Colon Cancer Screening and Surveillance

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Outline

- Colon cancer screening
  - Why do we do it?
  - Guidelines
    - When to start
    - Options on modality
- Colon cancer surveillance
  - Guidelines
  - Serrated polyps

Definitions

- Screening
  - To identify polyps/cancer in a patient without a personal history of cancer or precancerous lesions
  - No signs/symptoms of suspected colorectal disease
- Surveillance
  - To identify polyps/cancer in an individual with previously identified polyps/cancer
  - No signs/symptoms of suspected colorectal disease

Baron et al. Recommended Intervals Between Screening and Surveillance Colonoscopies. Mayo Clin Proc. 8.2013.

Why is colon cancer important?

- 3rd most common cancer in women and men
  - 8% of all new cancer diagnoses
- Overall lifetime risk is ~ 5-6%

American Cancer Society, 2014 estimates

Colon Cancer Screening

- **Multiple modalities have been shown to reduce colon cancer mortality**
  - **Colonoscopy**
    - Zauber et al. Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. NEJM 2/23/12.
  - **Flexible sigmoidoscopy**
    - Nishihara et al. Long-term colorectal-Cancer Incidence and Mortality after Lower Endoscopy. NEJM 9.2013.
  - **Fecal occult blood testing (FOBT)**
    - Shaukat et al. Long-Term Mortality after Screening for Colorectal Cancer. NEJM 9.2013
  - **Fecal immunochemical testing (FIT)**
    - Chiu et al. Effectiveness of Fecal Immunochemical Testing in Reducing Colorectal Cancer Mortality From the One Million Taiwanese Screening Program. Cancer 2015.

*** Remember - Whatever screening your patient will accept is better than none…**

Colon cancer screening

- **Multiple guidelines exist and updates are reported to be coming soon:**
  - **American College of Gastroenterology (ACG, 2008)**
  - **National Comprehensive Cancer Network (NCCN, updated continuously)**
  - **US Multi-Society Task Force on Colorectal Cancer (USMSTF, 2008) aka "Joint Guidelines"**
  - **US Preventative Services Task Force (2008)**

Colon cancer screening guidelines

- I generally use ACG 2008 guidelines due to simplicity
- Average risk screening should start at age 50
  - African Americans should begin at age 45
- Recommend cancer prevention tests first
  - Both prevent and detect colon cancer
- Colonoscopy is preferred, if normal repeat in 10 years

Colon cancer screening guidelines

- Alternative cancer prevention tests
  - Flexible sigmoidoscopy
    - If normal, repeat in 5-10 years (USMSTF – every 5 years)
    - If polyp found, requires colonoscopy for completion
      - Detects 60-70% of neoplasia found at colonoscopy

ACG 2008

Colon cancer screening guidelines

- CT colonography
  - If normal, repeat in 5 years
    - –Performs fairly well for polyps > 1 cm (90% detection)
    - –Does not detect polyps 5 mm or smaller
  - –Still requires bowel prep (despite "virtual colonoscopy" tagline)
  - If polyp found, requires colonoscopy for completion

ACG 2008

Why start African Americans early?

- **Average annual age-specific colorectal cancer incidence rates by race in California (per 100,000 persons)**

Age (yr)	Asian	**Black**	Latino	White
45	18.4 (13.6–23.2)	**23.2 (16.5–29.9)**	10.2 (7.68–12.8)	16.0 (14.2–17.8)
50	35.2 (27.4–42.9)	**56.6 (44.8–68.4)**	26.6 (21.7–31.4)	33.2 (30.3–36

Theuer et al. Racial and ethnic colorectal cancer patterns affect the cost-effectiveness of colorectal cancer screening in the United States. Gastroenterology 2001.

Colon cancer screening guidelines with family history

- First degree relatives (FDR) with colon cancer or advanced adenoma at age < 60 years or 2 FDR with this
  - Start screening at age 40 or 10 years younger than age of youngest affected relative
  - Colonoscopy every 5 years
- FDR ≥ 60 years with CRC or adv. Adenoma
  - Treat as average risk
- ACG 2008 – no comment on 2nd degree relatives

ACG 2008

Colon cancer screening guidelines with family history

- I use USMSTF 2008 guidelines when a patient has 2nd degree relatives with CRC
- If colon cancer or adenomas in 2 or more second degree relatives
  - Start screening at age 40
  - Screening intervals are same as average risk

*FDR with small adenomas – Increased risk USMSTF
Average risk ACG

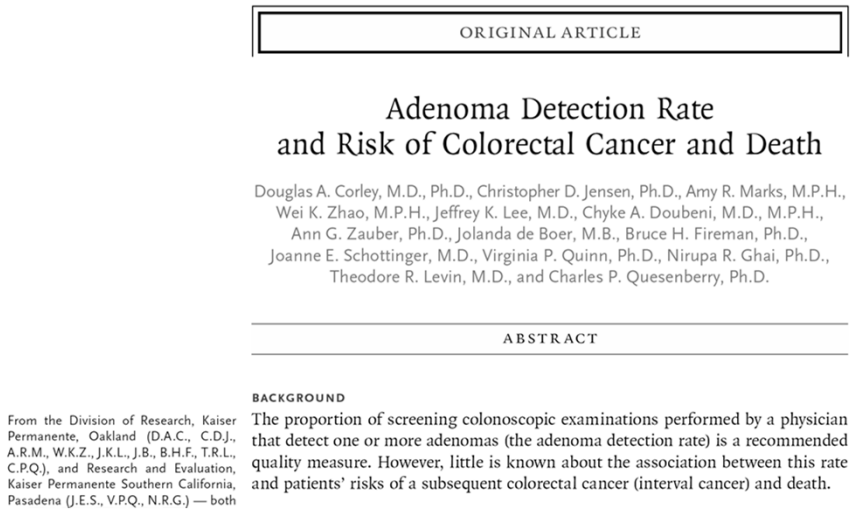
Levin et al. Screening and Surveillance for the Early Detection of Colorectal Cancer and Adenomatous Polyps, 2008: A Joint Guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. *CA: A Cancer Journal for Clinicians, 2008.*

Colon cancer screening guidelines with family history

- **Why do we care about second degree relatives (SDR)?**
- **Population-based studies have shown SDR of patients with colon cancer have:**
  - **Increased risk of colon cancer : 1.32 (CI 1.19 – 1.47)**
  - **Increased risk of adenomas: 1.19 (CI 1.08 – 1.31)**

Sammader et al. Increased Risk of Colorectal Neoplasia Among Family Members of Patients with Colorectal Cancer: a Population-Based Study in Utah. Gastro 2014.

Importance of EFFECTIVE CRC screening



ORIGINAL ARTICLE

Adenoma Detection Rate and Risk of Colorectal Cancer and Death

Douglas A. Corley, M.D., Ph.D., Christopher D. Jensen, Ph.D., Amy R. Marks, M.P.H., Wei K. Zhao, M.P.H., Jeffrey K. Lee, M.D., Chyke A. Doubeni, M.D., M.P.H., Ann G. Zauber, Ph.D., Jolanda de Boer, M.B., Bruce H. Fireman, Ph.D., Joanne E. Schottinger, M.D., Virginia P. Quinn, Ph.D., Nirupa R. Ghai, Ph.D., Theodore R. Levin, M.D., and Charles P. Quesenberry, Ph.D.

ABSTRACT

BACKGROUND

The proportion of screening colonoscopic examinations performed by a physician that detect one or more adenomas (the adenoma detection rate) is a recommended quality measure. However, little is known about the association between this rate and patients' risks of a subsequent colorectal cancer (interval cancer) and death.

