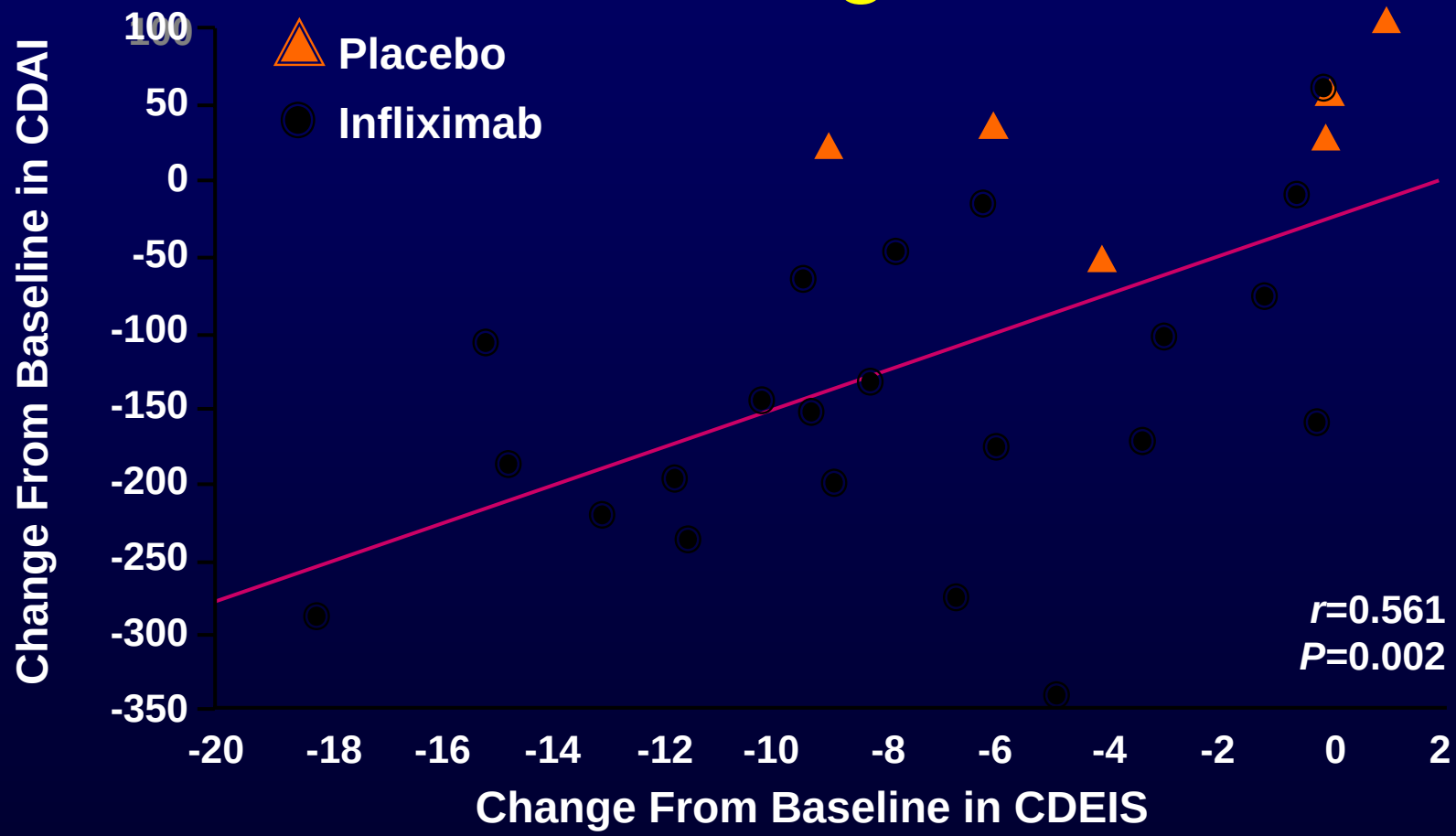
Effect of steroids (1 mg/kg/d) on endoscopic lesions in CD after 3-7 weeks





Modigliani et al, Gastroenterology, 1990

Symptom Improvement with Mucosal Healing



D'Haens G et al. *Gastroenterology* 1999

Treatment of CD: Mucosal Healing

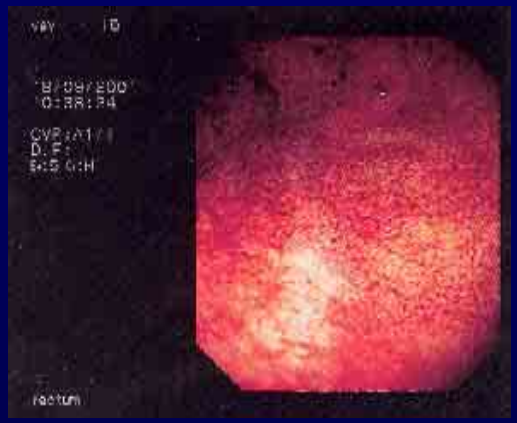
No or only Limited Healing	*Important but Slow Healing*	*Important and Rapid Healing*
Aminosalicylates	**Azathioprine**	**Infliximab**
Steroids	**6-MP**	
	Natalizumab ?	
		Adalimumab?
Antibiotics	**Methotrexate (?)**	**Certolizumab?**

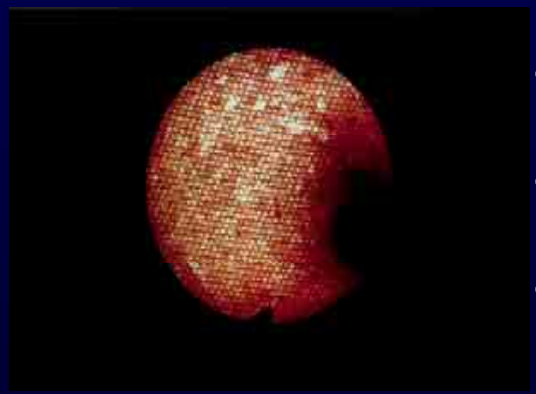
IOIBD CONSENSUS

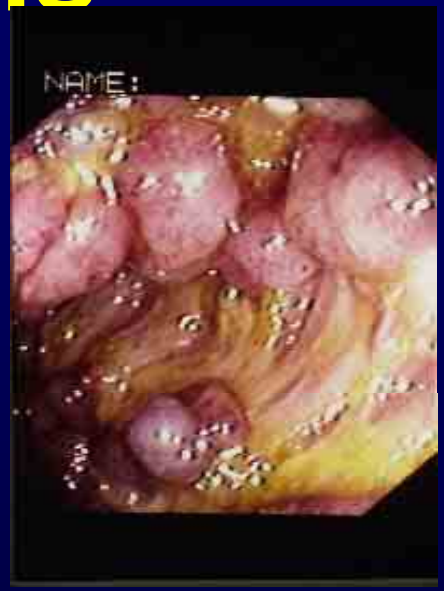
- CDEIS to be used a secondary endpoint in studies looking at inflammatory activity
- Rutgeerts' score to be used in studies for postoperative recurrence
- Significant recurrence = i3 or i4

