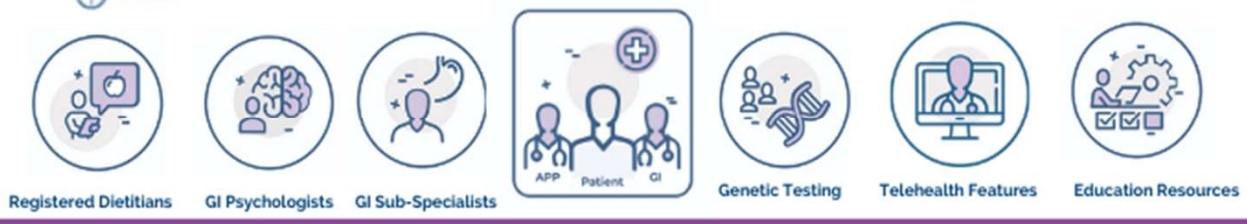
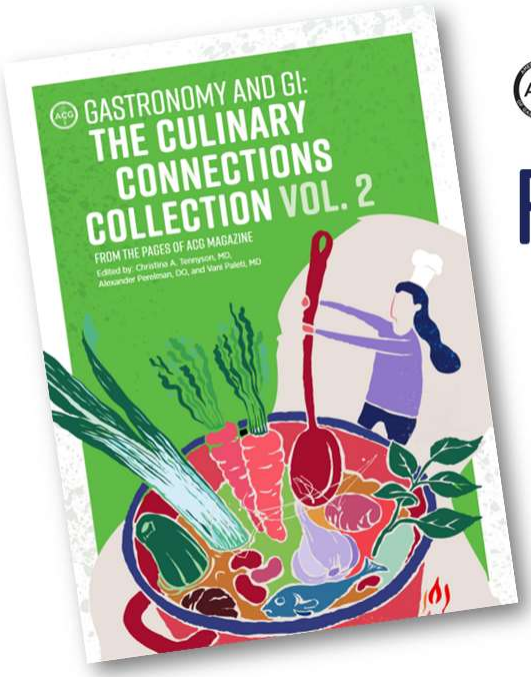
GI ON DEMAND

Access GI Expertise, Educational Resources and Support for You and Your Patients



A Free ACG Member Benefit Designed to Help You and Your Patients!
Learn More and Join Today at
GIONDEMAND.COM