From the Division of Research, Kaiser Permanente, Oakland (D.A.C., C.D.J., A.R.M., W.K.Z., J.K.L., J.B., B.H.F., T.R.L., C.P.Q.), and Research and Evaluation, Kaiser Permanente Southern California, Pasadena (J.E.S., V.P.Q., N.R.G.) — both

NEJM April 3, 2014

Importance of EFFECTIVE CRC screening

Adenoma detection rate	Hazard Ratio	# of interval cancers
Quintile 1 - Low performers	Reference	9.8
ADR: 7 -19%		
Quintile 3	0.85	8
ADR: 24 -28%		
Quintile 5 - High performers	0.52	4.8
ADR: 33-52%		

Corley et al. Adenoma Detection Rate and Risk of Colorectal Cancer and Death. NEJM 4.2014.

Importance of EFFECTIVE CRC screening

Adenoma detection rate	Hazard Ratio	# of interval cancers
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Each 1.0% increase in the adenoma detection rate was associated with a 3.0% decrease in the risk of cancer

Corley et al. Adenoma Detection Rate and Risk of Colorectal Cancer and Death. NEJM 4.2014.

Importance of Adenomas
–or –
Why high quality colonoscopy is king

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Corley et al. Adenoma Detection Rate and Risk of Colorectal Cancer and Death. NEJM 4.2014.

Non-Endoscopic options

- **FIT preferred to FOBT**
  - **Better performance**
  - **Less reliance on dietary restrictions**
  - **Less samples to collect (FOBT is usually 2-3 samples)**
  - **Remember – FOBT in the office with rectal exam is NOT ACCEPTABLE**

Levin et al. Screening and Surveillance for the Early Detection of Colorectal Cancer and Adenomatous Polyps, 2008: A Joint Guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. *CA: A Cancer Journal for Clinicians, 2008.*

Non-Endoscopic options

- **Fecal DNA testing – Testing for CRC DNA from a stool sample**

  Benefit: No prep, no procedure (good for average risk patients unwilling/unable to undergo colonoscopy)

Downsides:

1. **Only works for cancer, inadequate for polyps**
2. **3 year interval has no basis in literature at this point**
3. **If positive but no colon lesions, is this a marker from above in GI tract or a false positive?**
4. **People do not like to collect stool samples**

Imperiale et al. Multitarget Stool DNA Testing for Colorectal-Cancer Screening. N Engl J Med 4.2014

Fecal DNA testing

- **Performed well for cancer detection**
  - **92.3% (60/65) CRC detected**
  - **Significantly better than FIT (92.3% vs 73.8%, P = 0.002)**
- **True colon cancer screening - no polyp detection/removal!**
  - **<u>42% (321/758) of advanced adenomas detected</u>**

***Wait for guidelines to endorse prior to using given questions regarding safe intervals**

Imperiale et al. Multitarget Stool DNA Testing for Colorectal-Cancer Screening. N Engl J Med 4.2014

Colon cancer surveillance recommendations

- No polyps (average risk): 10 years
- No polyps (increased risk due to FH): 5 years

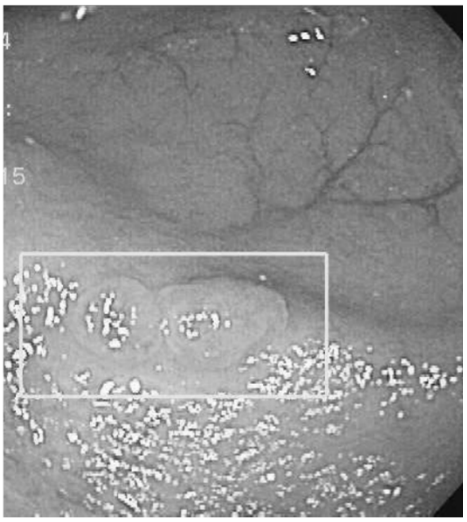
- 1-2 small adenomas (< 1 cm): 5 - 10 years
  - Most recommend 5 years

- ≥ 1 large adenoma (≥ 1 cm): 3 years
- Any high grade dysplasia: 3 years
- Any villous histology: 3 years
- 3-10 adenomas: 3 years

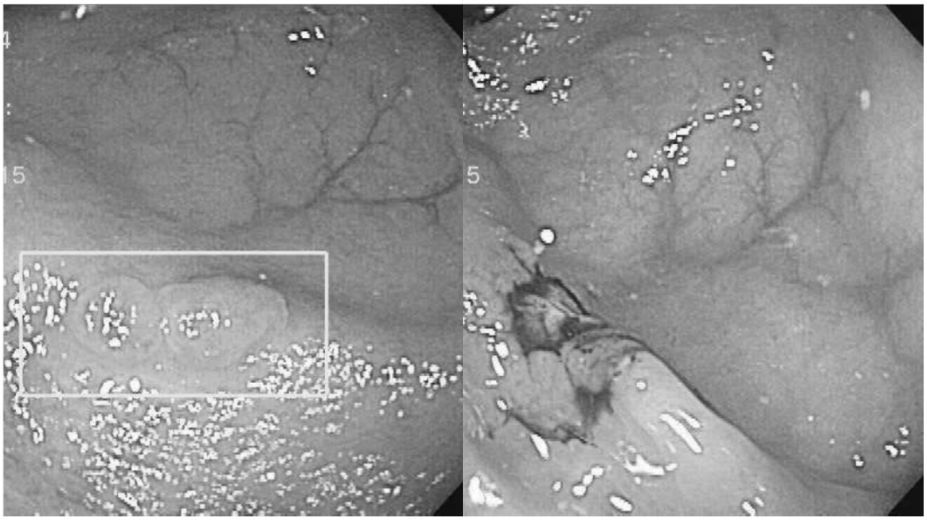
- ≥ 10 adenomas: < 3 years (most do 1 year, refer to Genetics)

Lieberman et al. Guidelines for Colonoscopy Surveillance After Screening and Polypectomy: A Consensus Update by the US Multi-Society Task Force on Colorectal Cancer. Gastroenterology 2012.

