Classification of polyps

- Neoplastic
  - Carcinoma
  - Adenoma
    - Tubular
    - Tubulovillous
    - Villous
  - Hamartoma
    - Hyperplastic
    - Inflammatory (psuedopolyps)

- Non-Neoplastic
  - Hyperplastic Polyps
    - Common in the colon.
    - Polyps are usually small (<5 mm) and show histologic characteristics of hyperplasia without any dysplasia.
    - Not considered premalignant, but cannot be distinguished from adenomatous polyps colonoscopically and are therefore often removed.
    - Large hyperplastic polyps (>2 cm) may have a slight risk of malignant degeneration.
    - Moreover, large polyps may harbor foci of adenomatous tissue and dysplasia.
    - Hyperplastic polyposis is a rare disorder in which multiple large hyperplastic polyps occur in young adults.

- Inflammatory Polyps (Pseudopolyps)
  - Occur most commonly in the context of inflammatory bowel disease, but may also occur after amebic colitis, ischemic colitis, and schistosomal colitis.
  - These lesions are not premalignant, but they cannot be distinguished from adenomatous polyps based upon gross appearance and therefore should be removed.

- Inflammatory pseudo-polyps
  - Inflammatory pseudopolyps are irregularly shaped islands of residual intact colonic mucosa that are the result of the mucosal ulceration and regeneration that occurs in inflammatory bowel disease (IBD).
  - Typically multiple, often filliform and scattered throughout the colitic region of the colon. They may also be more isolated and semipedunculated in areas of more active recent inflammation, and have mucus adherent to their apices.

- Hamartomatous Polyps (Juvenile Polyps)
  1. Familial juvenile polyposis
  2. Peutz-Jeghers syndrome
  3. Cronkite-Canada syndrome
  4. Cowden's syndrome

- Familial juvenile polyposis
  - AD disorder
  - Hundreds of polyps in the colon and rectum.
  - Degenerate into adenomas, and eventually carcinoma.
  - Annual screening should begin between the ages of 10 and 12 years.
  - Treatment is surgical and depends in part upon the degree of rectal involvement.
  - A total abdominal colectomy with ileorectal anastomosis may be performed with subsequent close surveillance of the retained rectum.
  - A total proctocolectomy with ileal pouch–anal reconstruction to avoid a permanent stoma.
**Peutz-Jeghers syndrome**
- characterized by polyposis of the small intestine, colon and rectum.
- Characteristic melanin spots are often noted on the buccal mucosa and lips.
- The polyps considered to be hamartomas and are not thought to be at significant risk for malignant degeneration.
- Because the entire length of the gastrointestinal tract may be affected, surgery is reserved for symptoms (obstruction or bleeding or for patients in whom polyps develop adenomatous features.)
- Screening consists of a baseline colonoscopy and upper endoscopy at age 20 years, followed by annual flexible sigmoidoscopy thereafter.

**Cronkite-Canada syndrome**
- polyposis in association with alopecia, cutaneous pigmentation, and atrophy of the fingernails and toenails.
- Diarrhea is a prominent symptom, and vomiting, malabsorption, and protein-losing enteropathy may occur.
- Surgery is reserved for complications of polyposis such as obstruction.

**Cowden's syndrome**
- AD disorder with hamartomas of all three embryonal cell layers.
- Facial trichilemmomas, breast cancer, thyroid disease, and gastrointestinal polyps are typical of the syndrome.
- Patients should be screened for cancers.
- Treatment is otherwise based upon symptoms.

**Inherited Colorectal Carcinoma**
1. Familial Adenomatous Polyposis
2. Attenuated FAP
3. Hereditary Nonpolyposis Colon Cancer (Lynch's Syndrome)

**Clinical Features of FAP**
- Estimated penetrance for adenomas >90%
- Risk of extracolonic tumors (upper GI, desmoid, osteoma, thyroid, brain, other)
- CHRPE may be present
- Untreated polyposis leads to 100% risk of cancer

**Genetics of FAP**
- Autosomal dominant inheritance
- Caused by mutations in APC tumor suppressor gene on chromosome 5q
- Up to 30% of patients have de novo germline mutations
- Most families have unique mutations
- Most mutations are protein truncating
- Genotype/phenotype relationships emerging
Attenuated FAP

- Later onset (CRC ~age 50)
- Few colonic adenomas
- Not associated with CHRPE
- UGI lesions
- Associated with mutations at 5' and 3' ends of APC gene

Clinical Features of HNPCC

- Early but variable age at CRC diagnosis (~45 years)
- Tumor site in proximal colon predominates
- Extracolonic cancers: endometrium, ovary, stomach, urinary tract, small bowel, bile ducts, sebaceous skin tumors

Amsterdam Criteria

- 3 or more relatives with verified CRC in family
- One case a first-degree relative of the other two
- Two or more generations
- One CRC by age 50
- FAP excluded