Sandborn et al.: A REVIEW OF ACTIVITY INDICES AND EFFICACY ENDPOINTS FOR CLINICAL TRIALS OF MEDICAL THERAPY IN ADULTS WITH CROHN'S DISEASE. Gastroenterology, 2002

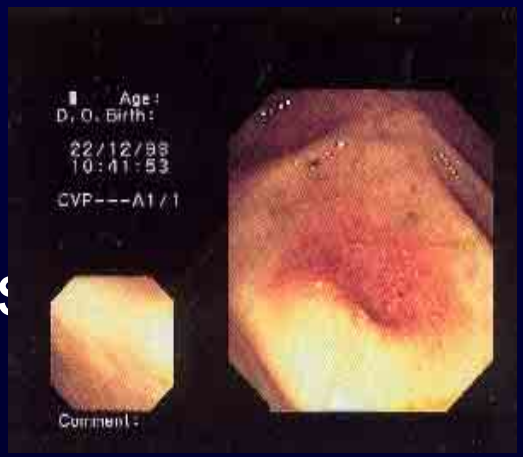
Typical lesions in Active Ulcerative Colitis



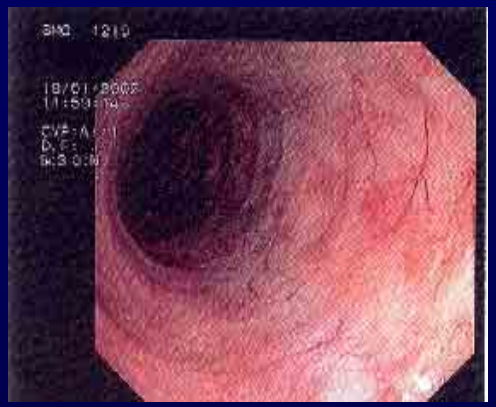


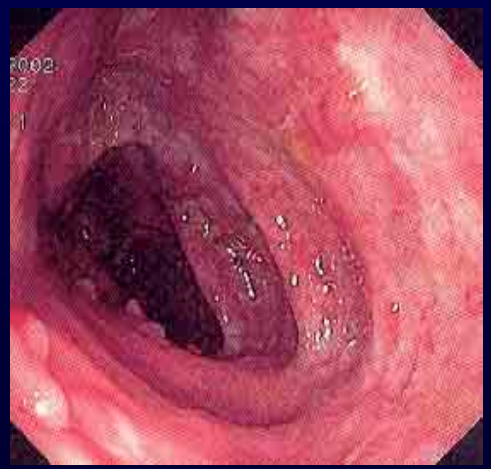


- Continuous involvement (caution: treatment effects)
- Erythema
- Friability
- Granularity
- Micro-ulcerations
- Shallow ulcerations
- Cecal patch



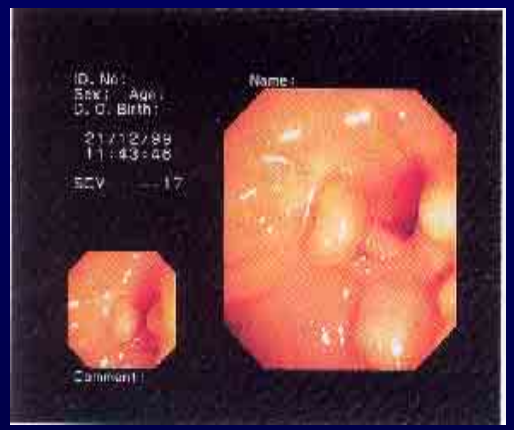
Typical lesions in Quiescent Colitis

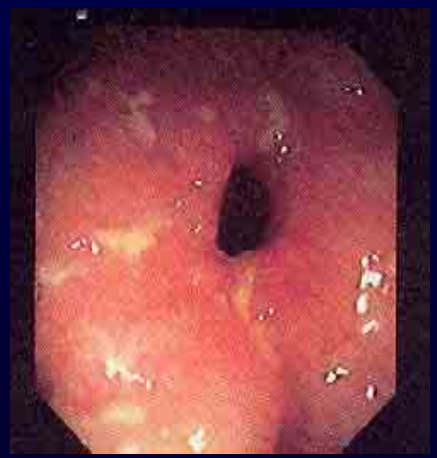




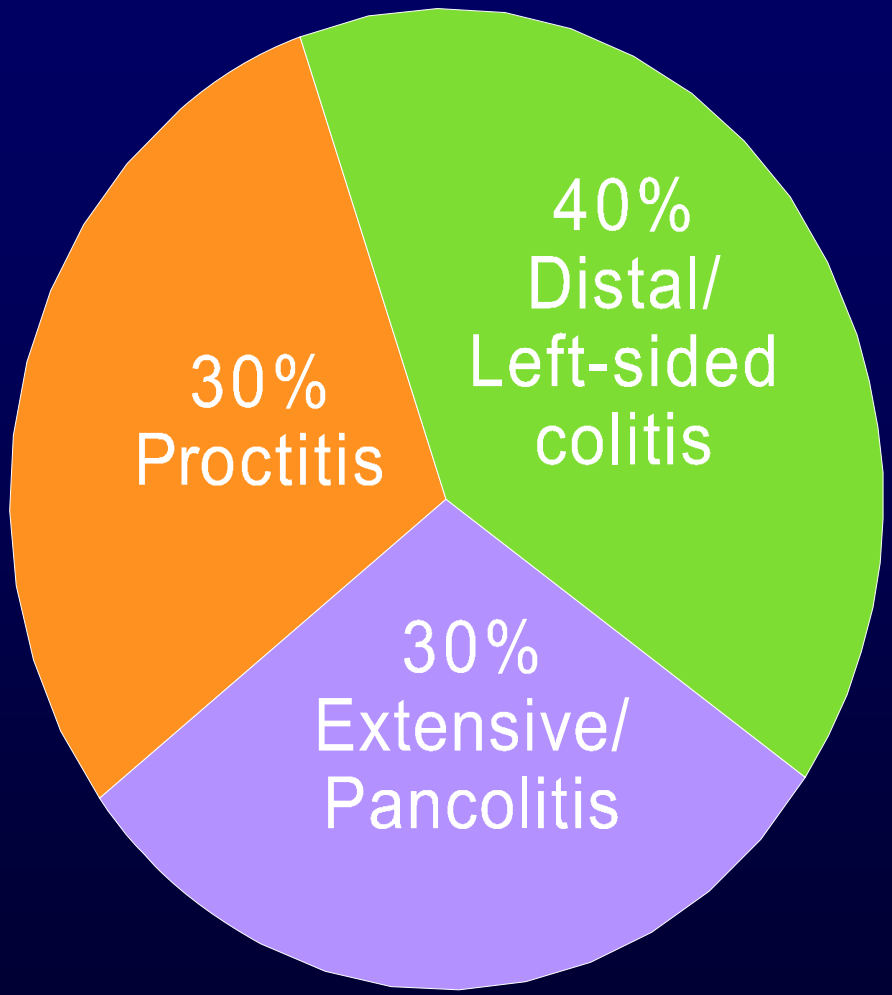
- Attenuated vascular pattern/ loss of vascular pattern
- Mucosal bridging
- Pseudopolyps
- Stricture formation: pylorus, ileocecal valve, rectosigmoid junction