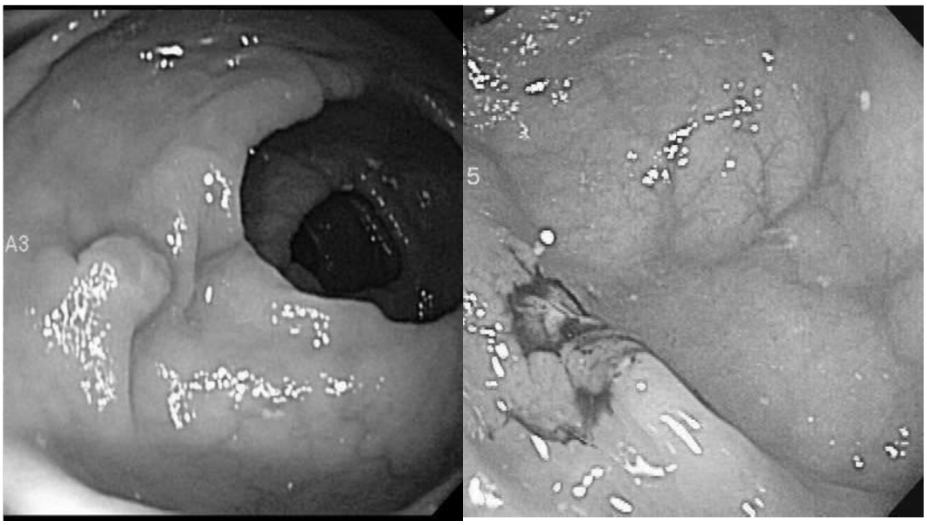
Adenomatous polyps



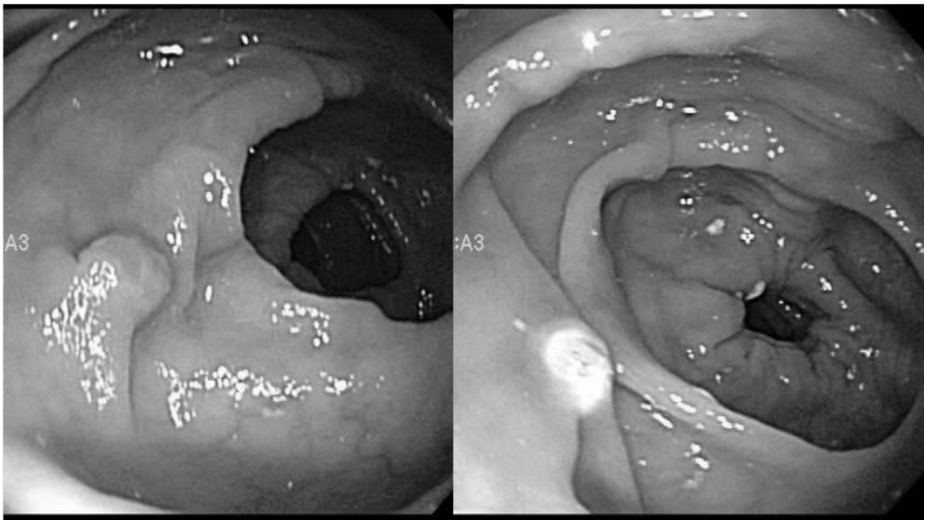
Adenomatous polyps



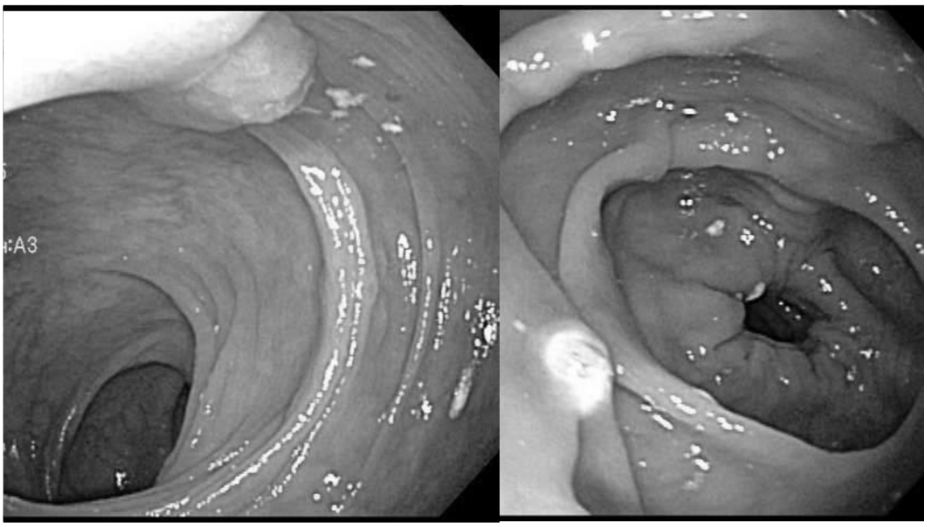
Adenomatous polyps



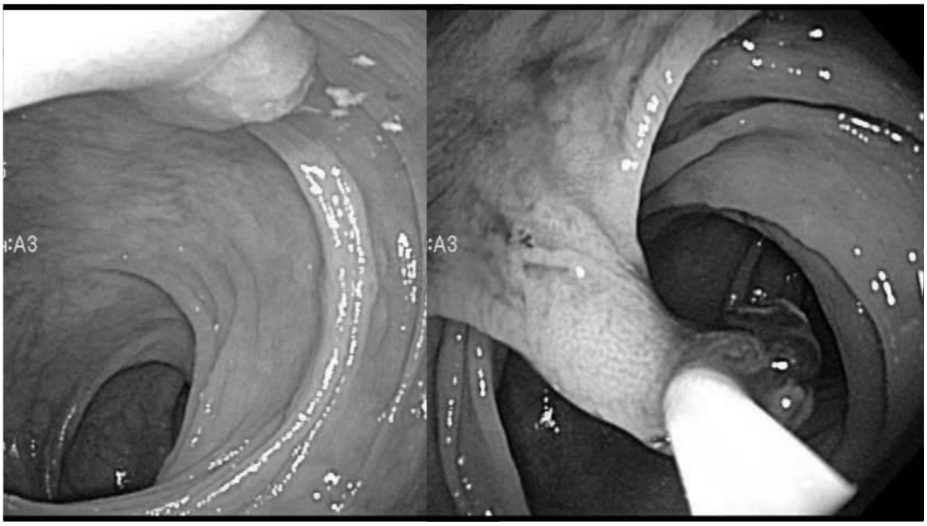
Adenomatous polyps



Adenomatous polyps



Adenomatous polyps



Colon cancer surveillance

- **Recommendations after the 1st Surv. Colonoscopy**

LRA – Low risk adenoma
HRA – High risk adenoma (>1 cm, high grade dysplasia, villous histology, ≥3 adenomas)

- **<u>Index procedure: LRA</u>, then on first surveillance:**
  - **If no adenomas, can return to 10 years.**
  - **If LRA/HRA, continue with standard surveillance recs**
- **<u>Index procedure: HRA</u>, then on first surveillance:**
  - **If no adenomas, repeat in 5 years.**
  - **If LRA/HRA, continue with standard surveillance recs**

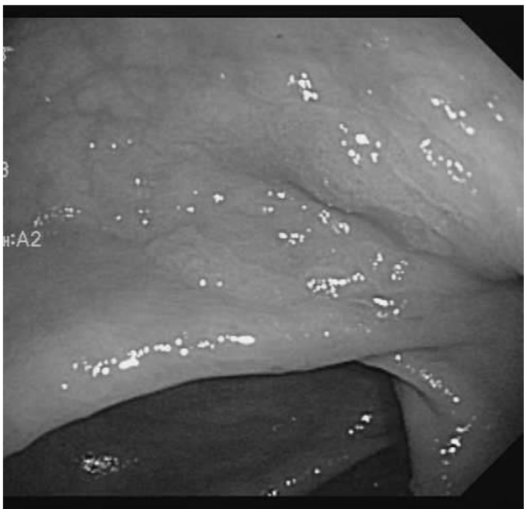
Lieberman et al. Guidelines for Colonoscopy Surveillance After Screening and Polypectomy: Consensus Update by the US Multi-Society Task Force on Colorectal Cancer. Gastroenterolog 2012.

Serrated colon polyps

- Includes:
  - Sessile serrated adenomas (SSA)
  - Sessile serrated polyps
    - Use interchangeably with SSA
  - Proximal hyperplastic polyps
    - Difficult for pathologists to differentiate from an SSA/P
  - Traditional serrated adenomas.
- <u>SSA/P likely the source of most interval cancers</u>
- Rectal and sigmoid hyperplastic polyps are not thought to confer an increased risk

Serrated colon polyps

- They can be very hard to see!



