Polyps & Colorectal cancer

K. Geboes

Colorectal cancer

- **Sporadic type** **94%**
- **Hereditary background** **4%**
  - **Familial Adenomatous Polyposis**
  - **Hereditary NonPolyposis CC**
  - **Juvenile polyposis**
  - **Hyperplastic polyposis**
- **IBD-related** **1%**

Content

- Precursor lesions
  - Definition
  - Subtypes
  - Microscopy
    - Sporadic
      - Flat lesions
      - Polyps
    - IBD
  - Handling specimens and risk factors

Colorectal cancer and precursor lesions

Sporadic ca – FAP - IBD

- **Polyp – cancer sequence**
  - **Adenoma – cancer sequence** (Morson et al 1984)
- **Flat adenoma (Muto et al 1985)**
  - **Nonpolypoid lesion**
  - **Height < 3 mm**
  - **Mucosal thickness is twice or less that of the surrounding mucosa**
- **Sessile serrated adenoma/polyp/lesion**
- **Dysplasia**

Polypoid (pedunculated adenoma)
Flat adenoma (668888/1)

Colorectal cancer and precursor lesions : IBD

- **Flat dysplasia** **95%**
- **Elevated lesions**

Hurlstone et al., Endoscopy 2005, Chromoendoscopy in UC

	HMCC group	*Control group*	*Total*	*P value HMCC vs. Control*
No. of intraepithelial neoplastic lesions detected	69	24	93	< 0.0001
Low-grade dysplasia	44	19	63	< 0.05
High-grade dysplasia	25	5	30	< 0.01
No. of invasive neoplastic lesions detected (T2 or beyond)	3	1	4	n.s.
No. of flat mucosal lesions (JRSC II) with intraepithelial neoplasia	53	14	67	< 0.001
No. of exophytic lesions (JRSC I) with intraepithelial neoplasia	16	10	26	> 0.1

Flat lesions

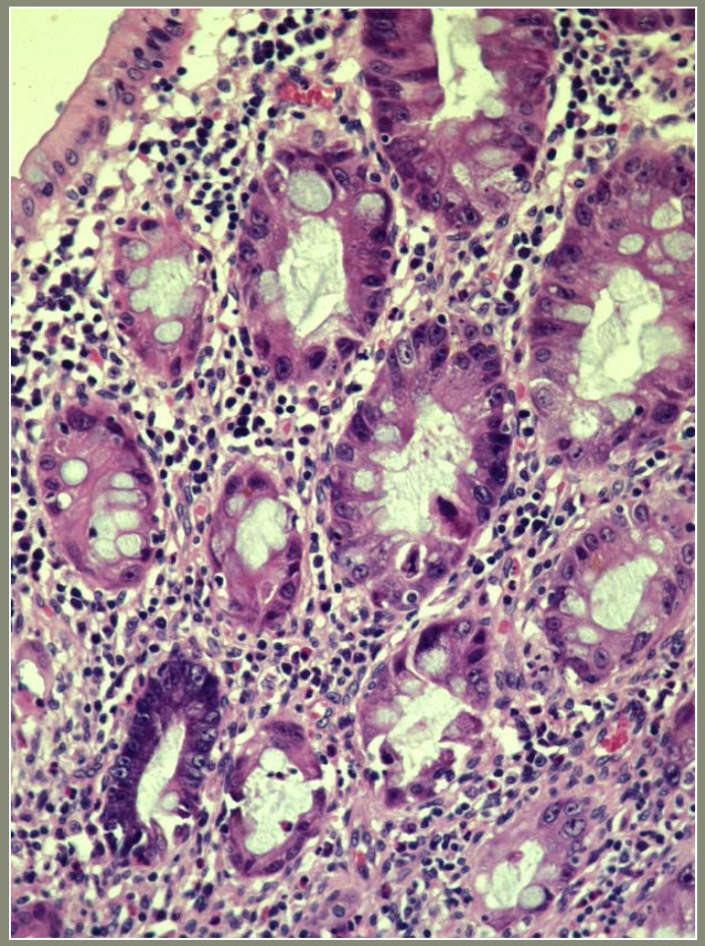
Colorectal cancer and precursor lesions : Macroscopy

- Stereomicroscopy Magnifying endoscopy
  - Aberrant Crypt focus (micro-adenoma; unicryptal adenoma)
    - With hyperplastic – non-dysplastic epithelial lining
    - With intraepithelial neoplasia – dysplastic type

Precursor lesions

662079/6 **Aberrant crypt focus colon**

Microadenoma - monocryptal adenoma



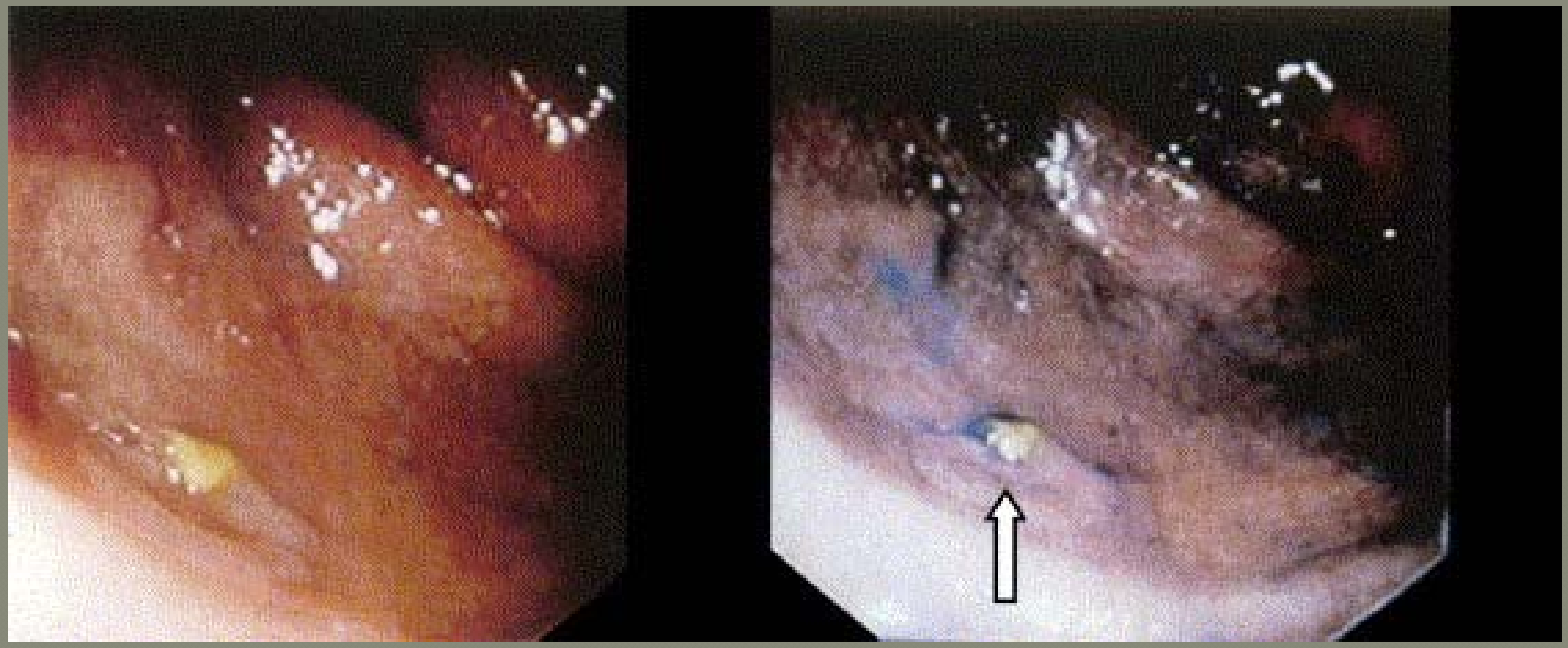
Adenomas – Special type

Muto T e.a. Small "flat adenoma" of the large bowel with special reference to the clinicopathologic features. Dis Colon and Rectum

1985; 28: 847-51

Definition

- **Flat elevated lesions (FELs)**
  - Lesions characterized by a slight elevation and a flat upper surface with a reddish colour
  - Generally smaller than 10 mm
  - Central depression with air insufflation
- Histology
  - Thickness : less than twice the surrounding mucosa
  - adenoma = **Flat adenomas (FAs)**



Histology of Flat elevated lesions

Gualco et al. Ann Diagn Pathol 2006; 10: 333

- 33 FELs less than 10 mm
  - 12 (36.4%) =adenoma
  - 10 = hyperplastic polyp
  - 1 = inflammatory polyp
- **Nonneoplastic lesions**
  - **Inflammatory polyps**
  - **Lymphoid nodules**
- **Flat adenomas**
- **Flat serrated lesions**

Flat adenoma

Flat adenoma : significance

- **Originally difficult diagnosis at endoscopy**
- **Frequency : 6.8% - 44.4% of all colorectal adenomas**
- **Flat adenomas at small size demonstrate a higher incidence of**
  - Advanced histology (villous aspect…)
  - High grade dysplasia
  - Submucosal cancer
  - Aneuploidy

Small flat colorectal Ca in the UK population (Tweede e a Colorectal Disease 2007)

1763 surgically resected Colorectal cancers

- 61 small cancers < 20 mm across
- **39/61 (64%) flat morphology**
- 20/61 (33%) polypoid cancers

Polyps

Definitions

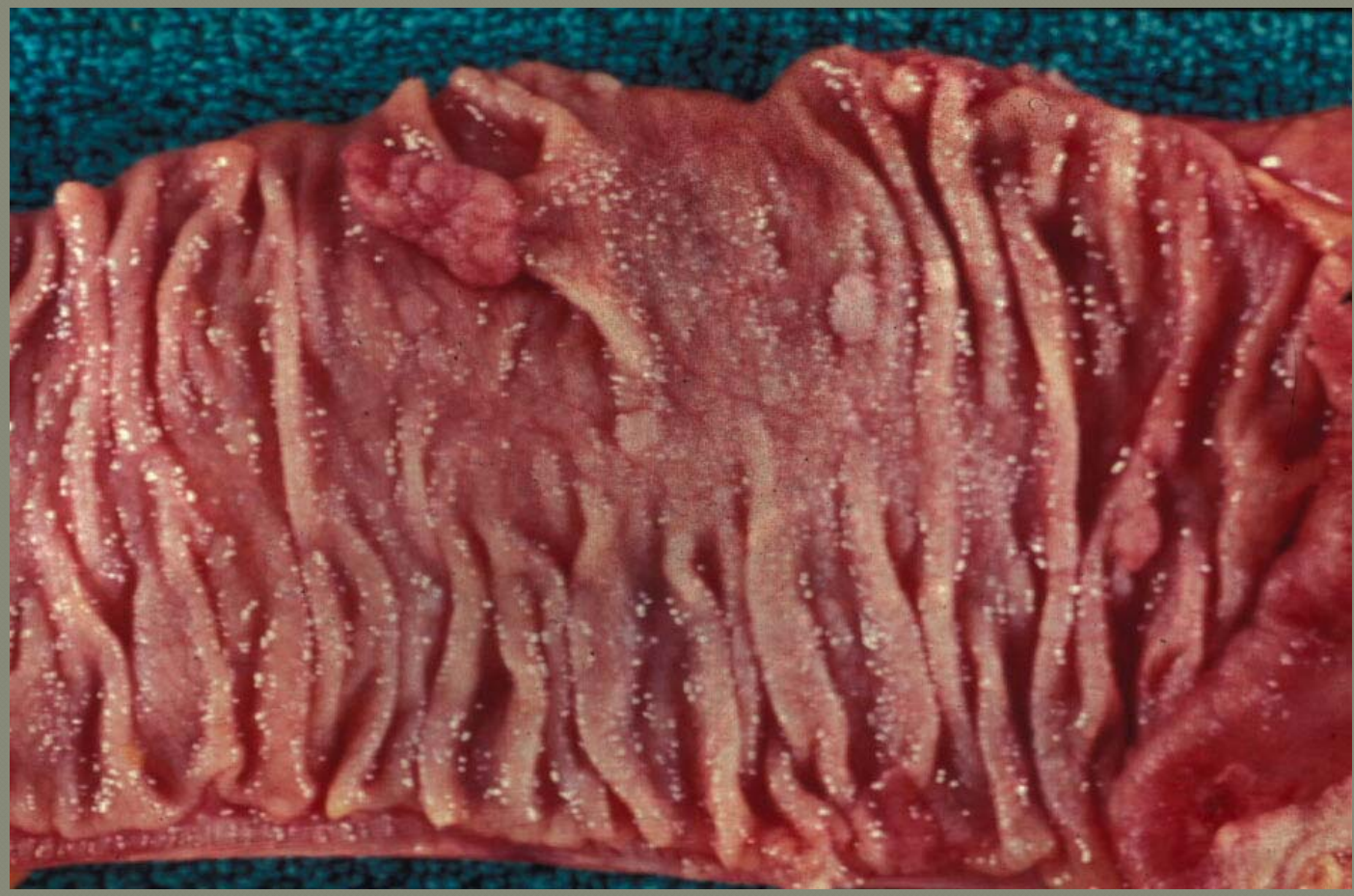
- Polyp : mass of tissue that arises from mucous membranes and protrudes into the lumen.

Macroscopy / precise nature unclear

Microscopy : neoplasm (= dysplasia); epithelial lesion

- Adenoma : circumscribed benign neoplasm composed of tubular and/or villous structures lined by dysplastic epithelium (WHO)
- Other

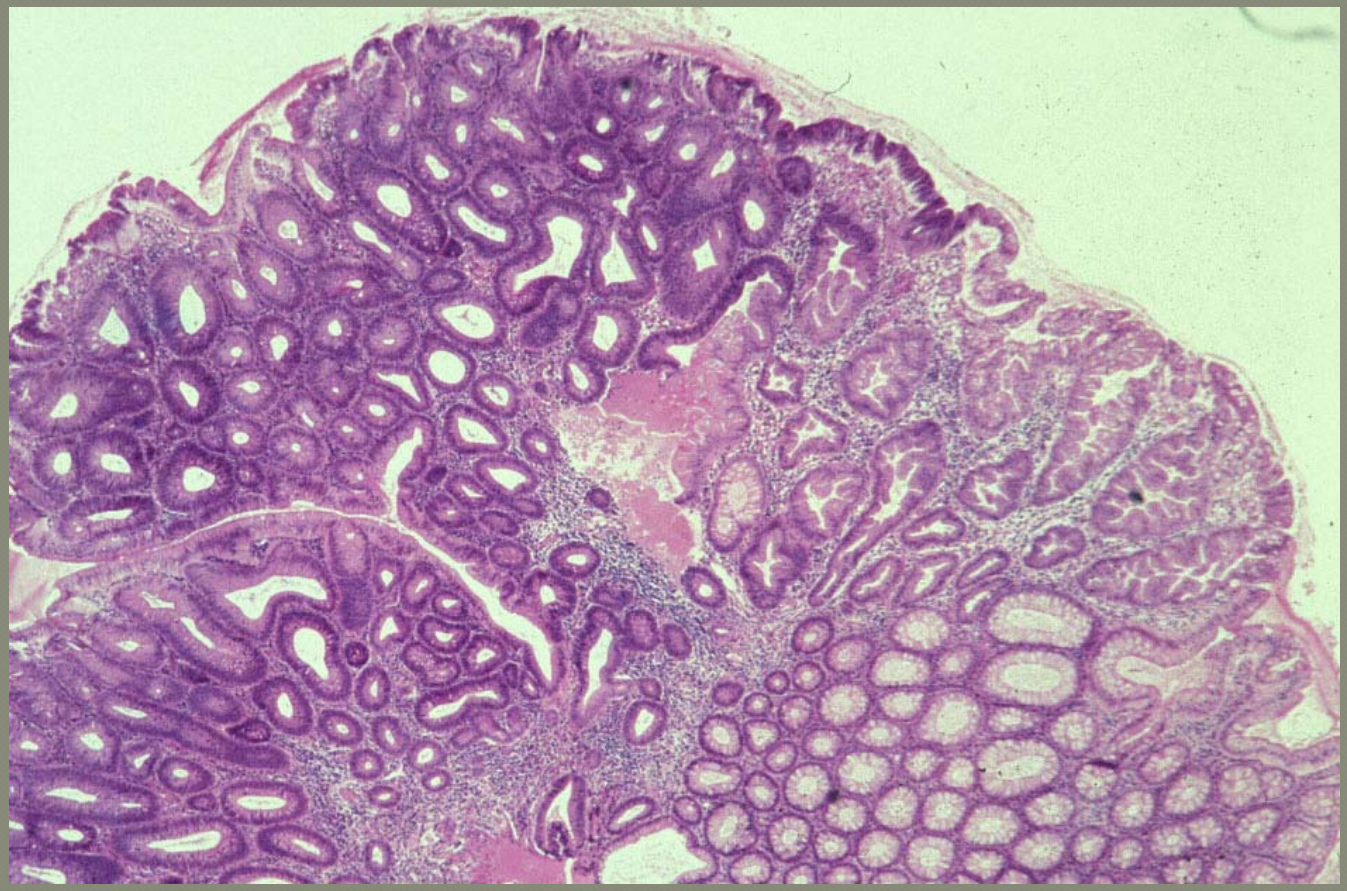
Pedunculated adenoma & Hyperplastic polyp