  (CD >> UC)



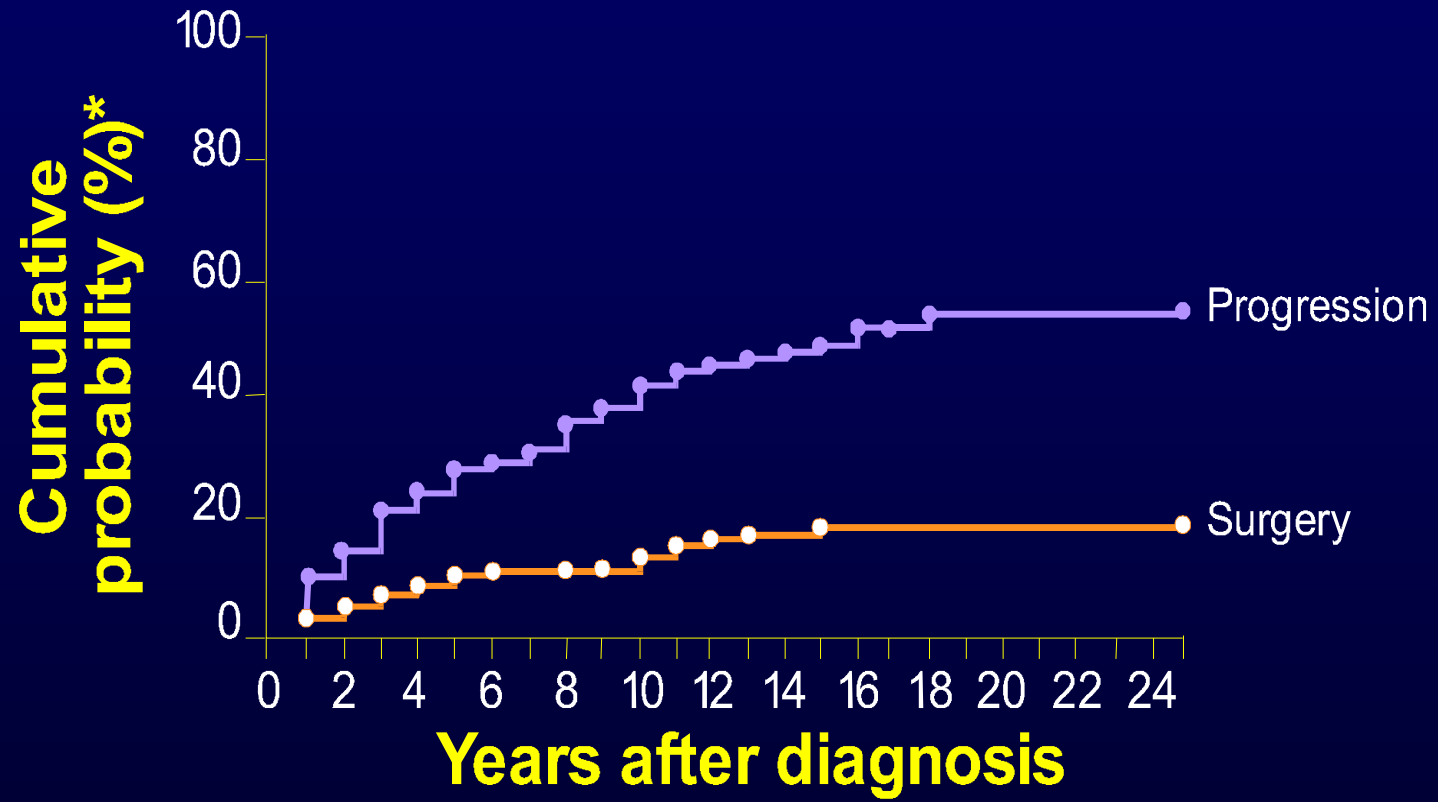


UC: Location and Extent



Percentages based on extent of disease at diagnosis.

