Hereditary Colonic Polyposis Syndromes

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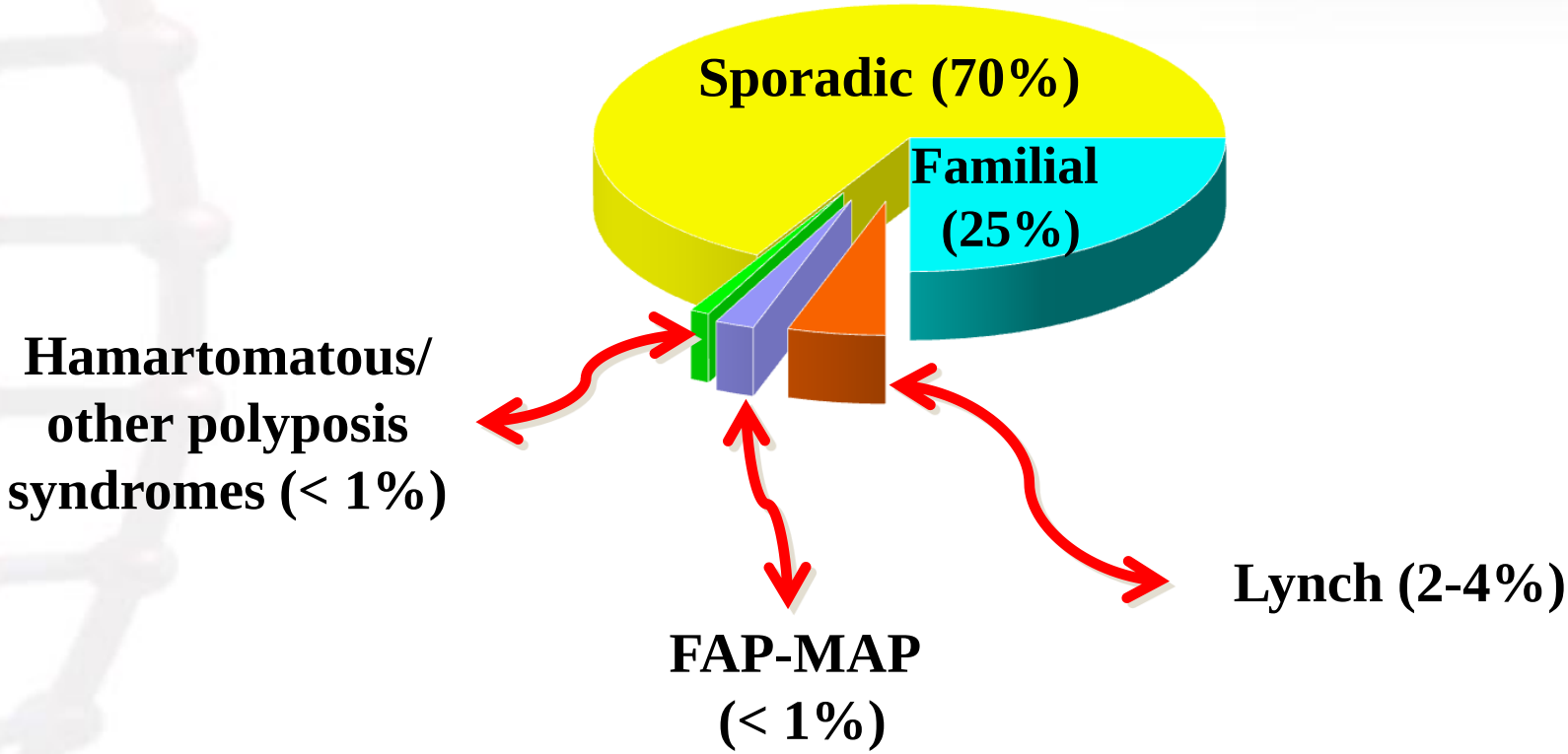
Disclosure

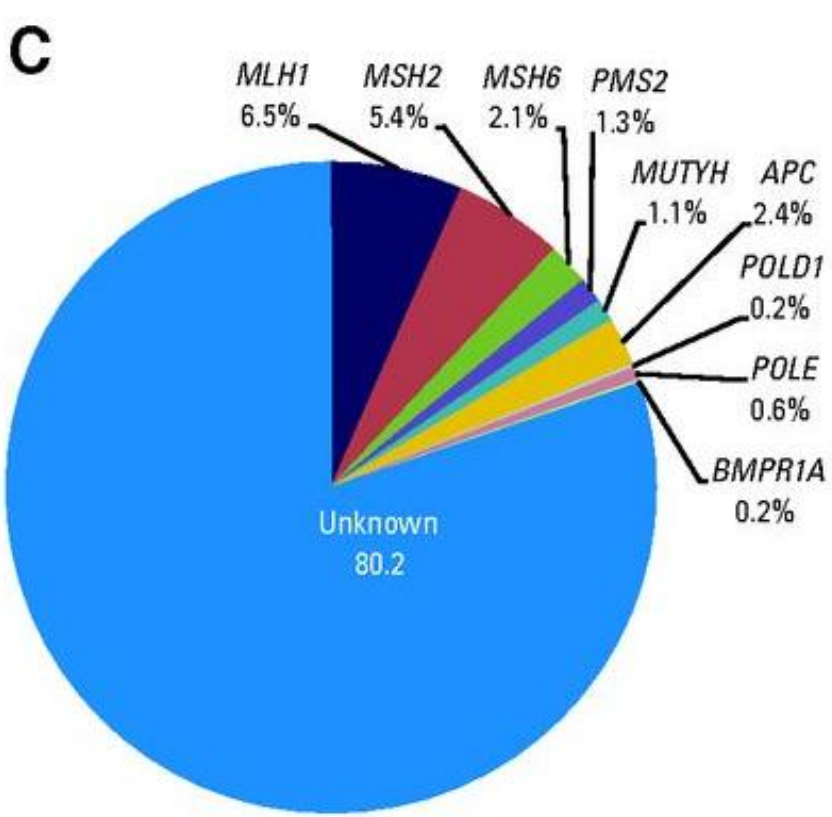
- Honorarium ad hoc consulting for Invitae

Colorectal Cancer



Familial CRC

- 626 CRCs < age 56 and family history of CRC
- *MLH1, MSH2, MSH6, PMS2, APC, MUTYH, SMAD4, BMPR1A, POLE, POLD1*
- 17% to 28% of familial CRCs were found to have a genetic diagnosis



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Chubb D et al. JCO doi:10.1200/JCO.2014.56.5689

Syndromes Associated With CRC

- Lynch syndrome (LS)
- Familial adenomatous polyposis (FAP)
- *MUTYH*-associated polyposis (MAP)

→ Adenomatous polyps

- Serrated polyposis syndrome (SPS) → Not really a syndrome: serrated polyps and adenomas
- Li-Fraumeni syndrome (LFS) → Pediatric cancer syndrome with increase risk of CRC
- Peutz-Jeghers syndrome (PJS)
- Juvenile polyposis syndrome (JPS)
- Cowden syndrome (CS)

→ Hamartomatous polyps

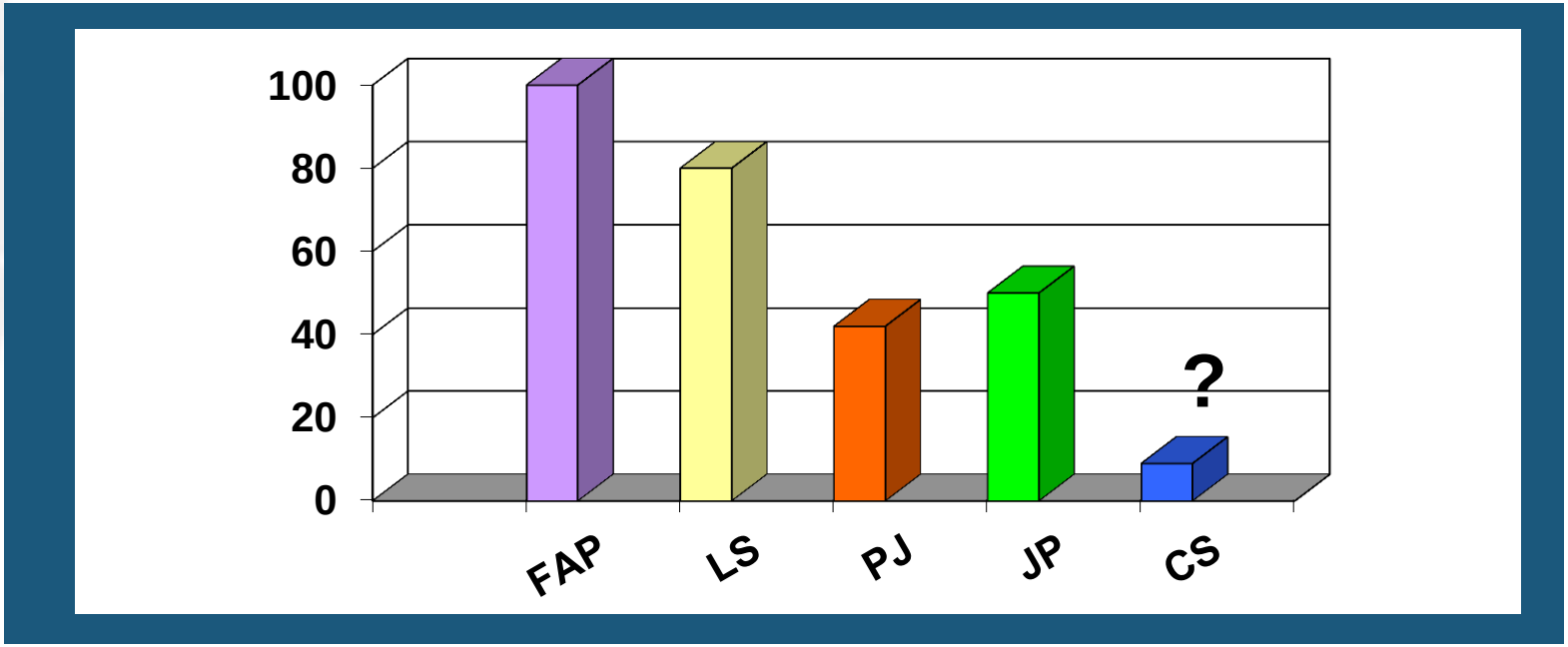
- Constitutional mismatch repair deficiency (CMMRD) syndrome
- *POLE and POLD1* (CRC and adenoma predisposition)
- *GREM1* (Hereditary mixed polyposis (HMP) syndrome)