1



GASTRONOMY AND GI:
FROM ACG MAGAZINE
THE CULINARY CONNECTIONS COLLECTION VOLUME 2

BIT.LY/ACG-FOODIES-2

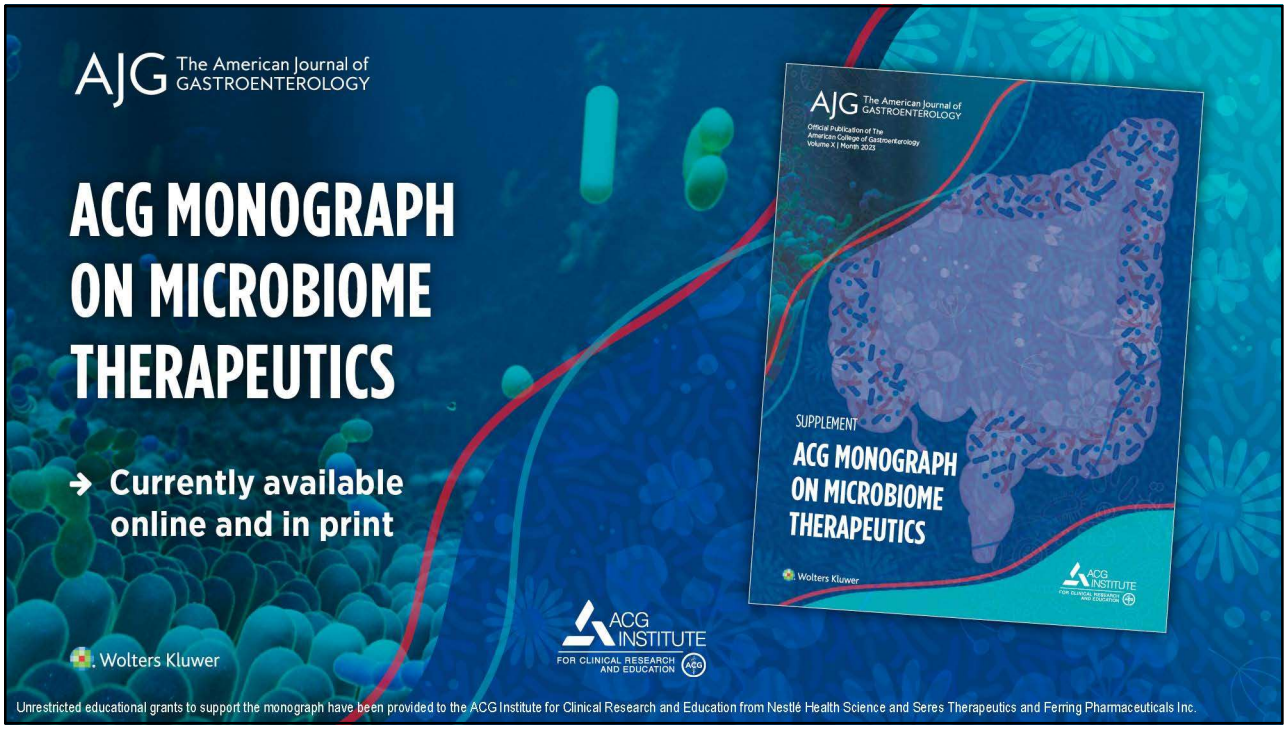
2


2024
ACG / FGS ANNUAL
SPRING SYMPOSIUM
MARCH 8-10, 2024
NAPLES GRANDE BEACH RESORT
NAPLES, FLORIDA
Register online: meetings.gi.org

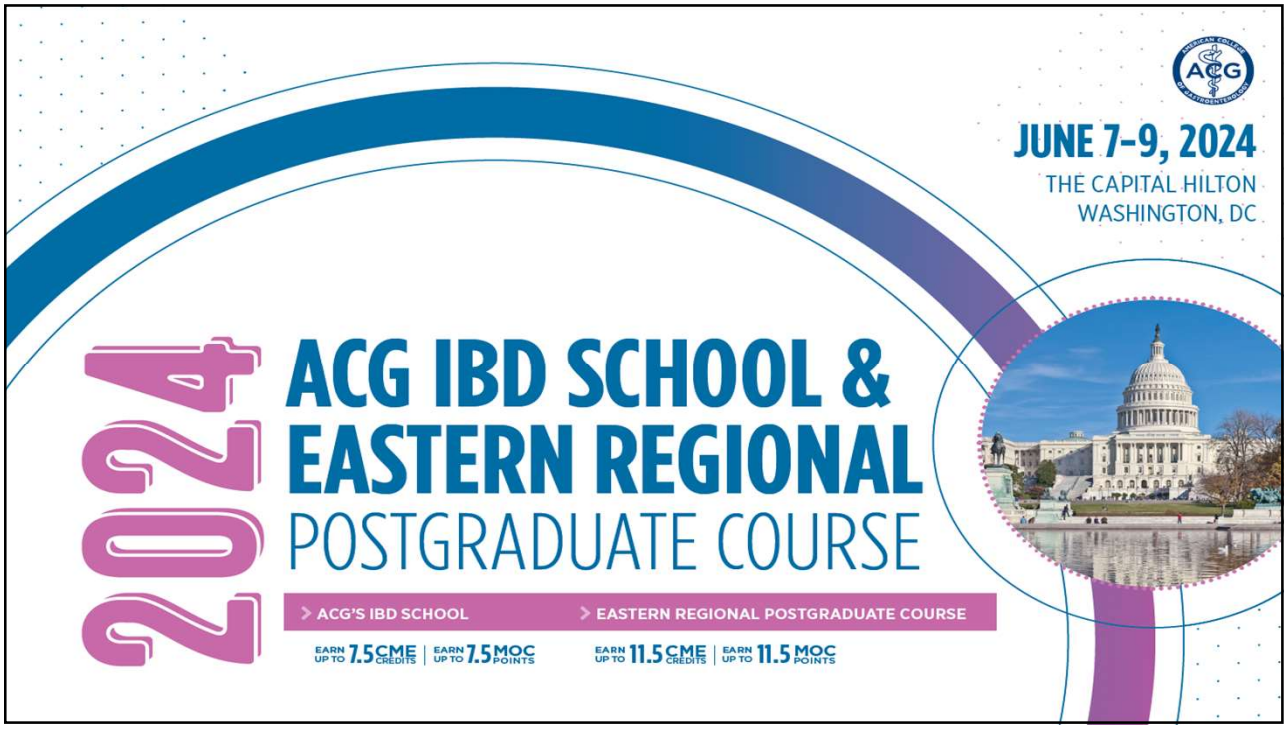
3


Special Issue:
WELL-BEING
JOY AND WELL-BEING IN THE PRACTICE OF MEDICINE – THE IMPORTANCE OF THE HUMAN CONNECTION
ACG MAGAZINE
BIT.LY/ACG-MAG-WELLBEING

4


AJG The American Journal of GASTROENTEROLOGY
ACG MONOGRAPH ON MICROBIOME THERAPEUTICS
Currently available online and in print
Wolters Kluwer
ACG INSTITUTE FOR CLINICAL RESEARCH AND EDUCATION
SUPPLEMENT
ACG MONOGRAPH ON MICROBIOME THERAPEUTICS
Unrestricted educational grants to support the monograph have been provided to the ACG Institute for Clinical Research and Education from Nestlé Health Science and Seres Therapeutics and Ferring Pharmaceuticals Inc.