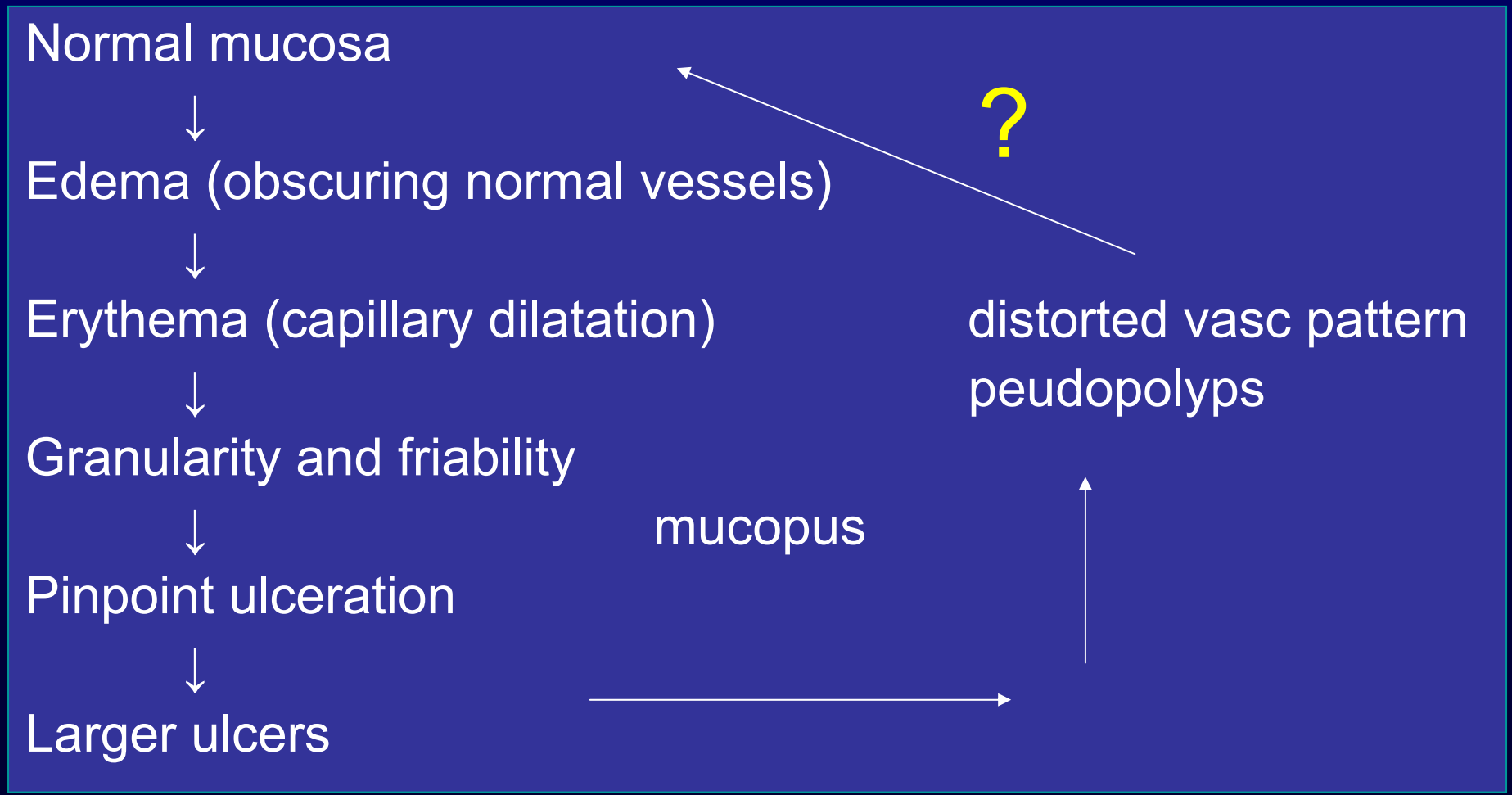
Natural Course of UC: Proctosigmoiditis



*Based on a multivariate analysis

Reprinted with permission from Langholz E et al. *Scand J Gastroenterol*. 1996;31:260-266.

Endoscopic changes in UC



Endoscopy in Active Ulcerative Colitis

- Full ileocolonoscopy recommended at diagnosis
- Flexible sigmoidoscopy sufficient for F/U
- No bowel prep needed in pts with active symptoms
- Continuous involvement (caution: treatment effects)
- Caution in fulminant colitis !
- Deep ulcers in spite of therapy : poor prognostic sign
- Biopsies to be taken in relapse ! (CMV, C Diff, …)

Endoscopic scores for UC

- Useful since endoscopic improvement lags behind symptom improvement and endoscopic healing is an endpoint that is aimed at
- Problematic ‘inter-observer variability’
- Problem of definitions: friability ? granularity ? Ulcers ?

Baron Endoscopic score for UC: 'Activity variables'

- 0= Normal: mat mucosa, ramifying vascular pattern clearly visible throughout, no bleeding spontaneous or to light touch
- 1= Abnormal but not hemorrhagic (between 0-2)
- 2= moderately hemorrhagic: bleeding to light touch but no spontaneous bleeding
- 3= severely hemorrhagic= spontaneous bleeding
- *Problem: no description of 'ulcers'*

Baron et al, BMJ 1964

Endoscopic score for UC: Baron

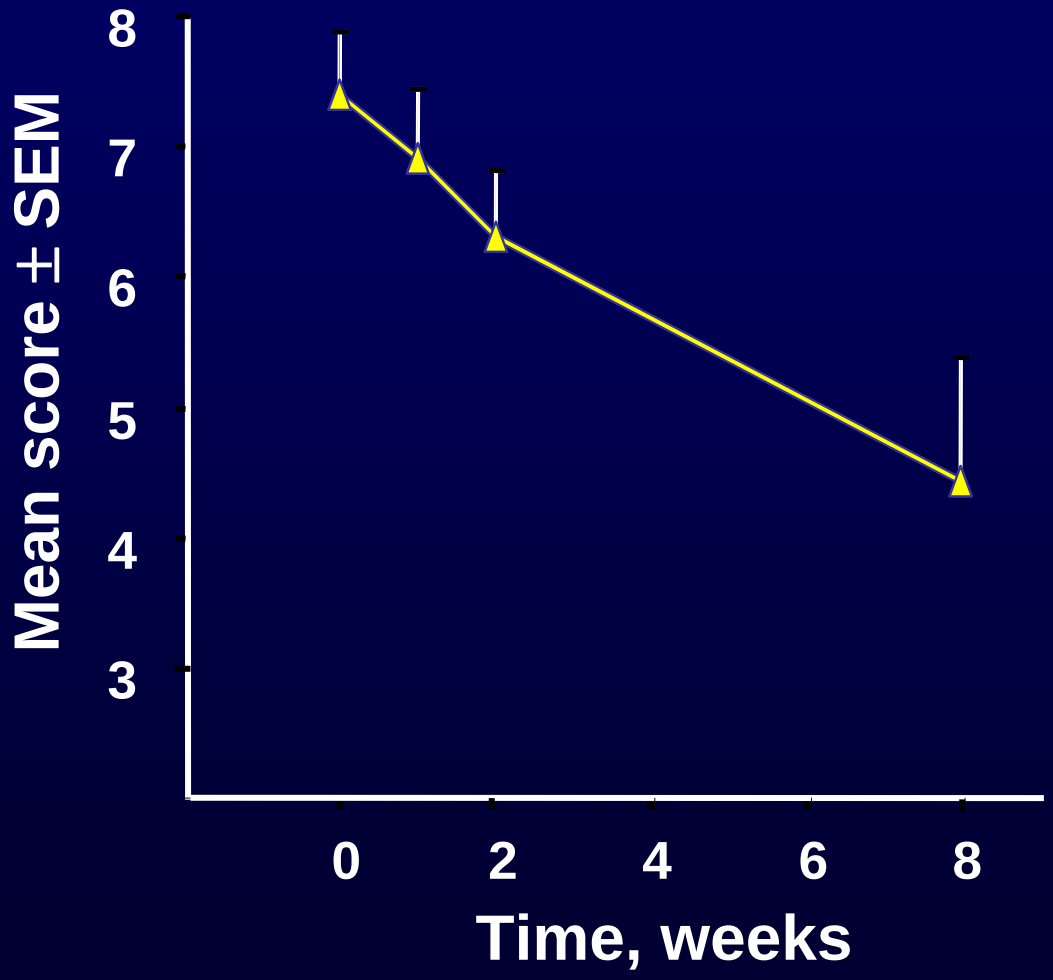
- Interobserver variation highest for ‘graded’ variables (eg ‘redness’)
- Score developed in mild/moderate cases (no ulcers !)
- Best agreement: friability (bleeding to light touch) spontaneous bleeding
- Lowest agreement: granularity