→ Rare syndromes/Genes associated with CRC

Syndromes/Genes

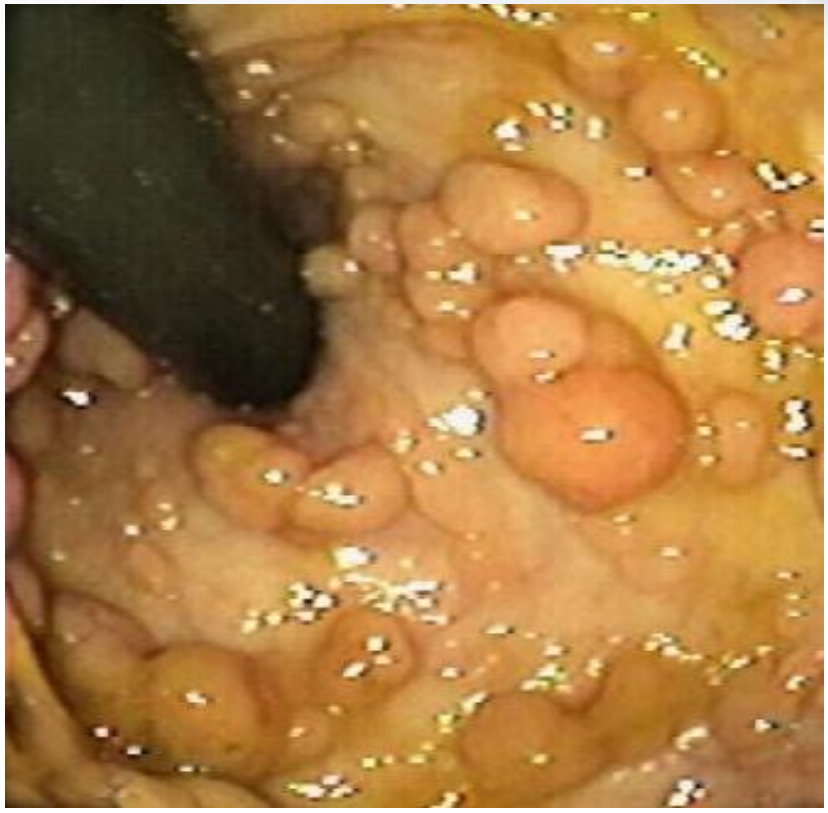
Syndrome	**Gene(s)**
FAP/AFAP	*APC*
MAP	Biallelic *MUTYH*
CMMRD	Biallelic MLH1, MSH2, MSH6, PMS2, EPCAM
PJS	*STK11*
JPS	*SMAD4, BMPR1A*
CS	*PTEN*
HMP	*GREM1*
?	*POLE, POLD1*
SPS	?

Inherited Syndromes and CRC Risk



Familial Adenomatous Polyposis (FAP)

- 100’s to 1000’s of colonic adenomatous polyps
- Penetrance for colorectal adenomas > 90% by age 40
- ~100% risk for CRC in untreated cases
- Risk of extra-colonic cancer

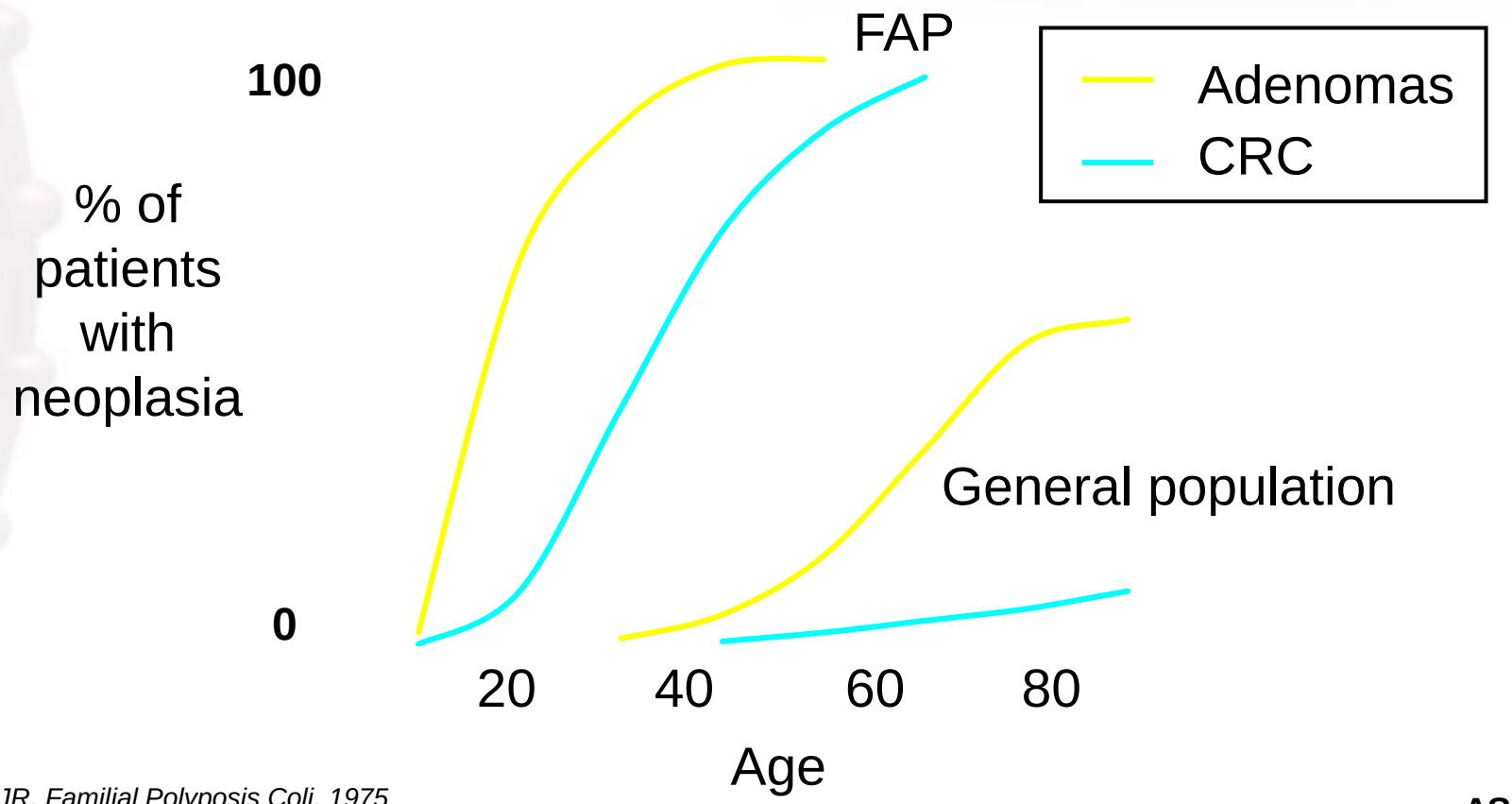


ASCO

FAP: Genetics

- Incidence: ~1 in 10,000 births
- Genetics
  - Autosomal dominant
  - Gene: *APC* (5q)
  - ~ 25% of patients have negative family history
  - Genotype/phenotype correlations

FAP: Age and Development of Adenomas and CRC

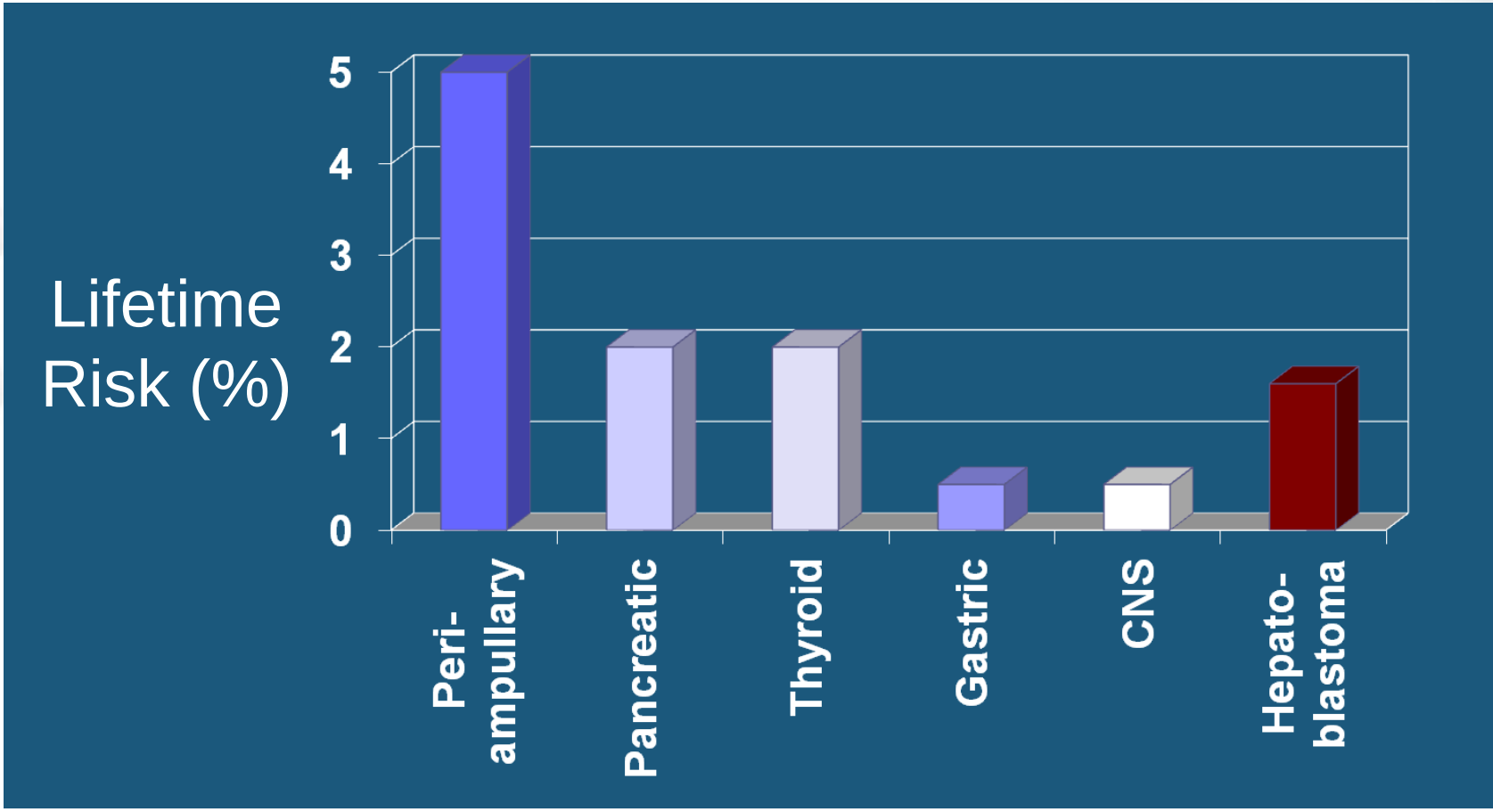


Bussey HJR. Familial Polyposis Coli, 1975
Petersen GM et al. Gastro 100:1658, 1991