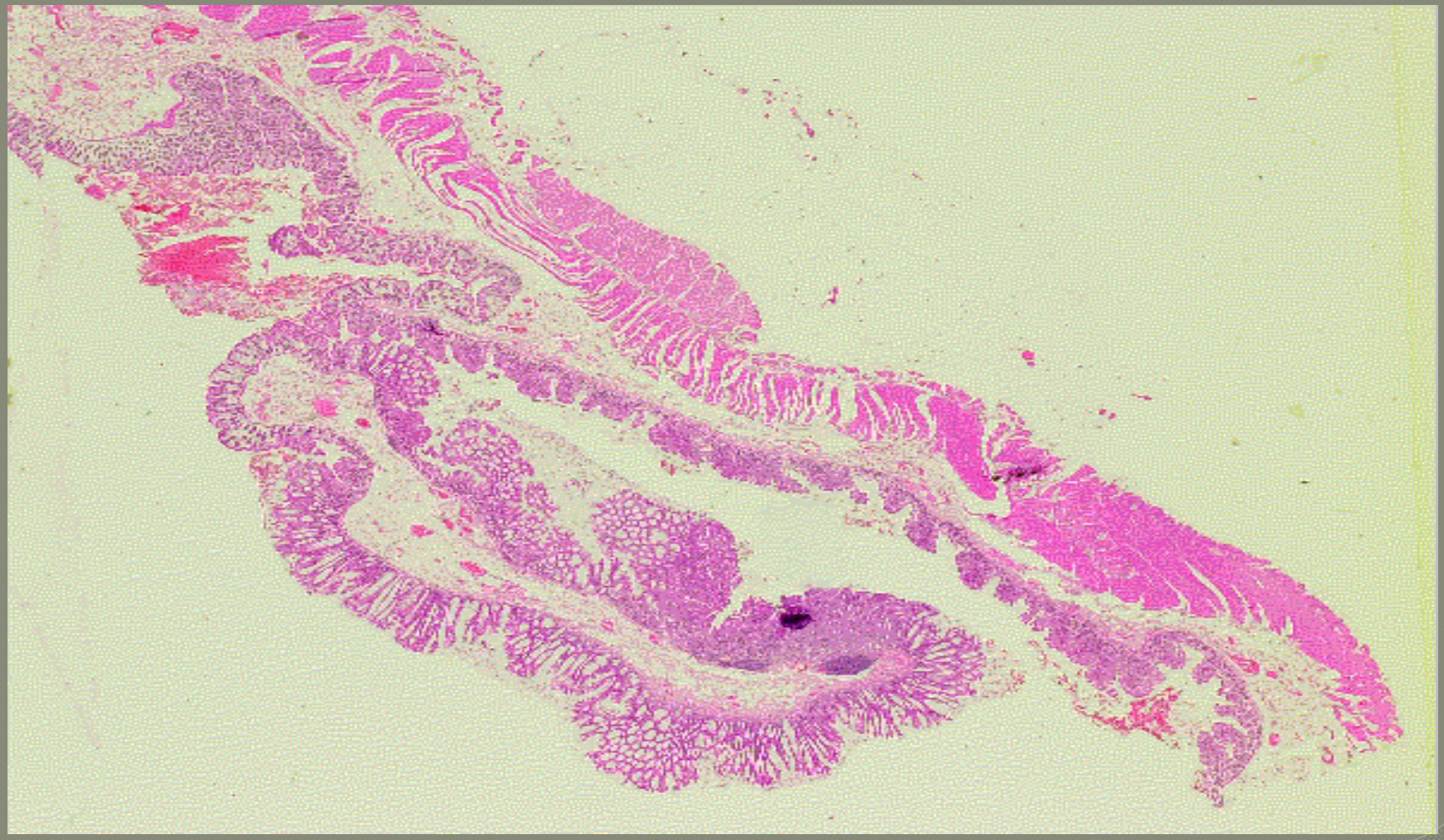
Colorectal cancer and precursor lesions

- Juvenile polyposis
  - Juvenile polyp
- Peutz-Jeghers
- Hyperplastic polyposis

Sessile serrated adenoma with dysplasia (B557607)



Serrated polyp with dysplasia and (intramucosal) carcinoma/ colon

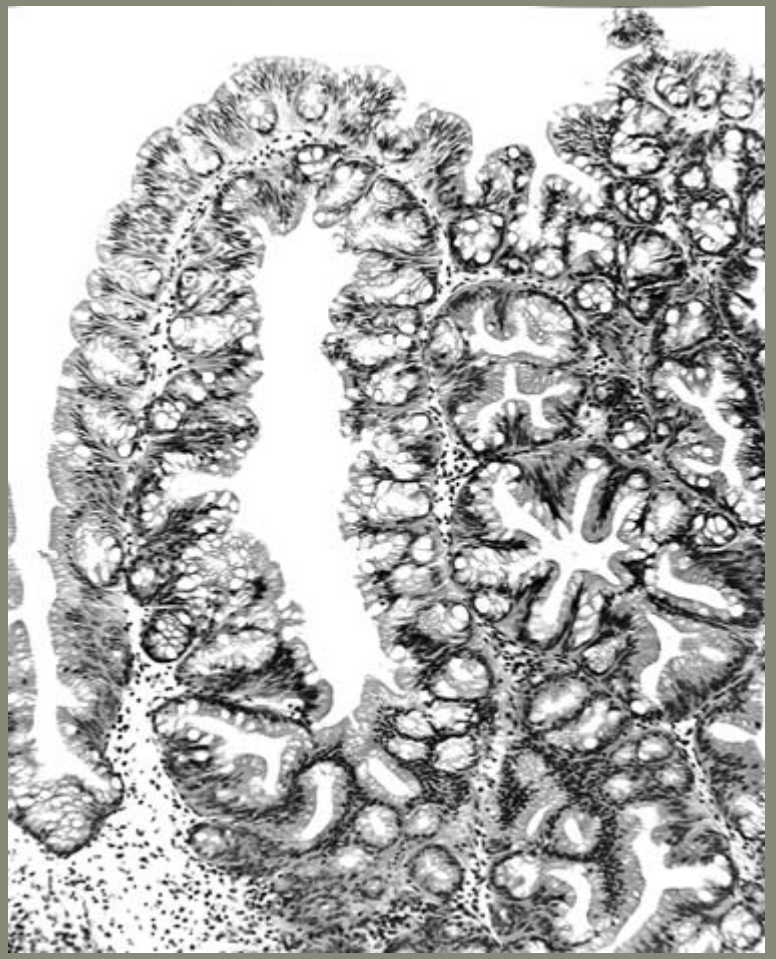


Microtubular adenoma (MTA)?

Rubio & Jamarillo Anticancer res 2013

Dysplastic epithelium arranged in closed rings (microtubules), with sideways-elongated outgrowth.

High frequency of Submucosal carcinom strongly suggests that MTA is an important alternative pathway in colorectal carcinogenesis.



IBD

Elevated lesions in IBD Terminology

Not related to colitis

- **Sporadic adenoma - adenoma-like lesion (ALM)**
- **Sessile serrated adenoma (?)**

Colitis associated

- **Flat dysplasia**
- **DALM**
- **Sessile serrated adenoma (non-dysplastic and dysplastic DALM?)**

Essentially two types OF LESIONS depending mainly on the presence of surrounding flat dysplasia

- Sporadic adenoma or adenoma-like lesion - mass (ALM) (in healthy, non-colitic areas)
(Neuman H et al WJG 2011)

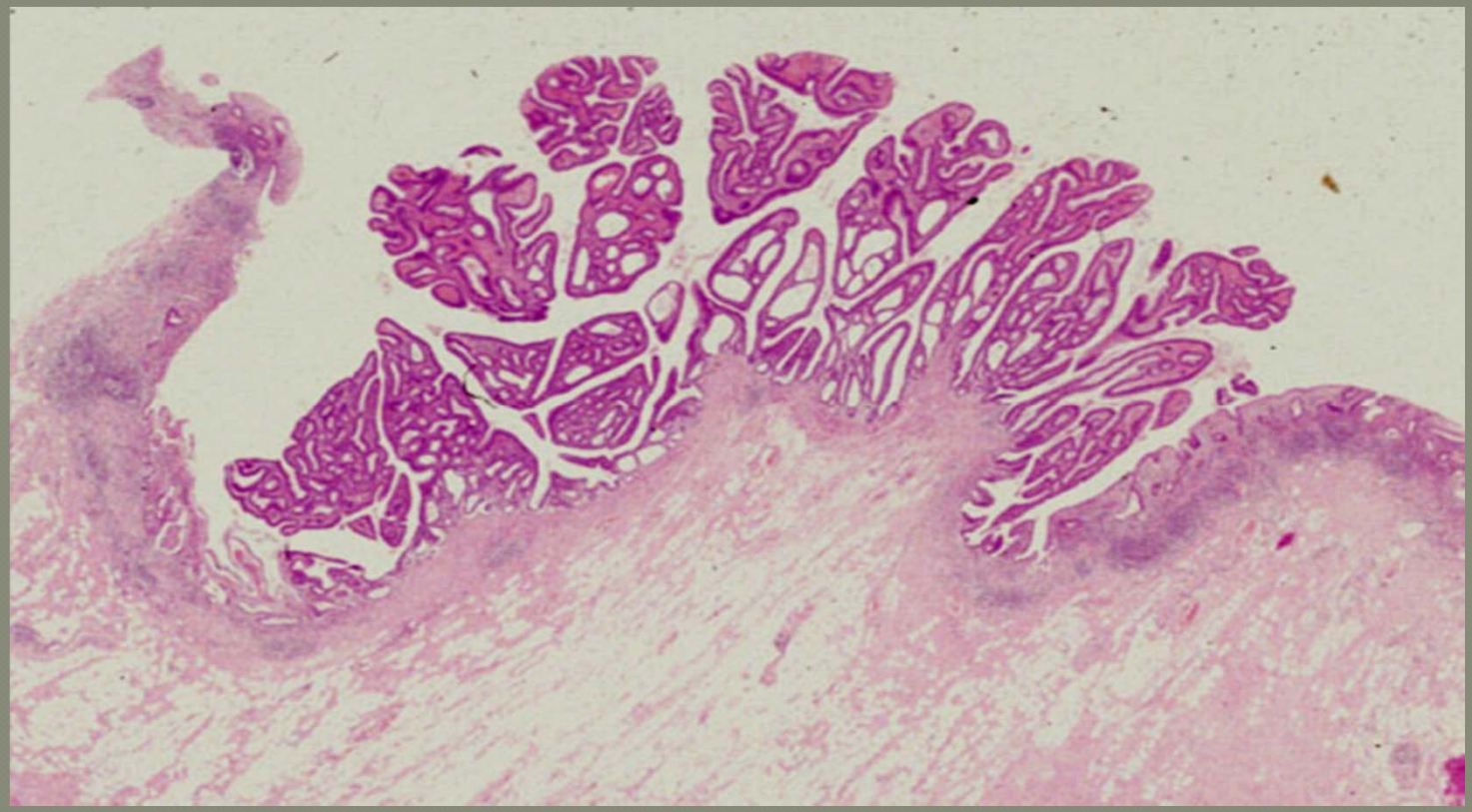
and

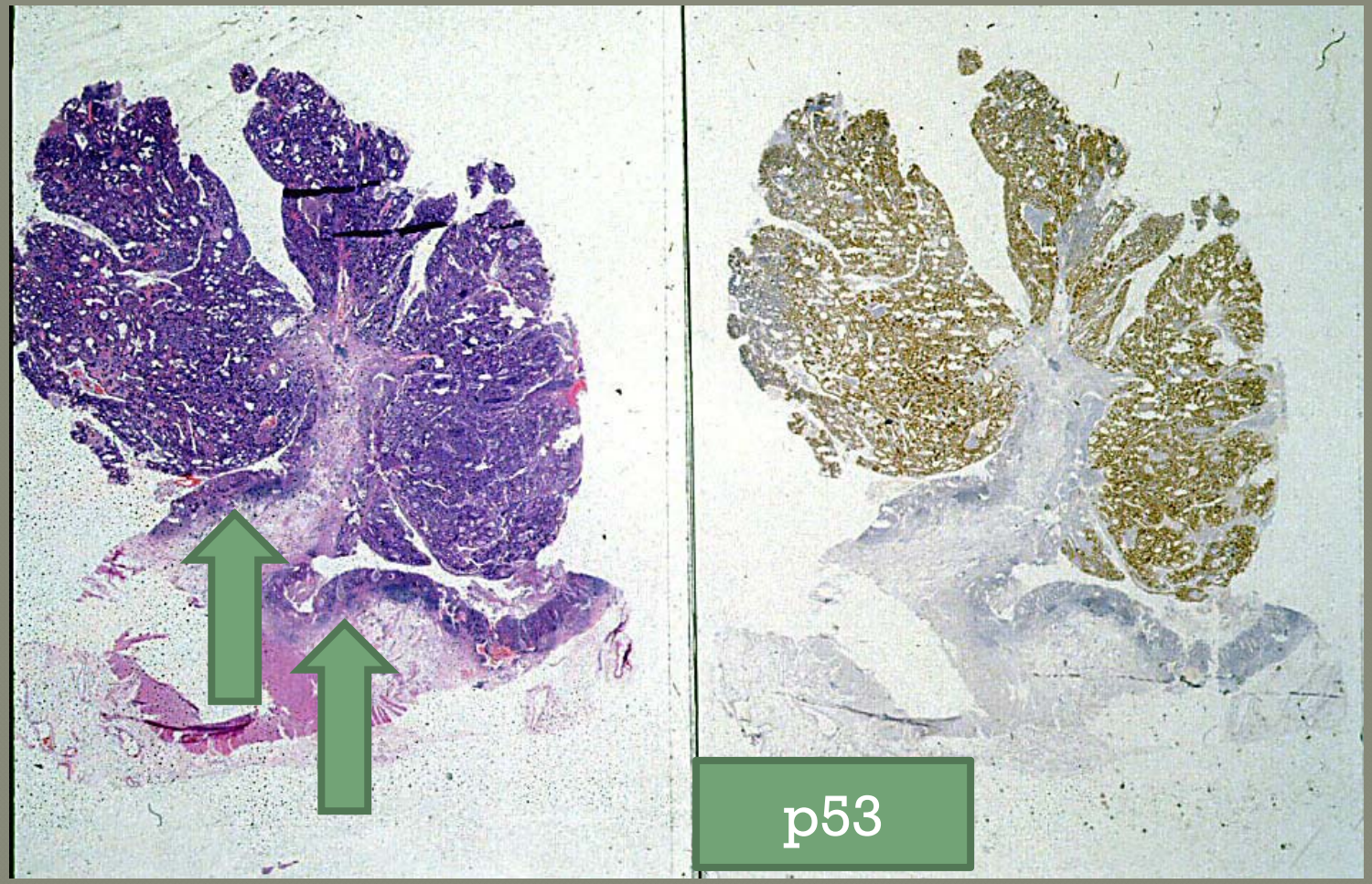
- Adenoma-like DALM (in colitic areas) (ALD) in US

- DALM : non-adenoma-like dysplasia (NALD) in US

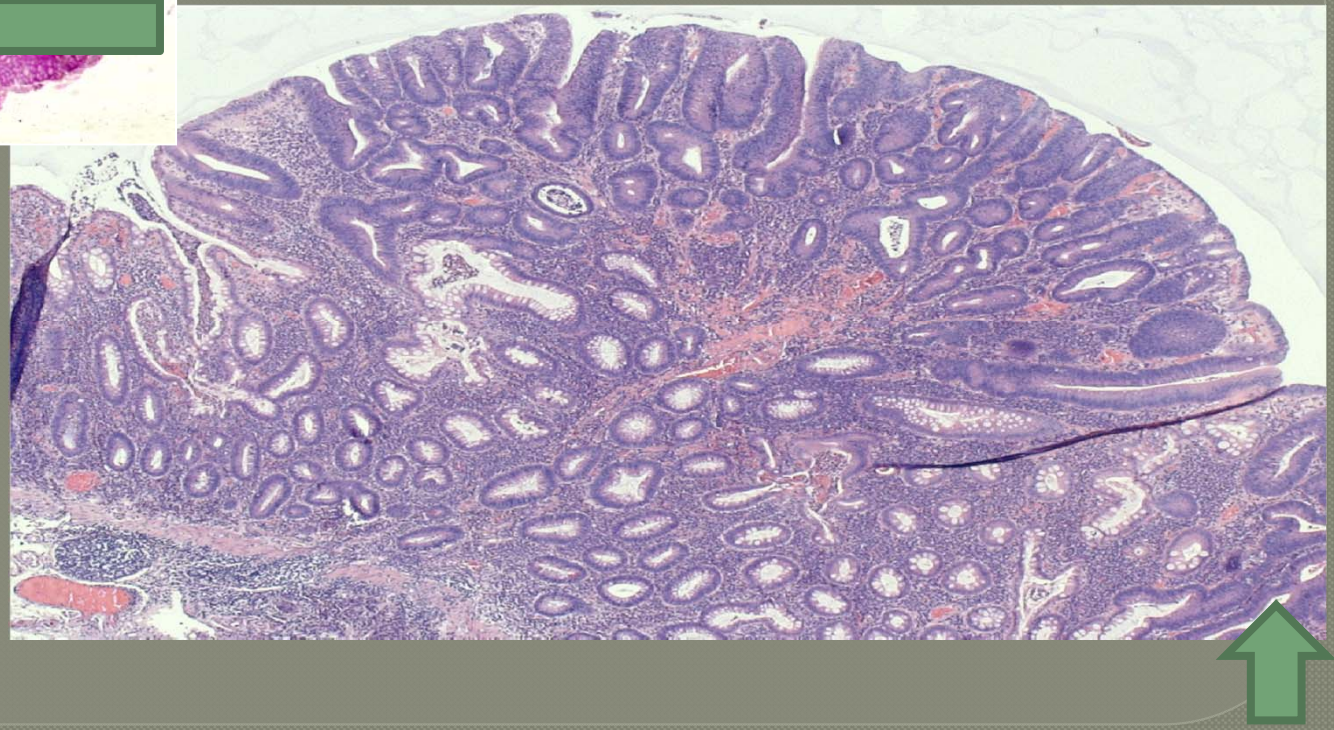
(Friedmann e.a. 2003, Farraye e.a; 2007, Thomas &Robinson 2007, Neurath et al 2011)

