Outline

• Types of polyps
• Polyposis
• Management of polyps
Types of Polyps

- Schwartz - “Polyp is a nonspecific clinical term that describes any projection from the surface of the intestinal mucosa regardless of its histologic nature”
- Colorectal polyps may be classified as:
  - Non-neoplastic (inflammatory, hyperplastic, mucosal, submucosal)
  - Hamartomatous (juvenile, Peutz-Jeghers, Cronkite-Canada)
  - Neoplastic (tubular adenoma, villous adenoma, tubulovillous adenomas)
Nonneoplastic Polyps

• Hyperplastic Polyps
  • Most common colonic polyp
  • Normal cellular components
  • Do not exhibit dysplasia
  • Difficult to distinguish from adenomatous polyps endoscopically
  • Serrated ‘saw-tooth’ pattern on pathology
  • Hematoxylin and eosin stains can distinguish from adenoma
  • Typically in rectosigmoid and < 5mm
• What risk does a small left sided hyperplastic polyp confer for CRC?
  • Not clear, generally considered NOT premalignant.
  • A systematic review of 4 studies addressing this found a RR of 1.3 for a proximal CRC when small hyperplastic polyp was found distally on sigmoidoscopy

• Do large hyperplastic polyps confer a CRC risk?
  • Greater risk of adenomatous or dysplastic foci
  • > 2cm hyperplastic polyps may be considered pre-malignant and should be removed completely
Hyperplastic Polyposis Syndrome

WHO Dx criteria:
- $\geq 5$ HPs proximal to sigmoid of which at least two are $>1\text{cm}$ or
- $\geq 30$ HPs throughout colon & rectum or
- Any # HPs prox to sigmoid and +FHx of HPS

Excess gene methylation affecting several TSG’s

 CRC risk 50%

Tx depends on location, number and characteristics of polyps - EMR vs colectomy

1-3 year surveillance starting 10 yrs earlier than earliest age dx’d
• **Inflammatory polyps**
  • Pseudopolyp
  • Most commonly occur with IBD, but can occur with any colitis
  • Not premalignant, but difficult to distinguish from adenomatous polyps endoscopically
  • Typically multiple
Hamartomatous Polyps

- Usually not premalignant when solitary
- Polyposis confers ↑ CRC risk
- More common in childhood
- Bleeding is common sx
- Protein-losing enteropathy
- Can be lead point for intussusception
- Grossly identical to adenomatous polyps
- Harmartomatous polyposis
  - Familial juvenile polyposis
  - PJS (Peutz-Jeghers syndrome)
  - Cronkhite-Canada syndrome
Familial Juvenile Polyposis

- Autosomal dominant
- Hundreds of hamartomatous polyps
- May degenerate into adenoma
- \( \uparrow \) CRC risk 9-50%
- Annual screening starting at age 10
- Germ-line mutations SMAD4 & BMPR1A genes associated with some subsets
- Dx -
  - > 5 JPs in colon
  - Multiple JPs throughout GIT
  - Any # JPs with +FHx
• Tx -
  • Colectomy with IRA if rectum spared with continued surveillance of rectum
  • Proctocolectomy with IPAA if rectum affected
  • OGD surveillance if UGI polyps
PJS

- Autosomal dominant
- STK-11 mutation (Serine Threonine Kinase - TSG)
- Small bowel hamartomas most common, gastric and colon also occurs
- RF for SB intussusception
- Distinguished from FJP by presence of smooth muscle bundles in submucosa
- Dx - PJS polyps + 2 of following:
  - + FHx
  - Hyperpigmentation of lips/buccal mucosa (mucocutaneous melanocytic macule)
  - SB polyposis
• PJS has ↑ extracolonic malignancy risk and ↑ CRC risk 15 - 84 X
• Tx-
  • Endoscopic surveillance - OGD, capusule endo, and colonoscopy q 3-4 years starting at age 20 (+/- FS annually)
  • Surgical tx of complications like SBO, bleeding, and intussusception…at same time take a ‘clean sweep’ approach and remove as many polyps as safely possible
Cronkhite-Canada Syndrome

- Rare non-familial d/o
- Hamartomatous polyposis associated with alopecia, cutaneous hyperpigmentation, onychodistropy (atrophy of fingernails and toenails), diarrhea, wt loss, abdo pain
- Unknown etiology
- Surgery reserved for complications
Neoplastic/Adenomatous Polyps