Other Polyps

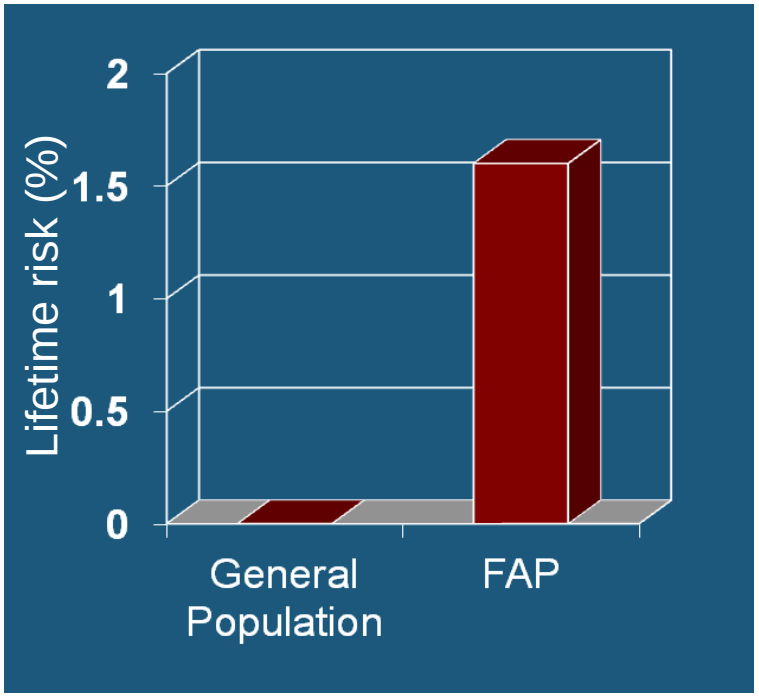
- Small bowel polyps (adenomas)
  - Typically occur in the duodenum and ampulla
  - Occur in approximately 60-80%
  - Approximately 4-12% risk for duodenal/ampullary malignancy
  - Spigelman staging criteria used to predict degree of dysplasia and how frequently to screen
- Gastric polyps (mainly fundic gland polyps)
  - ~90% will have fundic gland polyps
  - Low risk of gastric malignancy but still increased compared to general population

FAP: Extra-Colonic Cancers



FAP: Hepatoblastoma Risk

- General Population
  - 1% of all pediatric cancers
  - 0.5 - 1.5 diagnosis per 1 million children (younger than 15 years)
- FAP
  - 0.7 to 1.6% in children under age 5



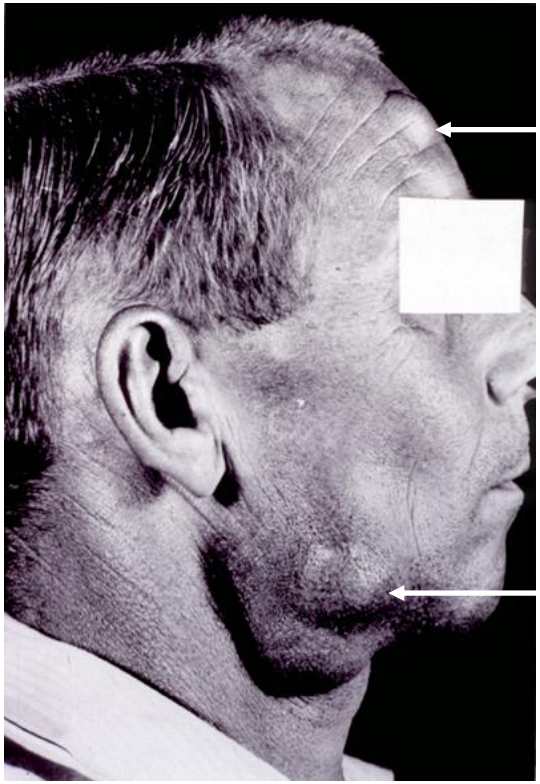
Giardiello et al. 1993, Garber et al 1988, LeSher et al 1989, Nandakumar et al 2004

FAP Variants

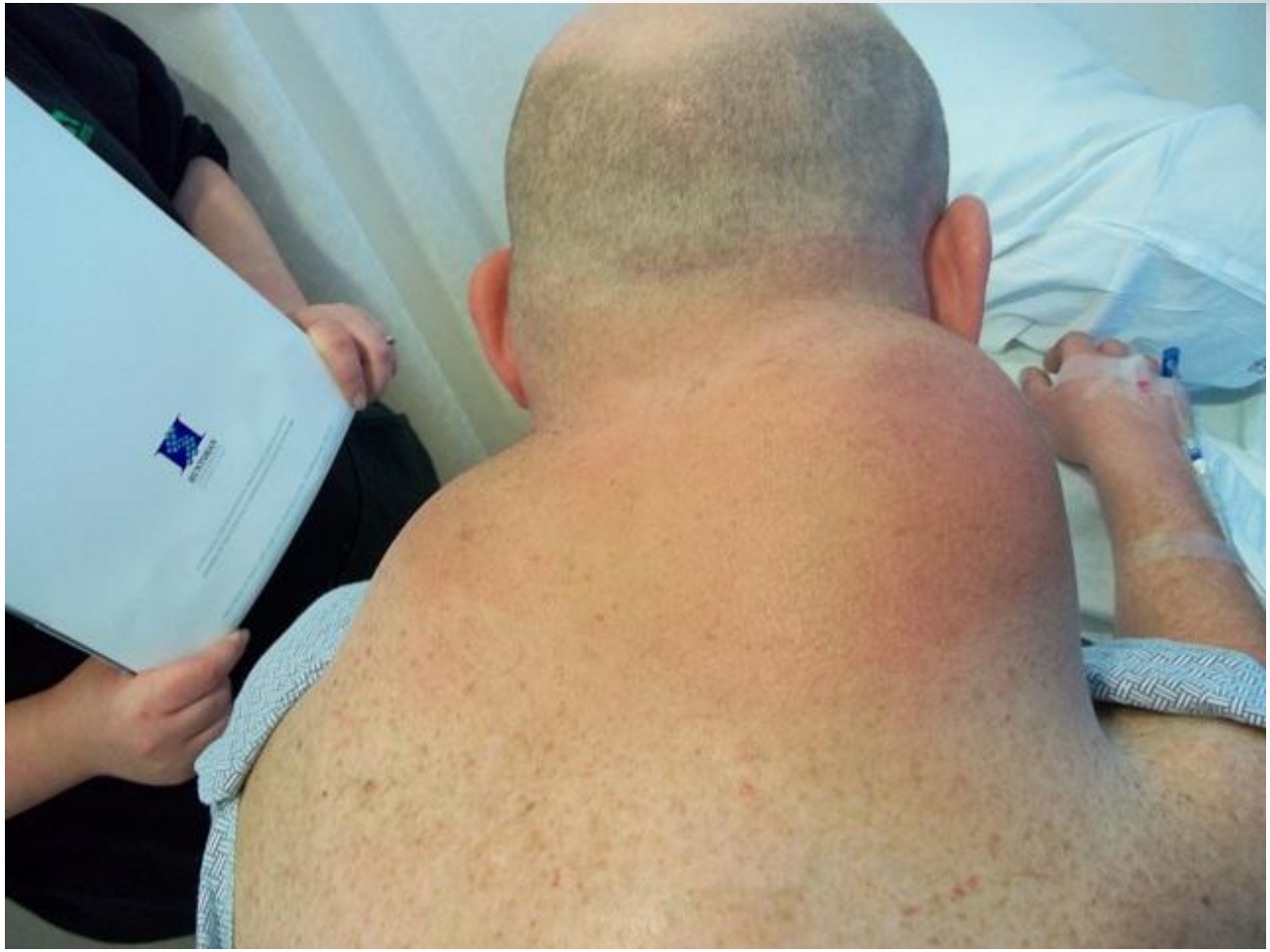
- **Gardner syndrome**
  - FAP with extra-intestinal growths
- **Turcot syndrome**
  - FAP and brain tumor (medulloblastoma)
  - 2/3 of Turcot have *APC* mutations
- **Attenuated FAP**
  - < 100 polyps and older age of CRC onset ~50's

Gardner Syndrome

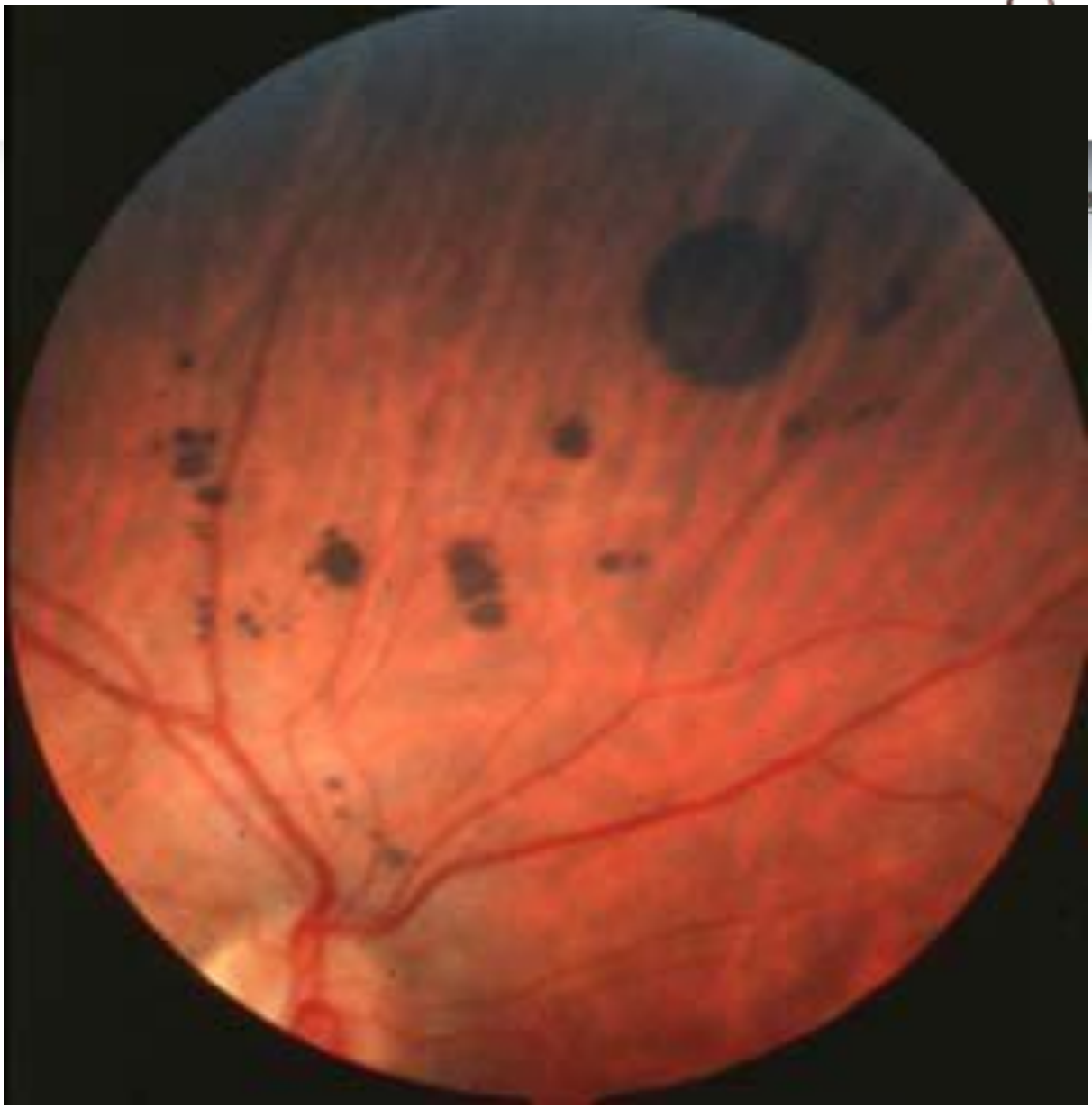
- **Desmoid tumors**
- **Osteomas**
- **Supernumerary teeth**
- **CHRPE**
- **Soft tissue skin tumors**