Adenoma-like Dalm (ALD)




p53

Non-adenoma-like DALM (NA



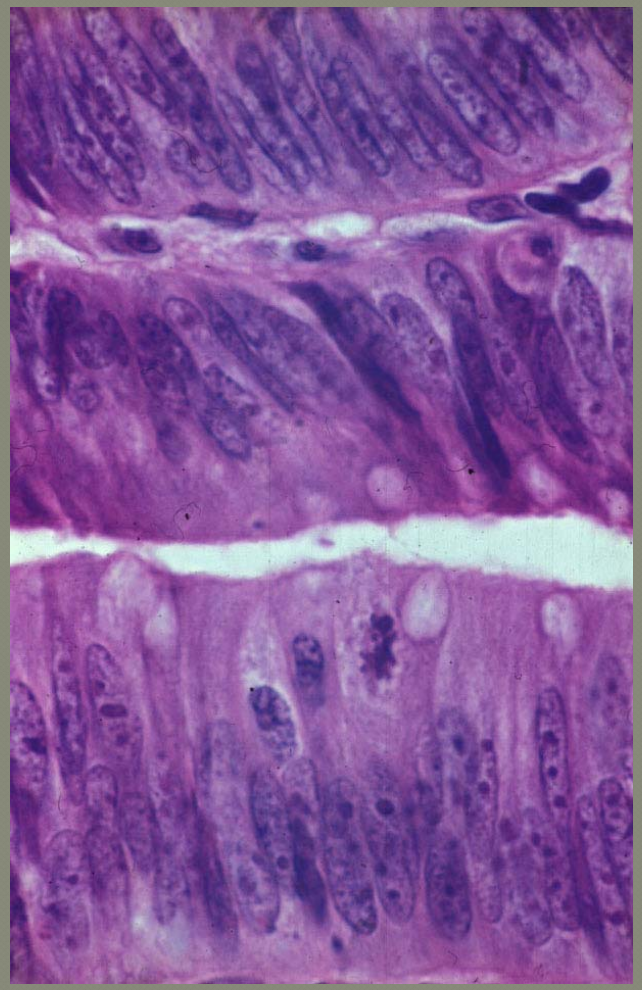
Definitions

- Dysplasia
  - Microscopy
    - structural changes of epithelium related to neoplasia
      - Definition : "atypical mucosa restricted to the epithelial layer" (Oehlert 1979; Grundmann 1982) Stomach
      - **Definition : Precise "unequivocal non-invasive (confined within the basement membrane) neoplastic transformation of the epithelium exclduding reactive changes (Riddell e.a. 1983) IBD**
    - **Abnormalities of**
      - **Architecture**
      - **Cytology including differentiation**

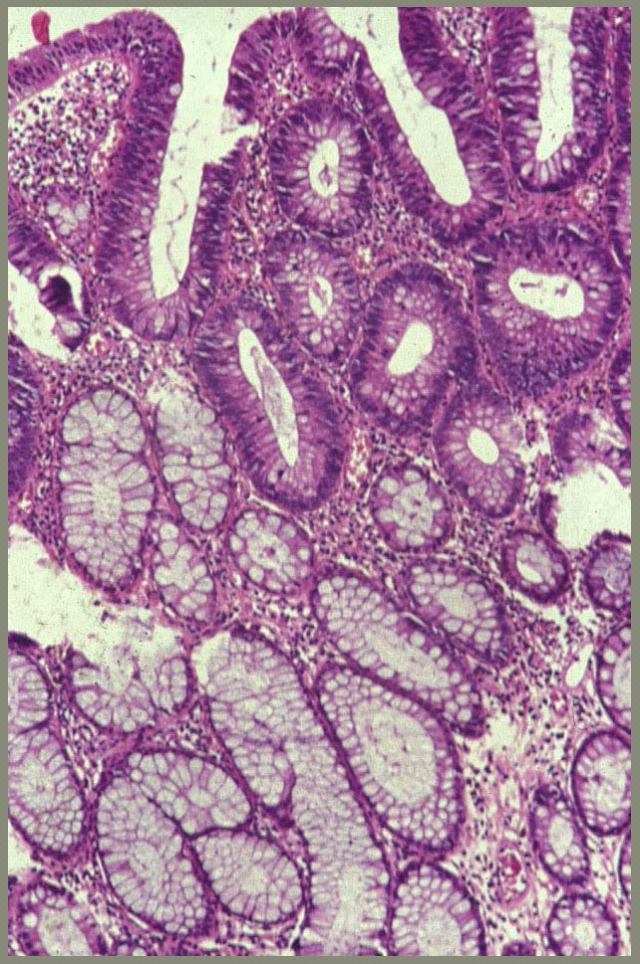
Intraepithelial neoplasia Microscopy

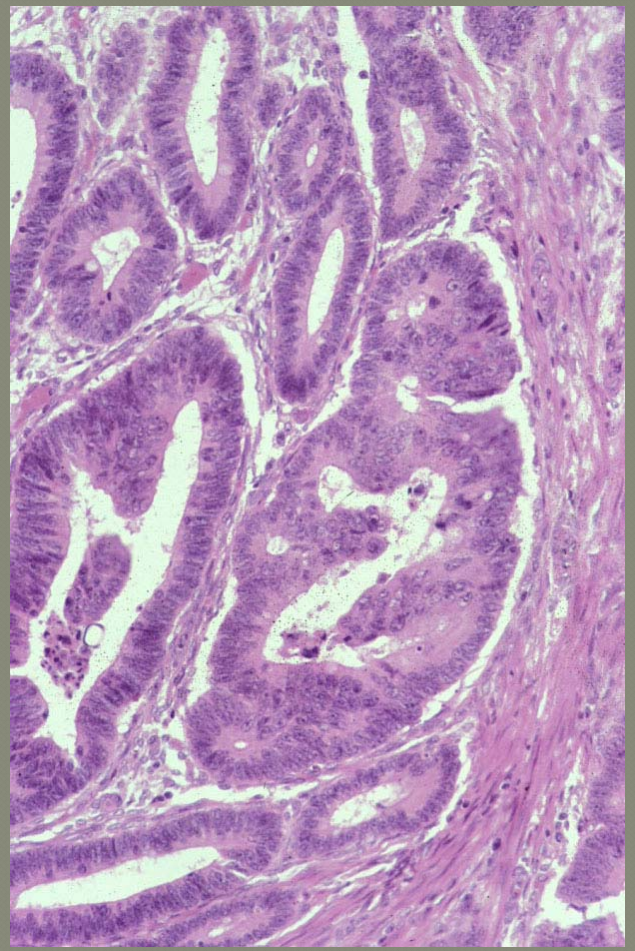
- **Cytology**
  - **Nuclear enlargement**
  - **Elongation**
  - **Relocation (farther from basement membrane)**
  - **Hyperchromatism**
  - **Polarity**
- **Differentiation**
  - **Mucin secretion**
  - **Hyperchromatic – basophilic cytoplasm**
- **Architecture**
  - **Crowding**
  - **budding**

Intraepithelial neoplasia
Microscopy : cytology



Intraepithelial neoplasia Microscopy : architecture





Intraepithelial neoplasia
Malignancy

- Japanese viewpoint
  - Cytology (rounded – enlarged nuclei)
  - Architecture (budding)
- Western viewpoint
  - Cribriform – solid patterns = High-grade dysplasia - **intraepithelial carcinoma** or non-invasive carcinoma
  - US : ?
  - Invasion of the lamina propria of the mucosa through the basement membrane = **intramucosal carcinoma**

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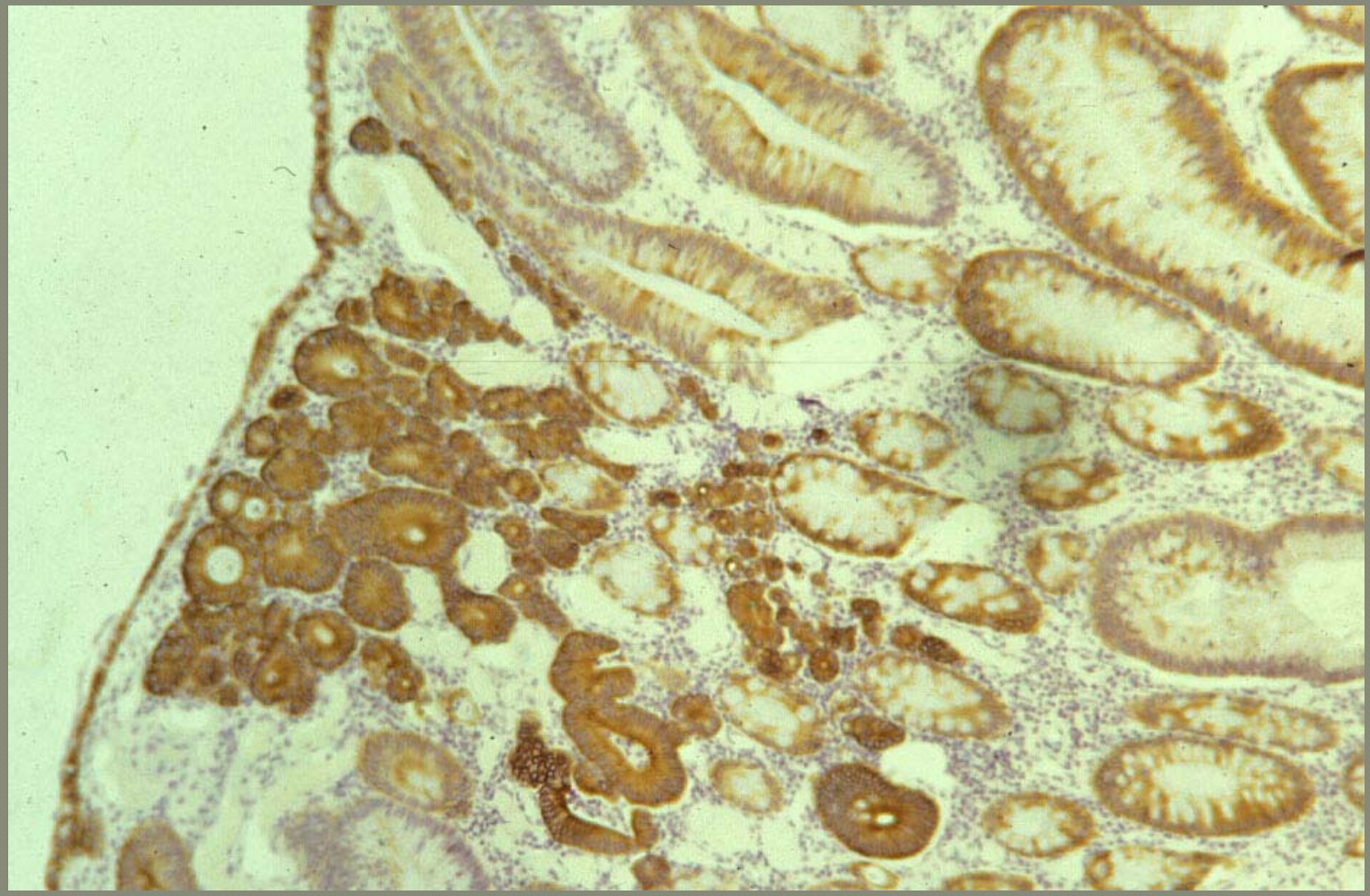


Colorectal adenomas containing invasive adenocarcinoma that extends through the muscularis mucosae into the submucosa have been defined as "malignant polyps."

This term encompasses cases in which the entire polyp head is replaced by carcinoma and adenomas with focal malignancy

But the definition excludes adenomas with high-grade dysplasia (intraepithelial carcinoma) or intramucosal carcinoma (invasive carcinoma limited to the lamina propria or invading no deeper than the muscularis mucosae) because these polyps possess negligible biologic potential for metastasis.

Arch Pathol Lab Med. 2009

Intraepithelial neoplasia & Malignancy COLON

- The mucosa of the colon lacks lymphatics
- Therefore "intramucosal cancer" will not disseminate

Digestive tract Colon

- High-grade Intraepithelial neoplasia (or intraepithelial carcinoma) = pTis (in situ cancer)
- High-grade Intraepithelial neoplasia (or intraepithelial carcinoma) and intramucosal carcinoma = pTis (in situ cancer)

Colorectal cancer and the pathologist

- Diagnostic biopsies
- Surgical specimens

- Polypectomy
- Transanal Endoscopic Microsurgery (TEM)
  - Surgical « conservative » technique for small rectal lesions, applied more commonly because of less morbidity.

Colorectal cancer and the pathologist

- Polypectomy
- Transanal Endoscopic Microsurgery (TEM)

RISK ASSESSMENT FOR RESIDUAL TUMOR

Colorectal cancer and the pathologist

- **Risk assessment depends**
  - **Upon the patient**
  - **Upon the specimen**

Young active male (?)

Elderly person

Elderly

sexually active male

What about the specimen?