5


JUNE 7–9, 2024
THE CAPITAL HILTON
WASHINGTON, DC
2024
ACG IBD SCHOOL & EASTERN REGIONAL POSTGRADUATE COURSE
ACG'S IBD SCHOOL
EARN UP TO 7.5 CME CREDITS | EARN UP TO 7.5 MOC POINTS
EASTERN REGIONAL POSTGRADUATE COURSE
EARN UP TO 11.5 CME CREDITS | EARN UP TO 11.5 MOC POINTS

6

Virtual Grand Rounds universe.gi.org

Participating in the Webinar

Moderator:
Pallavi Patil, MD

All attendees will be muted and will remain in "Listen Only Mode"

Type your questions here so that the moderator can see them.
Not all questions will be answered but we will get to as many as possible.

A handout with the slides and room to take notes can be downloaded from your control panel.

Exit

7

Virtual Grand Rounds universe.gi.org

ACG Virtual Grand Rounds

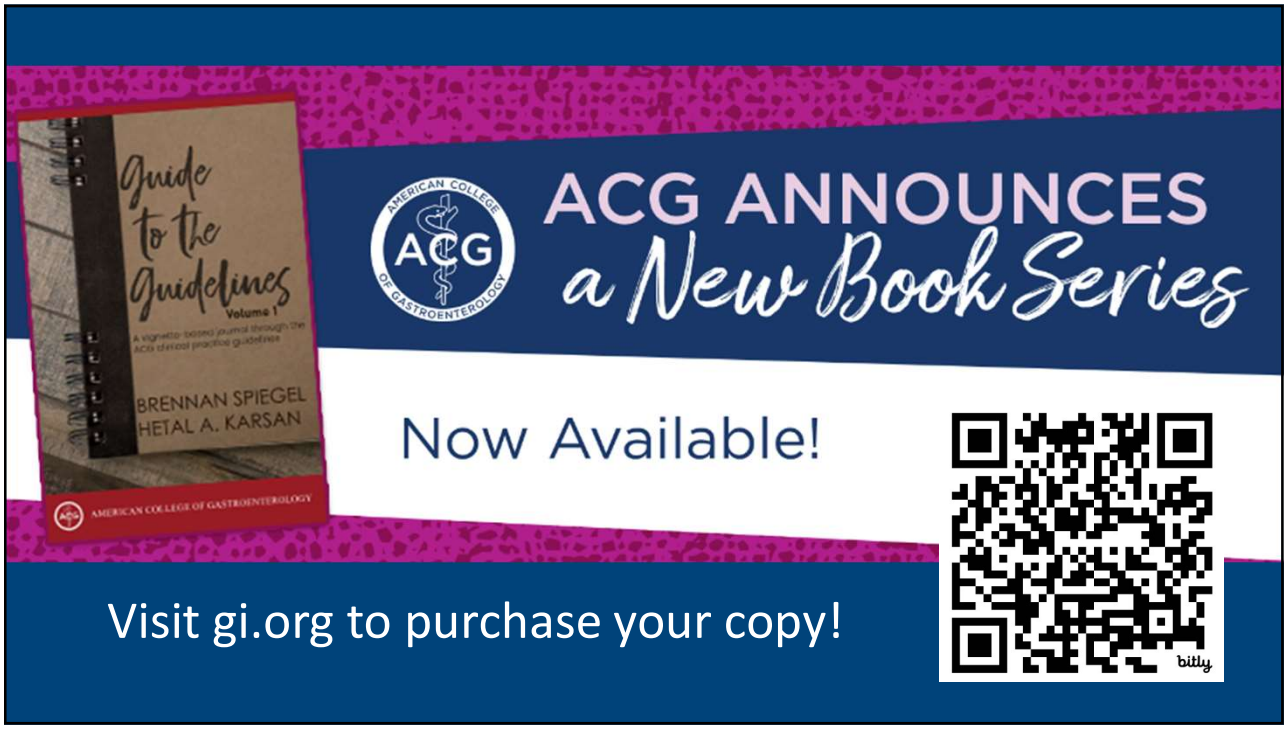
Join us for upcoming Virtual Grand Rounds!

Week 11 – Thursday, March 14, 2024
Exocrine and Endocrine Complications of Pancreatitis
Faculty: Philip S. Schoenfeld, MD, MSEd, MScEpi, FACG
Moderator: Philip N. Okafor, MD, MPH, FACG
At Noon and 8pm Eastern

Week 12 – Thursday, March 21, 2024
I See a Large Polyp During Routine Colonoscopy: How Do I Deal With It?
Faculty: Mohit Girotra, MD, FACG
Moderator: James Tabibian, MD, PhD, FACG
At Noon and 8pm Eastern

Visit **gi.org/ACGVGR** to Register

8


Guide to the Guidelines
Volume 1
BRENNAN SPIEGEL
HETAL A. KARSAN
AMERICAN COLLEGE OF GASTROENTEROLOGY
ACG
ACG ANNOUNCES
a New Book Series
Now Available!
Visit gi.org to purchase your copy!
bitly