Desmoid Tumor

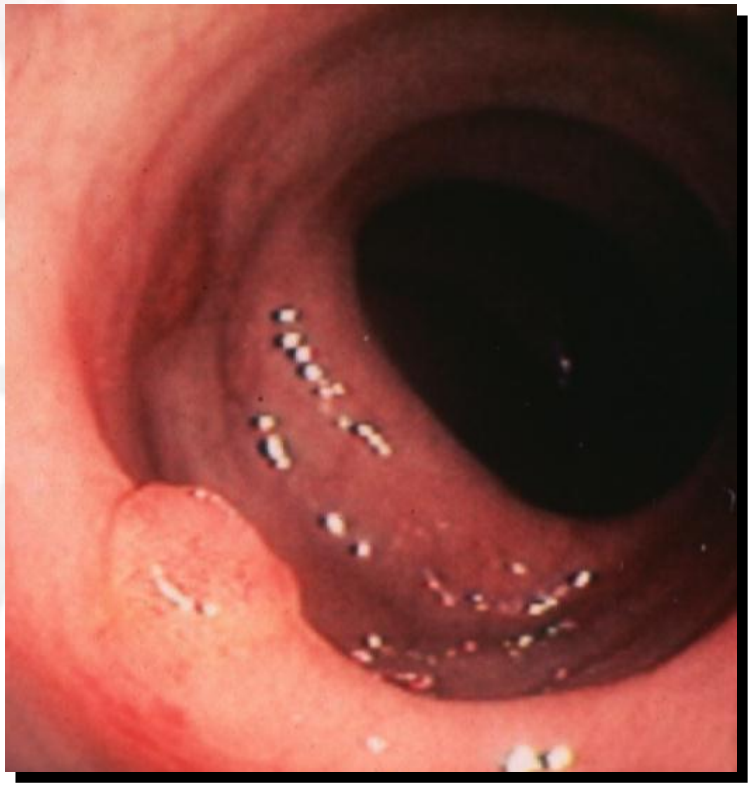


CHRPE



http://www.gfmer.ch/genetic_diseases_v2/gendis_detail_list.php?cat3=1369

Attenuated FAP (AFAP)



- Average 30 colonic polyps (may be more than 100, but typically at later ages), more proximal in location
- CRC ~70% lifetime risk
- Later onset (CRC ~age 50)
- Fundic gland polyps and duodenal adenomas: similar presentation as classic FAP

FAP: Colorectal Management

- Annual colonoscopy
  - Start at age 10 to 12 years for FAP
  - 18-20 for AFAP
- Prophylactic colectomy in all FAP and in some AFAP cases
- Subsequent surveillance for rectal, pouch, and extracolonic tumors

MUTYH Associated Polyposis (MAP)

- Similar to AFAP phenotype
- 15 - 100 adenomas, can be > 100
- Multiple serrated polyps may occur
- Older age of CRC onset (~50’s)
- Autosomal recessive!

MAP

- *MUTYH* (*MYH*) gene-accomplishes oxidative damage repair
- Part of base excision repair pathway
- Two common mutations in Caucasian population (Y165C and G382D)

MAP

- Reviewed 276 MAP cases
  - Seventy-seven (28%) had at least 1 extra-intestinal tumor
  - Compared to the general population, the incidence of extraintestinal malignancies was almost doubled in MAP patients (SIR: 1.9; 95% CI: 1.4 –2.5) and lifetime risk was 38% (95% CI: 23%–52%)
  - No osteomas or desmoids
- Of 150 patients who underwent EGD
  - 17 (11%) had gastric lesions
  - 26 (17%) had duodenal polyposis
  - Cumulative lifetime risk was 4% for duodenal cancer

Gastroenterology Vol 137, issue 6December 2009, Pages 1976-1985.e10

Genetic Testing: *APC* and *MUTYH*

- Colonic adenomas: ≥ 20 or fewer (>10) if young)
  - *APC* and *MUTYH*
- Genetic diagnosis
  - ↑ adenomas = ↑ % *APC* mutation
  - ↑ other types of polyps = ↓ % *APC* mutation
  - *> 500 adenomas = ↓ % MUTYH*
  - Fundic gland polyposis = ↑ % *APC* mutation
  - Family history of colonic polyps: =
    - ↑ *% APC if in parent or child*
    - ↑ *% MUTYH if in siblings only*

Early Onset CRC w/o Polyposis

- Early onset CRC with few adenomas and normal tumor testing
  - Limited data to support APC, MUTYH, or p53

- **89 Dutch patients with CRC < 40 (or meeting other BGs) and MSS/MSI-low tumors**
  - **MUTYH (common mutations) no mutations found**

Contribution of bi-allelic germline MUTYH mutations

Table 1 Study population characteristics and MUTYH analysis results

Population	Selection criteria	CRC characteristics	Polyps	Bethesda	Amsterdam II	MUTYH
Groningen: Dutch, white Caucasian N = 47	CRC < 40 yrs, MSS tumor and normal tumor MMR protein staining <20 polyps	Mean age: 33.9 yrs Range: 22–39 yrs	6 patients with adenomatous polyps (range: 1–8 polyps)	47/47 (100 %)	8/47 (17.0 %)	Full gene analyzed Mut/mut: 0/47 Mut/wt: 0/47 WT/WT: 47/47(100 %)
Leiden: Dutch, white Caucasian N = 42	CRC Bethesda criteria positive < 20 polyps MSS of MSI-L Normal MMR protein IHC	Mean age 52.2 yrs (Range: 29–71)	11 patients with adenomatous polyps (range 1–4 polyps)	42/42 (100 %)	30/42 (71.4 %)	Full gene analyzed Mut/mut: 0/42 Mut/wt: 2/42 (4.8 %; 1 × Y179C and 1 × G396D)* Wt/wt: 40/42 (95.2 %)
Wageningen: Dutch, white Caucasian N = 693	One or more adenomatous polyps Colonoscopy perfomed because of clinical complaints or follow-up after previous polyp No previous history of CRC or other CR disease	Not applicable	100 % had between 1 and 13 adenomatous polyps: 1–2 polyps in 69.7 %; 3–4 in 16.2 %; 5–6 in 8.2 %; 7–8 in 3.8 % and 8–13 polyps in 2.1 % of cases. Ages at diagnosis 35–75 years (see Fig. 1)	0/693	0/693	3 hotspot mutations analyzed: Y179C; G396D and P405L Mut/mut 0/693 Mut/wt: 15/693 (2.1 %; 4 × Y179C, 11 × G396D)*

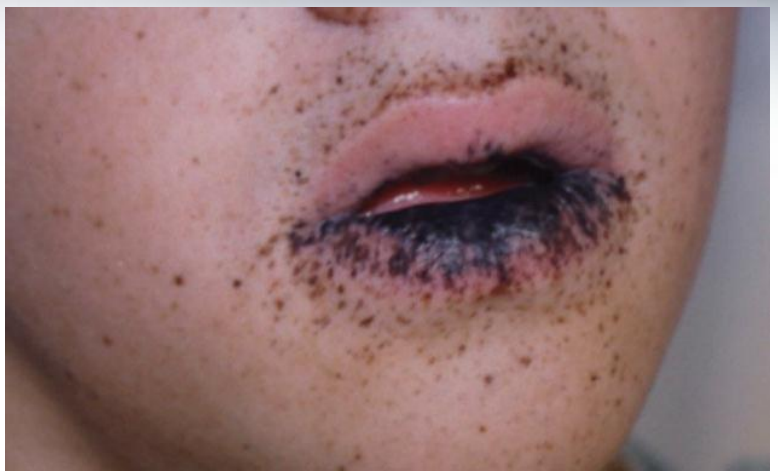
CR colorectal, *CRC* colorectal cancer, *IHC* immunohistochemical staining for the Lynch syndrome-associated MMR gene-coded proteins, *MMR* DNA mismatch repair genes, *MSI* microsatellite instability, *MSS* microsatellite stable, *MSI-L* microsatellite instability - low, *Mut* MUTYH gene germline mutation, *Wt* wild type MUTYH allele, *Yrs* age in years

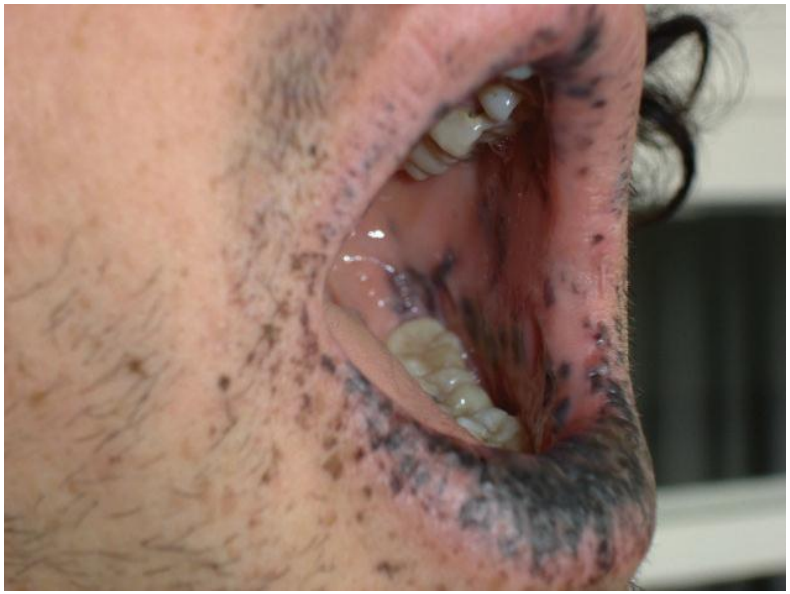
* not significantly different from the heterozygote frequency of 2.2 % in 668 Dutch controls ($p > 0.1$)

Fam Cancer. 2013 Mar;12(1):43-50.