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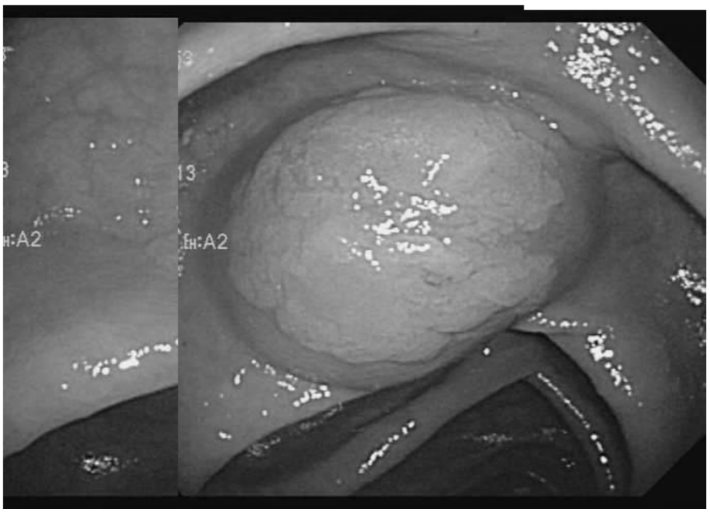

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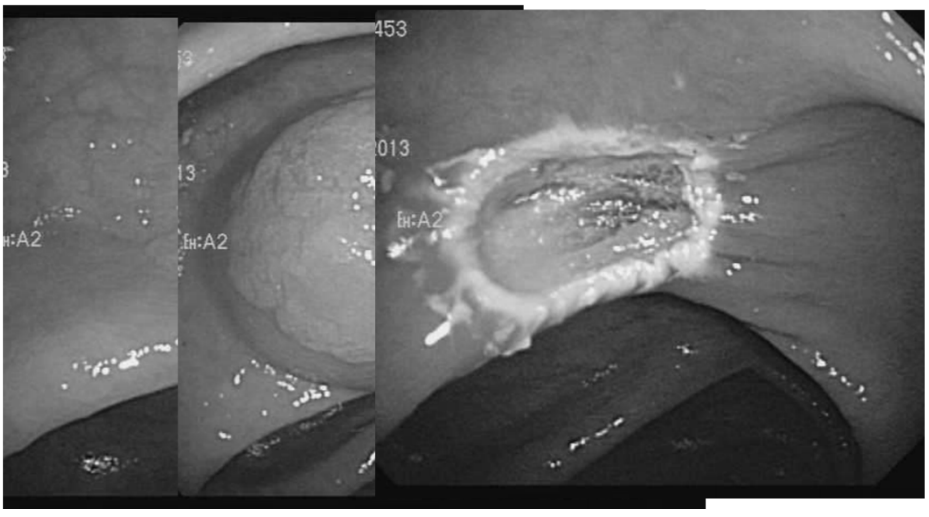

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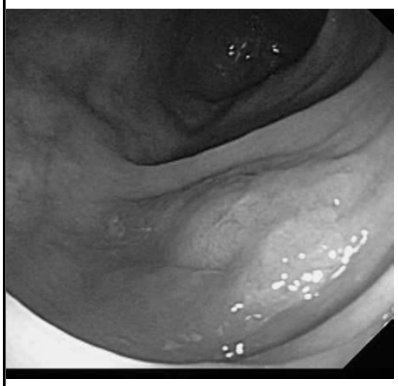

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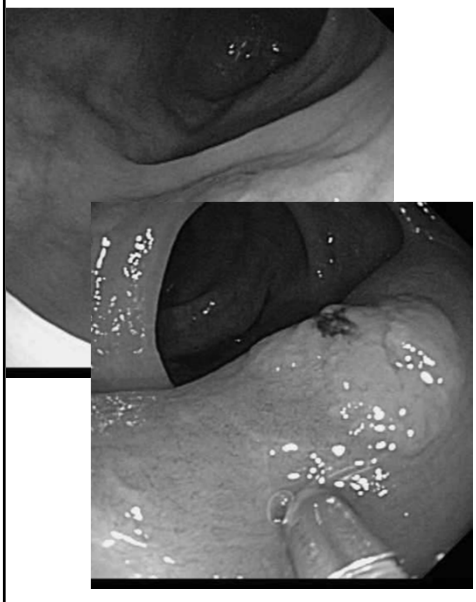
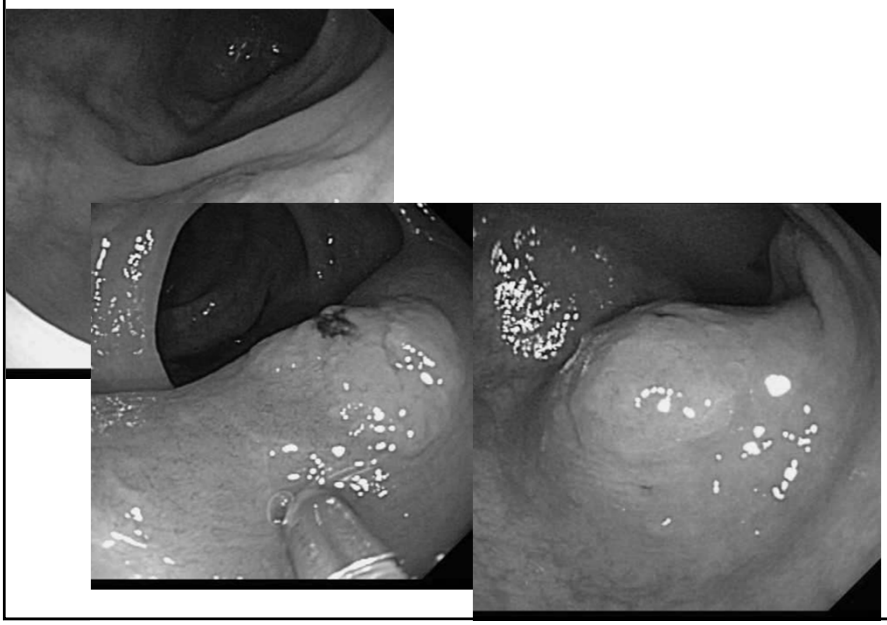
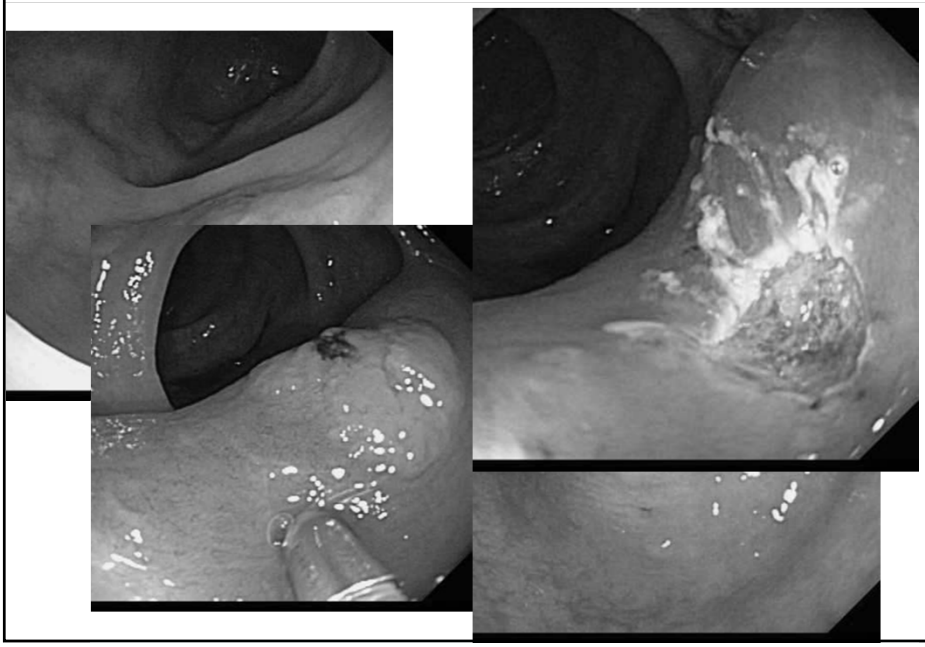


Serrated polyps



Serrated polyps



Serrated polyp surveillance intervals

- Sessile serrated adenomas/polyps (SSA/P)
  - Also applies for traditional serrated adenomas (TSA)
  - SSA / P: < 1 cm, 1 or 2 polyps: 5 years
  - SSA / P: ≥ 1 cm, 1 polyp: 3 years
  - SSA / P: ≥ 1 cm, ≥ 2 polyps: 1 – 3 years
    - Consider serrated polyposis syndrome
  - SSA / P: < 1 cm, ≥ 3 polyps: 3 years
  - SSA / P: Any with dysplasia: 1 – 3 years

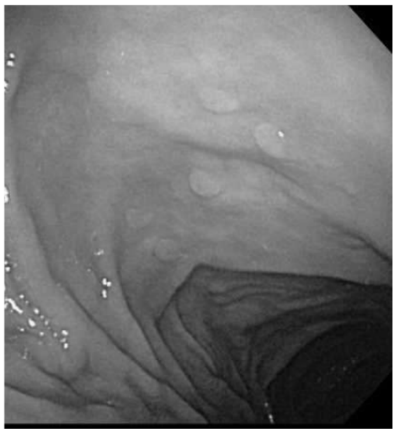
Rex et al. Serrated lesions of the colorectum: review and recommendations from an expert panel. AJG 2012.