- Handling the specimen
- Histology

Handling the specimen

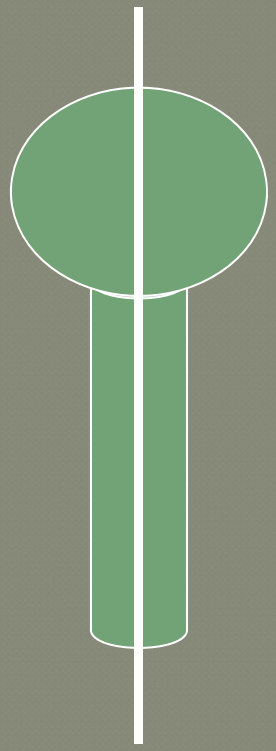
- Orientation
- Cutting

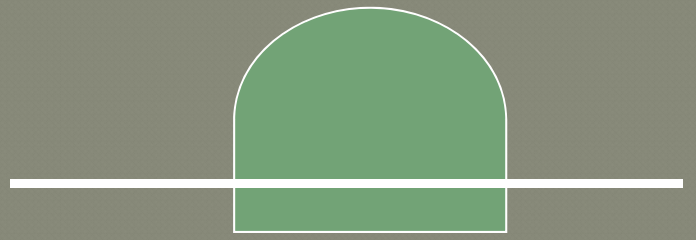
Orientation

needle

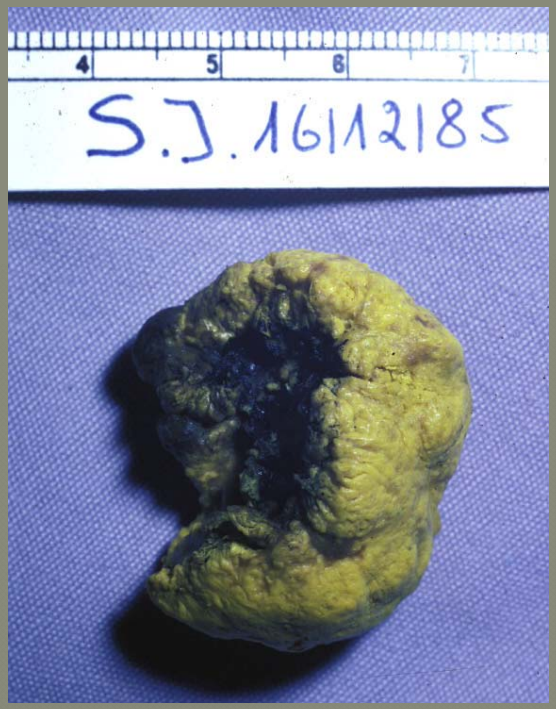
Stalked lesion

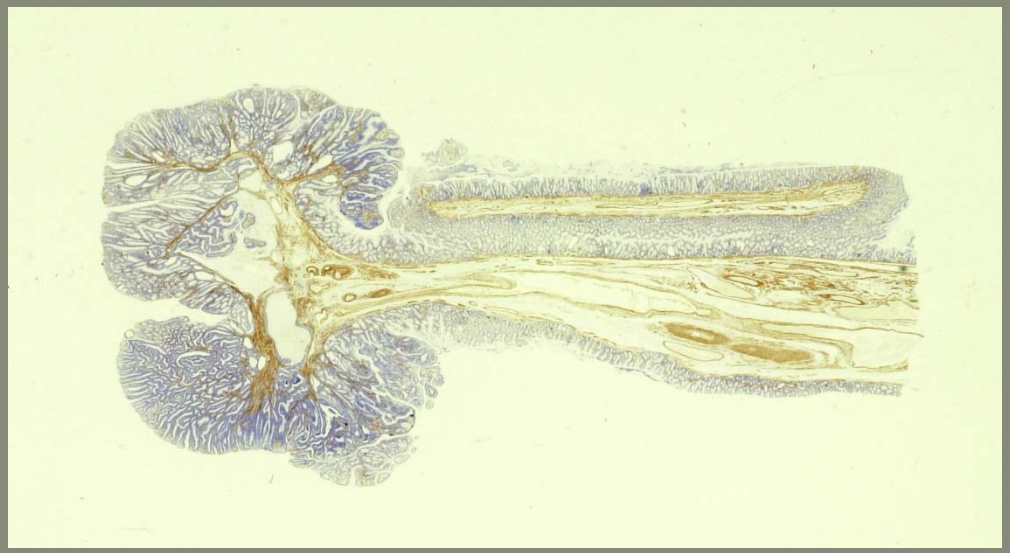
Sessile lesion



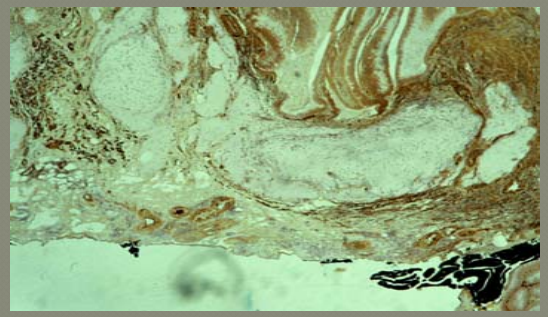


Orientation

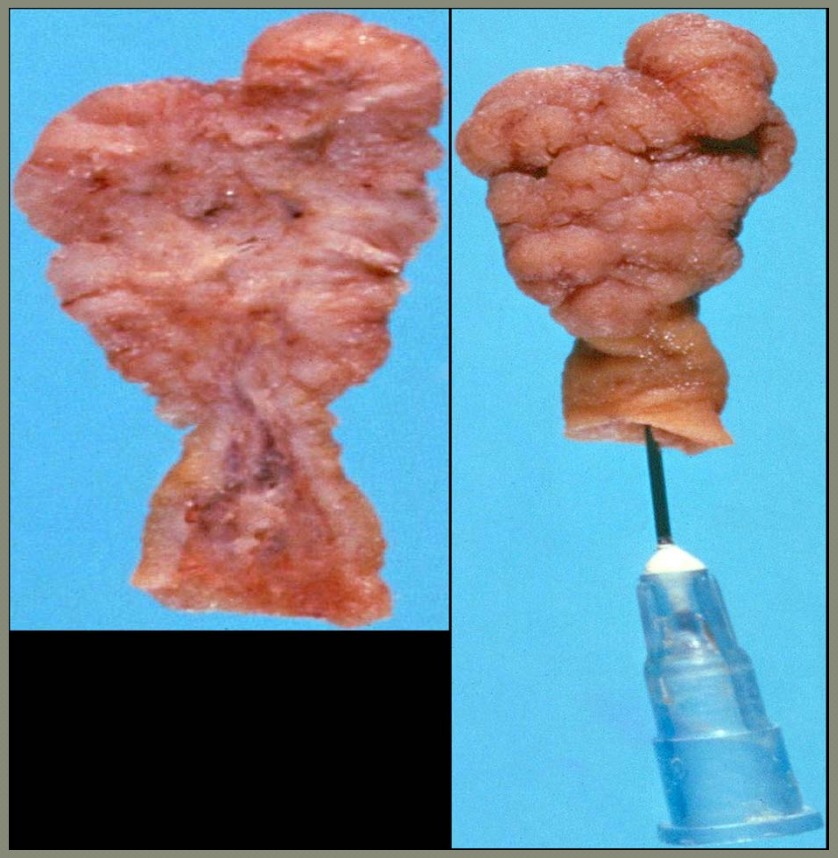


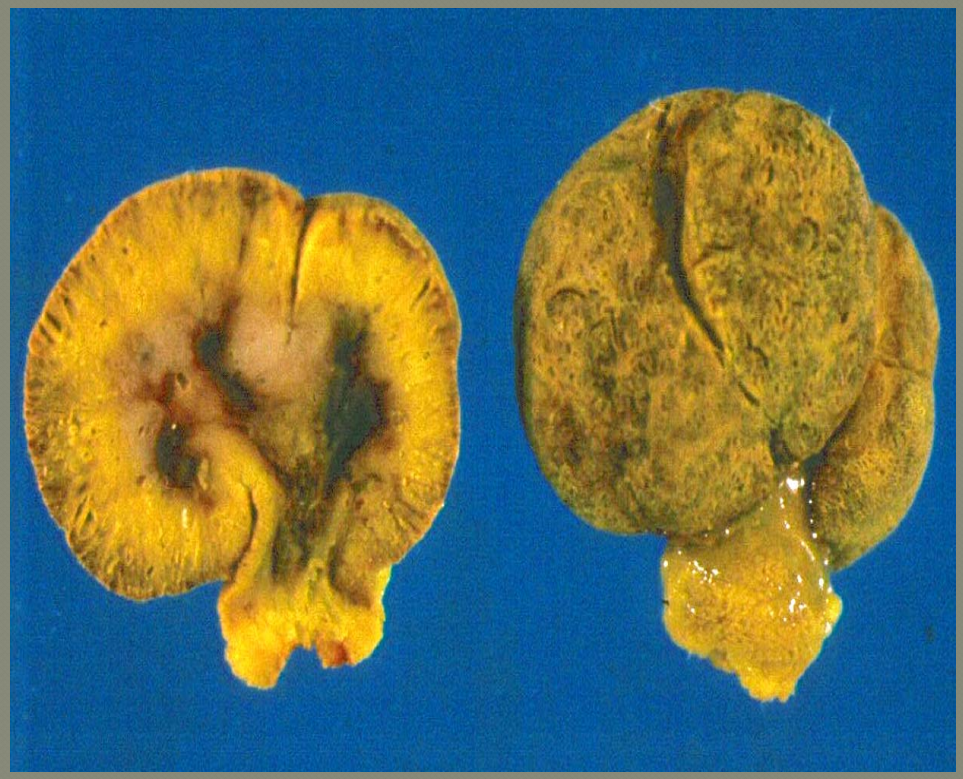


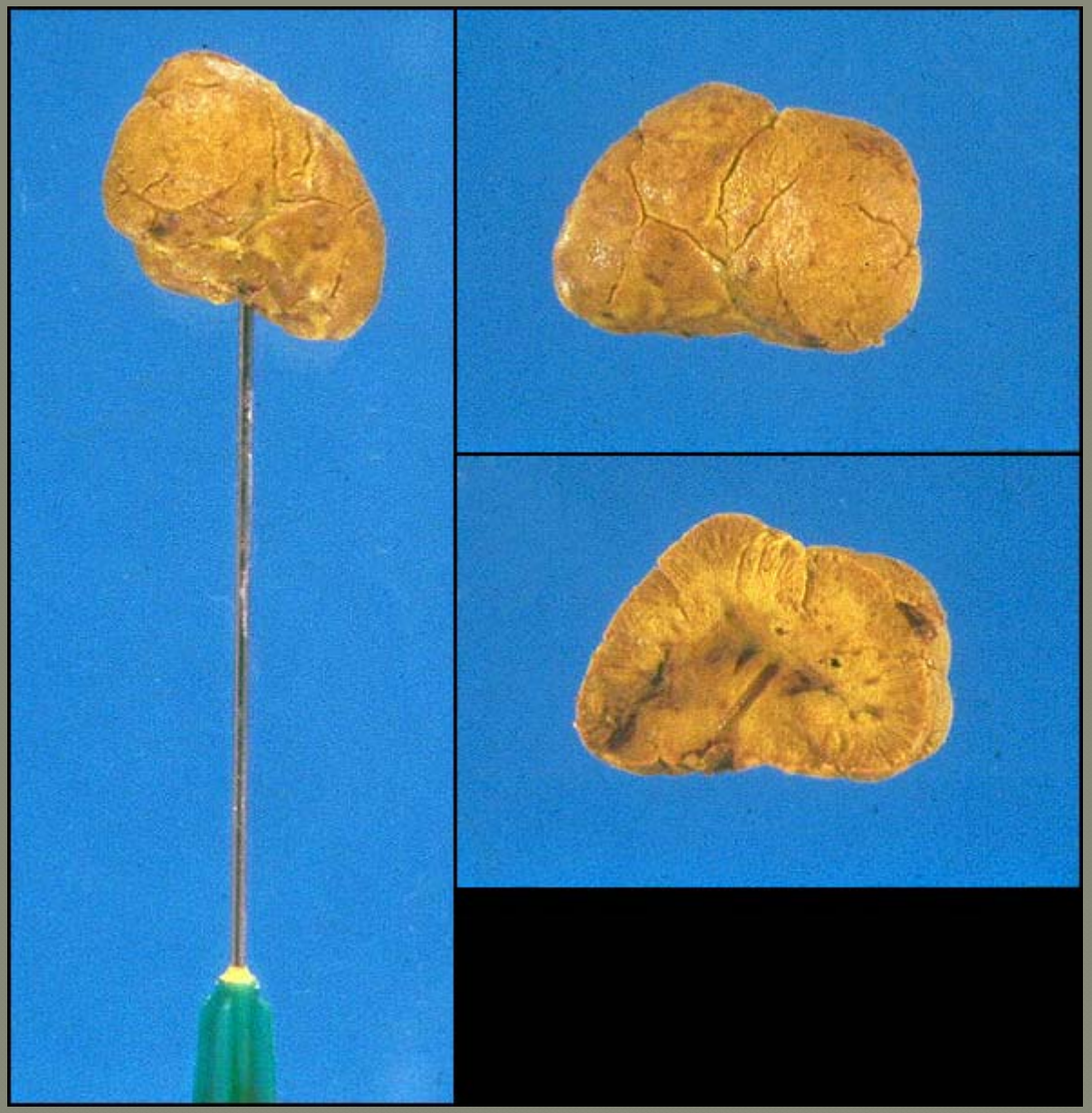
Stalked lesion



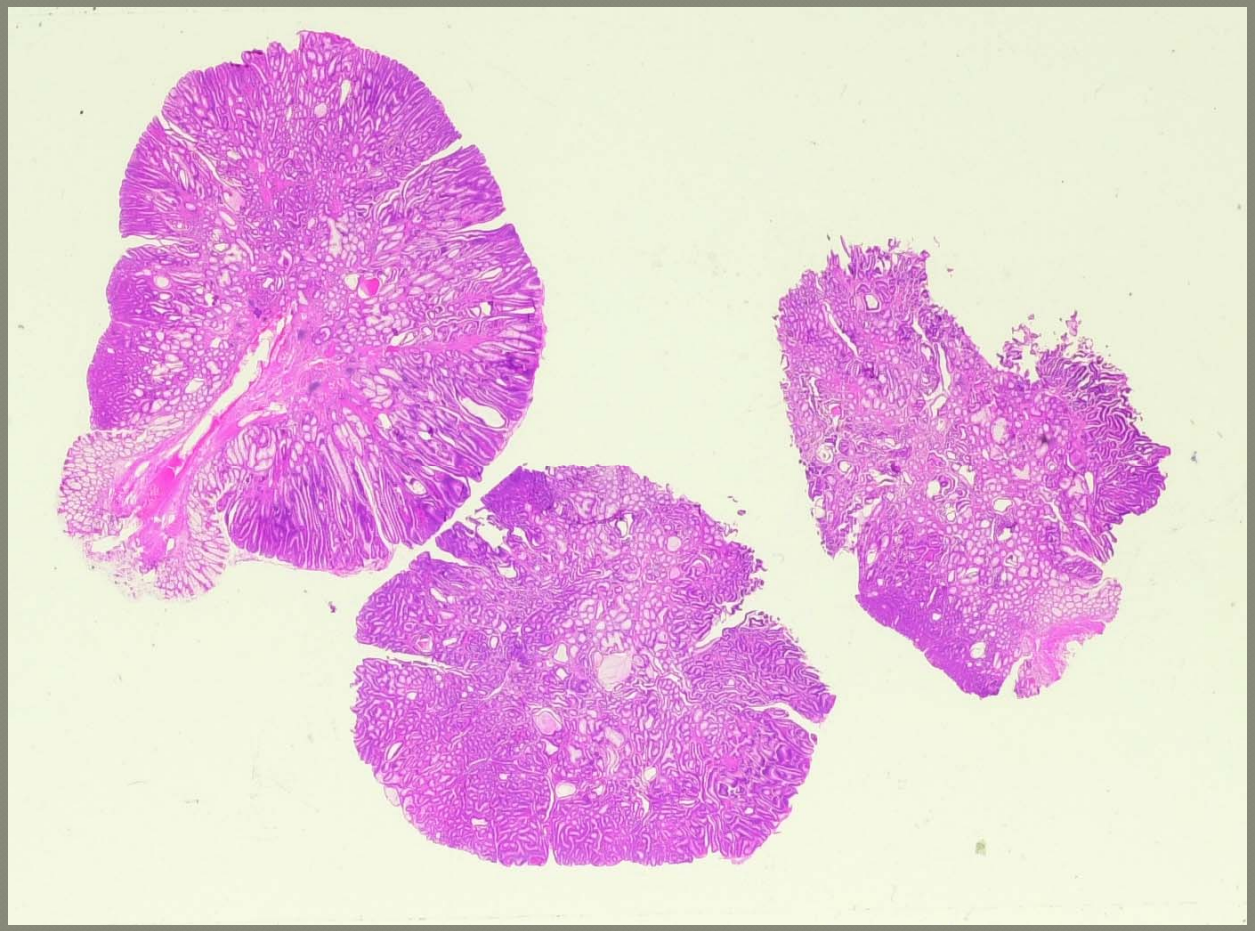
Sessile lesion



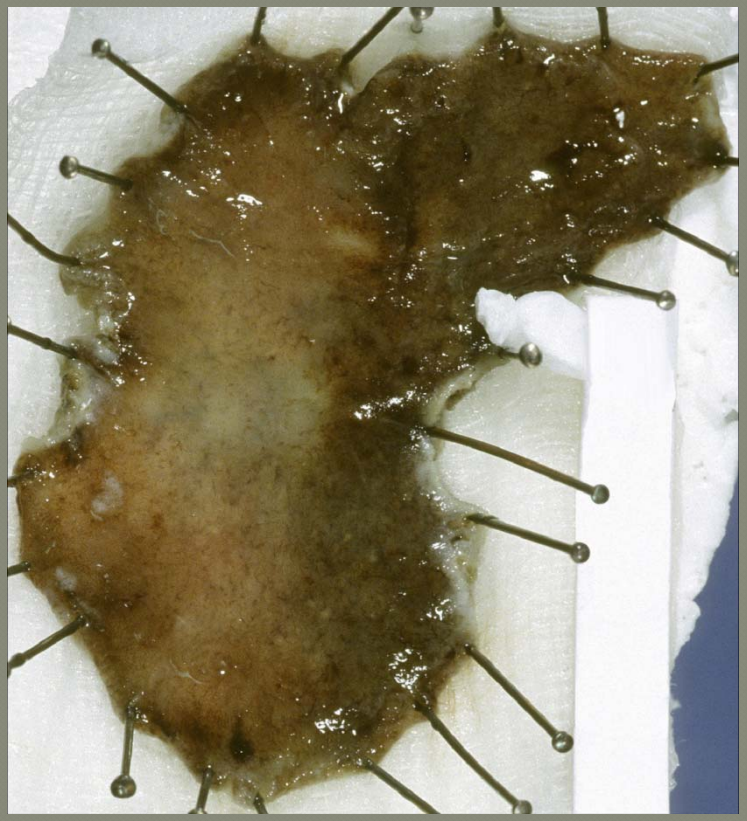


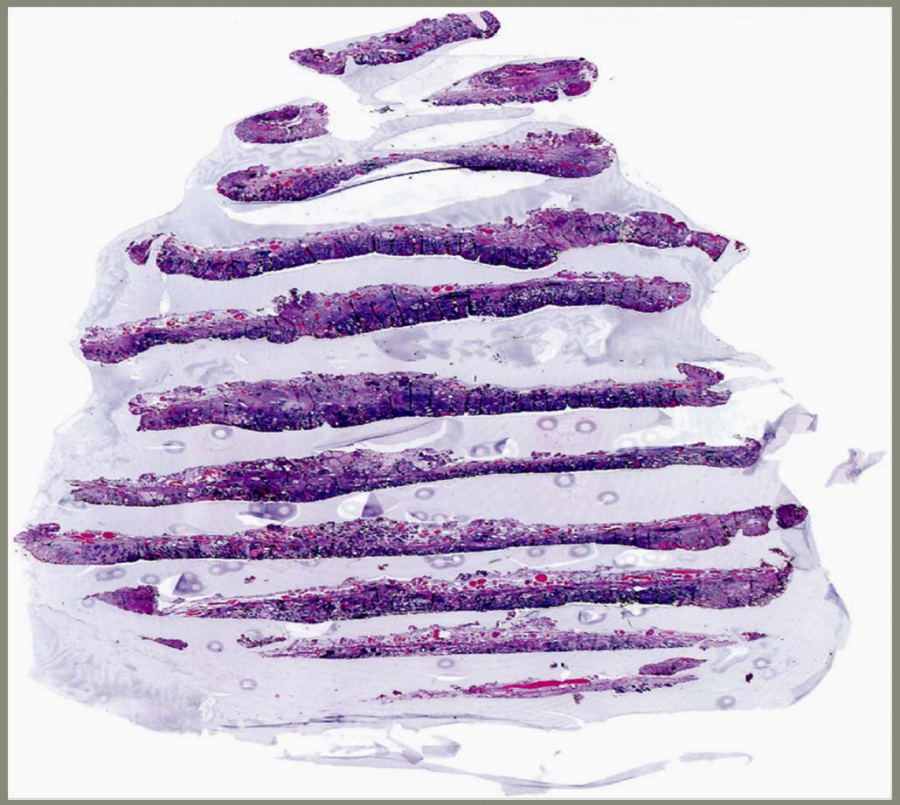


Cutting



TEM





Histology

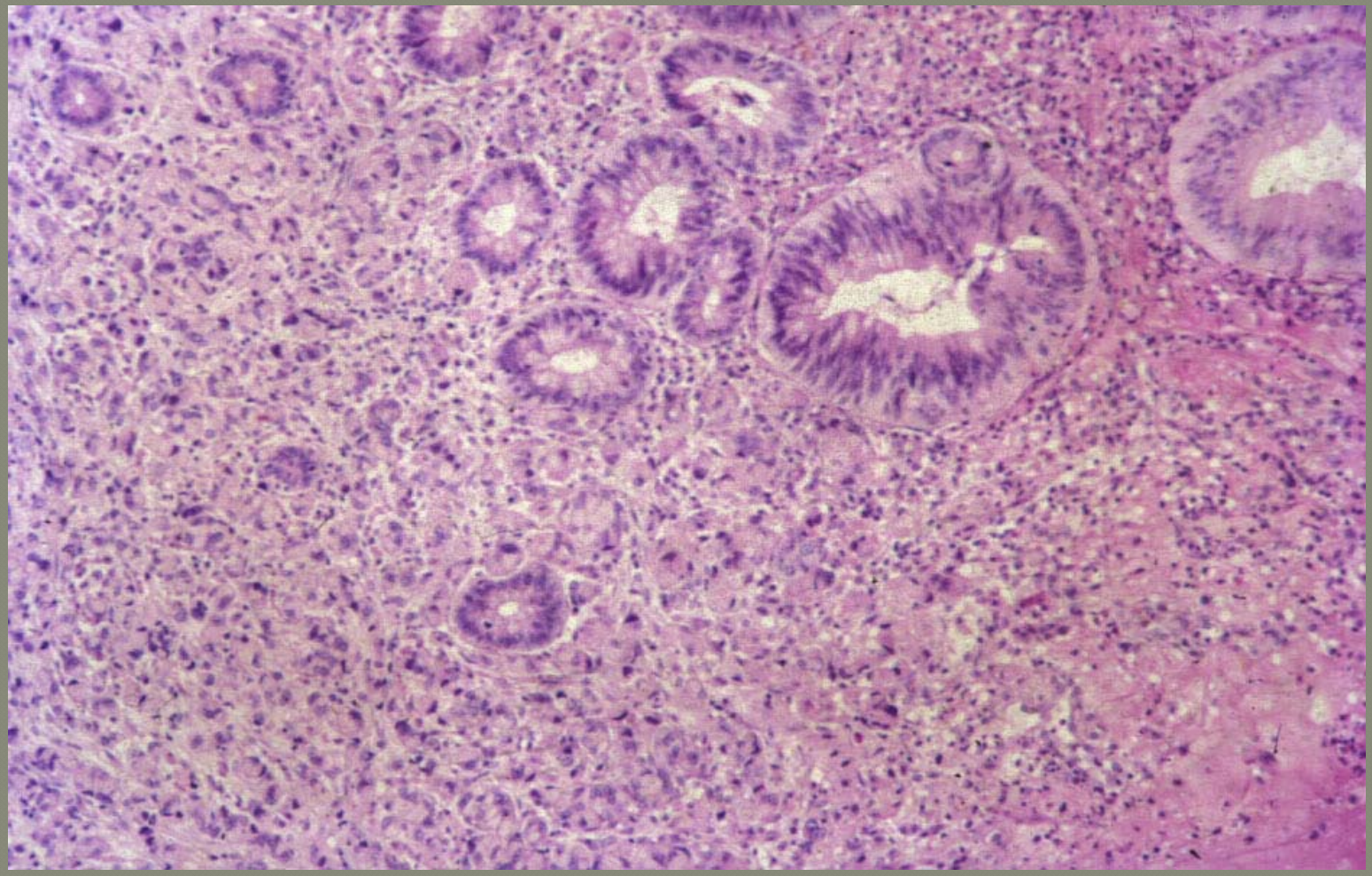
Risk factors and adverse outcome

Author	Number of cases	Adverse outcome
Colacchio 1981	24	6 (LN)
Lipper 1983	51	2 (1 residual)
Haggitt 1985	64	8 (4=LN)
Cranley 1986	38	10 (3=LN)
Richards 1987	80	10 (6=LN)
Kikuchi 1995	182	21 (13=LN)
Cooper 1995	140	16 (13=LN)
Ueno 2004	292	50 (33=LN)