Peutz-Jeghers Syndrome (PJS)

- Autosomal dominant
- 1 in 200,000 live births
- Peri-oral melanin pigment >95% of cases
- Characteristic polyps throughout GI tract
  - Occur more commonly in small bowel
- Commonly presents with intussusception in childhood
- Gene: *STK11*





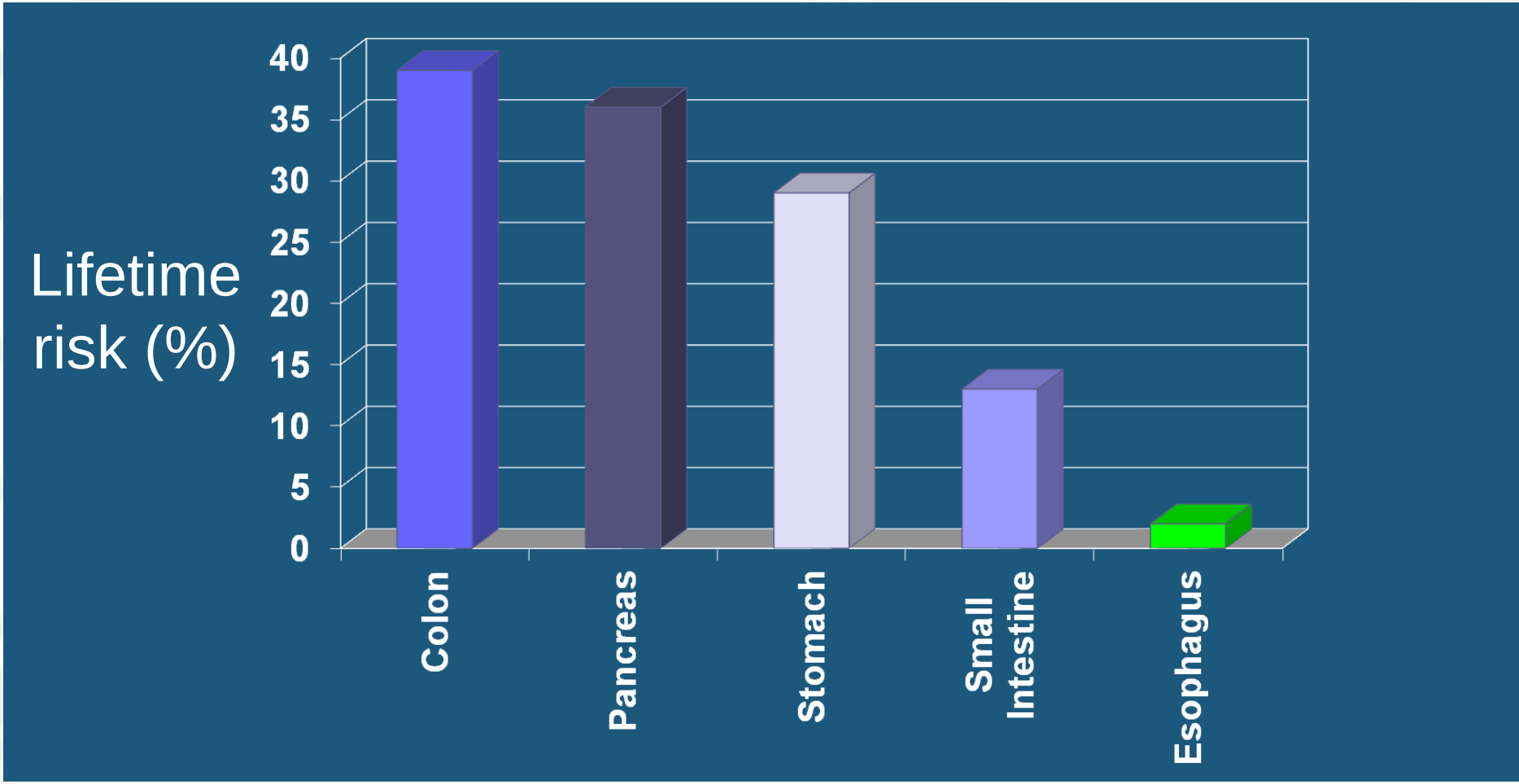
PJS

- Tumor risks
  - Colorectal cancer (39%)
  - Esophageal (0.5%)
  - Small bowel (13%)
  - Gastric (29%)
  - Pancreatic (36%)
  - Sex cord tumors with annular tubules (SCTAT) (21%)
  - Breast cancer (54%)
  - Adenoma malignum of the cervix (10%)
  - Sertoli cell tumors of the testes (9%)

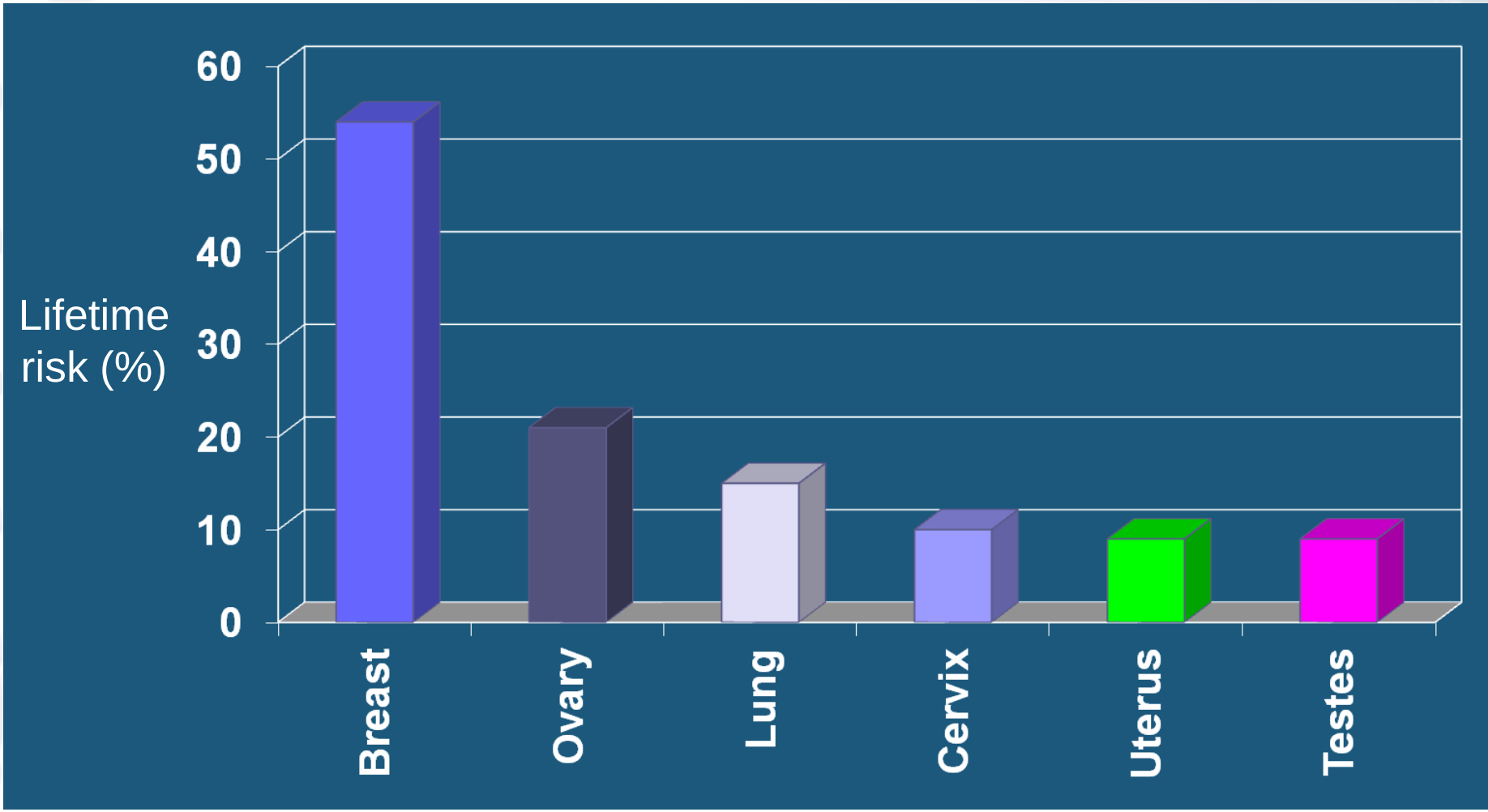
Cancer risks sited are cumulative risks from age 15-64

Giardiello FM et al. 2000

PJS, GI Cancers



PJS, Non-GI Cancers



PJS: Diagnostic Criteria

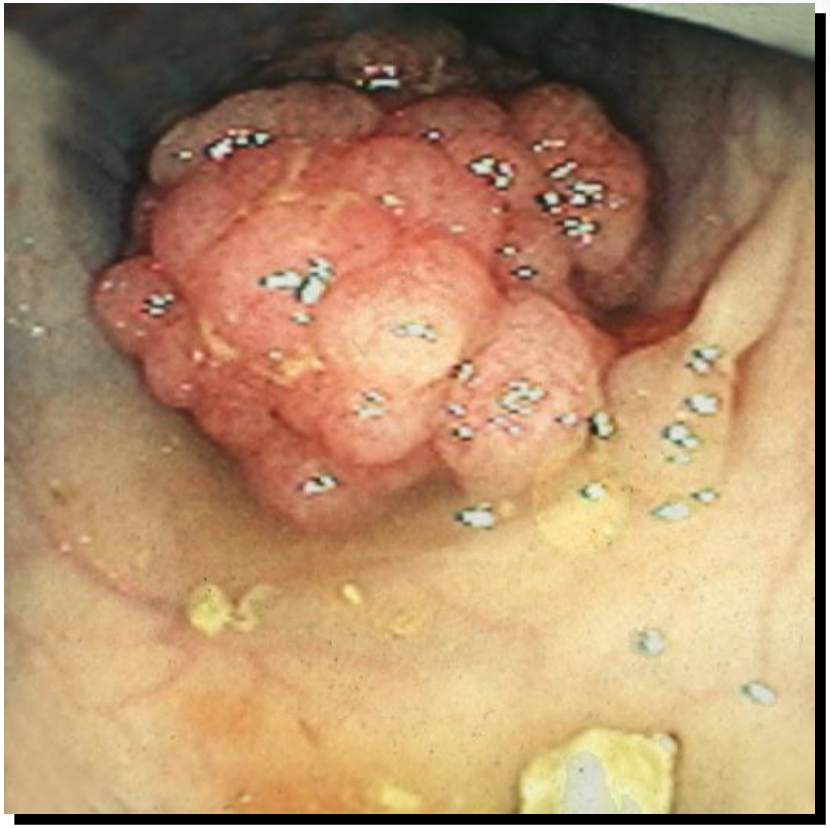
Proband meets both criteria

- Two or more histologically confirmed PJS-type hamartomatous polyps
- Any number of PJS-type polyps detected in one individual who has a family history of PJS in a close relative(s)
- Characteristic mucocutaneous pigmentation in an individual who has a family history of PJS in a close relative(s)
- Any number of PJS-type polyps in an individual who also has characteristic mucocutaneous pigmentation