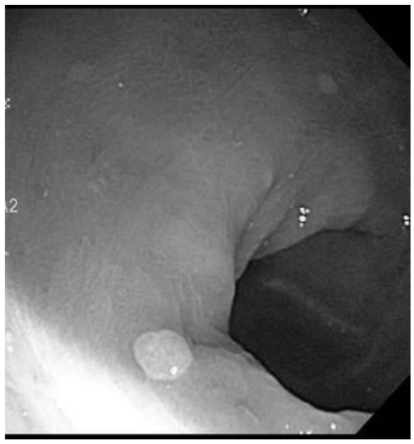
Serrated polyp surveillance intervals

- Hyperplastic polyps
  - Rectosigmoid: < 1 cm, any number polyps: 10 years
  - Proximal: small (≤ 5 mm), ≤ 3 polyps: 10 years
  - Proximal: Any size, ≥ 4 polyps: 5 years
  - Proximal: > 5 mm, ≥ 1 polyps: 5 years

Rex et al. Serrated lesions of the colorectum: review and recommendations from an expert panel. AJG 2012.

Rectal hyperplastic polyps





Colon cancer surveillance guidelines

<table>
<tr><th colspan="3">No polyps, or hyperplastic polyps in rectum/sigmoid</th></tr>
<tr><td colspan="3">Repeat in 10 years</td></tr>
<tr><td colspan="3">Neoplasia found</td></tr>
<tr><td>Serrated polyps/lesion</td><td>High risk adenomas</td><td>Low risk adenomas</td></tr>
<tr><td rowspan="2">Serrated polyposis
Repeat in 1 year</td><td>>10 Adenomas
Repeat in less than 3 years</td><td rowspan="4">1-2 Tubular adenomas
< 10 mm
Repeat in 5 – 10 years</td></tr>
<tr><td rowspan="3">3-10 Adenomas
Repeat in 3 years

Villous adenoma(s) or tubular adenoma(s) ≥ 10 mm
Repeat in 3 years

Adenoma(s) with high grade dysplasia
Repeat in 3 years</td></tr>
<tr><td>≥ 10mm or With dysplasia or traditional serrated adenoma
Repeat in 3 years</td></tr>
<tr><td>< 10 mm in Proximal colon and without dysplasia
Repeat in 5 years</td></tr>
</table>

These recommended intervals assume a complete exam to cecum, adequate bowel prep, and complete removal of polyps at the baseline exam.

Lieberman. Colon Polyp Surveillance: Clinical Decision Tool. Gastro 2013.

Why might clinical recommendations differ?

- **Piecemeal resection - If polyp was not removed in one piece, follow-up in 3-6 months recommended**
- **Large polyp requiring mucosal resection - Similar**
- **Bowel prep – if prep is not up to par, then shorter intervals likely to be recommended**
- **Not aware of personal or family history – might give average risk recommendations when should be high risk**

If not sure, ask the endoscopist for clarification

When to stop?

- **Screening – USPSTF recommends stopping at 75, with consideration of continuing through 85 based on comorbidities**
- **Surveillance – Should be individualized, based on assessment of risks, benefits and comorbidities**
  - **75-85 is likely reasonable**
  - **If colon cancer found, would patient accept/be offered surgery and/or chemotherapy?**

Lieberman et al. Guidelines for Colonoscopy Surveillance After Screening and Polypectomy: A Consensus Update by the US Multi-Society Task Force on Colorectal Cancer. Gastroenterology 2012.

Key Points

- Colon cancer screening is important and effective
  - Start at age 50, consider starting at age 45 in African Americans
- Colonoscopy is preferred as it both prevents and detects colon cancer in a single session
- Any screening modality is better than none
- Surveillance recommendations are more complicated than screening – but equally or more important!

Thank you

- For any questions or referrals, please contact me at:
  - Peter.Stanich@osumc.edu
  - http://go.osu.edu/INHP
  - (614) 293 – 6255

What is the best bowel prep for a colonoscopy?

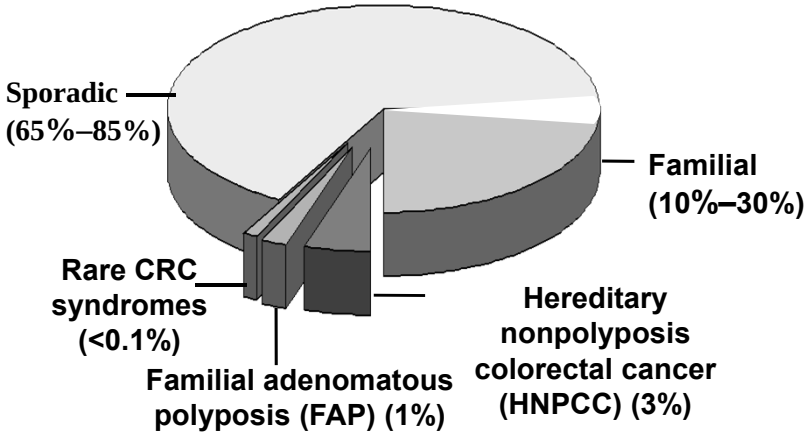
Capsule endoscopy

Recognizing the Red Flags: Does my patient have Hereditary Colorectal Cancer?

Heather Hampel , MS, LGC
Associate Director, Division of Human Genetics
Associate Director, Biospecimen Research
Professor, Internal Medicine
The Ohio State University Comprehensive Cancer Ctr.
The Ohio State University Wexner Medical Center

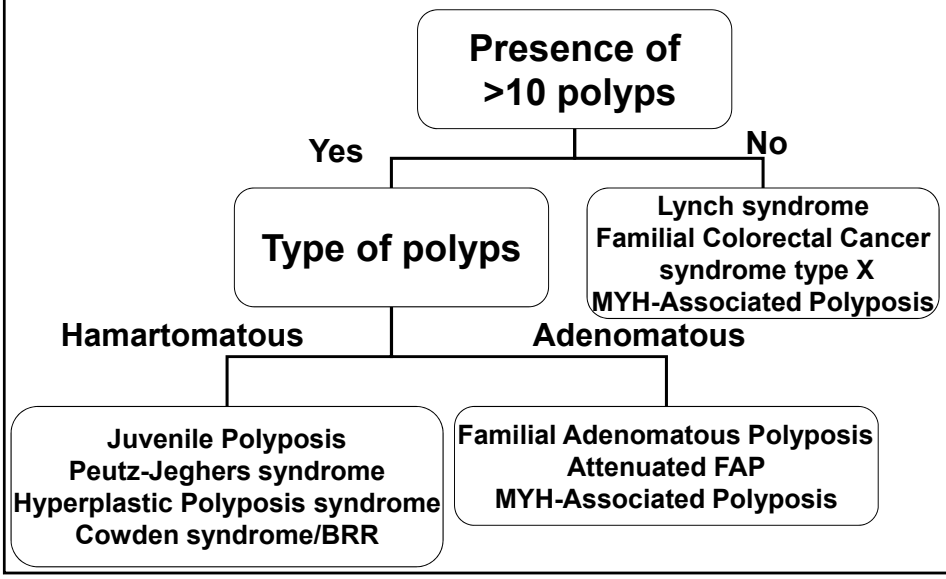
1. **Major Hereditary Causes of Colorectal Cancer**
2. **Red Flags for Polyposis**
3. **Red Flags for Lynch syndrome**
4. **Tumor Screening Red Flags for Lynch syndrome**
5. **Tools to Use in Clinic**
6. **Genetic Information Nondiscrimination Act**