9


Virtual Grand Rounds
universe.gi.org
Disclosures
Aasma Shaukat, MD, MPH, FACG:
Iterative Scopes Inc.: Advisory BoardFreenome:
ConsultantMedtronic: ConsultantMotus GI: Consultant
Pallavi Patil, MD: Astellas Pharma –
Advisory board (terminated 2022)
*All of the relevant financial relationships listed for these individuals have been mitigated

10

Virtual Grand Rounds universe.gi.org

Application of Genetic and Molecular Testing for the Management of Colon Polyps and Cancer

Aasma Shaukat, MD, MPH, FACG
Robert M. and Mary H. Glickman Professor of Medicine
Professor of Public Health
Director GI outcomes Research
NYU Grossman School of Medicine

11

Virtual Grand Rounds universe.gi.org

Outline

- Importance of family history
- Spectrum of increased CRC risk based on family history
- Review the risk of other cancers
- Screening and surveillance for CRC and other cancers

12

Cases

Case 1: A 40 yo female reports mother diagnosed with endometrial cancer at age 50

Case 2: A 35 yo male presents with rectal bleeding. Colonoscopy shows 100+ polyps, mostly <1cm, a few 1.5-2 cm. Pathology reports tubular adenomas.

13

Family history of CRC is common

- 10% adults (20-79) report a family history of CRC
- The rate increases with age
- 20% of CRC cases report a family history of CRC in a FDR

Lowery JT, et al. Understanding the contribution of family history to colorectal cancer risk and its clinical implications. Cancer 2016;122:2633-45

14

Virtual Grand Rounds

universe.gi.org

Risk Assessment

- Ask family history before age 40
  - Any relatives with CRC or precancerous polyps
  - If yes, how many and first or second degree
  - Age at onset of cancer or polyps diagnosed
- Update every 5 years
- Eliciting family history is cost effective strategy

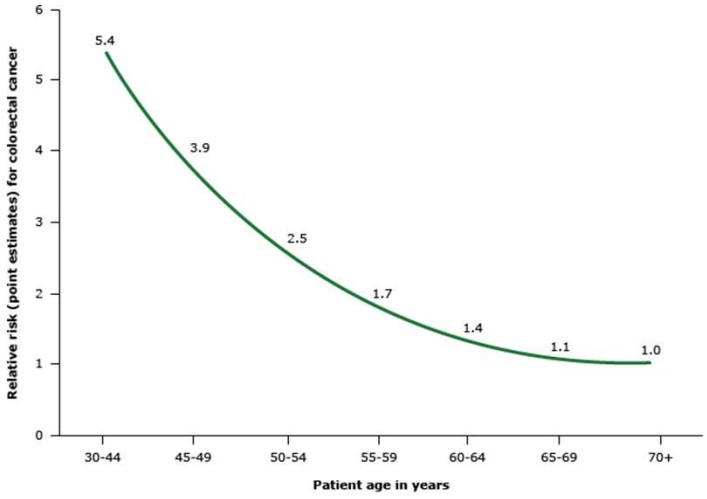
Ramsey SD et al. Family history assessment to detect increased risk for colorectal cancer: conceptual considerations and a preliminary economic analysis Cancer Epidemiol Biomarkers Prev. 2005;14:2494-5

15

Virtual Grand Rounds

universe.gi.org

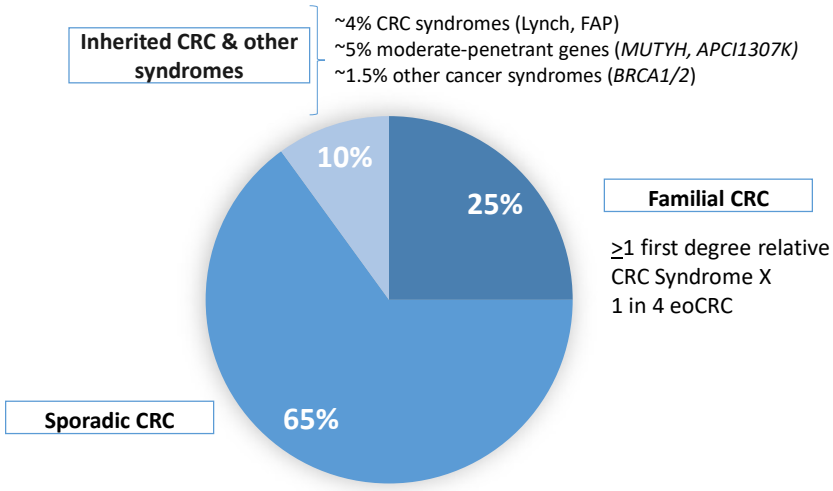
Risk of CRC associated with a FDR with CRC declines with age



Fuchs CS, Giovannucci EL, Colditz GA, et al. A prospective study of family history and the risk of colorectal cancer. N Engl J Med 1994; 331:1669