Risk factors for residual tumor

- ***Tumor grade - Poor differentiation***
- ***Vascular invasion***
- ***Positive section margin***
- ***Budding (solitary cells or small groups of cells < 5)***
- ***Haggitt's classification : width and depth of submucosal invasion***

450143
Poorly differentiated CRC



By convention, signet-ring cell carcinomas, small cell carcinomas, and undifferentiated carcinomas are high grade

High grade: Less than 50% gland formation

High grade (Grade III) defined by the least differentiated area

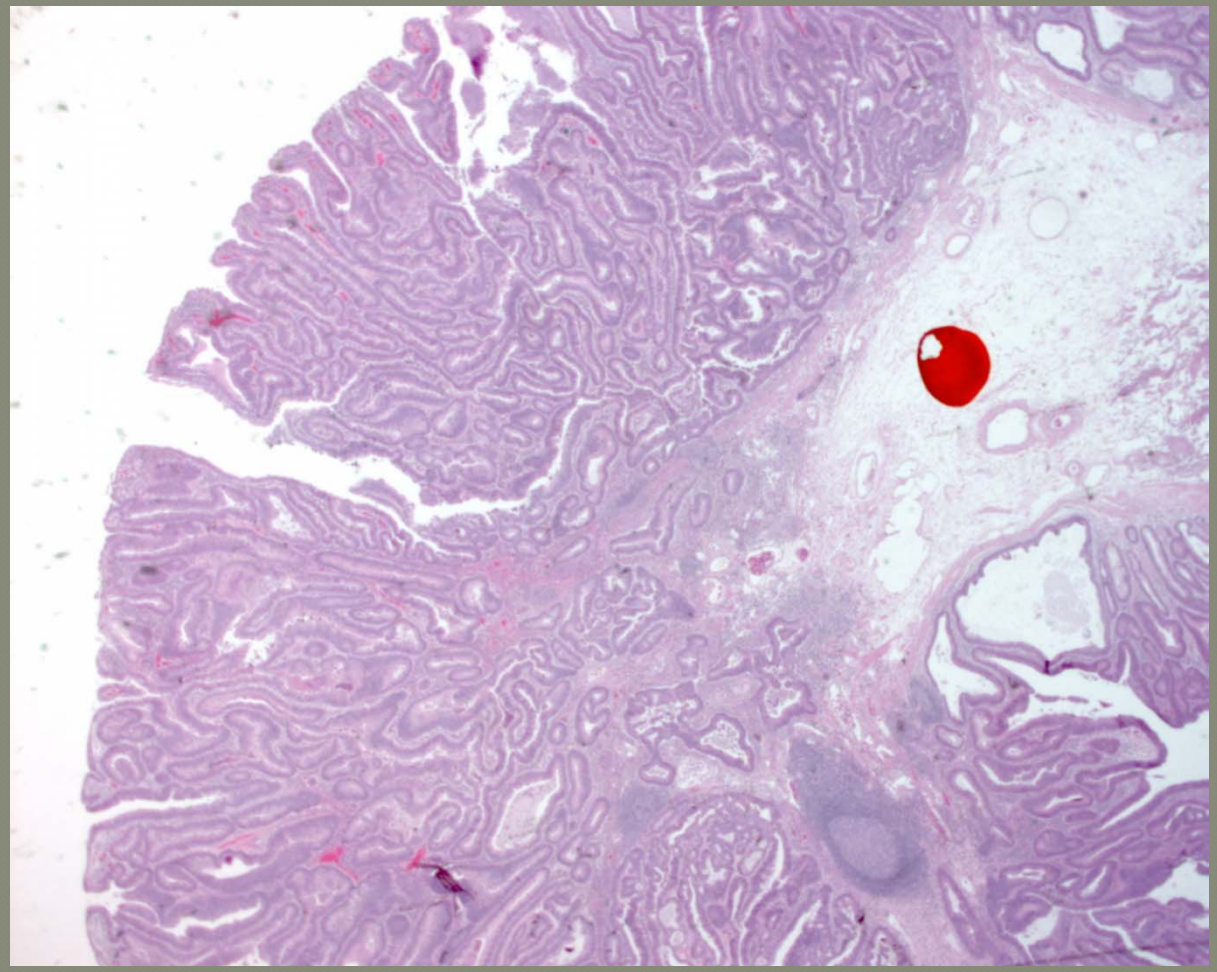
1	II	Unassessable	Rectum Subtotal colectomy	Residual carcinoma
2	II	0	Sigmoid colon Subtotal colectomy	Residual cammoma
3	II	0	Rectum Subtotal colectomy	Residual carcinoma
4	Ill	0	Rectum Subtotal colectomy	Residual carcinoma
5	tl	0	Rectum Subtotal colectomy	Residual carcinoma
6	**II**	**< 2**	**Rectum Subtotal colectomy**	Residual carcinoma
7	il	0	Rectum Subtotal colectomy	No residual carcinoma, metastasis, died of disease
8	II	0	Rectum Local radiation	Recurrence, metastasis, died of disease
9	Ill	0	Rectum Local radiation	Metastasis, died of disease
10	**II**	**< 2**	**Rectum Local radiation**	Metastasis, died of disease
11	ill	0	Sigmoid colon Subtotal colectomy	No
12	II	0	Sigmoid colon Subtotal colectomy	No
13	III	0	Rectum Subtotal colectomy	No
14	II	<2	Colon Subtotal colectomy	No
15	I	0	Rectum Subtotal colectomy	No
16	I	0	Colon Subtotal colectomy	No
17	II	0	Sigmoid colon Subtotal colectomy	No
18	II	< 2	Rectum Subtotal colectomy	No
19	II	< 2	Sigmoid colon Subtotal colectomy	No
20	III	> 2	Rectum Subtotal colectomy	No
21	III	> 2	Sigmoid colon Subtotal colectomy	No
22	I	< 2	Sigmoid colon Subtotal colectomy	No
23	II	Unassessable	Sigmoid colon Subtotal colectomy	No
24	I	Unassessable	Sigmoid colon Subtotal colectomy	No
25	II	<2	Rectum Local radiation	No
26	Ill	> 2	Rectum Local radiation	No
27	I	< 2	Sigmoid colon Polypectomy only	No
28	III	< 2	Rectum Polypectomy only	No
29	I	0	Sigmoid colon Polypectomy only	No
30	I	0	Colon Polypectomy only	No

-Patient nr
-Tumor grade
- Section margin
- Treatment

Volk e.a.
Gastroenterology 109; 1995

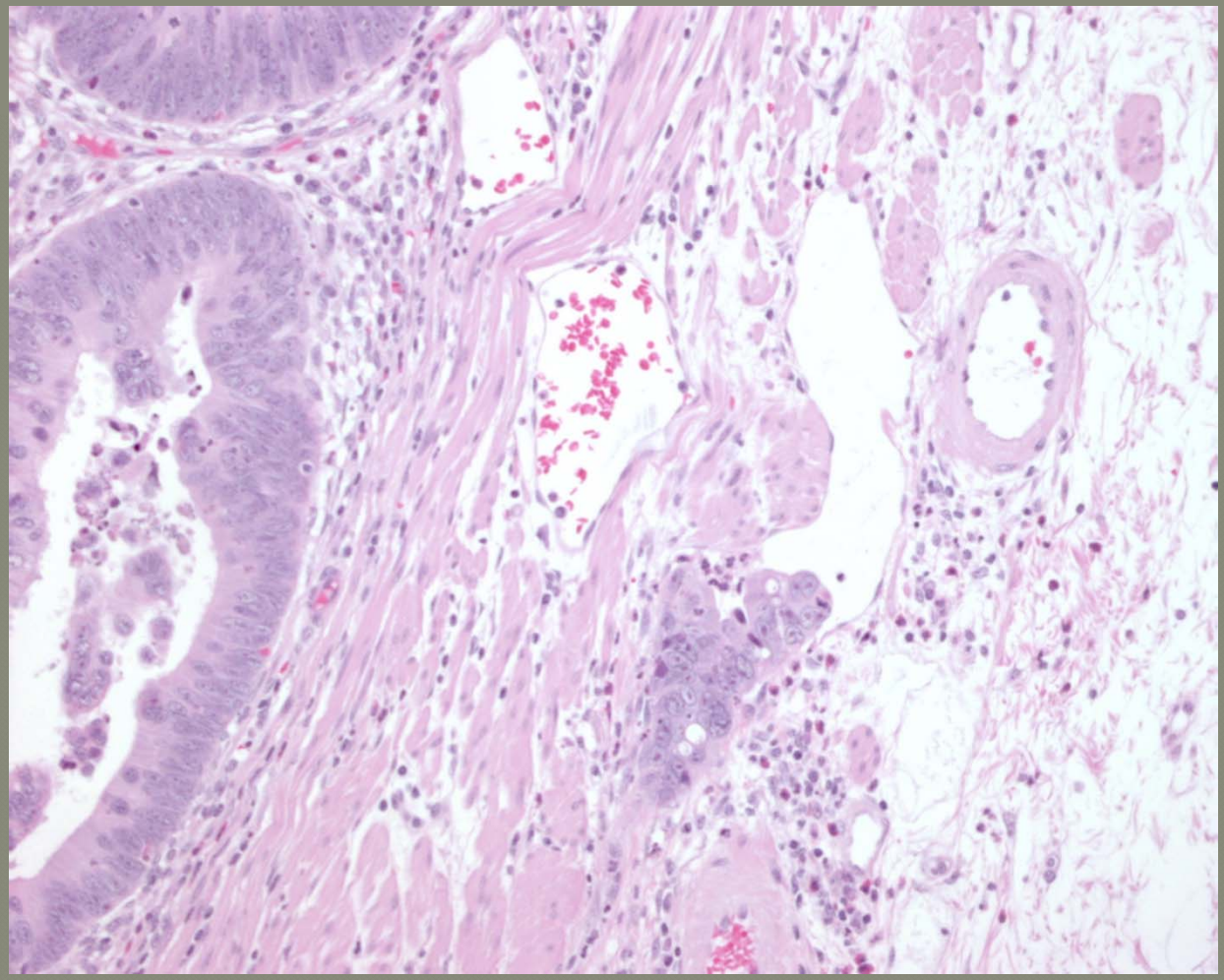
- Male Patient
- °1948
- Red blood loss per anum
- Polypectomy

Vascular invasion

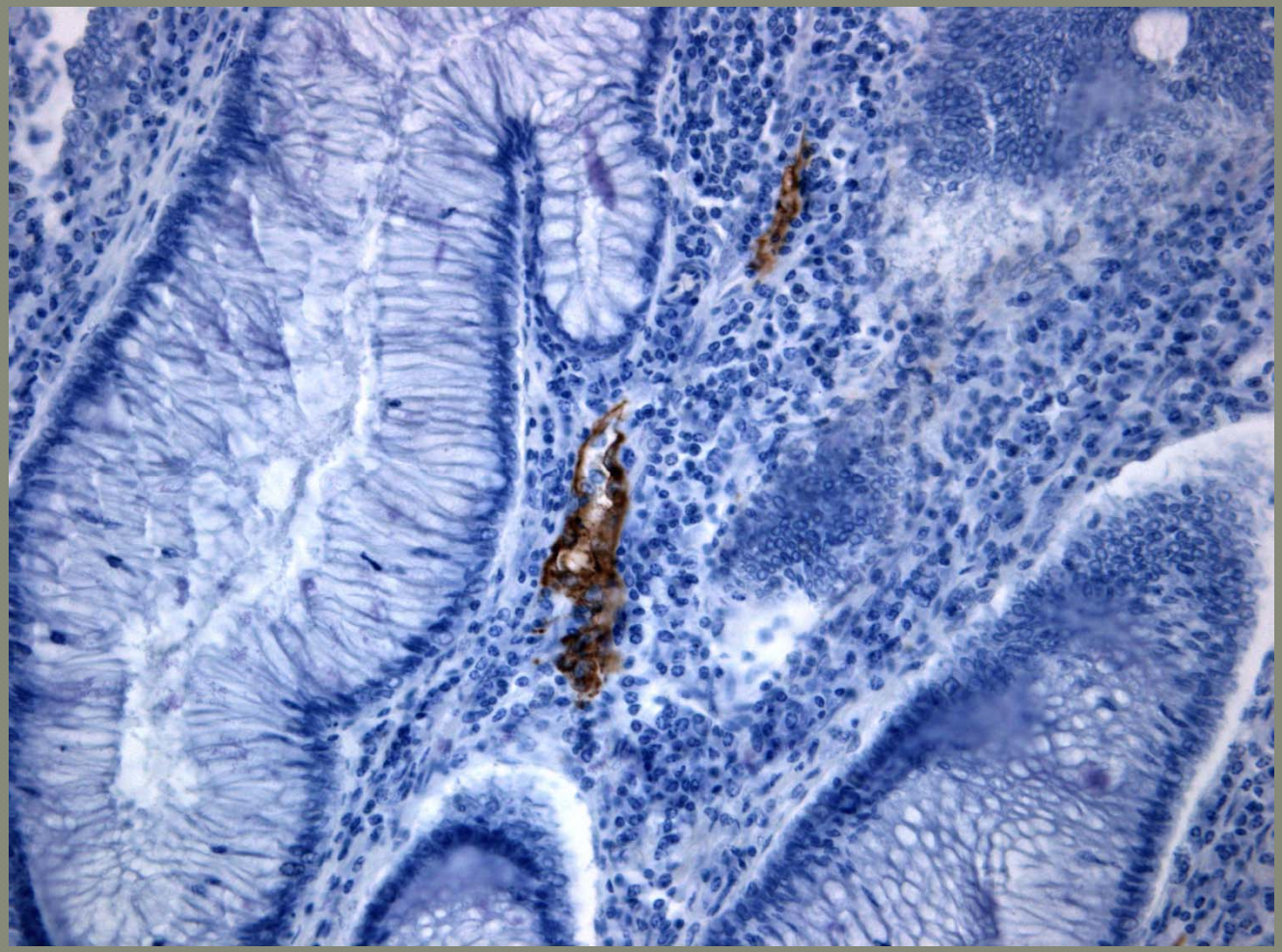


Low rectal lesion Invades just into the submucosa but has LVI, which is ?? still in the musc mucosae. Margin is clear (wmm)

So Questions.
A) What is the likelihood of any nodes being involved
B) Does she need her nodes removed?
c) If this involves an APR
d) If this involves a TME



Lymphatics in the mucosa (lymphangiogenesis)



Comments (R. Odze)

- nice and difficult clinical decision , here is my view if the patient is young and healthy, and the lvi is real(which it appears to be), then the guidelines say a resection should be strongly considered due to increased risk of lymph node mets, i believe the risk is anywhere from 10-20 percent, to me lvi is lvi regardless if its IN muscularis or BELOW it. They all connect!
- if it means an APR, its a BIG decision .If its a simple LAR, i think its an easier one. Of course, it all depends on the age and health and input and desire of the patient ultimately

Comments
(J. Greenson)

- **I reviewed a nearly identical case for a lawyer wherein the initial pathologist missed the LVI and the cancer penetrating the muscularis mucosae and stated that the polyp had been completely removed and was just an adenoma. Nothing further was done and the patient presented about 2 years later with a mass invading the sacrum and metastatic disease.**

Comments (G Williams)

- I would be more cautious about this. Is this genuine lymphatic invasion?
- **this lesion is otherwise a very superficially invasive well differentiated tumour that seems to be miles from the resection margin. So the putative lymphatic invasion is the only indication for radical surgery, and the evidence for isolated lymphatic invasion being an adverse prognostic indicator in the literature is not very convincing**

Intern Emerg Med. 2012

Clinical outcome of low- and high-risk malignant colorectal polyps: results of a population-based study and meta-analysis of the available literature.

Di Gregorio C, et al

Fifty-five malignant polyps were classified as low-risk lesions and 50 as high-risk.

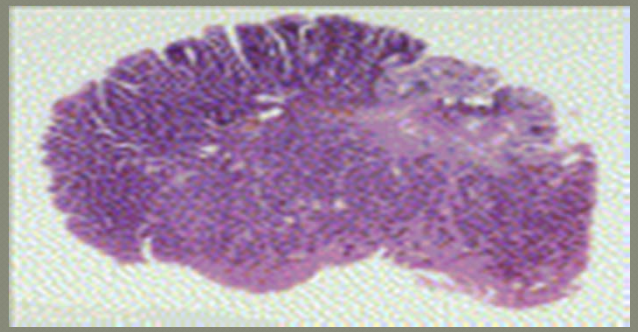
None of the patients at low-risk died of colorectal cancer.

Of the patients at high-risk, three died of cancer; all three cases showed lymphatic/vascular invasion.