Hereditary Susceptibility to CRC

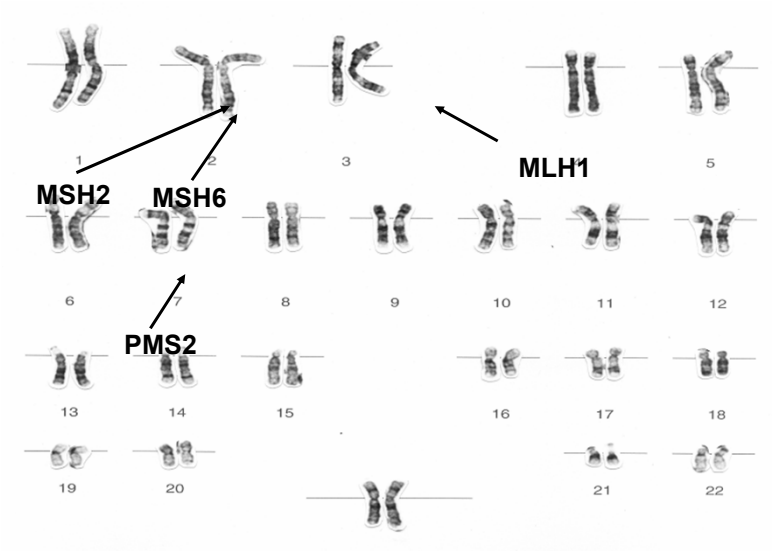


Adapted from Burt RW et al. *Prevention and Early Detection of CRC*, 1996

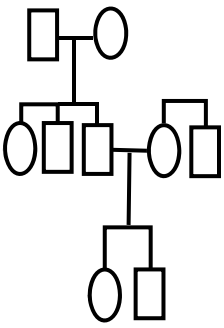
Flowchart for Hereditary Colon Cancer Differential Diagnosis

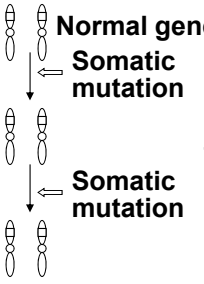


Lynch Syndrome Genes



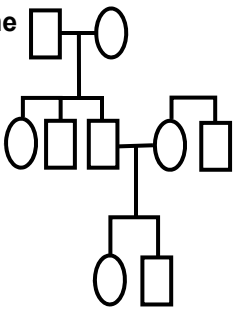
Sporadic

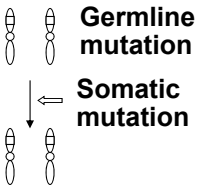




- Later age at onset (60s or 70s)
- Little or no family history of cancer
- Single or unilateral tumors

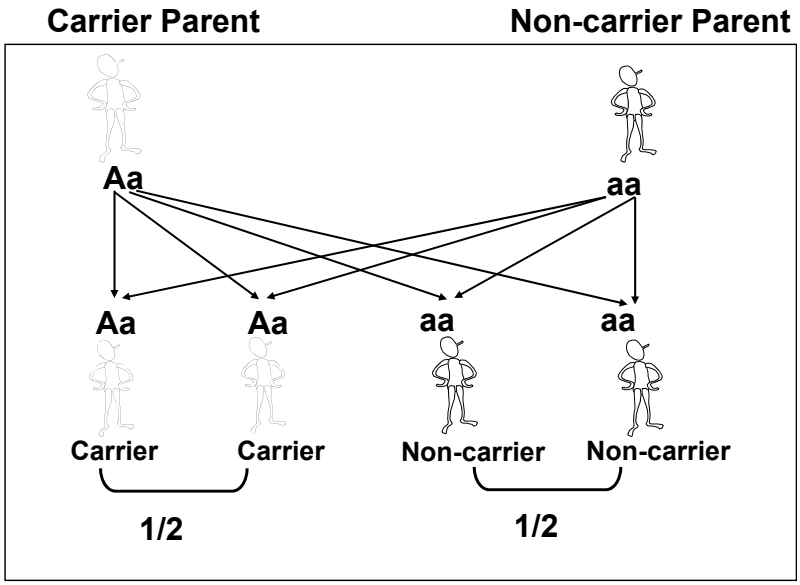
Inherited





- Early age at onset (<50)
- Multiple primary tumors
- Multiple generations with cancer
- Clustering of certain cancers (i.e. breast/ovarian)

Autosomal Dominant Inheritance



Lynch Syndrome Cancer Risks (to 70)

Cancer type	MLH1& MSH2	MSH6	PMS2	General Public
Colon cancer	40-80%	10-22%	15-20%	5.5%
Endometrial cancer	25-60%	16-26%	15%	2.7%
Stomach	1-13%	$\leq$ 3%	6%	<1%
Ovarian	4-24%	1-11%	6%	1.6%

NCCN Guidelines for Colorectal Cancer Screening 2.2013; Bonadona V. JAMA 2011;30-5:2304-10.; Senter L. Gastroenterology 2008:135:419-48.

Lynch Syndrome Surveillance Options

Intervention	Recommendation
Colonoscopy	Every 1-2 y beginning at age 20-25 (MLH1 & MSH2), or 25-30 (MSH6 & PMS2); or 2-5 y prior to the earliest colon cancer
Endometrial sampling	No clear evidence to support but could consider every 1 y beginning at age 30-35
Transvaginal U/S & CA-125	No clear evidence to support but clinicians could consider at their discretion every 1 y beginning at age 30-35
EGD with extended duodenoscopy	Every 2-3 y beginning at 30-35
Urinalysis	Every 1 y beginning at age 25-30
History & Exam w/ review of systems	Every 1 y beginning at age 25

NCCN Guidelines for Colorectal Cancer Screening 2.2012

Lynch Syndrome Prophylactic Surgery Options

- **Options include subtotal colectomy, hysterectomy, and oophorectomy**
- **Subtotal colectomy does not eliminate cancer risk**
- **Hysterectomy eliminates risk of endometrial and ovarian cancer**
- **Expert panels made no recommendation for or against surgery due to unproven efficacy**

Schmeler et al. NEJM 2006;354:261-9 &
NCCN Guidelines for Colorectal Cancer Screening 2.2012

Tumor Tests to Screen for Lynch Syndrome

- Microsatellite Instability (MSI) testing
  - Performed on DNA extracted from tumor and normal tissue – requires laboratory
  - Test is positive in 15% of CRC cases
  - Test is positive in 77-89% of LS cases
- Immunohistochemistry staining
  - Performed on thin slide of tumor – can be done in pathology department
  - 1-2 proteins are absent in 20% of CRC cases
  - 1-2 proteins are absent in 83% of LS cases