Baron et al, BMJ 1964

Endoscopic Indices for UC

Powell-Tuck	0:no bleeding	1: bleeding on light touch	2: spontaneous bleeding	
Sutherland	0: normal	1: mild friability	2:moderate friability	3:exsudation
Schroeder	0: normal	1: disturbed vessels	2: loss of vasc pattern	3:ulcers

Daclizumab in UC: Pilot Study Endoscopy Scores

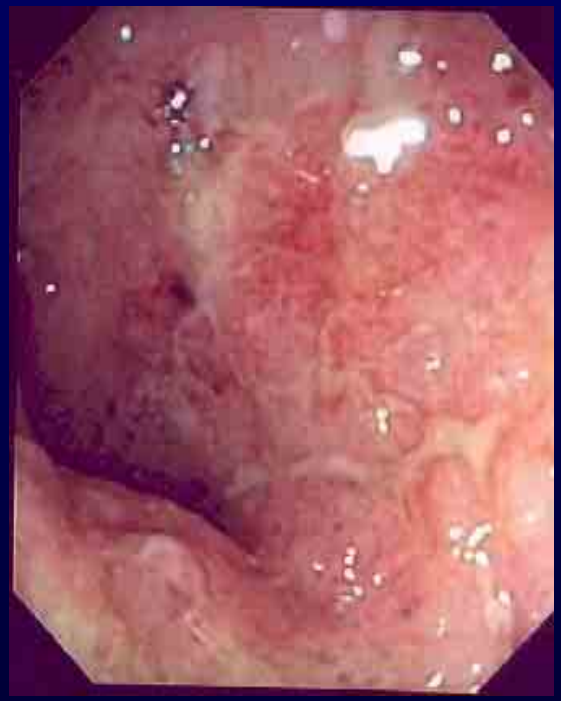


Endoscopic score
Granularity
Vascular pattern
Vulnerability
Mucosal damage

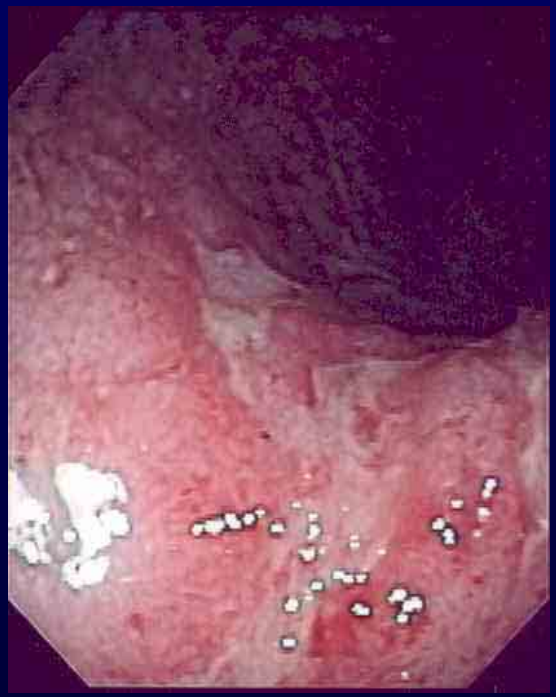
min 0, max 12

Van Assche G, et al. *Am J Gastroenterol*. 2003; Vol. 98, No. 2: 369-376.

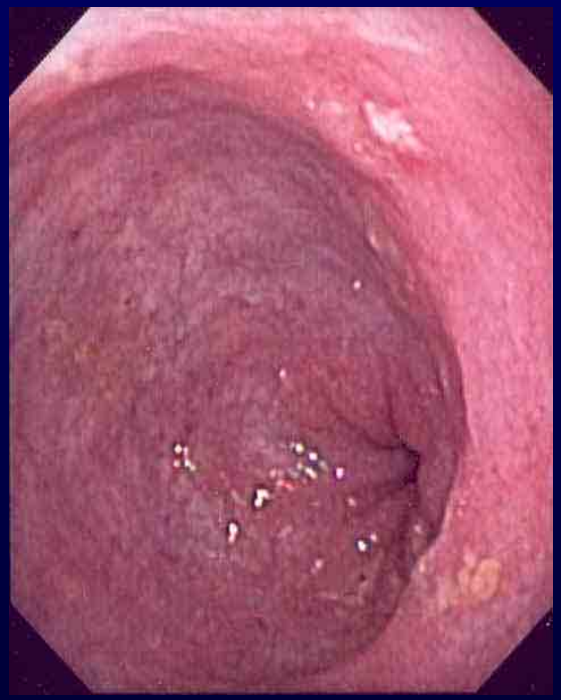
Daclizumab in UC: Pilot Study Results
Mucosal Improvement After Treatment With Daclizumab



Week 0



Week 1



Week 8

Adapted with permission from Claessens C, et al. Presented at Digestive Disease Week. May 2002.