Negative Margin
no consensus definition

- not within the actual diathermy,
- more than one high-power field from the diathermy,
- greater than 1 mm from the margin, and
- more than 2 mm from the margin

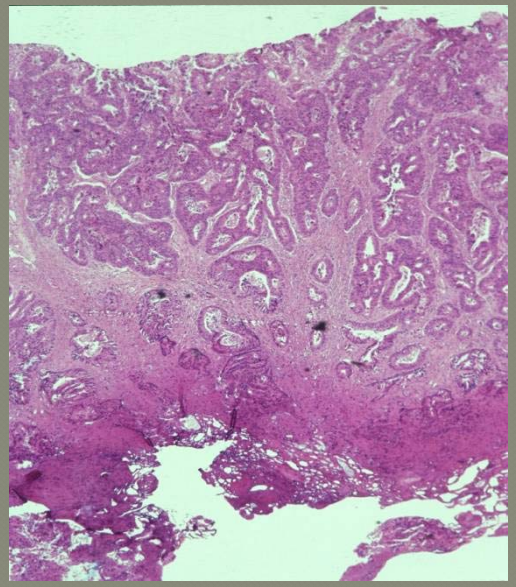
Polyp with negative margin

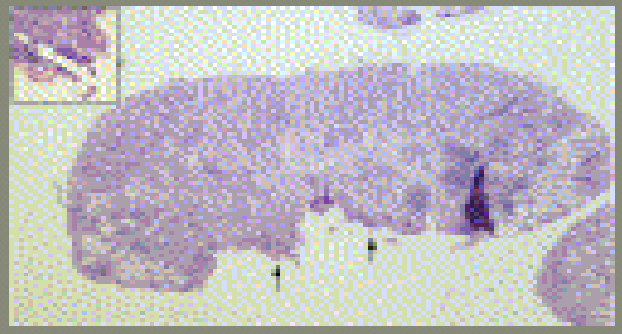


Cancer near the margin
No consensus definition

- **cancer cells 1 mm or less from the transected margin,**
- **cancer cells 2 mm or less from the transected margin,and [**
- **cancer within the diathermy and/or within one high-power field of the diathermy.**

Cancer & Polyp with positive margin

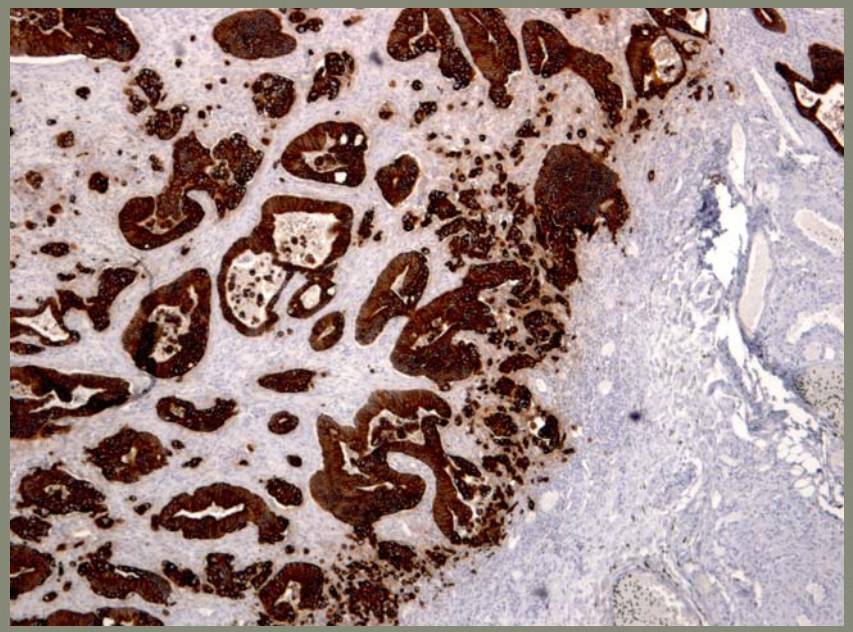


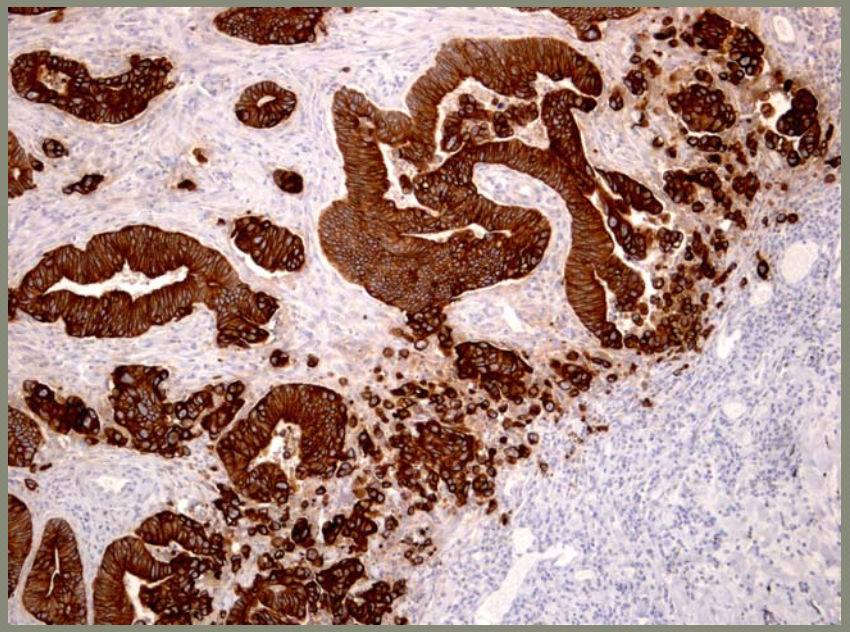


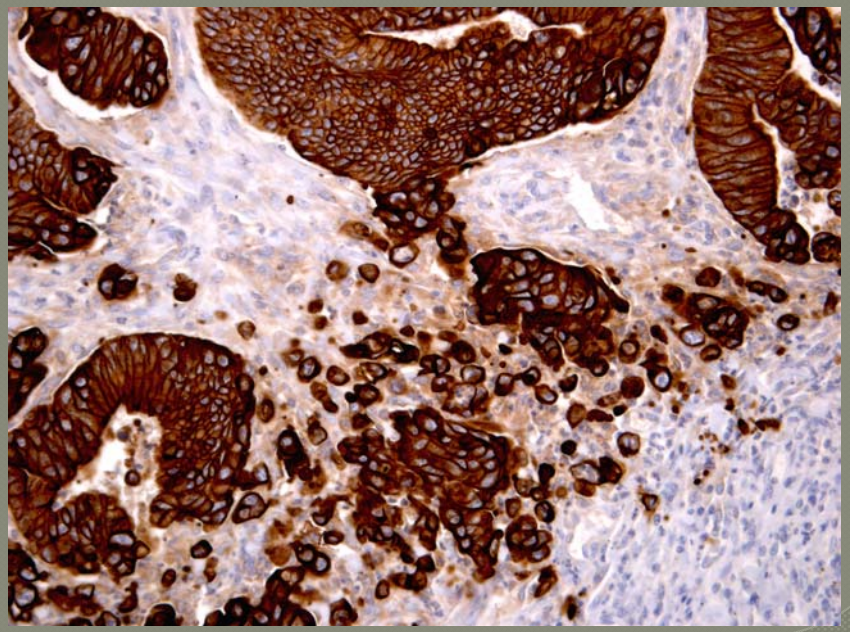
Tumor budding = activity

- Definition
  - Presence of isolated single cells or small clusters (up to four cells) scattered in the stroma at the invasive tumor margins
- Scoring
  - Field : X 20 objective lens
  - Number counted in the field with the most frequent tumor budding
  - Counts of 0-9 : low-grade
  - Counts of 10 or >10 : high grade

Budding keratin stain



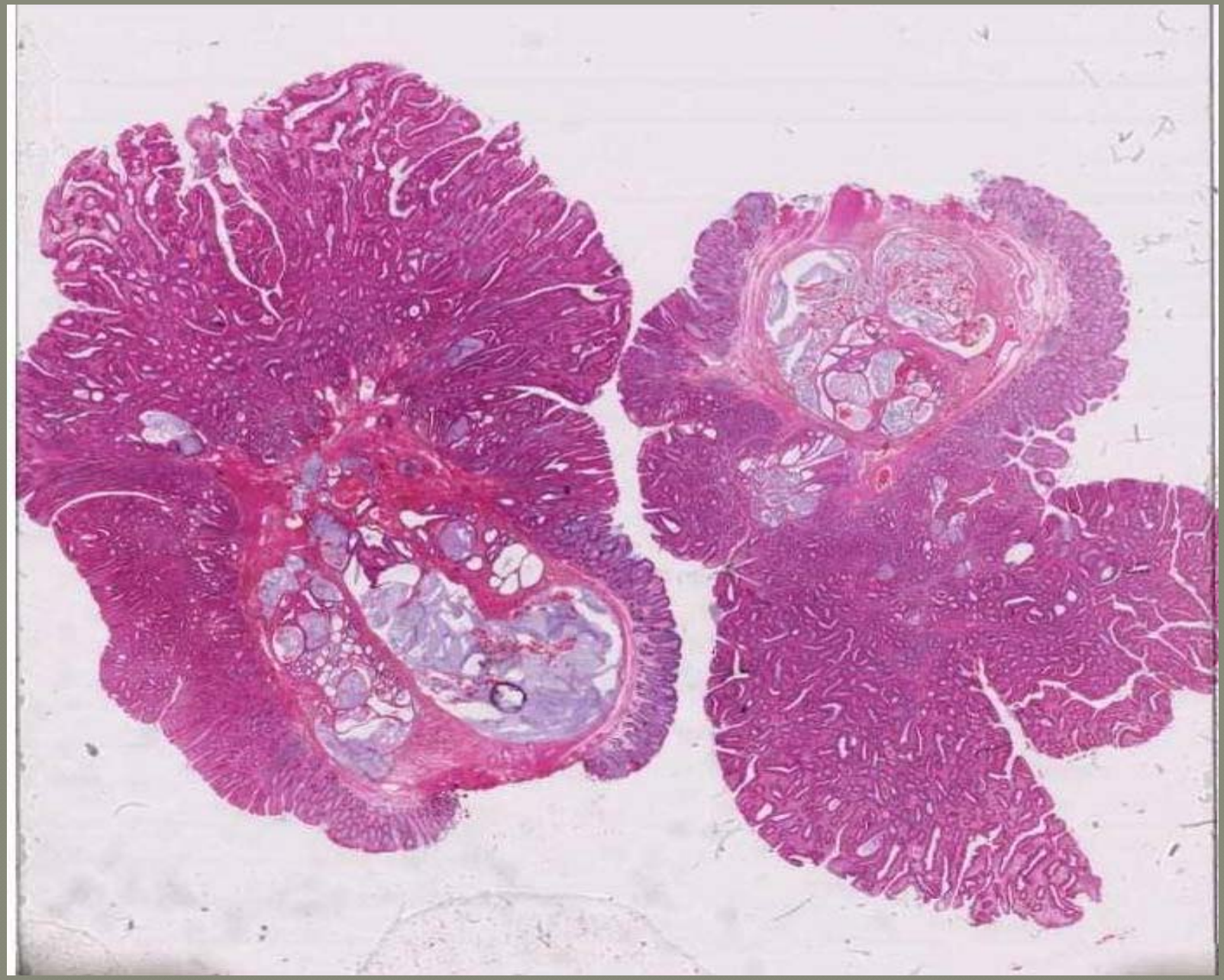




Tumor budding is predictive of lymphatic involvement

Ogawa e a Scan J Gastroenterol 2009;44:605-14

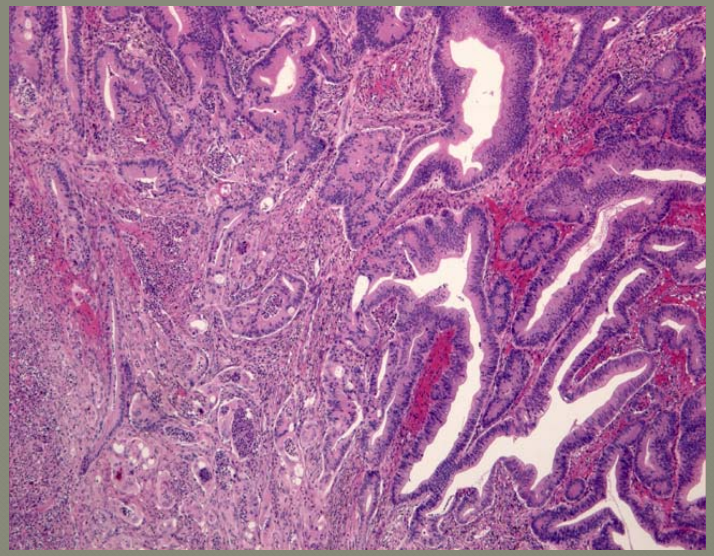
- Tumor budding is higher in non-polypoid ca
- Positive link with lymph node metastasis and lymphatic involvement

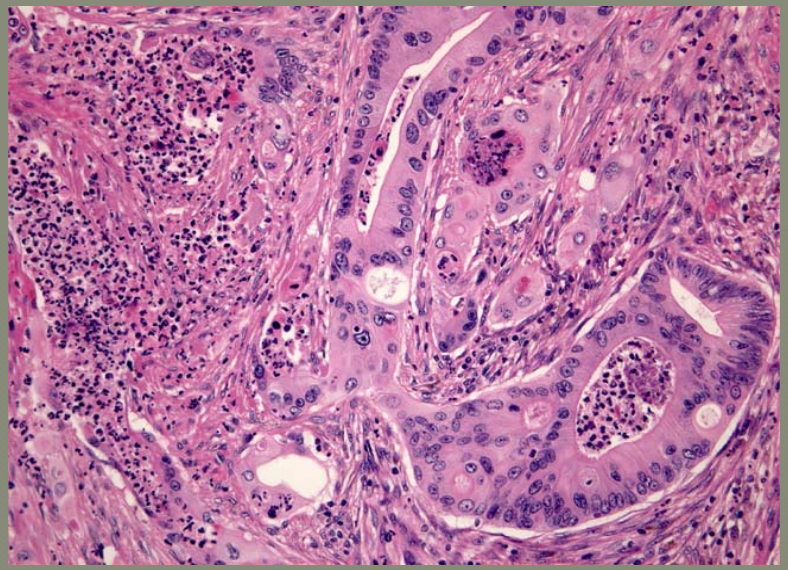


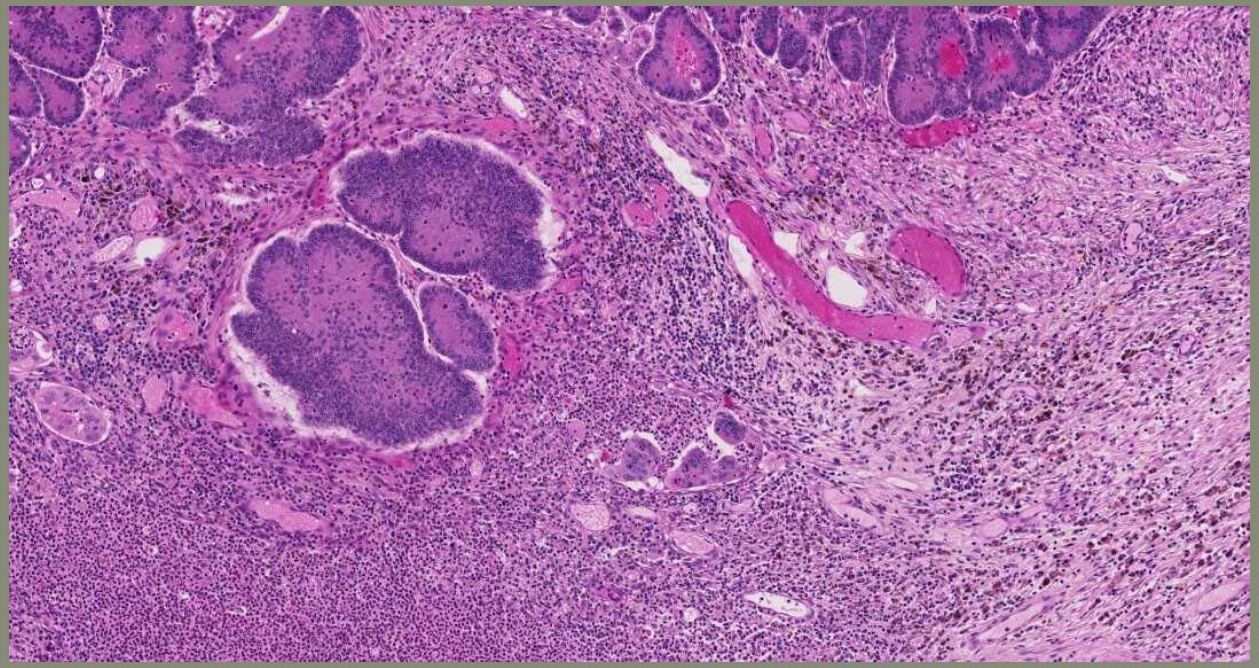
Invasion or pseudo-invasion

- Glandular pseudo-invasion occurs in 2.5-10% of adenomas
- Diff diagnosis
  - Presence of loosely arranged stroma (lamina propria) between the glands
  - Absence of desmoplastic reaction around the glands
  - Haemosiderin pigment
  - Smooth muscle cells
  - Absence of cytologic and architectural features of high-grade intraepithelial neoplasia.