Red Flags for Polyposis

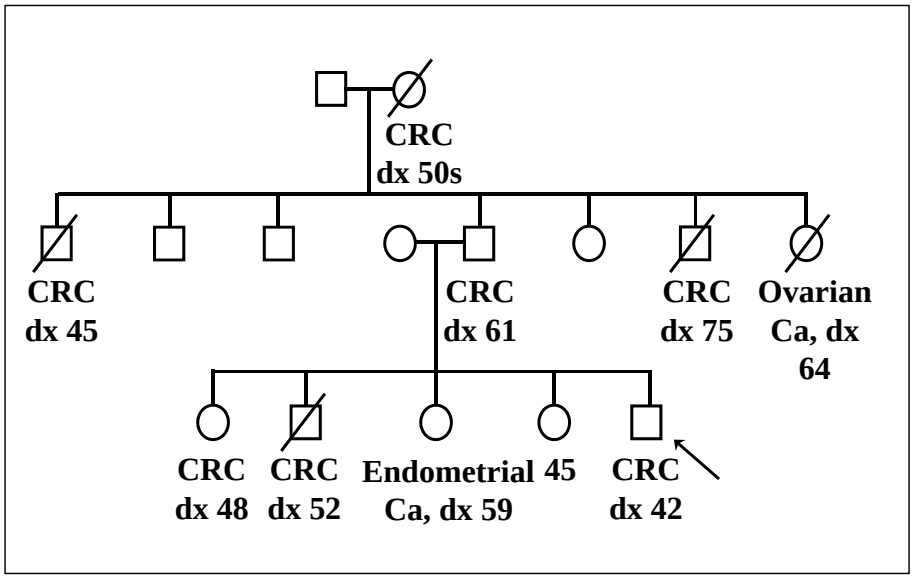
- >10 adenomas (at one time)
  - Familial Adenomatous Polyposis (FAP) and Attenuated FAP due to *APC* mutations
  - MUTYH-Associated Polyposis (MAP) due to biallelic *MUTYH* mutations (*Note this is the only recessive hereditary colon cancer syndrome)
  - Polymerase Proofreading Associated Polyposis (PPAP) due to mutations in *POLE* or *POLD1*
- >5 juvenile polyps
  - Juvenile Polyposis due to SMAD4 or BMPR1A mutations
- >2 Peutz Jegher polyps
  - Peutz Jegher syndrome due to STK11 mutations

Red Flags for Lynch Syndrome

- **Bethesda Guidelines**
  - **CRC dx <50**
  - **Synchronous or metachronous CRC, or other Lynch syndrome-associated tumors regardless of age**
  - **CRC with MSI-H histology dx <60**
  - **CRC with ≥1 FDR with an HNPCC-associated tumor, with one cancer dx <50**
  - **CRC with ≥2 FDRs or SDRs with an HNPCC-associated tumor, regardless of age**
  - **82% Sensitivity**
  - **77% Specificity**

Umar A, et al. JNCI. 2004;96(4):261-268.

Family History is Key to Diagnosing Lynch Syndrome – or is it?



Warning: Family Histories can be Deceiving

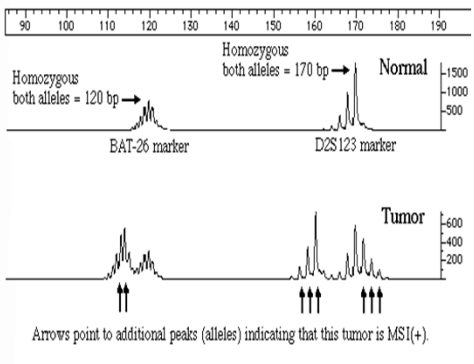
- Family size is getting smaller
- Wider use of colonoscopy likely to prevent many colon cancers
- MSH6 & PMS2 have lower cancer risks

Tumor Red Flags for Lynch Syndrome

- Microsatellite Instability (MSI) testing
  - Performed on DNA extracted from tumor and norma tissue – requires laboratory
  - Test is positive in 15% of CRC cases
  - Test is positive in 77-89% of LS cases
- Immunohistochemistry staining
  - Performed on thin slide of tumor – can be done in pathology department
  - 1-2 proteins are absent in 20% of CRC cases
  - 1-2 proteins are absent in 83% of LS cases
- Recommended to be performed routinely on CRC biopsy or surgical resection specimens
  - EGAPP, US Multi-Society Task Force on CRC, NCCN
  - Can be requested on TVAs on a case-by-case basis

Giardiello FM et al. Am J Gastroenterol. 2014;109(8):1159-79. EGAPP. Genet Med. 2009;11(1):35-41.

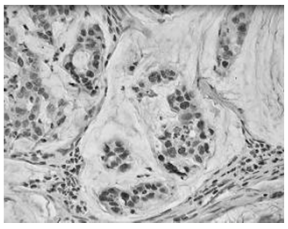
Tumor Red Flags for Lynch Syndrome: Microsatellite Instability Testing (MSI)



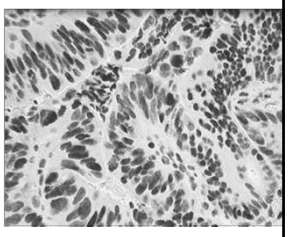
- Microsatellites are repetitive sequences in the DNA (eg. BAT-26)
- 5 microsatellites are usually assessed during testing
- If 2 or more are unstable, tumor is considered MSI-high > likely LS
- If 1 is unstable, tumor is considered MSI-low (can be treated like MSI-negative)
- If 0 are unstable, tumor is considered MSI-negative or MSS (microsatellite stable) > unlikely LS

Tumor Red Flags for Lynch Syndrome: Immunohistochemistry

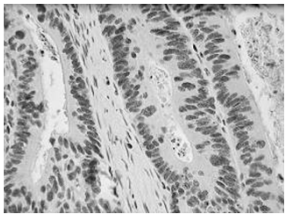
- Identify MMR proteins
- Normally present
- If protein is absent, gene is not being expressed (mutation or methylation)
- Helps direct gene testing by predicting likely involved gene
- If abnormal IHC (absent), MSI+



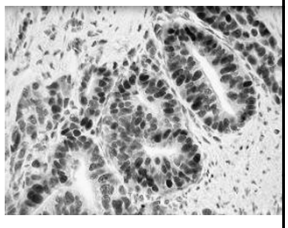
MLH1



MSH2



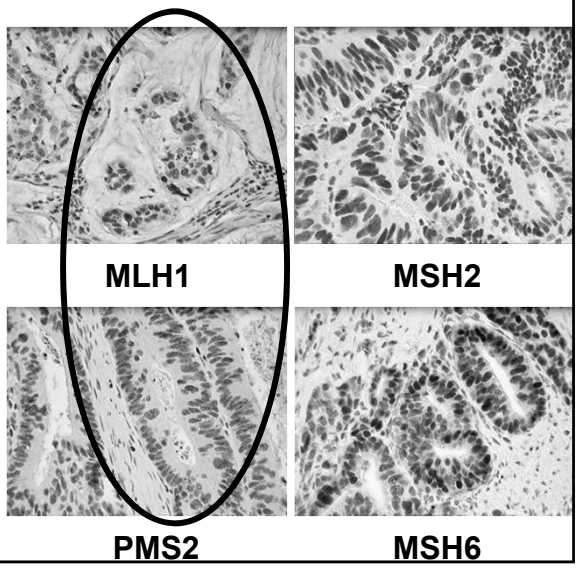
PMS2



MSH6

Tumor Red Flags for Lynch Syndrome: Immunohistochemistry

- Identify MMR proteins
- Normally present
- If protein is absent, gene is not being expressed (mutation or methylation)
- Helps direct gene testing by predicting likely involved gene
- If abnormal IHC (absent), MSI+