16

Familial risks of colorectal cancer



Kastrinos F et al *Gastroenterol* 2020

17

Virtual Grand Rounds

universe.gi.org

ACG guidelines: Approach to Family History in CRC Screening

CRC Risk Group	Guideline Recommendations
Average Risk: No personal or FH of CRC neoplasia	Start screening at 45, menu of options
Increased risk : 1 FDR ≥ age 60	Start screening earlier, menu of options
High Risk: 1 FDR <60 or >1 FDR	Start earlier, use colonoscopy, repeat more often
Very high risk - Hereditary syndromes	Start much earlier, use colonoscopy repeat more often

Shaukat A, Kahi CJ, Burke CA, Rabeneck L, Sauer BG, Rex DK. ACG Clinical Guidelines: Colorectal Cancer Screening 2021. Am J Gastroenterol. 2021;116(3):458-479

18

ACG Guideline recommendations

HIGH ← *Risk based on family history* → **LOW**

	2+ FDR CRC	1 FDR<=60y CRC/AdvA	1 FDR >60y CRC/AdvA	1+ SDR CRC
Screen vs. not	✓	✓	✓	Average risk
Preferred test	Colonoscopy	Colonoscopy	Colonoscopy or stool based	
Age to start	40	40 or 10 years younger than FDR	40	
Interval	5 yrs	Col 5 years	Col: 10 y FIT: 1y Mts-DNA 3y	

19

Virtual Grand Rounds

universe.gi.org

Case 1: A 40 yo female reports mother with endometrial cancer at age 50

1. What are the D/Dx?
2. What is management?
3. What surveillance for CRC would you recommend?
4. What other tests would you recommend?

20

Virtual Grand Rounds

universe.gi.org

1 FDR <60 w CRC or adv adenoma or 2 SDR with CRC or adv adenoma (any age) or adv serrated polyps

Increase risk of CRC

Familial CRC

>1 FDR/SDR w CRC or other cancer OR younger age of onset of cancer

Hereditary cancer syndrome?

Lynch syndrome

FAP/AFAP

MYH-associated polyposis

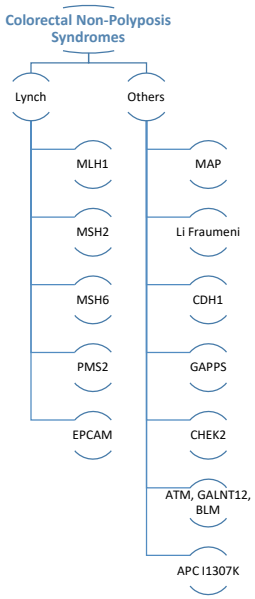
Colon cancer syndrome X

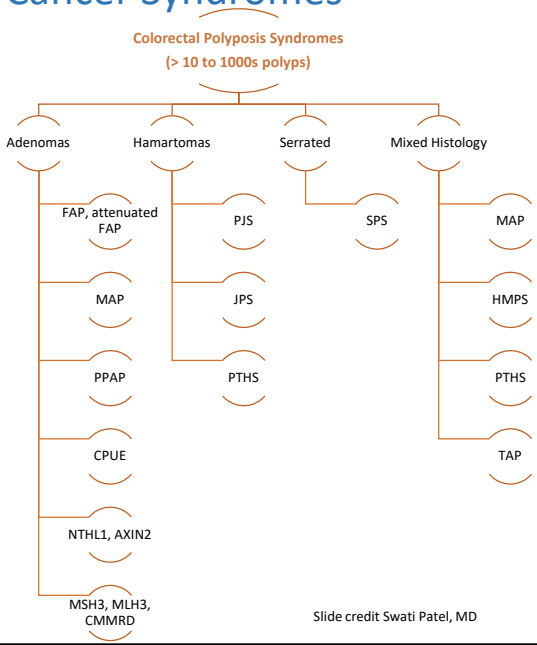
21

Virtual Grand Rounds

universe.gi.org

Hereditary Colorectal Cancer Syndromes





Slide credit Swati Patel, MD

22

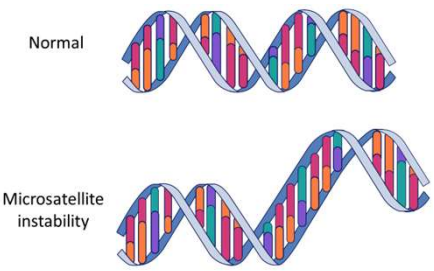
Hereditary Colorectal Cancer Syndromes

- Lynch Syndrome / Hereditary Nonpolyposis Colorectal Cancer (HNPCC)
- Familial Adenomatous Polyposis (FAP)
- Attenuated familial adenomatous polyposis (AFAP)
- MYH-Associated Polyposis (MAP)

23

LYNCH SYNDROME

- Autosomal dominant
- Occurrence: 3% of all CRC and 3% of endometrial cancer
- Germ-line mutations in one of the DNA mismatch repair (MMR) or *EPCAM* gene, leading to a microsatellite instability (MSI) phenotype
- 80% affected individuals will develop CRC
- Average age of onset of CRC: 44 years



24

Lynch syndrome

- *Oligopolyposis: Few/ scant /no polyps!*
- Polyp: Cancer ratio is 1:1 or 1:2
- Rt sided, mucin-rich, poorly diff tumors, good prognosis
- Increased risk of extracolonic malignancies: Endometrial, ovarian, renal, small bowel, biliary, pancreatic, brain, stomach
- 2nd most common cancer site is endometrial

25

Amsterdam Criteria for the Diagnosis of HNPCC
The "3-2-1" Rule

- Three or more relatives with CRC (or related HNPCC cancer*), one of whom is a 1st degree relative of the other 2,
- Two or more generations with lynch-associated cancer,
- One or more cancer case diagnosed before age 50.