Failure to meet these criteria does not exclude HNPCC


Genetic Features of HNPCC

- Autosomal dominant inheritance
- Penetration ~80%
- Genes belong to DNA mismatch repair (MMR) family
- Genetic heterogeneity (MLH1, MSH2, MSH6, PMS1, PMS2)

Adenomatous polyp

- About 2/3 of all colonic polyps are adenomas
- Can take 5-10 years for polyp to develop
- Up to 10% of polyps develop into cancer
- Size and histology are risk factors for polyp to cancer progression
Clinical presentation and natural history of Adenomas

- Adenomas are generally asymptomatic and are most often detected by colon cancer screening tests.
- Small adenomas do not typically bleed.
- Adenomas are found in 17 to 43 percent of patients with a positive FOBT but they are also detected in 32 to 41 percent of asymptomatic men with a negative FOBT.
- Advanced adenomas are more likely to bleed and cause a positive fecal occult blood test.

Synchronous lesion

- An adenoma that is diagnosed at the same time as an index colorectal neoplasm is called a synchronous lesion.
- Thirty to 50 percent of colons with one adenoma will contain at least one other synchronous adenoma.

Metachronous lesion

- One that is diagnosed at least six months later is considered metachronous lesion.

Pathologic classification

- The histologic features and size of colonic adenomas are the major determinants of their malignant potential.
- The glandular architecture of adenomas is characterized as tubular, villous, or a mixture of the two.

Polyp base

- Sessile - base is attached to the colon wall,
- Pedunculated if a mucosal stalk is interposed between the polyp and the wall.
- Adenomas are most commonly found within raised lesions, up to 27 to 36 percent are flat (having a height less than one-half the diameter of the lesion) and up to 1 percent are depressed.

Malignant change

- Type
  - Tubular 5%
  - Tubulovillous 22%
  - Villous 40%
- Size
  - <1 cm 1%
  - 1 – 2 cm 10%
  - >2 cm 53%
**Size as a risk of cancer of a polyp**

<table>
<thead>
<tr>
<th>Size in cms</th>
<th>Risk of cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.6 – 1.5</td>
<td>2%</td>
</tr>
<tr>
<td>1.5 - 2.5</td>
<td>19%</td>
</tr>
<tr>
<td>2.6 – 3.5</td>
<td>43%</td>
</tr>
<tr>
<td>&gt; 3.5</td>
<td>76%</td>
</tr>
</tbody>
</table>

Nusco et al Endoscop 1997

**Malignant change**

- Size of polyp > 2 cm
  - Tubular 35%
  - Tubulovillous 46%
  - Villous 53%

- Timing
  - 5 years 2.5%
  - 10 years 8%
  - 20 years 20%

**Grades of adenocarcinoma**

- Well-diff. + Grade 1
- Mod-diff. + Grade 2
- Poorly differentiated + Grade 3
- Mucin-producing

**Lymphovascular invasion**

- Cancer cells in endothelial lined channels
- Poor interobserver varied by studies (6-52%)
- Sampling error
- Artifact

**Histopathologic parameters**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Cancer risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unfavorable histology</td>
<td>19.7 %</td>
</tr>
<tr>
<td>Indefinite</td>
<td>8.6%</td>
</tr>
<tr>
<td>Favorable histology</td>
<td>0 %</td>
</tr>
</tbody>
</table>

Cooper et al., 1995

**Haggitt’s System**

Depth of Invasion
Level 4 = 27% LN +ve
**SM classification**

Significant for Lymph Node Metastasis ($p < 0.001$)

<table>
<thead>
<tr>
<th></th>
<th>node metastasis</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>sm1</td>
<td>sm2</td>
<td>sm3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>no.</td>
<td>%</td>
<td>no.</td>
<td>%</td>
</tr>
<tr>
<td>Kudo</td>
<td>96</td>
<td>1</td>
<td>63</td>
<td>6.3</td>
</tr>
<tr>
<td>Igarashi</td>
<td>47</td>
<td>0</td>
<td>49</td>
<td>16</td>
</tr>
<tr>
<td>Kodaira</td>
<td>3.2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Well-known high risk factors of MP**

1. Depth of Invasion
   - $< 2$ mm margin
   - Haggitt level 4 (27% LN – Nivatvongs et al 1991)
   - Kudo SM 3 (25% LN – Kikuchi et al 1995)

2. Grade 3 adenocarcinoma
   - poorly differentiated (50% LN – Coverlizza et al. 1989)
   - mucin producing

3. Lymphovascular invasion

**Recently Proposed Adverse risk factors**

4. Grade 3 cancer at the invasive front (Budding) (21% LN + Masaki 2000)

5. Site of MP in the lower third of rectum (10 - 34% LN)

**Budding**

- Undifferentiated cancer cells at the invasive front
  $\rightarrow$ 21% Lymph nodes +ve and/or