Tumor Red Flags for Lynch Syndrome: Immunohistochemistry

- Identify MMR proteins
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- Helps direct gene testing by predicting likely involved gene
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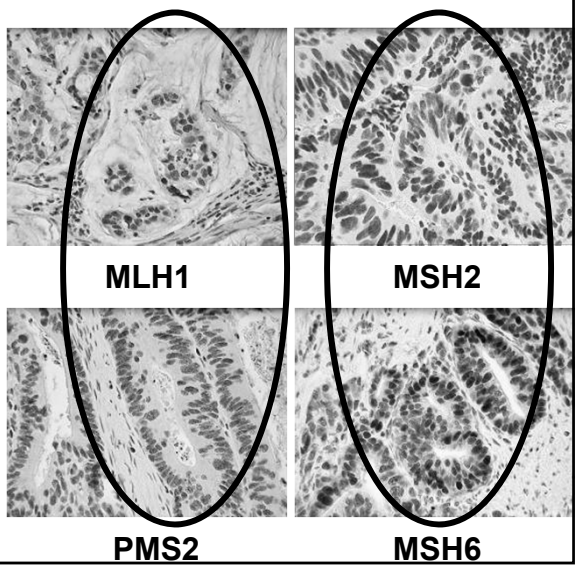
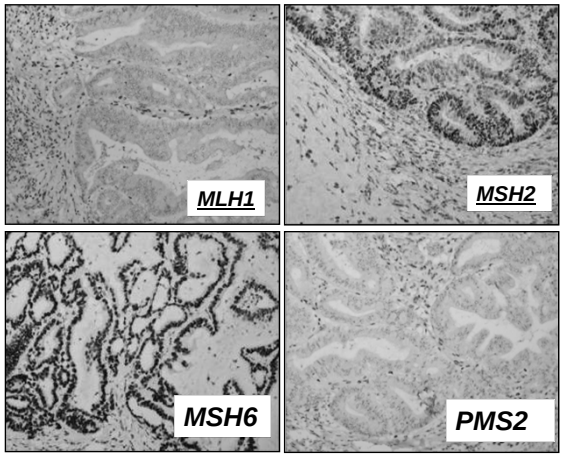


Tumor Red Flags for Lynch Syndrome: Normal – All 4 Stains Present

- 80% of the time you will get this result
- CRC is probably not MSI+
- Prognosis worse than if MSI+
- Refer to Genetics ONLY if
  - you suspect polyposis
  - patient dx <45
  - patient has had multiple CRC primaries, or
  - patient has a FDR with CRC at any age

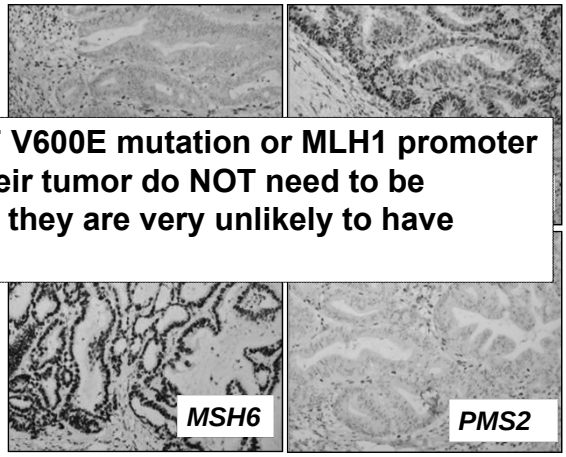
Tumor Red Flags for Lynch Syndrome: Abnormal – MLH1 & PMS2 Absent

- 15% of the time
- CRC is MSI+
- Better prognosis
- 80% acquired methylation of *MLH1*
- 20% will be LS
- BRAF test or MLH1 promoter methylation test is done to help sort this out.



Tumor Red Flags for Lynch Syndrome: Abnormal – MLH1 & PMS2 Absent

- 15% of the time
- CRC is MSI+
- Better prognosis
- Patients with the BRAF V600E mutation or MLH1 promoter hypermethylation in their tumor do NOT need to be referred to Genetics as they are very unlikely to have Lynch syndrome.
- 20% will be LS
- BRAF test or MLH1 promoter methylation test is done to help sort this out.



Tools to Use in Clinic: Colorectal Cancer Risk Assessment Tool

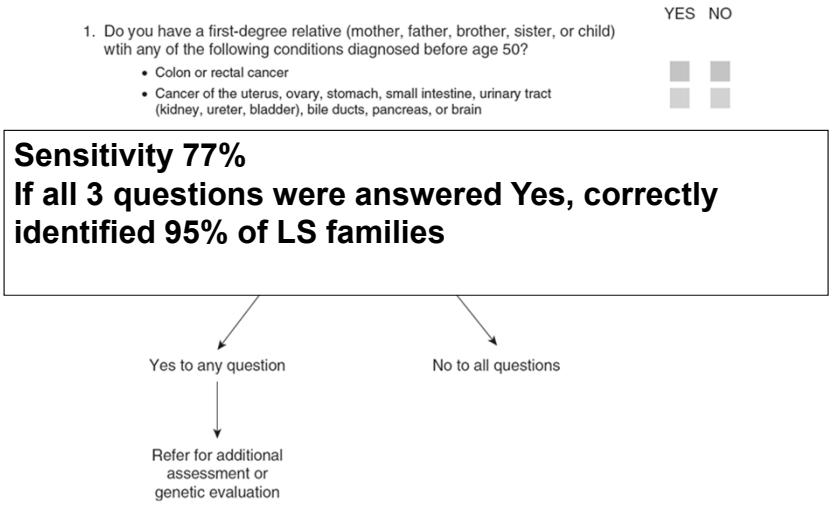
	YES	NO
1. Do you have a first-degree relative (mother, father, brother, sister, or child) wtih any of the following conditions diagnosed before age 50? • Colon or rectal cancer • Cancer of the uterus, ovary, stomach, small intestine, urinary tract (kidney, ureter, bladder), bile ducts, pancreas, or brain	☐	☐
2. Have you had any of the following conditions diagnosed before age 50: • Colon or rectal cancer • Colon or rectal polyps	☐	☐
3. Do you have three or more relatives with a history of colon or rectal cancer? (This includes parents, brothers, sisters, children, grandparents, aunts, uncles, and cousins.)	☐	☐

Yes to any question → Refer for additional assessment or genetic evaluation

No to all questions

Kastrinos F et al. Am J Gastroenterol 2009;104:1508-18.

Tools to Use in Clinic: Colorectal Cancer Risk Assessment Tool



Sensitivity 77%
If all 3 questions were answered Yes, correctly identified 95% of LS families

Kastrinos F et al. Am J Gastroenterol 2009;104:1508-18.

Tools to Use in Clinic: PREMM1,2,6 - http://premm.dfci.harvard.edu/

- Probability of *MLH1*, MSH2, or *MSH6* mutation
- Proband
  - # of CRCs & youngest age at dx
  - Y/N adenomas & youngest age at dx
  - Y/N EC & youngest age at dx
- FDRs & SDRs
  - # with CRC & youngest age at dx
  - # with EC & youngest age at dx
  - Y/N any with another HNPCC cancer
- Refer patients with >5% chance of having LS
- 90% Sensitivity
- 67% Specificity

Balmana J, et al. JAMA. 2006;296(12):1469-78.

Summary: Who should be referred to consider genetic testing

- Clinical testing criteria
  - Patients who meet Bethesda criteria
  - Patients with Endometrial cancer dx <50
  - Individuals with MMR mutation likelihood >5%
  - Individuals with abnormal tumor screening
  - Individuals with known dx of LS (or any hereditary cancer syndrome) in family
  - Individuals with >10 adenomatous polyps
  - Individuals with >5 juvenile polyps or >2 PJS polyps
- Routine tumor testing criteria
  - All CRC patients; OR
  - CRC patients dx <70 & CRC patients dx ≥70 who meet Revised Bethesda guidelines

Genetic Information Nondiscrimination Act (GINA)

- Prevents health insurers from denying coverage, adjusting premiums, or otherwise discriminating on the basis of genetic information.
  - Group and self-insured policies
- Insurers may not request that an individual undergo a genetic test.
- Employers cannot use genetic information to make hiring, firing, compensation, or promotion decisions.
- Sharply limits a health insurer's or employer's right to request, require, or purchase someone's genetic information.


The James
The Ohio State University
Comprehensive Cancer Center