*Endometrium, small bowel, ureter, renal

26

Revised Bethesda Guidelines

- CRC under age 50
- Synchronous or metachronous CRC or HNPCC-associated tumor
- CRC with one or more FDR with CRC or HNPCC tumor, one less than 50
- CRC with 2 or more FDR relatives with CRC or other HNPCC tumors, any age

27

Prediction models for Lynch Syndrome

- Provides quantitative risk of estimates of likelihood of MMR mutation
- If risk>5%, refer to genetic counselling
- MMRpredict (hnpccpredict.hgu.mrc.ac.uk/)
- MMRpro (www4utsouthwestern.edu/breasthealth/cagene/)
- PREMM (premm.dfci.harvard.edu)

28

Virtual Grand Rounds

universe.gi.org

Sensitivity for Diagnosis of Lynch syndrome

Test	Sensitivity	Specificity
• Amsterdam Criteria	• 22%	98%
• Bethesda Criteria	• 82%	77%
• IHC for MLH1 MSH2 PMS2 MSH6	• 83%	89%
• Tumor tissue MSI testing	• 85%	90%
• PREMM	• 90%	67%

29

Virtual Grand Rounds

universe.gi.org

Guidelines on genetic evaluation and management of Lynch syndrome: A consensus statement by the U.S. Multi-Society Task Force on Colorectal Cancer

	YES	NO
1. Do you have a first-degree relative (mother, father, brother, sister, or child) with 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

Giardiello FM et al. Gastrointestinal Endoscopy 2014;80:197-220

30

Virtual Grand Rounds universe.gi.org

Genetic counseling

Indication:

- Amsterdam criteria
- Bethesda Criteria
- Uterine cancer < 50y
- Known Lynch syndrome in family
- ≥5% chance of mutation by prediction models

Counseling:

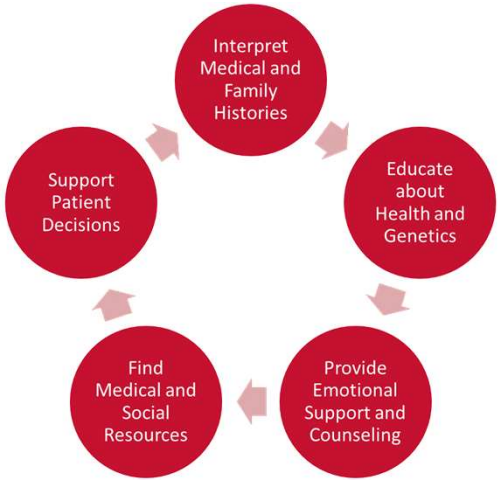
- Family history evaluation
- Education
- Risk assessment
- Management recommendations
- Informed consent for genetic testing
- Genetic testing and interpretation of results

31

Virtual Grand Rounds universe.gi.org

Post-testing Counselling

- Interpretation of results
  - Pathogenic vs VUS
- Implications of results
  - High-penetrance mutations
    - Guideline based medical management: chemoprevention, screening, prophylactic surgery
  - Low/moderate-penetrance mutations
- If no mutation is identified
  - Recommendations based on family history



32

Isn't Genetic testing Expensive?

•Cost is significantly lower with next-generation sequencing and competition from many companies

Most insurance companies (including CMS) pay for genetic testing if NCCN criteria are met

- Minimal out of pocket cost

Out of pocket costs

- Invitae: $295-495
- Color (direct consumer marketing): $249

33

Universal molecular testing for Lynch?

- Likely to be standard in the future
- 28% of Lynch syndrome patents missed with the most sensitive revised Bethesda criteria
- Endorsed by recent USMSTF for all patients with CRC ≤70 years of age when appropriate infrastructure exists