Beggs AD et al. Peutz-Jeghers syndrome: a systematic review and recommendations for management. Gut. 2010;59:975–86

Juvenile Polyposis Syndrome

- Juvenile polyps mainly in the colon
  - Anemia and obstruction due to size and number of polyps
- Characteristic cancers: colon (~40%) and gastric (20%, mainly in individuals with gastric polyps)
- Other cancers may occur
- Symptomatic presentations
  - <30 years, benign complications
  - >30 malignant complications
- Multiple congenital anomalies in some individuals(cardiovascular, urogenital or CNS abnormalities)

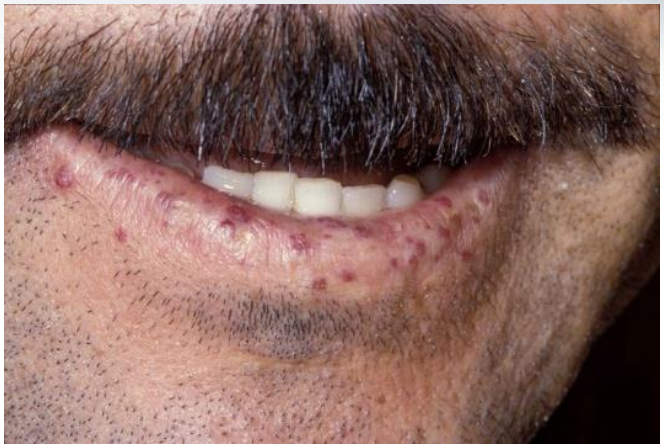


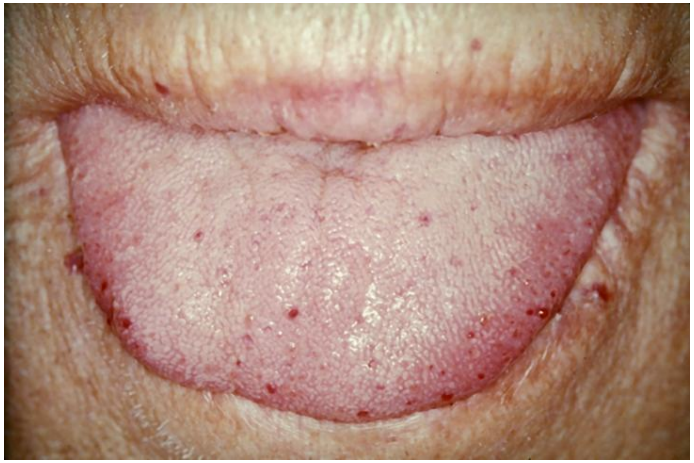
JPS: Genetics

- Incidence: ~1 in 100,000
- Genetics
  - Autosomal dominant
    - SMAD4 (18q21) ~20-25%
    - BMPR1A (10q22-23) ~20-25%

JPS/Hereditary Hemorrhagic Telangiectasia (HHT)

- ~ 15%-22% of individuals with *SMAD4* mutations will have the combined JPS/HHT syndrome
- Individuals with the combined JPS/HHT syndrome have variable findings of juvenile polyposis and some of the following:
  - epistaxis
  - mucocutaneous telangiectases
  - arteriovenous malformations (AVMs): pulmonary, hepatic AVMs, cerebral, and GI
  - intracranial bleeding
- Findings of HHT may manifest in early childhood.





Juvenile Polyposis

Diagnostic Criteria

Any one of the following:

- More than five juvenile polyps of the colorectum
- Multiple juvenile polyps of the upper and lower GI tract
- Any number of juvenile polyps and a family history of juvenile polyps

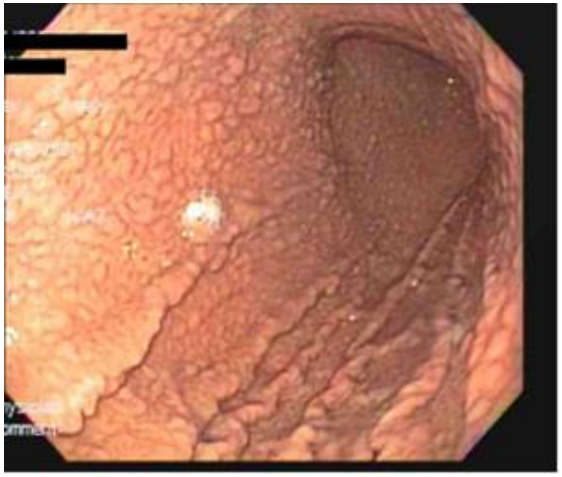
Cowden Syndrome
PTEN Hamartoma Tumor Syndrome

- Characteristic skin findings and macrocephaly
- Colon cancer risk 9-16%
- Extra-colonic cancers:
  - Thyroid: 3-10% lifetime risk (Tan et al. = 35.2%)
  - Endometrial: slightly increased over average (Tan et al. = 28.2%)
  - Urinary tract/kidney slightly increased: (Tan et al. = 33.6%)
  - Melanoma = not previously a recognized component of Cowden syndrome (Tan et al. = 6% risk)

Tan et al. Clin Cancer Res. 2012 Jan 15;18(2):400-7.

Cowden Syndrome

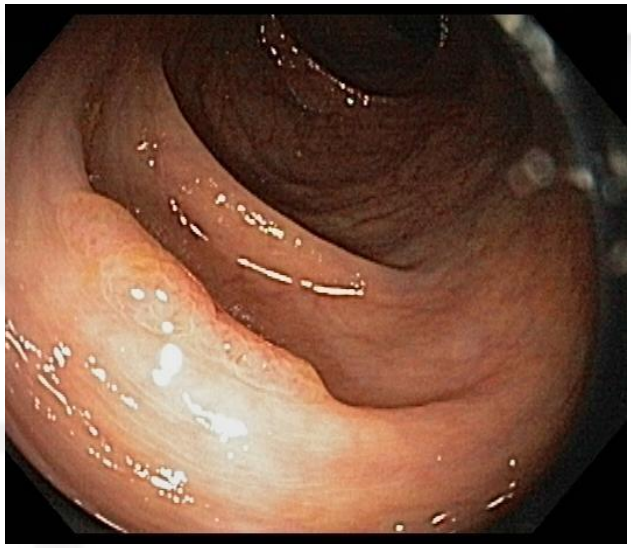
- Hamartomatous polyps throughout GI tract
  - Hamartomas are the most common histologic type, occurring in up to 29% in one study
- Colon polyps
  - Juvenile polyps, ganglioneuromas, adenomas, inflammatory polyps, hyperplastic polyps, sessile serrated polyps
  - Less commonly leiomyomas, lipomas and lymphoid polyps
- Hamartomatous polyps in the stomach, duodenum and small bowel
- Diffuse esophageal glycogenic acanthosis

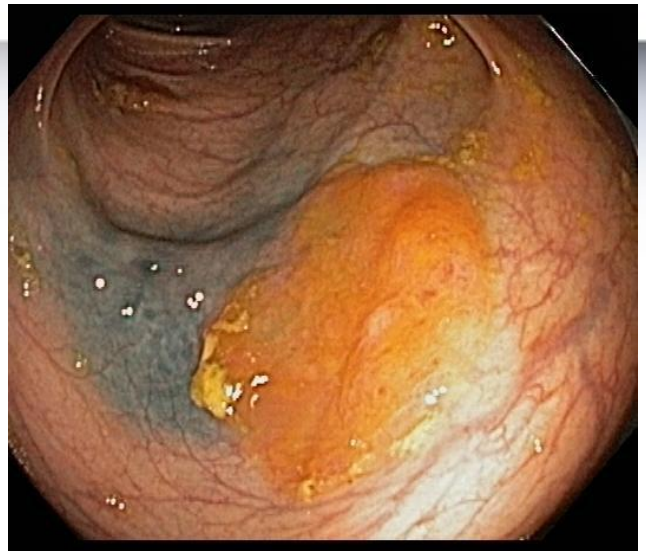


Serrated Polyposis Syndrome (Hyperplastic polyposis)

- Increased risk of CRC, magnitude unknown
- Serrated polyps: sessile serrated polyp (sessile serrated adenoma), hyperplastic polyp, traditional serrated adenoma
- No known genetic cause
  - Some cases with MAP will met criteria for SPS, although they usually have more adenomas than serrated polyps. Patients with Cowden syndrome may also technically meet criteria
- Family history of CRC is common, although these typically occur at older ages
- The risk of CRC for family members is unknown
- No proven extra-colonic features, though some studies suggest there is an increased risk