Healing in UC: points to consider

- Active UC is associated with a higher likelihood of dysplasia/cancer
- Endoscopy correlates well with histology and ‘histological healing’ predicts longer ‘time to relapse’ (Riley at al.)
- In ACT, if healing at w8 (score 0): 4 x higher likelihood of clinical remission at w 30 (43.8 % vs 9.5 %)

Differential diagnosis CD/UC

CROHN'S

- Discontinuous involvement
- Cobblestoning
- Aphthous ulcers
- Deep serpiginous ulcers
- Rectal sparing
- Anal lesions
- Ileocecal valve stenotic/ulcerated

UC

- Continuous involvement
- Erosions/microulcerations
- Loss of vascular pattern
- Rectal involvement
- Ileocecal valve patulous and free of ulceration

Indeterminate: 10 %

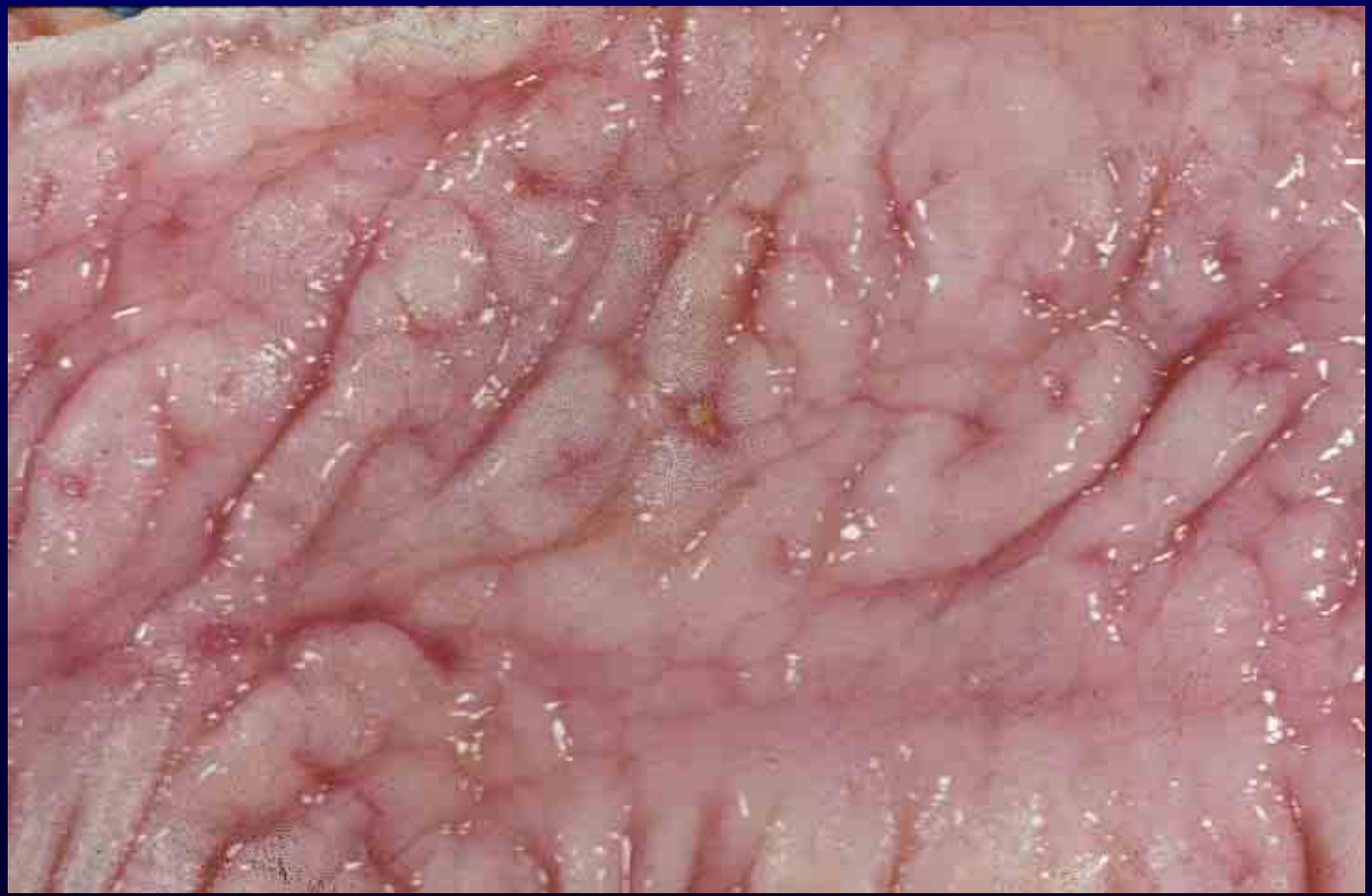
Crohn's disease histology: general features

- **CD can affect the entire GI tract**
- **CD is a segmental disease**
- **CD is a transmural disease**
  - **Mucosal lesions > endoscopic samples**
  - **Deeply situated lesions > surgical samples**