- Common ~ 25 % pop under 50
- Risk of malignant degeneration is related to polyp size, type, & degree of dysplasia
- ↑ polyp size = ↑ CRC risk
- CRC in polyp < 1cm is rare (1-2%)
- Risk CRC in polyp > 2cm is 35 - 50%
- Adenoma-Carcinoma sequence - activation of oncogenes (K-ras) and inactivation of tumor supressor genes (APC, p53, DCC)
Adenoma-Carcinoma Sequence

- Normal epithelium
- Initiation → 5q loss APC
- Hyperproliferative epithelium (dysplasia)
- Alterations in DNA methylation (early adenoma)
- Promotion → 12p activation K-ras
- Intermediate adenoma
- 18q loss DCC
- Late adenoma
- Malignant conversion → 17p loss p53
- Carcinoma
- Metastasis
Types of Adenomatous Polyps

- **Tubular adenoma**
  - Most common - 65-80%
  - ~ 5% CRC risk
  - ↑ polyp size = ↑ CRC risk
    - <1cm polyp assoc w < 5% CRC risk
    - >2cm polyp assoc w ~ 35% CRC risk
  - Branching adenomatous epithelium = tubular
• **Villous adenoma**
  - 5-15% of adenomatous polyps
  - More often sessile
  - Often have severe atypia or significant dysplasia
  - Long glands extending down from surface to centre of polyp
  - >2cm polyp assoc w ~ 50% CRC risk

• **Tubulovillous adenoma**
  - 10-25% of adenomatous polyps
National Polyp Study Workgroup
advanced pathologic features for CRC:

- Adenomatous polyps > 1cm
- Adenomatous polyps with HG dysplasia
- Adenomatous polyps with >25% villous histology
- Adenomatous polyps with invasive ca
Adenomatous Polyposis Syndromes

• FAP
  • Gardner Syndrome
• MYH Associated Polyposis
• Turcotte Syndrome
• HNPCC

Management of Polyps

- Removal of adenomatous polyps recommended b/c or CRC risk over time
- Small adenomas are less likely to bleed than larger advanced lesions
- **Villous histology, ↑polyp size, high-grade dysplasia, & older age are all independent risk factors for focal ca within an adenoma**
- Endoscopic polypectomy
- Surgical resection
• If invasive ca penetrates the muscularis mucosa, consideration of the risk for lymph node metastasis and local recurrence is required
• Must now determine whether a more extensive resection is required
• Hence…
• …the Haggitt classification for polyps containing cancer according to the depth of invasion
Haggitt Classification for Polyps with Invasive Ca

- **Level 0** = Ca in situ, not invade mm
- **Level 1** = Ca invades thru mm into submucosa, limited to head of polyp
- **Level 2** = Ca invades neck of polyp
- **Level 3** = Ca invades stalk of polyp
- **Level 4** = Ca invades submucosa of bowel wall = T1

- *All sessile polyps with invasive Ca are level 4 by Haggitt's criteria*
- *Level 1-3 are limited to polyp wall & do not involve normal bowel wall*
Haggitt Levels

QuickTime™ and a decompressor are needed to see this picture.
Polyp Tx/Removal

- Colonscopy is gold standard for detection and removal of polyps...but it’s not perfect...it operator dependent
- CT colonography may identify missed polyps, however is not therapeutic
- Bowel prep, endoscopic experience, and withdrawal time are all factors in polyp detection
- Colonscopic polypectomy techniques:
  - Cold bx, hot bx, cold snare, hot snare, fulguration (argon), piecemeal excision, saline assisted mucosal resection (EMR)

- 7882 colonoscopies by 12 experienced gastroenterologists over 15 months.
- 2053 screening
- Compared rates of detection of neoplastic lesions - mean withdrawal times <6 min vs mean withdrawal times of ≥6 min
- 11.8% vs 28.3% (p<0.001) for any neoplasia
- 2.6% vs 6.4% (p=0.005) for adv neoplasia
- Conclusion - observed greater rates of detection of adenomas among endoscopists who had longer mean times for withdrawal of the colonoscope
Summary of ACG Guidelines

- Small polyps should be completely removed. If numerous >20, representative bx’s should be done.
- Large pedunculated polyps are usually easily removed with hot snare.
- Large sessile adenomas may require piecemeal resection or mucosal saline injection to raise them away from the muscularis propria for EMR.
- If polyp does not raise then is suggests invasion of mp and EMR not advisable.
- F/u colonoscopy 3-6/12 after removal of large (>2cm) polyps if there is concern regarding incomplete removal.
• No lymphatics above musc mucosa, thus HG dysplasia is non-invasive if it is limited within a resected polyp & requires no further therapy if resection margins neg

• Adenomas with early invasive ca have < 1% risk of lymphatic mets...polypectomy is usually adequate if neg margins
Mgt of Malignant Polyps