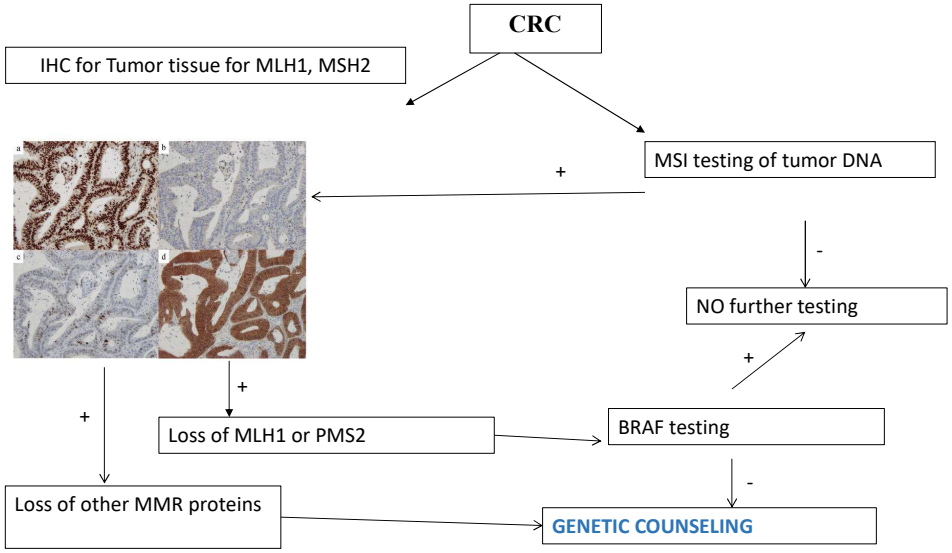
Giardiello FM et al. Gastrointestinal Endoscopy 2014;80:197-220

34

Virtual Grand Rounds

universe.gi.org

Universal screening by tumor testing



Giardiello FM et al. Gastrointestinal Endoscopy 2014;80:197-220

35

Virtual Grand Rounds

universe.gi.org

Surveillance recommendations for patients with Lynch syndrome

- Colonoscopy every 1-2 years beginning at age 20-25

❑Colonoscopy + Ileoscopy

- MLH1/MSH2, > 40, hx of adenoma—1 year
- PMS2/MSH6, <40, no adenoma—1-2 years

- Transvaginal ultrasound and endometrial aspirate annually starting age 30-35
- Urinalysis annually beginning age 35
- EGD with gastric biopsies q2-3 years starting age 30-35
- Long-term use of aspirin may reduce risk of cancer

Burn J et al. Aspirin prevents cancer in Lynch syndrome. Eur J Cancer 2009;7:320-21

36

Virtual Grand Rounds universe.gi.org

Case 1: A 40 yo female reports mother with endometrial cancer at age 50

1. What are the D/Dx?
2. What is management?
3. What surveillance for CRC would you recommend?
4. What other tests would you recommend?

1. Lynch syndrome
2. Genetic counseling and testing for mutation in MMR, EPCAM genes
3. Colonoscopy now, then every 1-2 years
4. TV ultrasound and endometrial aspirate
   Urinalysis
   EGD +/- gastric sampling

37

Virtual Grand Rounds universe.gi.org

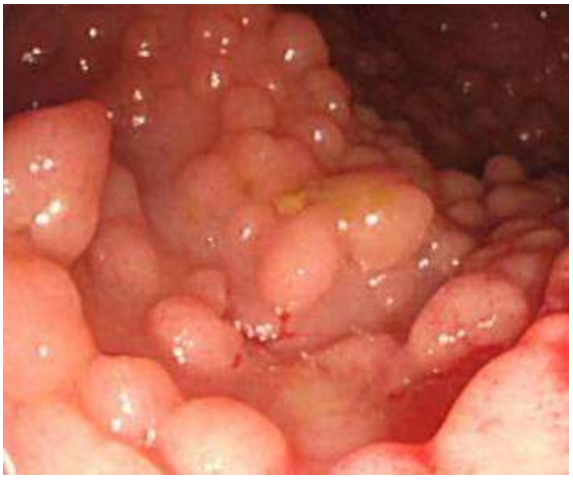
Case 2: A 35 yo male presents with rectal bleeding. Colonoscopy shows 100+ polyps, mostly <1cm, a few 1.5-2 cm. Pathology reports tubular adenoma

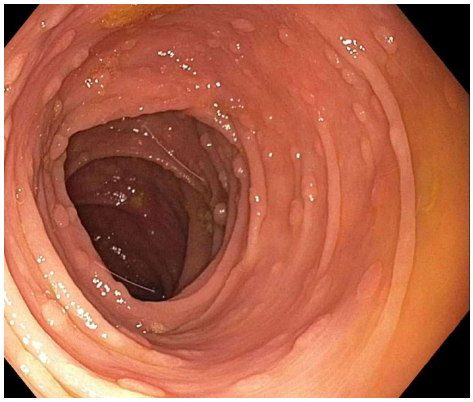
1. What are the D/Dx?
2. What is surgical management?
3. What other tests would you recommend?
4. What genetic tests would you order?