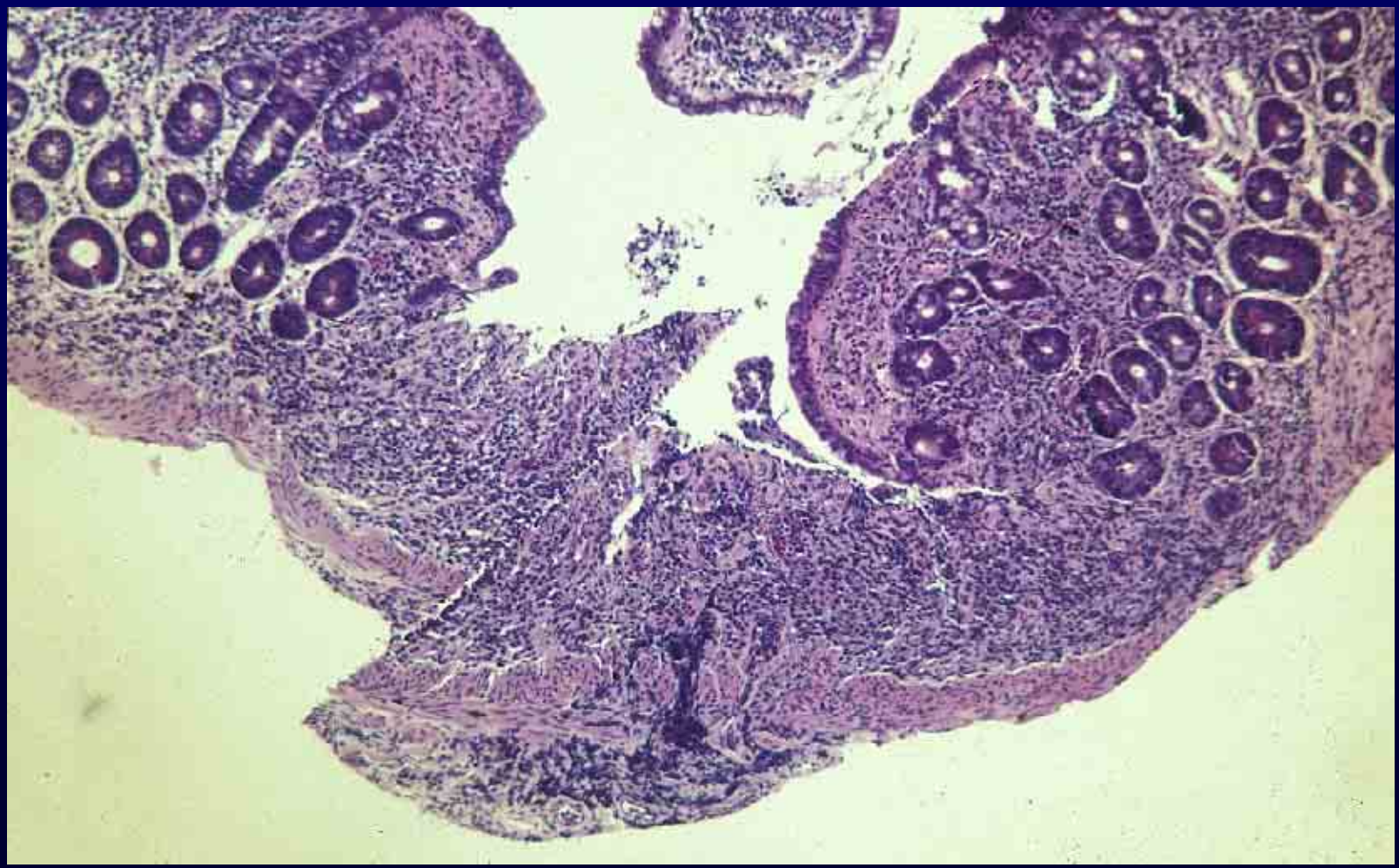
Crohn's disease microscopic features : early lesions

- **Early lesions occur in a background of normal mucosa (focal lesions)**
- **Types**
  - **Summit lesions : damage of small capillaries and loss of epithelial cells**
  - **Epithelial patchy necrosis**
  - **Mucosal microulcerations (loss of up to 6 cells)**
  - **Aphthoid ulcer**
  - **Mountain peak ulcer : ulcers at the base of crypts**

Crohn’s disease : Aphthoid ulcer



Crohn’s disease : Mountain peak ulcer



Crohn's disease microscopic features & diagnosis

- **Epithelial alterations**
  - **Cytological changes > damage & repair**
  - **Architectural changes**
  - **Metaplastic changes**
- **Inflammatory response**
  - **Intensity**
  - **Composition**
  - **Distribution**

Histologic Disease Activity in CD

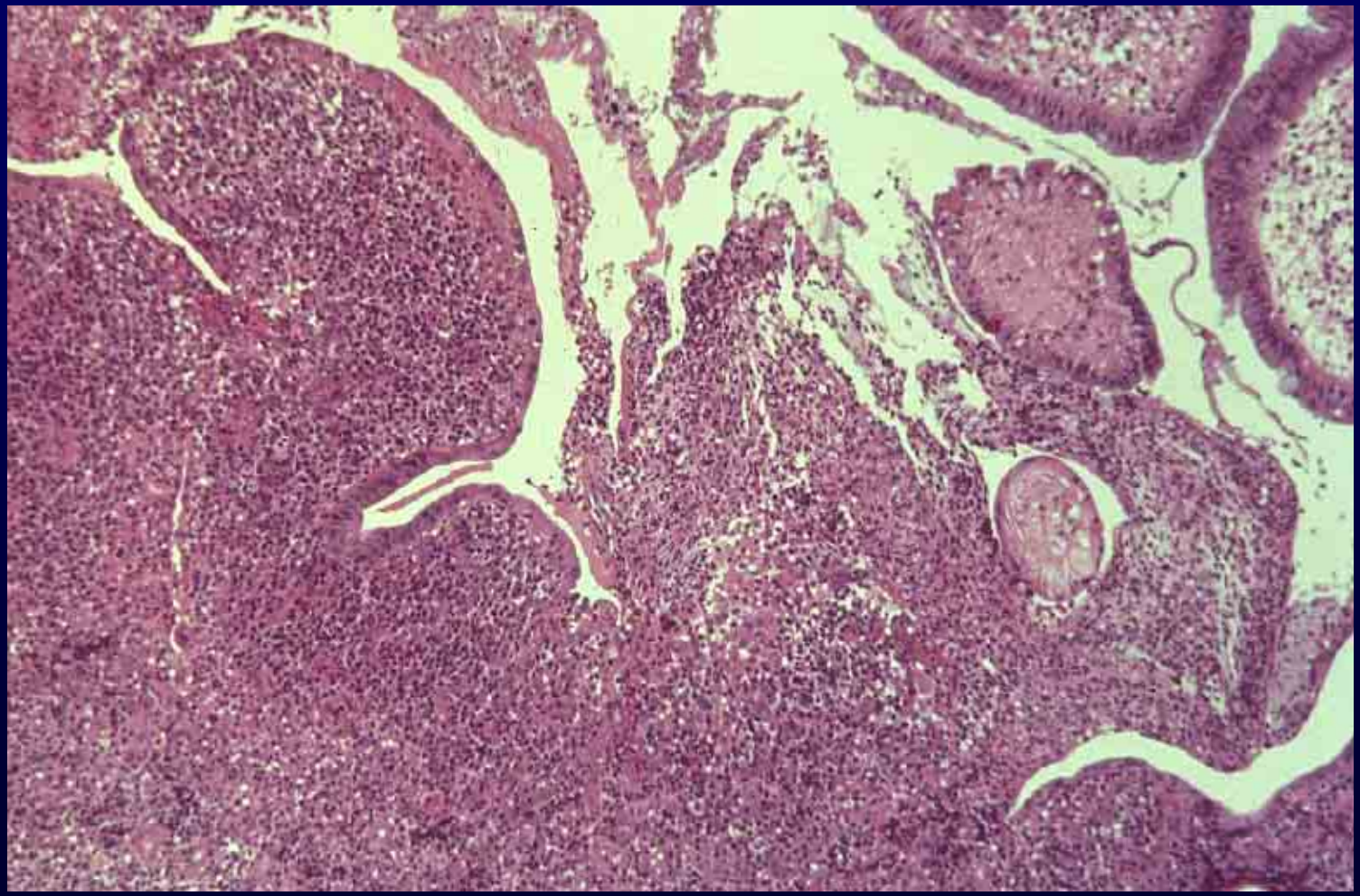
- Epithelial damage 0-2
- Architectural changes 0-2
- Mononuclear infiltrate in LP 0-2
- PMN infiltrate in LP 0-2
- PMN infiltrate in epithelium 1-3
- Erosion/ulcers 0-1
- Granulomas 0-1
- Proportion of biopsies affected 0-3