B-657099





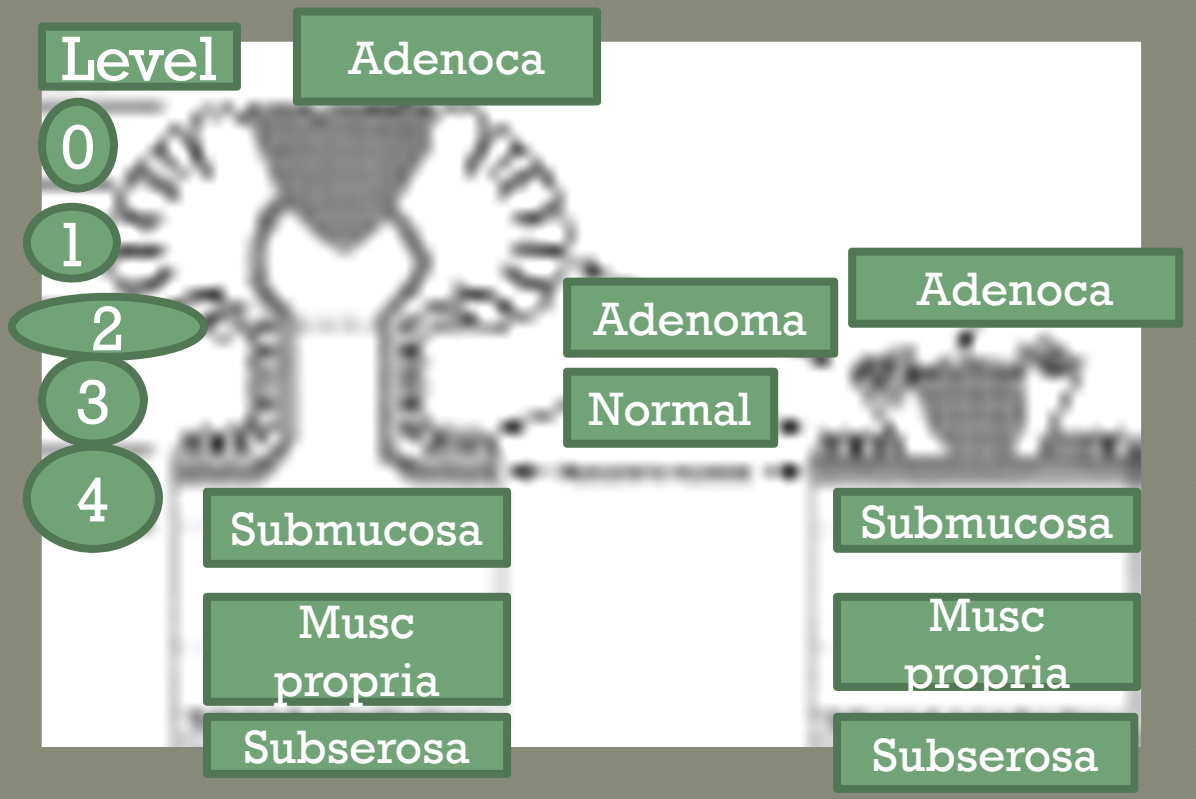


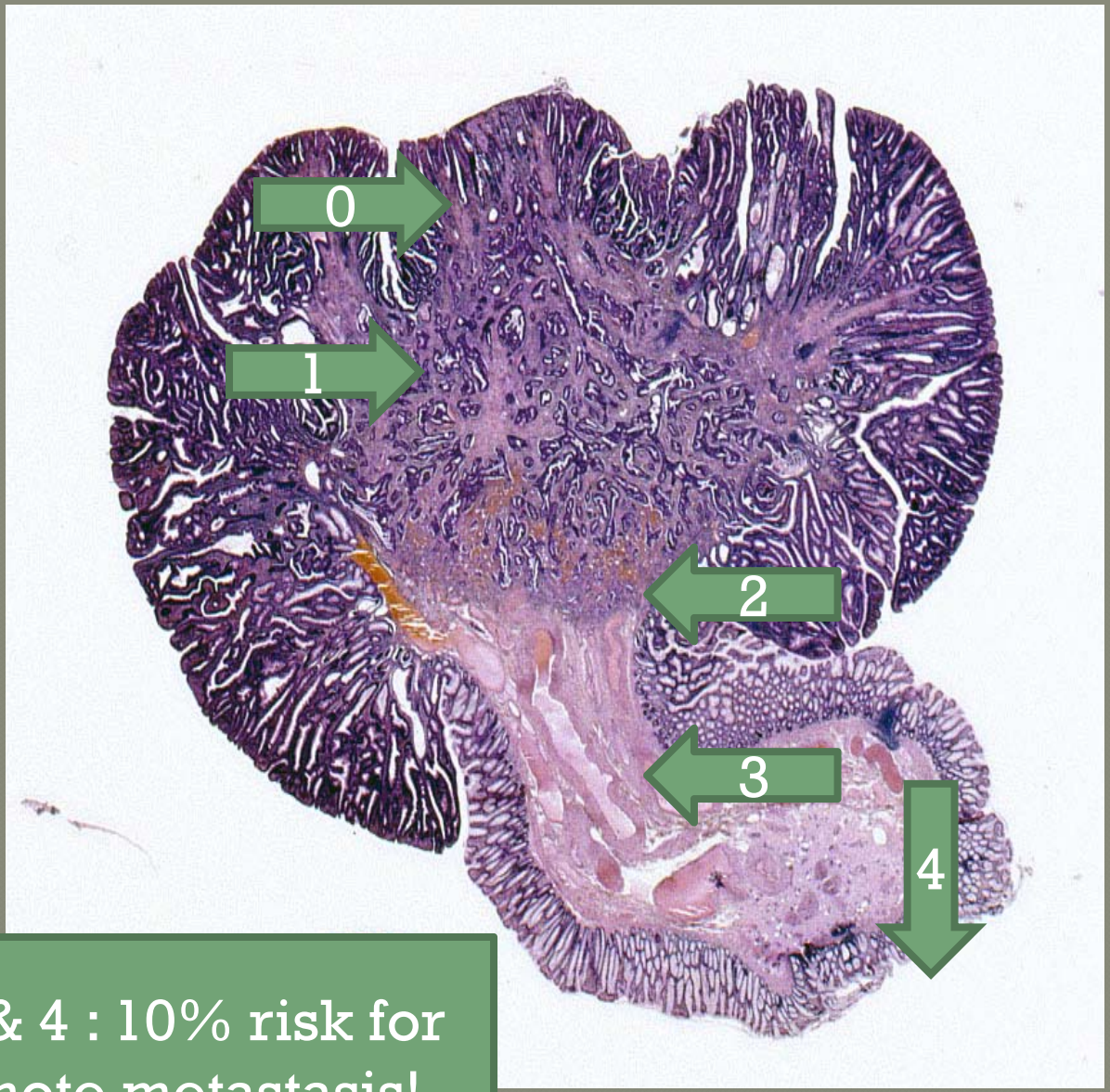
Haggitt's level of invasion

Cooper H, Pathology of the endoscopically removed malignant colorectal polyp Curr Diagn Pathol 2007; 13: 423-37

- ***Level 1***: **Carcinoma invading into the submucosa, but limited to the head of the polyp.**
- ***Level 2***: **Carcinoma invading to the level of the neck (the junction of the head and stalk) of the adenoma.**
- ***Level 3***: **Carcinoma invading any part of the stalk.**
- ***Level 4***: **Carcinoma invading into the submucosa of the bowel wall below the stalk of the polyp but above the muscularis propria**.

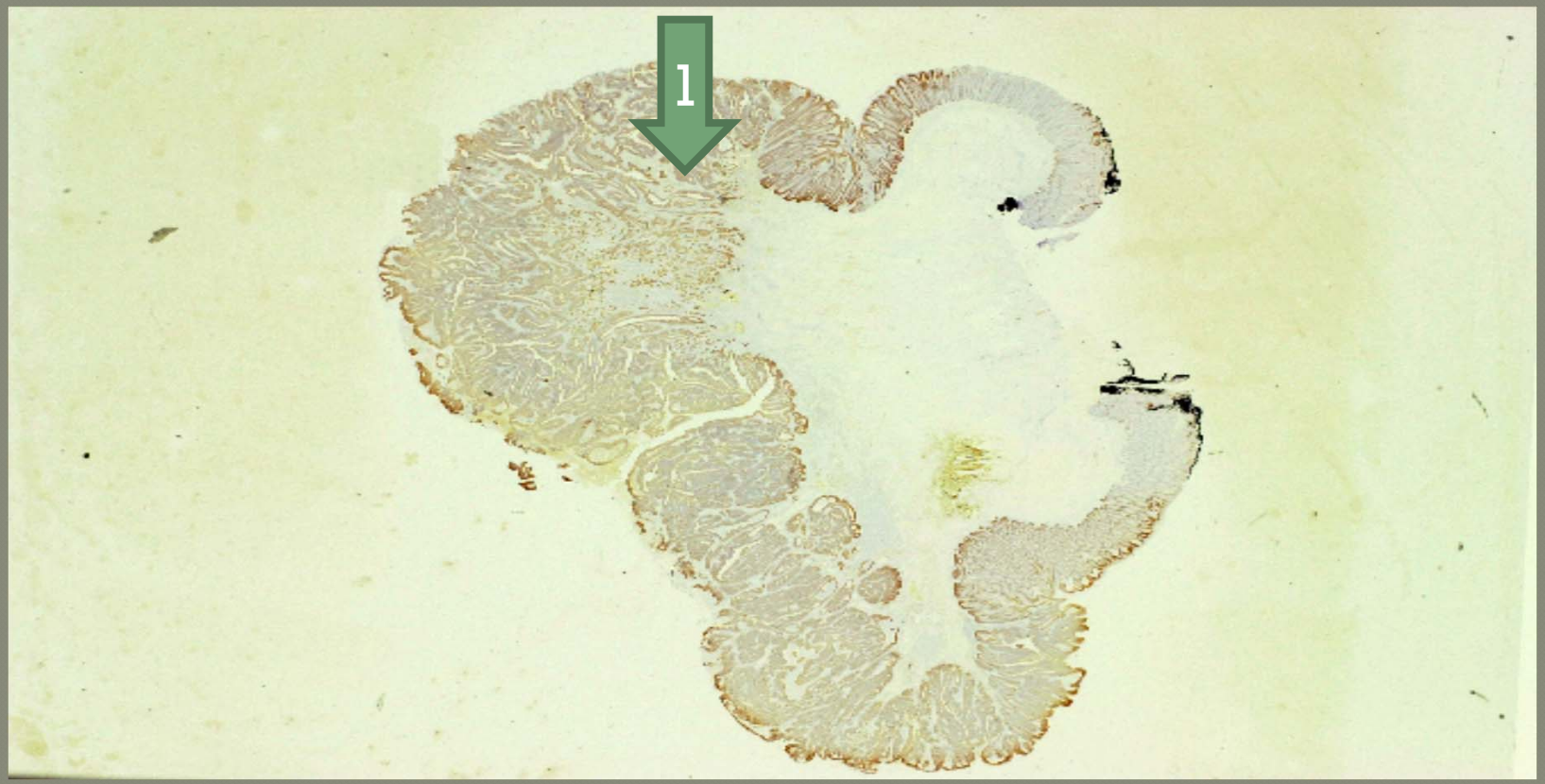
Haggit's level of invasion



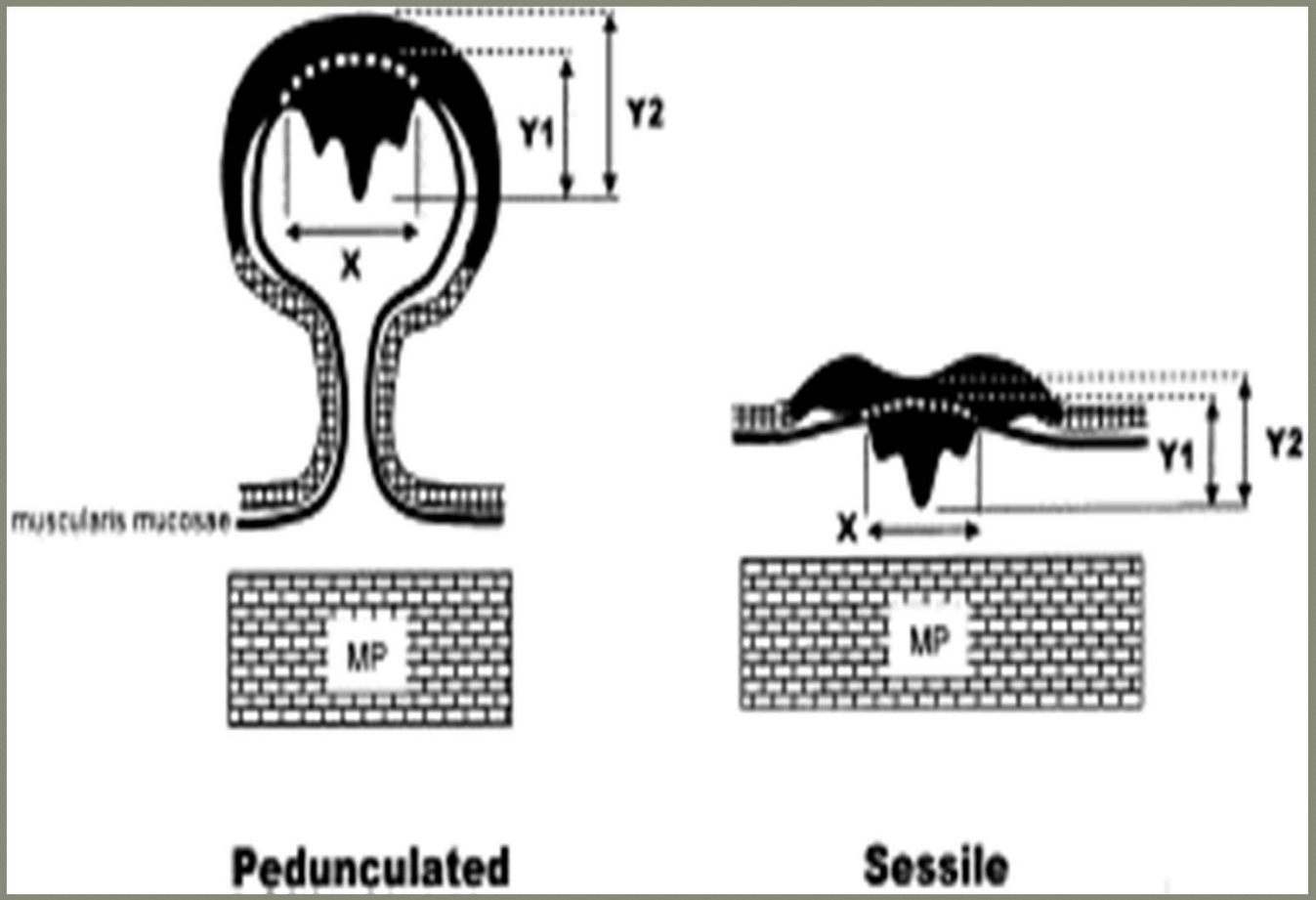


Level 3 & 4 : 10% risk for lymph note metastasis!

Adenoma with area of invasive carcinoma/ malignant adenoma Colon/ cytokeratin stain

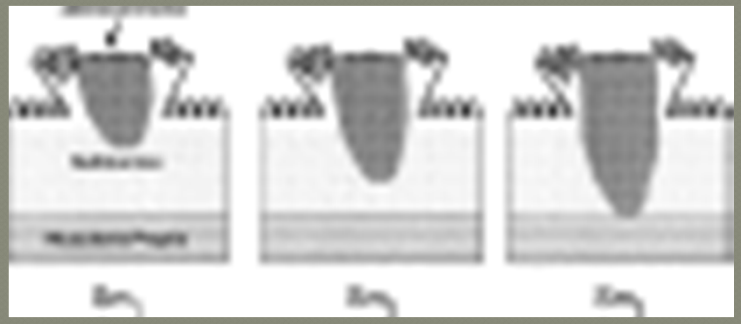


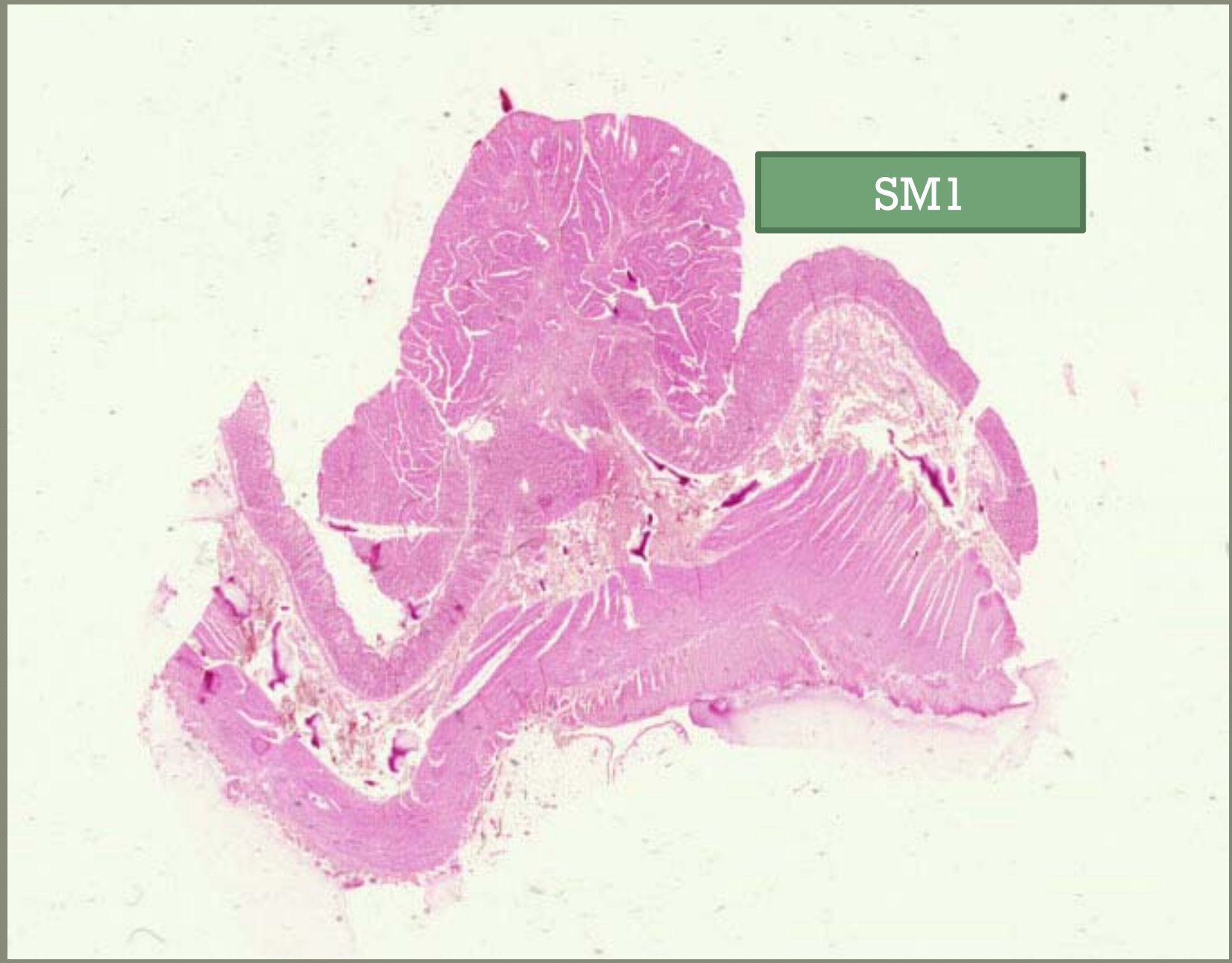
Measurement of extent of invasion in the submucosa
(Ueno et al Gastroenterology 2004)
X : width of invasion; Y1 : depth of invasion (when muscularis mucosae is present) Y2
: depth of invasion (within muscularis mucosae)



TEM & Early colorectal carcinoma Risk factors

- Maximum diameter (in mm)
  - Local recurrence rates at 3 years for tumors 3 cm in size or smaller are significantly lower than for tumors larger than 3 cm (16 vs. 39%; P < 0.03).
- Depth of submucosal invasion
  - Sm1 superficial third < 0.5mm
  - Sm2 middle third 0.5 – 1 mm
  - **Sm3 deep third > 1 mm (1000 μm)**




SM1

Kikuchi e.a. Dis Col Rectum 1995

After endoscopic polypectomy or local resection, 4 patients showed local recurrence and 13 patients showed lymph node metastasis.
None of these 17 patients had sm1 disease.