Serrated Polyposis



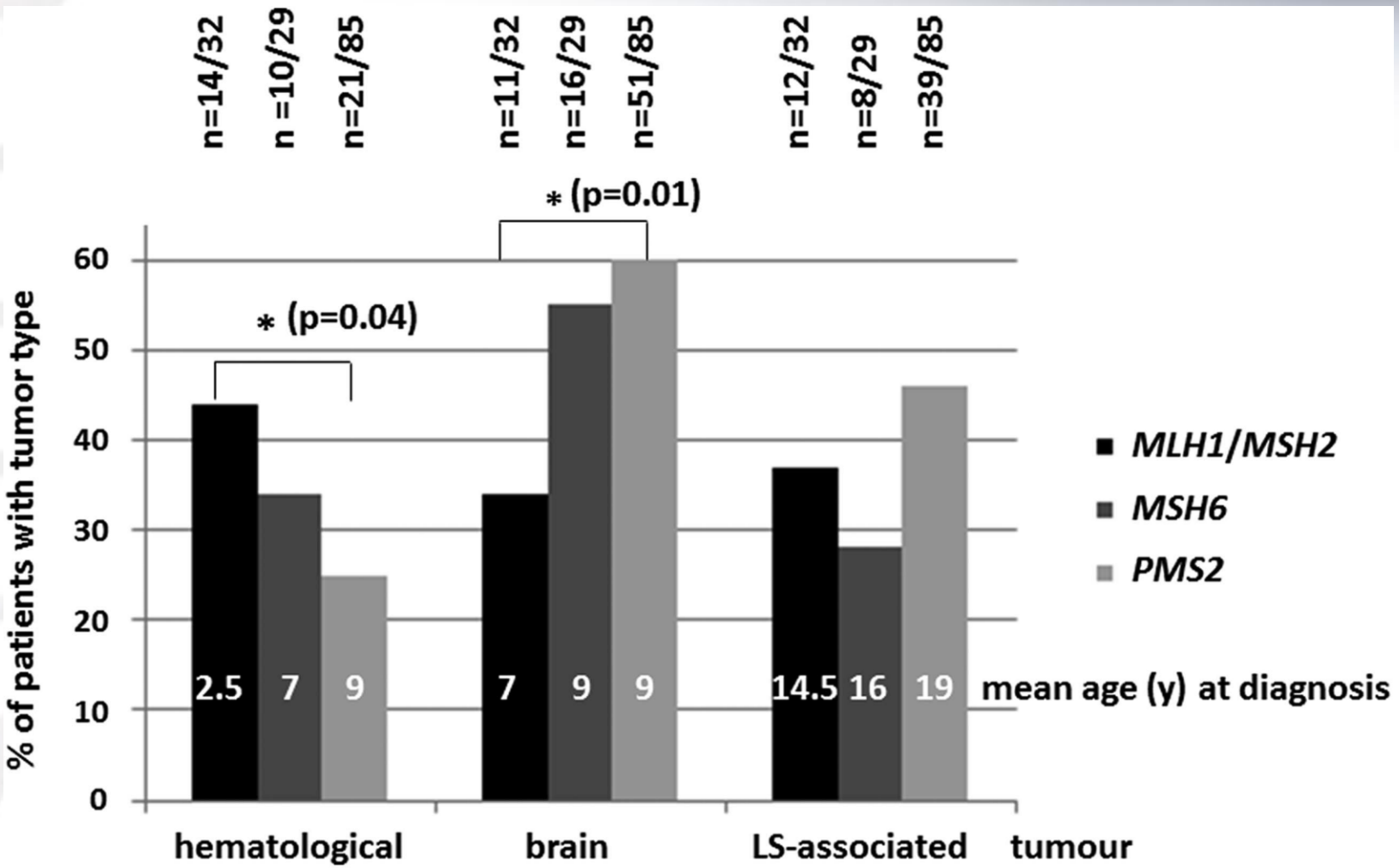


- WHO Diagnostic criteria, any one of the following:
  - > 20 serrated polyps distributed throughout colon
  - ≥ 5 serrated polyps proximal to the sigmoid colon, 2 of which are greater than 10 mm
  - ≥ 1 serrated polyps occurring proximal to the sigmoid colon in an individual who has at least one first-degree relative with serrated polyposis

Constitutional MMR deficiency (CMMRD) syndrome

- Autosomal recessive, biallelic MMR
- Childhood onset, sometimes infancy
- Characteristic features:
  - Hematologic malignancies
  - Brain tumors
  - Lynch syndrome tumors (colon, uterine, small bowel, etc)
  - Signs of NF1
    - Café au lait spots, skin-fold freckling, Lisch nodules and neurofibromas

CMMRD Cancers



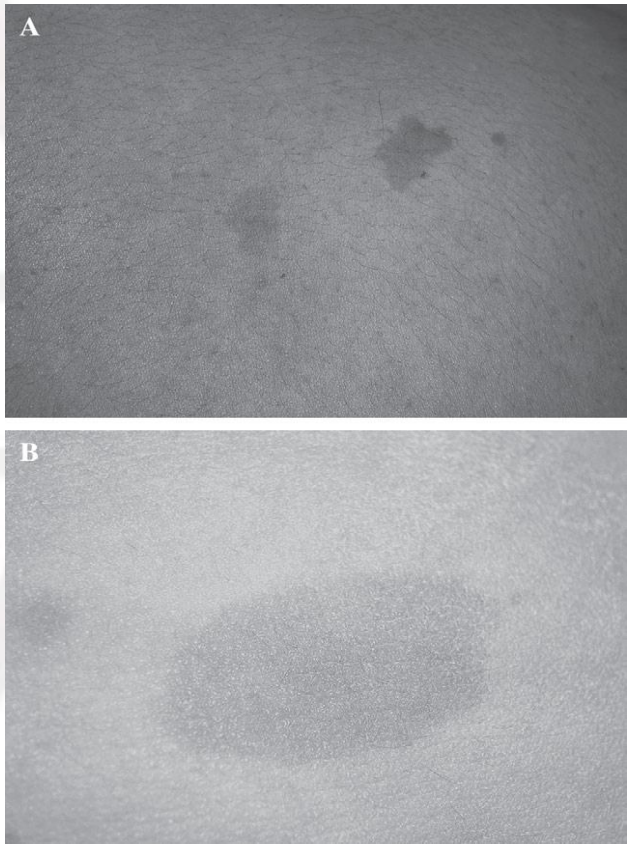
CMMRD Non-Malignant Tumors

Premalignancies and non-malignant tumours in 146 CMMRD patients

Type of neoplasia	Number of patients	Median age at first diagnosis in years	Age range at first diagnosis in years
Adenomas/polyps of colon and rectum	52	14	6–46
Duodenal adenomas/polyps	8	14	10–32
Gastric polyps	1	n.r.	n.r.
Hepatic adenomas	3	9	–
Neurofibromas	7	n.r.	n.r.
Optic glioma	1	3	
Pilomatricomas (epithelioma of Malherbe)	2	2 years 8 months	–
Polyps of vocal cord	1	in infancy	–

Wimmer et al. J Med Genet. 2014 Jun;51(6):355-65.

NF Features



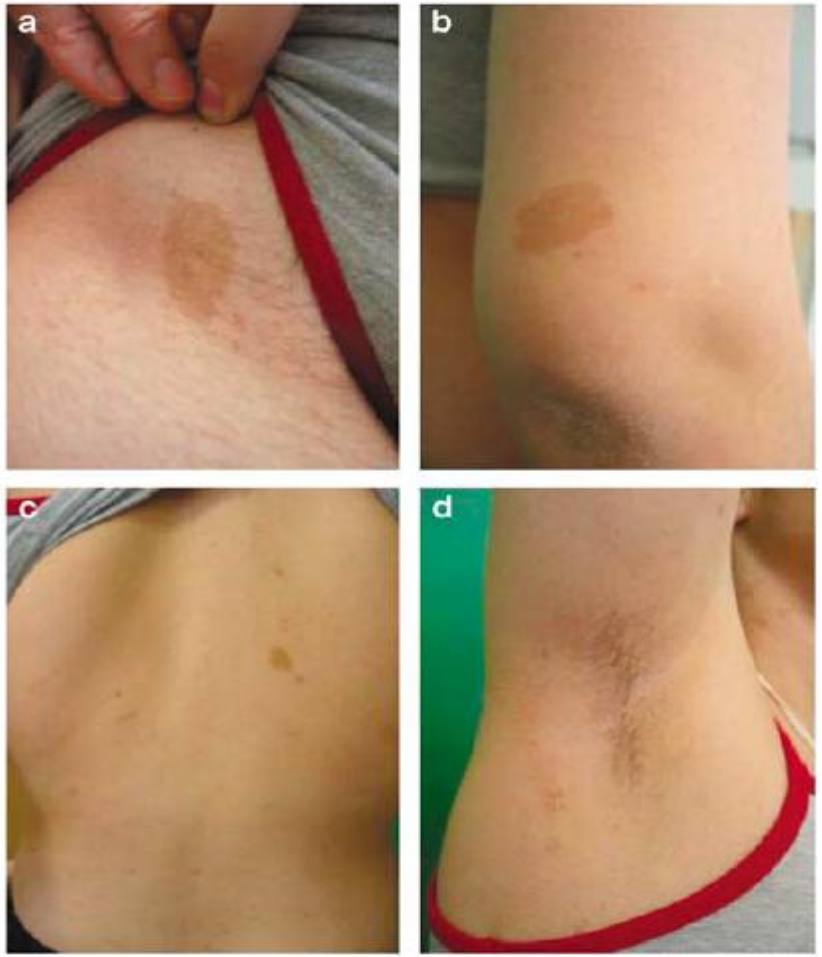


Figure 3 Signs of NF1 in the index patient of family 2. (**a**–**c**) CALS in the right inguinal region, right upper arm, and dorsum, respectively. (**d**) Freckling in the right axilla.

European Journal of Human Genetics (2008) 16, 62–72

Case 1

- 35 yo male presents with hematochezia
- Colonoscopy reveals obstructing descending colon mass, scope not completed
- Biopsy reveals invasive moderately differentiated adenocarcinoma. No mention of polyps
- Subtotal colectomy was performed
- Referred to genetics

Case 1 Continued

- No family history of cancer or polyps
- Proband reports no personal history of polyps (surgical report not available during visit)
- MSI and IHC performed revealed
  - MSI-high
  - IHC (absent MLH1 and PMS2, normal MSH2 and MSH6)
- Differentials
  - Lynch syndrome
  - Sporadic colon cancer
  - Others?

Case 1 Continued

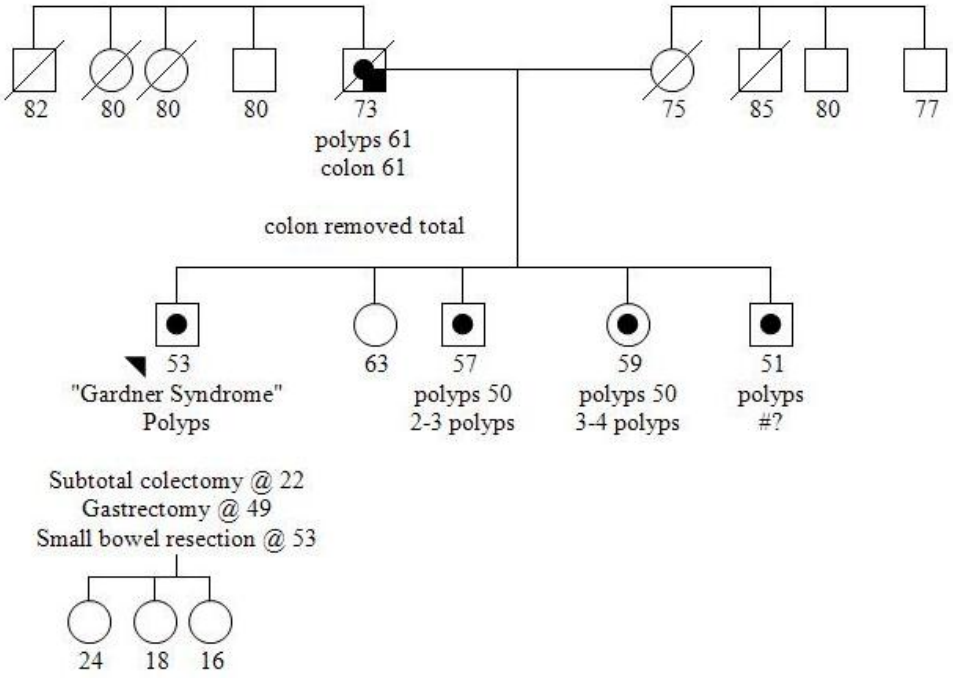
- Genetic testing of MLH1 and PMS2 revealed no mutation
- Promoter MLH1 hypermethylation testing was positive
- Confused yet???
- Surgical path report has one line out of four or five pages that reads: numerous polyps in surgical specimen, sessile serrated polyps
- Follow up completion colonoscopy reveals > 20 sessile serrated and/or hyperplastic polyps