- ACG recommends no further Tx if all of the following criteria are met:
  - Polyp endoscopically considered completely excised
  - Pathology able to accurately determine depth invasion, grade, & completeness of excision
  - Ca is not poorly diff
  - Margin of excision is not involved

- When all of these low risk criteria are not met, segmental colectomy must be considered - individualized
Indications for Colectomy

- Large adenomas not amenable to safe polypectomy
- Incomplete resection and pathology revealing foci of ca or HG dysplasia
- Repeated failed endoscopic removal of large polyp
- All low risk ACG criteria not met after endo Tx
Surveillance

- *Pooled analysis* of 8 RCTs estimated risk of CRC ~ 12% within 5 years post polypectomy of adenoma
- Strongest risk factors
  - Invasive ca in initial polypectomy
  - Older age
  - Size and number of adenomas

- [http://www.gastro.org/wmspage.cfm?parm1=4453](http://www.gastro.org/wmspage.cfm?parm1=4453)
ACG, AGA, ACS, SAGES Surveillance Guidelines

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• **National Polyp Study (NEJM 1993)**
  • 1418 pts with colonic adenomas randomly assigned to surveillance at 1 & 3yrs or 3yrs only
  • % of pts with adenomas with adv pathologic features was the same in both groups
  • Frequency of ca was not different in the two groups and only 0.5%
  • Established that a 3yr interval for surveillance is safe for most pts
Polyp Prevention

- ACG Recommendations (limited data):
  - Diet low in fat & high in fruits and fibre
  - Normal body wt and regular exercise
  - No smoking, no excess EtOH
  - Dietary supp with 3g CaCO3
- Insufficient data to recommend ASA or NSAIDs or selenium supp
- 2 large RCTs evaluating COX-2 inhibitors for chemoprevention of polyps showed significant reductions in advanced adenomas with high doses of celecoxib
- However, vascular events (stroke & MI) were significantly higher

- Regular use of aspirin reduced the incidence of colonic adenomas in RCTs, case-control studies, and cohort studies.
- In cohort studies, regular use of aspirin was associated with RR reductions of 22% for incidence of colorectal cancer.
- Two RCTs of low-dose aspirin failed to show a protective effect.
- Data for colorectal cancer mortality were limited.
- Benefits of chemoprevention more evident when aspirin was used at a high dose and for >10yrs.
- Aspirin use was associated with a dose-related increase in incidence of GI complications.

- One cohort study showed no effect of non-ASA NSAIDs on death due to CRC.
- CRC incidence was reduced with non-ASA NSAIDs in other cohort studies & case-control studies.
- Adenoma incidence was also reduced with non-ASA NSAID use in cohort studies & case-control studies.
- Colorectal adenoma incidence was reduced by COX-2 inhibitors in RCTs.
- The ulcer complication rate associated with non-ASA NSAIDs was 1.5% per year.
- Compared with non-ASA NSAIDs, COX-2 inhibitors reduce this risk but, in multiyear use, have a higher ulcer complication rate than placebo.
- COX-2 inhibitors increase the risk for serious cardiovascular events.
• **Conclusion:**
  • COX-2 inhibitors and NSAIDs reduce the incidence of colonic adenomas.
  • However, these agents are associated with important cardiovascular events and gastrointestinal harms.
  • The balance of benefits to risk does not favor chemoprevention in average-risk individuals.

  • Baron et al. *A randomized trial of rofecoxib for the chemoprevention of colorectal adenomas*. Gastroenterology 2006; 131:1674.

- 4 clinical trials with 2967 randomly assigned participants.
- Each trial evaluated aspirin for the secondary prevention of colorectal adenomas.
- Doses of aspirin tested ranged from 81-325 mg/d.
- Adenomas were found in 424 (37%) of the 1156 participants allocated to placebo and in 507 (33%) of the 1542 participants allocated to any dose of aspirin.
- Advanced lesions were found in 12% of participants in the placebo group and in 9% of participants allocated to any dose of aspirin.
- Absolute risk reduction of 6.7% (95% CI = 3.2-10.2%)
- Conclusion - Aspirin is effective for the prevention of colorectal adenomas in individuals with a history of these lesions.
United States Preventive Services Task Force (USPSTF)

- Concluded that overall, the harms outweighed the benefits of aspirin and NSAIDs for use for the prevention of colorectal cancer in asymptomatic adults at average risk for colorectal cancer including those with a family history of colorectal cancer.
- These recommendations do not apply to individuals with familial adenomatous polyposis, hereditary nonpolyposis colorectal cancer, or a personal history of colorectal cancer or adenomas.
- Grade 1B
Thank you