38

Virtual Grand Rounds universe.gi.org

FAP – Endoscopic Findings





39

Virtual Grand Rounds universe.gi.org

Familial Adenomatous Polyposis (FAP)

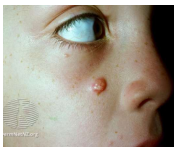
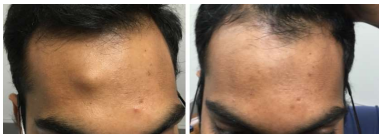
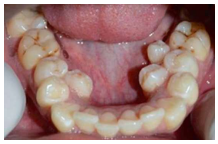
- Autosomal dominant
- Germ-line mutation in the *APC* gene
- Occurrence: ~ 1% of CRC
- Characterized by multiple (>100) adenoma in the colon beginning around 15 years of age
- Colon cancer develops around 35 years of age
- Extracolonic manifestations

40

Virtual Grand Rounds universe.gi.org

Benign Extra-Intestinal Manifestations of FAP

	Location	Risk
Osteomas	Jaw, skull	50-90%
Epidermoid Cysts	Legs, face, scalp, arms	50%
Missing teeth, late erupting teeth		90%
Supernumery teeth		11-27%
Congenital hypertrophy of the retinal pigmented epithelium (CHRPE)		70-80%
Desmoids	Anywhere	10-30%

Slide credit Swati Patel, MD

41

Virtual Grand Rounds universe.gi.org

Screening for other cancers in FAP

Starting at age 30-35 years:

- Upper GI endoscopy with a side-viewing endoscope q 1-3 years
- Endoscopic ultrasound of suspicious lesions at ampulla
- Sample gastric fundic gland polyps if large
- +/- Annual thyroid ultrasound

Gallagher MC et al. Surveillance and management of upper gastrointestinal diseases in familial adenomatous polyposis. Fam Cancer 2006;5:263-73;
Herraiz M et al. Prevalence of thyroid cancer in FAP and role of screening ultrasound. Clin Gastroentrol Hepatol 2007;5:367-373

42

Virtual Grand Rounds universe.gi.org

Screening Guidelines: Family History of FAP

- Genetic counseling
- Genetic testing (a negative genetic test result rules out FAP only if an affected family member has an identified mutation)
- Gene carriers or indeterminate cases should be offered flexible sigmoidoscopy every 12 months beginning at puberty
- If polyposis is present, consider colectomy

43

Virtual Grand Rounds universe.gi.org

Case 3: A 35 yo male presents with rectal bleeding. Colonoscopy shows 100+ polyps, mostly <1cm, a few 1.5-2 cm. Pathology reports tubular adenoma

1. What are the D/Dx?
2. What is surgical management?
3. What other tests would you recommend?
4. What genetic tests would you order?

1. D/Dx: FAP, AFAP, MAP,
2. Total colectomy with IPAA
3. EGD w side-viewing scope +/- biopsy of ampulla
4. Germline testing for mutations in APC, MYH

44

Virtual Grand Rounds universe.gi.org

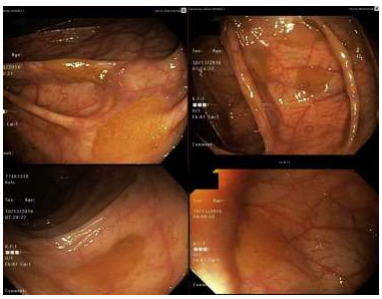
Serrated Polyposis Syndrome (SPS)

WHO criteria:

- >=5 SP Proximal to rectum, all >=5mm and >=2 10mm

OR

- >20 SPs any size in colon, with >=5 proximal to rectum
- Over lifetime (review prior records)



Management:

- Colonoscopy Q1-2 years
- Screen FDR start at age 40, q 5 yrs

Mankaney G et al. CGH 2019;18:777-779

45

Virtual Grand Rounds universe.gi.org

Colon cancer syndrome X

- Meet criteria for HNPCC but have microsatellite stable CRC
- Yet to be identified genes “type X”
- CRC risk is lower than Lynch syndrome and occurs 10 years later
- Colonoscopy every 3-5 years starting 10 years younger than age of diagnosis of youngest affected relative

Rex DK et al. Colorectal cancer screening: recommendations for physicians and patients from the US Multi-society task force on colorectal cancer Am J Gastrenterol 2017;112:1016-30

46

Genetic Malpractice

- Failure to make a diagnosis and use proper diagnostic tools
- Failure to recommend adequately aggressive cancer surveillance
- Failure to recommend surveillance or prophylactic surgery for associated cancers
- Failure of 'duty to warn' family members

47

Conclusions

- Accurate and frequent family history starting at a young age
- If 1 FDR, age of FDR and patient are important
- If multiple FDR or SDR, think of hereditary syndromes
- Earlier and more intense screening / surveillance depending on extent of family history
- Surveillance for extra colonic manifestations
- Document family history and discussions with patient!

48

Virtual Grand Rounds universe.gi.org

Thank you

Aasma.Shaukat@nyulangone.org
@aasmashaukatmd

49

Virtual Grand Rounds universe.gi.org

Questions

Aasma Shaukat, MD, MPH, FACG

Pallavi Patil, MD

50


CONNECT AND COLLABORATE IN GI
GI
ACG GI Circle
Connect and collaborate within GI
IBD Circle
A Partnership of the American College of Gastroenterology and the Crohn's & Colitis Foundation
ACG Hepatology Circle
ACG Functional GI Health and Nutrition Circle
ACG's Online Professional Networking Communities
LOGIN OR SIGN-UP NOW AT: acg-gi-circle.within3.com
ACG

51