**Local recurrence**

Masaki, J Gastroenterol 2000

**Nodal metastasis Risk factors**

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Nodal metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>No risk factor</td>
<td>0.7%</td>
</tr>
<tr>
<td>Single risk factor</td>
<td>20.7%</td>
</tr>
<tr>
<td>Multiple risk factors</td>
<td>36.4%</td>
</tr>
</tbody>
</table>
Oncologic Bowel Resection Indicated

MP in colon, upper & middle rectum
1. Pedunculated Haggitt level 4 with invasion into distal third of submucosa, or pedunculated lesions with lymphovascular invasion
2. Sessile lesions removed with margin < 2 mm
3. Sessile lesions removed piecemeal
4. Sessile lesions with depth of invasion into SM3
5. Sessile lesions with lymphovascular invasion

MP in distal third of the rectum
1. Pedunculated Haggitt level 4 with invasion into distal third of submucosa, or pedunculated lesion with lymphovascular invasion
2. All sessile lesions (An alternative may be a per anal full thickness excision plus chemoradiation)

Follow up colonoscopy


Small Large 1 - 6 3 - 5
+ve -ve +ve -ve

LVI and Risk of LNM in T1

<table>
<thead>
<tr>
<th>LVI</th>
<th>No.</th>
<th>LNM No. (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent</td>
<td>324</td>
<td>37 (11)</td>
<td>0.002</td>
</tr>
<tr>
<td>Present</td>
<td>28</td>
<td>9 (32)</td>
<td></td>
</tr>
</tbody>
</table>

LVI = lymphovascular invasion; LNM = lymph node metastasis.

- 114 Pts with endoscopically removed polyps
  - Complete resection
  - G1 G 2 grade
  - No Vascular invasion
  - Endoscopic polypectomy alone is adequate
• 47 pt
• 17 had favorable histology:
  16 → polypectomy alone → no adverse outcome
• 30 pt unfavorable
  21 → surgery
  10/30 had adverse outcome
• Conclusion:- Endoscopic polypectomy is adequate for polyps with favorable histology

Nascimbeni et al. showed that the lower third of rectum had a high risk of lymph node metastasis

Volk Fazio. Gastroenterology 1995

Nascimbeni R et al. Dis Colon Rectum 2002

**sessile lesions with invasive carcinoma <2 cm in diameter in the colon**
• upper third and middle third of rectum: snared in one piece via colonoscopy
• microscopic free margin of at least 2mm

**sessile lesion that has high risk factors**
(lymphovascular invasion and deep invasion into Sm3 level):
• oncologic resection
• lower third rectal lesion: full thickness transanal excision + postoperative radiation or chemoradiation

---

**TABLE 4** Selected Series of Local Recurrence and Survival After Transanal Excision for T1 Carcinoma of the Rectum

<table>
<thead>
<tr>
<th>Institution</th>
<th>No.</th>
<th>LR (%)</th>
<th>5-Yr Survival (% CSB)</th>
<th>F-U (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>University of Minnesota (68)</td>
<td>69</td>
<td>18</td>
<td>95</td>
<td>52</td>
</tr>
<tr>
<td>Memorial Skars-Kettering (46)</td>
<td>67</td>
<td>14</td>
<td>74</td>
<td>60</td>
</tr>
<tr>
<td>Cleveland Clinic (69)</td>
<td>52</td>
<td>29</td>
<td>75</td>
<td>55</td>
</tr>
<tr>
<td>Mayo Clinic (70)</td>
<td>70</td>
<td>7</td>
<td>89</td>
<td>60</td>
</tr>
</tbody>
</table>

Abbreviations: LR, local recurrence; CSB, cancer-specific survival; F-U, follow-up.

LITERATURE REVIEW
Local Excision Ca. Rectum (T1)

<table>
<thead>
<tr>
<th>Author</th>
<th>Yr</th>
<th>No.</th>
<th>Loc Recur(%)</th>
<th>FU/MO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Madboddy</td>
<td>2005</td>
<td>52</td>
<td>17</td>
<td>55</td>
</tr>
<tr>
<td>Nascimbeni</td>
<td>2004</td>
<td>70</td>
<td>7</td>
<td>60</td>
</tr>
<tr>
<td>Paty</td>
<td>2002</td>
<td>67</td>
<td>14</td>
<td>60</td>
</tr>
<tr>
<td>Mulhearn</td>
<td>2000</td>
<td>49</td>
<td>18</td>
<td>52</td>
</tr>
</tbody>
</table>
Transanal excision for a sessile polyp with invasive carcinoma or T1 carcinoma of the low rectum

- 3 to 5 fold higher risk recurrence compared with radical resection
- immediate radical resection after local excision (within 1 month) gives a better prognosis