The level of invasion, configuration, and location were significant risk factors for development of lymph node metastasis or local recurrence ($P < 0.05$),
but lymphovascular invasion, histologic grade, and diameter were not risk factors.

Comparison of various risk factors with outcome

Groups Risk factors (N) N Adverse outcome Odds ratio (95% CI) p Value (Netzer e.a. Gut 1998)

† factor important in combination with others

Polyp shape : †Sessile *v pendunculated 19 v 51* *10 v 9* ***8.3*** *(2.1 to 34.8) <0.001*

Polypectomy : Incomplete *v complete 8 v 62* *6 v 10* ***15.6*** *(2.2 to 169) 0.001*

*Margin of resection : Not cancer-free *v cancer-free 24 v 38* ***9 v 1*** *20.2 (2.6 to 998) <0.001*

*Lymphatic invasion †Present *v not present 6 v 56* *4 v 6* ***16.7*** *(1.8 to 204) 0.005*

*Venous invasion †Present *v not present 5 v 57* *2 v 8* *4.1 (0.3 to 40.7) 0.18*

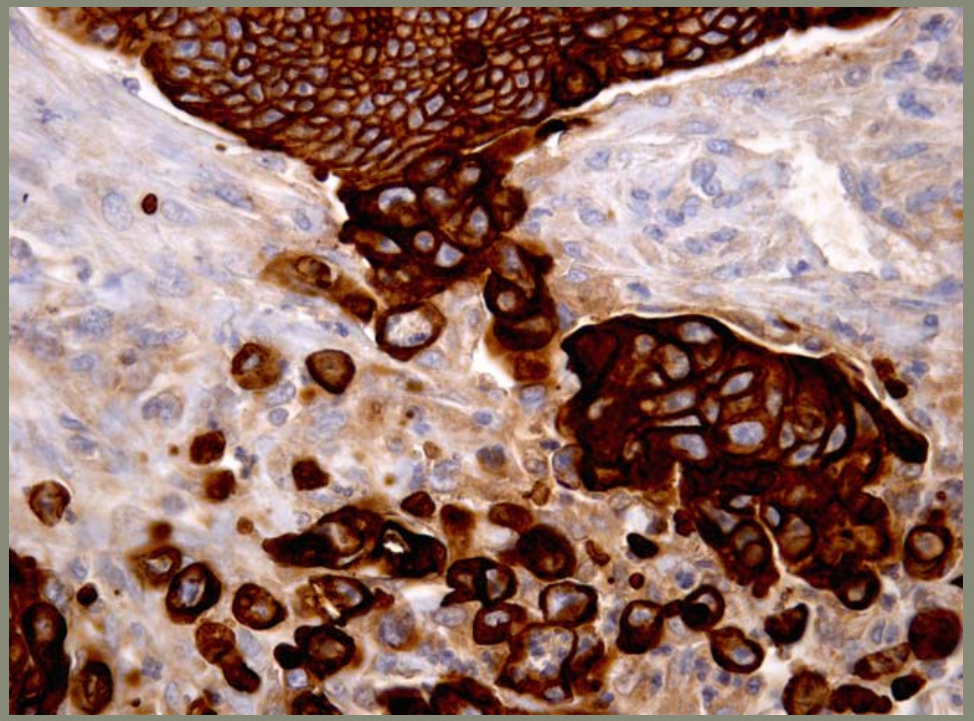
*Grade III cancer †Present *v not present 5 v 57* *2 v 57* *4.1 (0.3 to 40.7) 0.18*

*Polypoid cancer †Present *v not present 6 v 56* *3 v 7* *7 (0.7 to 60.6) 0.048*

Risk categories High risk *v low risk 38 v 32 16 v 0 Infinite (5 to infinite) <0.001*

Risk factors for residual tumor
Ueno et al Gastroenterology 2004; 127

- **Absence of unfavorable tumor grade**
- **Absence of vascular invasion**
- **Absence of tumor budding (sprouting)**
- **Absence of extensive submucosal invasion**



Early colorectal carcinoma Risk factors (Inoue 2004)

- Correlation with nodal involvement
  - Poor tumor grade
  - Vascular invasion (venous & lymphatic)
  - Tumor budding
- Absence of these parameters : low risk
- Coagulation involving tumor

TEM
Low risk

- Size < 3 cm
- Invasion limited to sm1 (recurrence rate 0)
  - Sm2 : recurrence rate 17%/ sm3 : 30%
- No lymphatic invasion
- Additional surgery needed for

Positive vertical margins at the site of submucosal invasion

Depth of submucosal invasion greater than 1000 μm

Vascular or lymphatic invasion

Poorly differentiated adenocarcinoma, signet ring cell carcinoma, or

mucinous carcinoma

High-grade tumor budding

SURGICAL PATHOLOGY CANCER CASE SUMMARY (CHECKLIST)

Colon and Rectum: Excisional Biopsy (Polypectomy)

Select a Single Response Unless Otherwise Indicated

* Data elements with asterisks are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.

Arch Pathol Lab Med. 2009 October ; 133(10): 1539–1551.

***Polyp Size**

* Greatest dimension: ____ cm
* Additional dimensions: ____ × ____ cm
* ____ Cannot be determined (see Comment)

***Polyp Configuration**

* ____ Pedunculated with stalk
* Stalk length: ____ cm
* ____ Sessile

Size of Invasive Carcinoma

Greatest dimension: ____ cm

* Additional dimensions: ____ × ____ cm

____Cannot be determined (see Comment)

Histologic Type (note B)

_____ Adenocarcinoma
_____ Mucinous adenocarcinoma
_____ Signet-ring cell carcinoma
_____ Small cell carcinoma
_____ Squamous cell carcinoma
_____ Adenosquamous carcinoma
_____ Medullary carcinoma
_____ Undifferentiated carcinoma
_____ Other (specify): _____
_____ Carcinoma, type cannot be determined

Histologic Grade (note C)

_____ Not applicable
_____ Cannot be determined
_____ Low grade (well differentiated to moderately differentiated)
_____ High grade (poorly differentiated to undifferentiated)

Microscopic Tumor Extension (note D)

____ Cannot be determined

Invasion (deepest):

____ Lamina propria

____ Muscularis mucosae

____ Submucosa

____ Muscularis propria

Margins (select all that apply)

Deep Margin (Stalk Margin)

____ Cannot be assessed

____ Uninvolved by invasive carcinoma

Distance of invasive carcinoma from margin: ____ mm

____ Involved by invasive carcinoma

Mucosal/Lateral Margin

____ Not applicable

____ Cannot be assessed

____ Uninvolved by invasive carcinoma

____ Involved by invasive carcinoma

____ Involved by adenoma

Lymph-Vascular Invasion (notes D and E)

____ Not identified
____ Present
____ Indeterminate

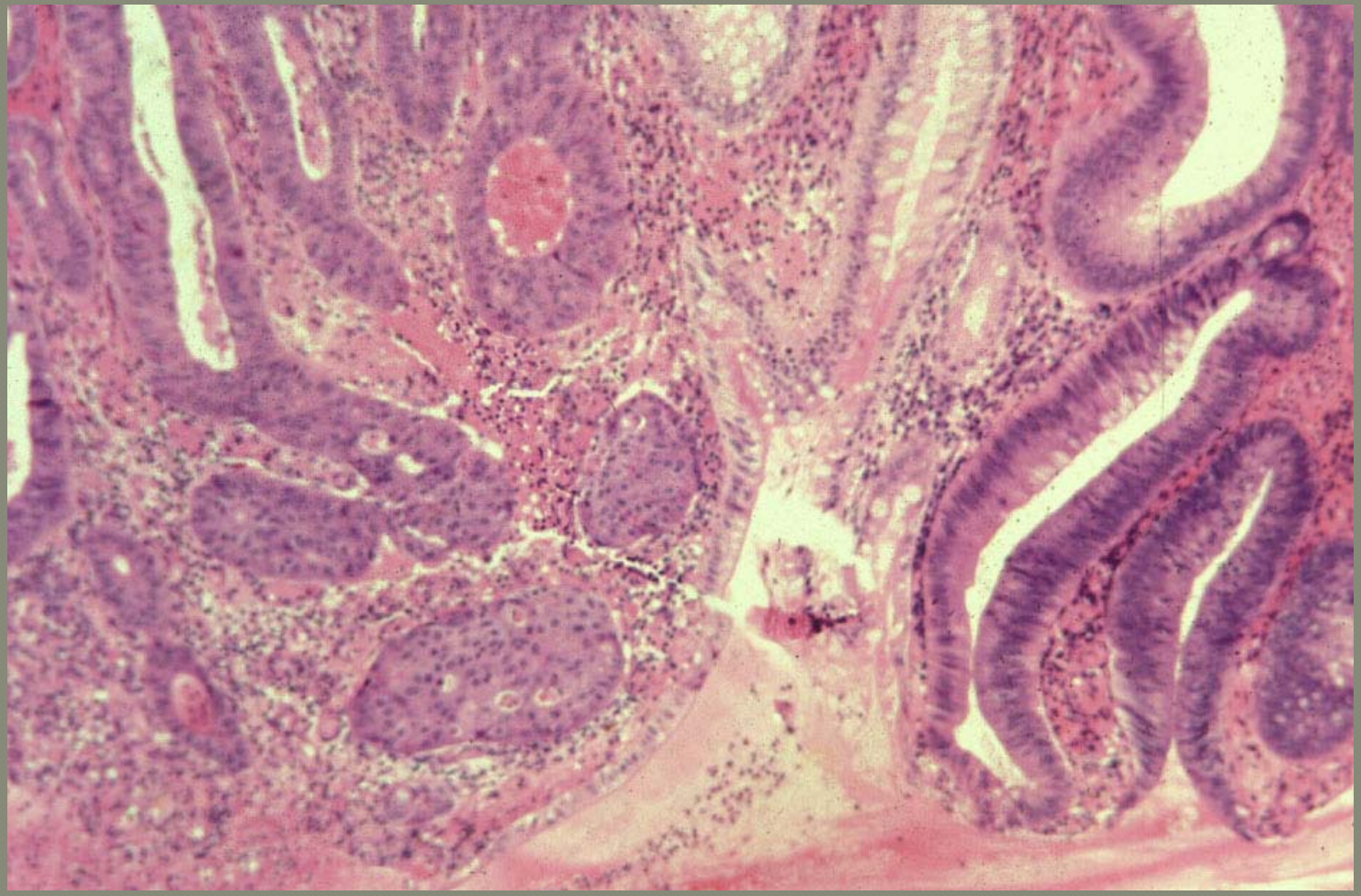
***Type of Polyp in Which Invasive Carcinoma Arose (note F)**

* ____ Tubular adenoma
* ____ Villous adenoma
* ____ Tubulovillous adenoma
* ____ Traditional serrated adenoma
* ____ Sessile serrated adenoma
* ____ Hamartomatous polyp
* ____ Indeterminate

Conclusions

- There is a variety of precursor lesions
- Handling the specimen is important
- Risk factor analysis
  - Size
  - Tumor grade
  - Depth of invasion
    - Haggit's level
    - Submucosal invasion
  - Lymphovascular invasion
  - Budding
  - Margin
- Final conclusion (risk factors – status of patient)

132548



Colorectal neoplasia and treatment

- Intraepithelial neoplasia : low- & high grade – polypoid and non-polypoid
  - Local – endoscopic treatment
  - Follow-up (guidelines)
- Intramucosal carcinoma - polypoid and non-polypoid
  - Local – endoscopic treatment
  - Follow-up
- Submucosal carcinoma - Early colorectal carcinoma
  - Local – endoscopic treatment
  - Follow-up or colon resection (depending on histology)

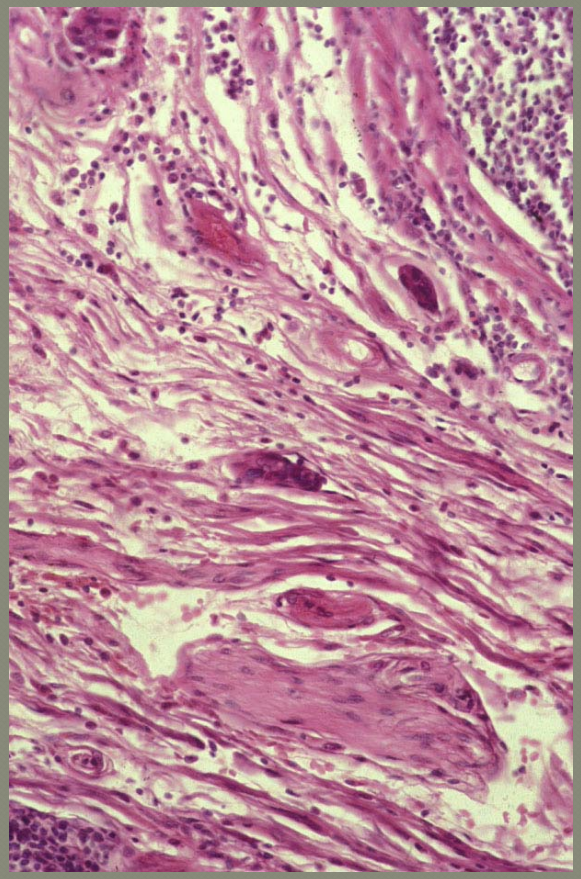
Early colorectal carcinoma

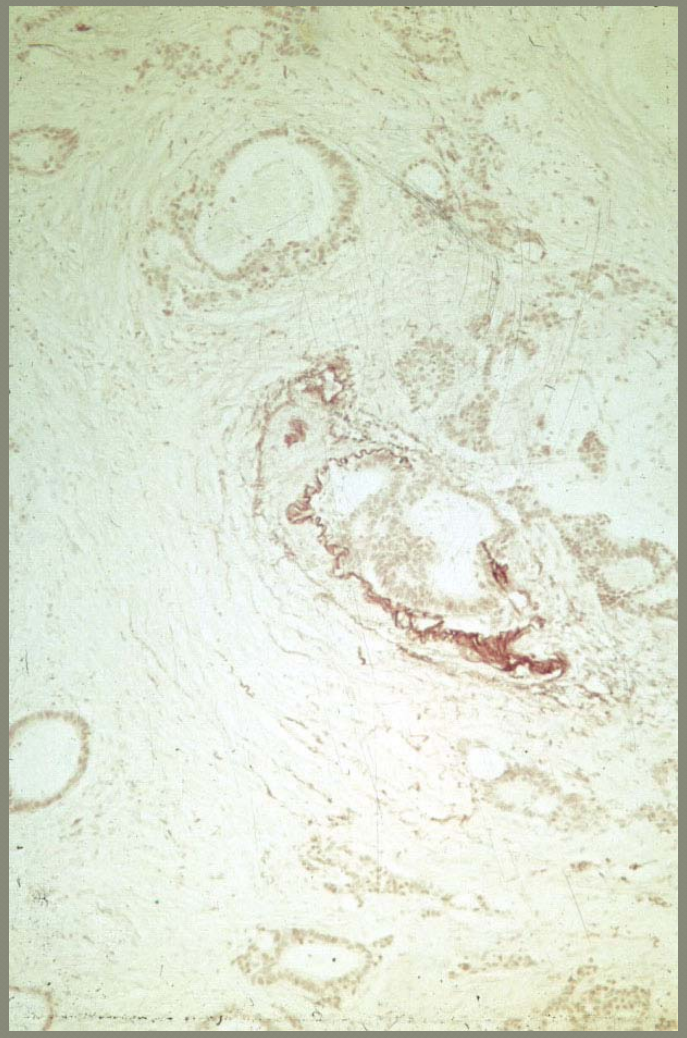
- Endoscopic resection
- Histopathological evaluation
  - Detection of risk factors for adverse outcome (presence of residual carcinoma in the bowel wall or in regional lymph nodes) necessitating subsequent colon resection

Early colorectal carcinoma Risk factors (Haggitt 1985)

- Level of invasion
  - 0 = mucosa
  - 1 = head of polyp
  - 2 = neck
  - 3 = stalk
  - 4 = submucosa
- Grading
- **Vascular invasion**
- **Carcinoma at or close < 1 mm from the resection margin**

CRC : 603160/4 lymphatic invasion
650438 Vascular invasion





Conclusion

- **Intraepithelial neoplasia is the equivalent of dysplasia and the preferable terminology**
- **Early colorectal cancer is limited to the submucosa and not beyond**
- **Early colorectal cancer can be treated with curative resection (EMR or surgery)**
- **Endoscopic mucosal resection specimens should be handled properly**
- **Risk factors for adverse outcome are poor grade; vascular involvement; tumor budding and coagulation involving tumor**

Inflammatory lesion
34yr old Cambodian male