D'Haens et al. Gastroenterology 1998

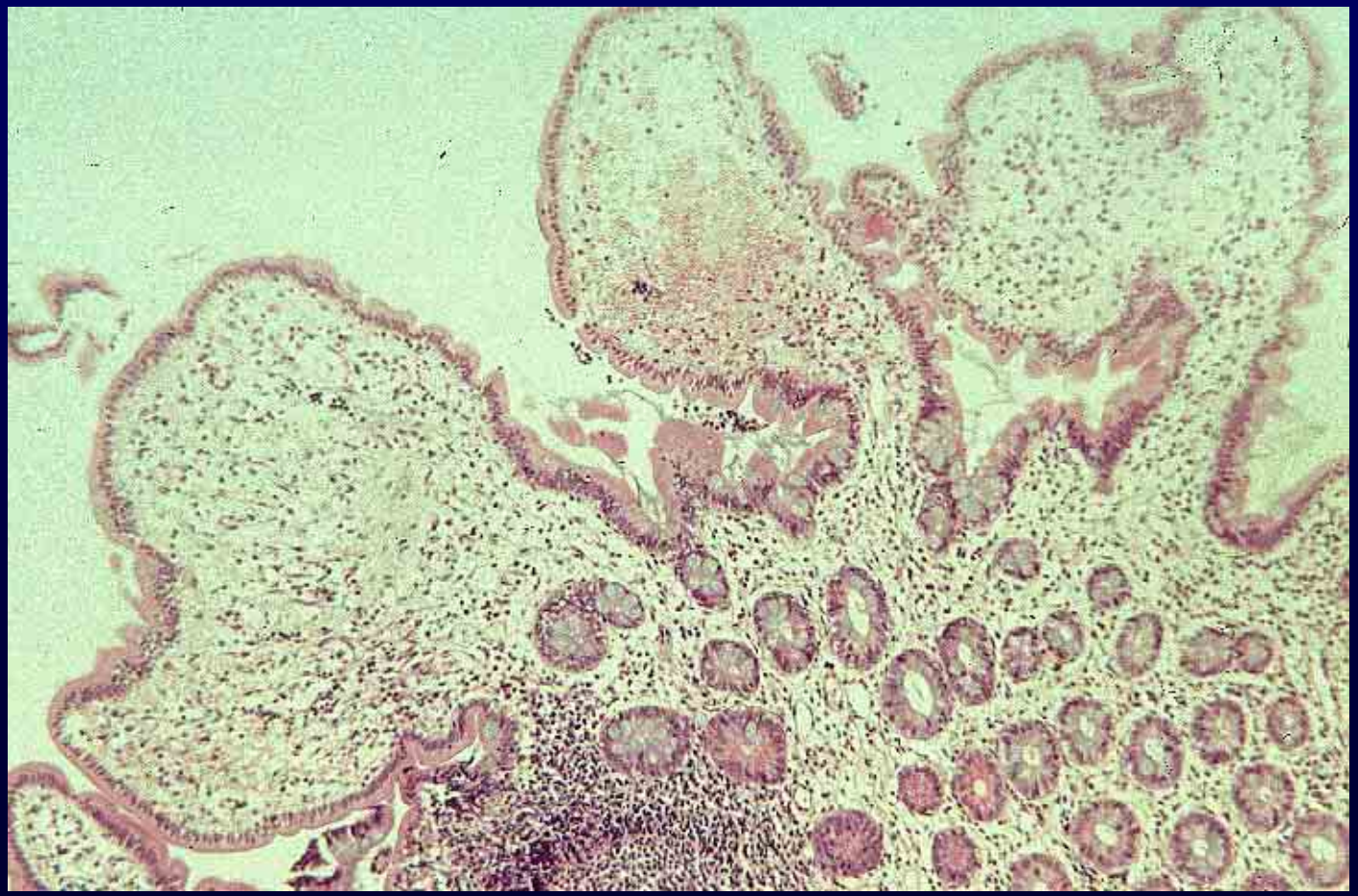
Histologic Disease Activity in CD

- Correlation between histological changes and clinical improvement is poor
- Score not validated prospecively
- Histology recommended for exploratory studies

Crohn’s disease : Before IFX



Crohn’s disease : 4w after IFX



Geboes Index: different grades used for evaluation of histologic disease severity in UC

Geboes Index:

Grade 0: Structural (architectural) changes

0= No abnormality, 1= Mild abnormality, 2= Mild or moderate diffuse or multifocal abnormalities, 3= Severe diffuse or multifocal abnormalities

Grade 1: Chronic inflammatory infiltrate

0= No increase, 1= Mild but unequivocal increase, 2= Moderate increase, 3= Marked increase

Grade 2: Lamina propria neutrophils and eosinophils

2A Eosinophils

0= No increase, 1= Mild but unequivocal increase, 2= Moderate increase, 3= Marked increase

2B Neutrophils

0= No increase, 1= Mild but unequivocal increase, 2= Moderate increase, 3= Marked increase

Grade 3: Neutrophils in epithelium

0= None, 1= < 5% crypts involved, 2=< 50% crypts involved, 3=> 50% crypts involved

Grade 4: Crypt destruction

0=None, 1=Probable – local excess of neutrophils in part of crypt, 2=Probable – marked attenuation, 3=Unequivocal crypt destruction

Grade 5:Erosion or ulceration

0=No erosion, ulceration, or granulation tissue, 1= Recovering epithelium + adjacent inflammation, 2= Probable erosion – focally stripped, 3= Unequivocal erosion, 4= Ulcer or granulation tissue

Conclusions

- In UC endoscopic (and histological) scores are absolutely recommended in the assessment of disease activity and effects of drug therapy
- In Crohn's disease endoscopic endpoints are gradually entering routine clinical practice and should be part of the evaluation of drug effects
- More research is needed to ascertain if 'healing of the mucosa' should be the ultimate goal of treatment in CD

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