Case 1 Conclusions

- Diagnosis: serrated polyposis syndrome
- Take home points:
  - SPS is associated with hypermethylation of MLH1 which is also seen in sporadic CRCs
  - Important to look at all/most colonoscopy and pathology records to determine appropriate differential diagnoses

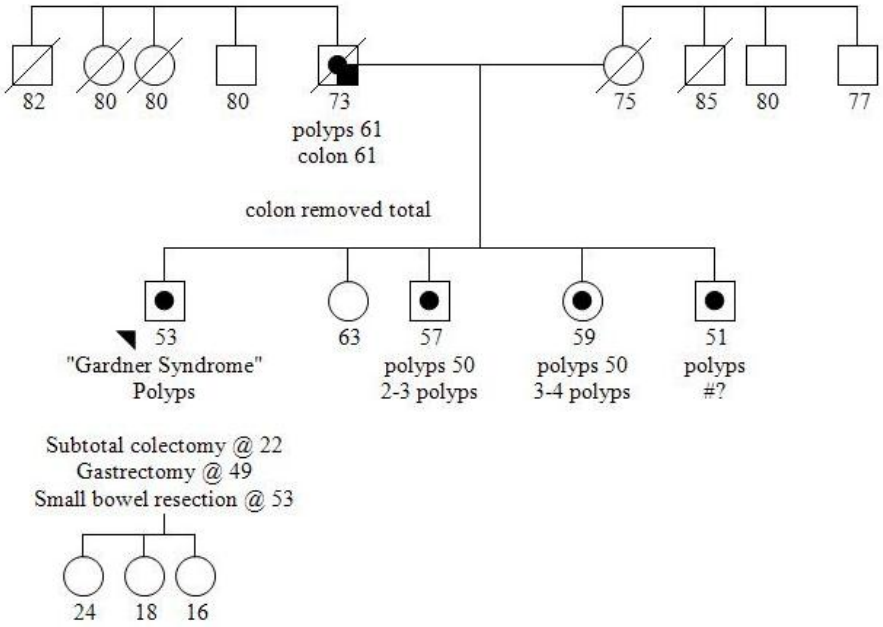
Case 2

- 53 year old male referred for Gardner syndrome originally diagnosed in his 20s
- Colonic and gastric polyposis: polyp types not know
- Small bowel polyp/s: adenomas
- Astrocytoma age 45
- APC/MUTYH negative
- Differentials
  - Mosaicism
  - Missed mutation
  - Other syndrome



Case 2 Conclusions

- Panel genetic testing
  - SMAD4 deleterious mutation confirming JPS
- Take home points:
  - JPS may be misdiagnosed as FAP
  - Important to look at all/most colonoscopy and pathology records to determine appropriate differential diagnoses
  - Genetic testing is key in confirming diagnosis

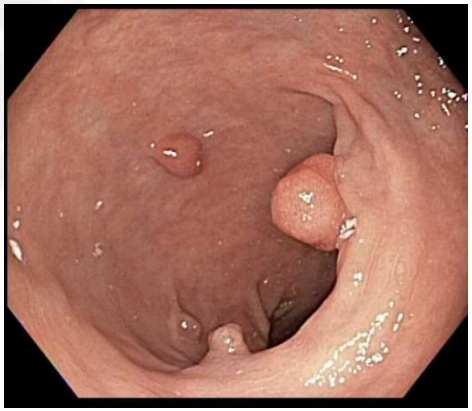


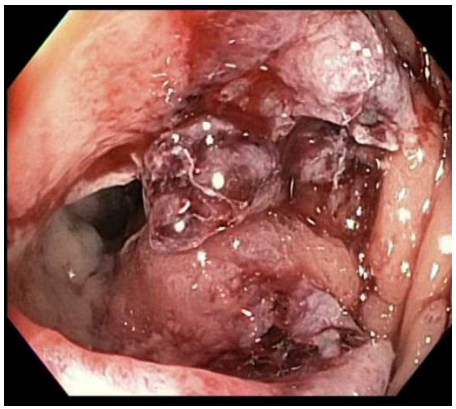
Case 3

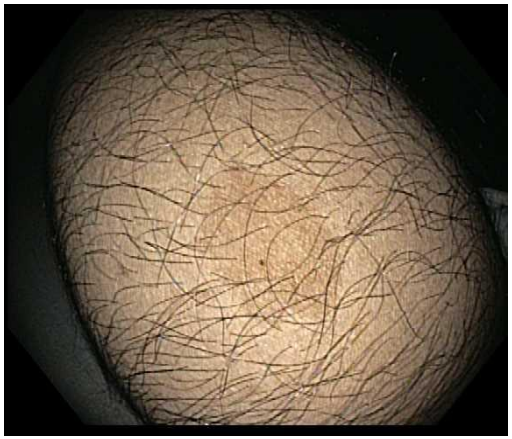
- 30 year old male presented to genetics with a recent diagnosis of descending colon cancer with > 20 adenomatous colon polyps
- Past history included
  - Colon cancer at 13 yo with subtotal colectomy (no records available)
  - Glioblastoma diagnosed at age 26
- Family history non-contributory
- Café au lait macules and axillary freckling
- Diagnosis?

Case 3 Continued

- Uninsured: Proceeded with panel genetic test because tumor testing was not an option
- MSI-high colon cancer
- MSI-stable brain tumor
- IHC
  - Absent PMS2 in colon cancer and normal tissue
  - Normal MLH1 and MSH2
  - Absent MSH6 in colon cancer, but present in normal tissue







Case 3 Conclusions

- Diagnosis:
  - Constitutional mismatch repair deficiency syndrome
- May present with colonic polyposis and look similar to other polyposis conditions
- Exceptionally young age of Lynch syndrome cancers
  - Childhood onset CRCs: CMMRD, LFS, others?
- Signs of NF1 are key
- IHC may be uninformative

Patterns or Something Unusual

Hereditary CRC Syndromes

Gene	Syndrome	Phenotype	Lifetime CRC Risk	Prevalence
APC	Familial adenomatous polyposis, attenuated familial adenomatous polyposis	>100 adenomas 10-100 adenomas	100% 80%	1 in 10,000
MYH	MYH Associated Polyposis	10-100s adenomas	~80%	1 in 40,000 to 1 in 20,000
POLE	Polymerase Proofreading Polyposis	>5 adenomas, young onset colorectal cancer	Unknown	Unknown
POLD1	Polymerase Proofreading Polyposis	>5 adenomas, young onset colorectal cancer	Unknown	Unknown
GREM1	Hereditary Mixed Polyposis	Multiple adenomas, hamartomas and serrated polyps Ashkenazi Jewish ancestry	Unknown	Unknown
MLH1	Lynch Syndrome	CRC, EC, other tumors, MSI	48-56%	1 in 400
MSH2	Lynch Syndrome	CRC, EC, other tumors, MSI	48-56%	1 in 400
MSH6	Lynch Syndrome	CRC, EC, other tumors, MSI	9-23%	1 in 400
PMS2	Lynch Syndrome	CRC, EC, other tumors, MSI	15-20%	1 in 400
EPCAM	Lynch syndrome	CRC, EC, other tumors, MSI	75%	1 in 400
SMAD4	Juvenile polyposis syndrome	≥5 juvenile polyps	9-50%	1 in 100,000 to 1 in 160,000
BMPRIA	Juvenile polyposis syndrome	≥5 juvenile polyps	9-50%	1 in 100,000 to 1 in 160,000
STK11	Peutz-Jehger's syndrome	P-J polyp/muco-cutaneous pigmentation, family history	36%	1 in 250,000 to 1 in 280,000
PTEN	Cowden syndrome	Macrocephaly, hamartomas, and cutaneous manifestations	9%	1 in 200,000
TP53	Li Fraumeni Syndrome	Early onset colorectal cancer	Unknown	1 in 5,000 to 1 in 20,000
CDH1	Hereditary diffuse gastric cancer	Signet ring cell colorectal cancer	Unknown	10 to 40 in 100,000

Courtesy Brandie Leach

Hereditary Polyposis syndromes

Syndrome	Gene (frequency mutation found)	CRC risk (mean age of diagnosis)	Polyp histology	Polyp distribution	Mean age of GI symptom onset	Other disease manifestations	
						Benign	Malignant
Familial adenomatous polyposis[1] (FAP)	APC (70-90%)	100% (39 years), AFAP[2] 69% (58 years)	Adenomatous, except stomach: fundic gland polyps	Stomach: 23%-100% Duodenum: 50%-90% Jejunum: 50% Ileum: 20% Colon: 100%	35.8 years, AFAP[2] 52 years	Desmoid tumors, epidermoid cysts, fibromas, osteomas, CHRPE[3], adrenal adenomas, dental abnormalities, pilomatrixomas, nasal angiofibromas	Duodenal or periampullary: 3%-5%, rare pancreatic, biliary, thyroid, gastric, CNS[4], hepatoblastoma, small bowel
MUTYH associated polyposis (MAP)	MUTYH recessive inheritance (16% to 40% if 15-100 adenomas and 7.5% to 12.5% if > 100 adenomas but not FAP)	93-fold increased risk (48 years)	Adenomatous, hyperplastic, sessile serrated	Stomach: 11% Duodenum: 17% Colon: usually	Not determined	Sebaceous gland adenomas and epitheliomas, lipomas, CHRPE[3], osteomas, desmoid tumors, epidermoid cysts, and pilomatrixomas	Duodenal 4%, sebaceous gland carcinoma
Serrated polyposis syndrome (SPS)	?	Up to 50% or greater in some studies (63 years)	Hyperplastic, sessile serrated, traditional serrated adenomas, adenomatous	Colon	48 years	None	Unknown
Peutz-Jeghers syndrome (PJS)	STK11 (80% to 94%)	39% (46 years)	Peutz-Jeghers, Adenomatous	Stomach: 24% Small bowel: 96% Colon: 27% Rectum: 24%	22-26 years	Mucocutaneous melanin pigment spots	Pancreatic 36%, gastric 29%, small bowel 13%, breast 54%, ovarian 21%, uterine 9% , lung 15%, testes 9%, cervix 10%
Juvenile polyposis syndrome (JPS)	SMAD4, BMPR1A (up to 60%)	Up to 68% (34 years)	Juvenile, Adenomatous	Stomach: 14% Duodenum: 7% Small bowel: 7% Colon: 98%	18.5 years	Macrocephaly, hypertelorism, 20% congenital abnormalities in sporadic type	Stomach and duodenum combined up to 21%
PTEN hamartoma tumor syndrome (PHTS)[5]	PTEN (30% to 55%)	9% to 16%	Juvenile, adenomatous, lipomas, inflammatory, ganglioneuromas, lymphoid hyperplasia	Esophagus: 66% Stomach: 75% Duodenum: 37% Colon: 66%	Not determined	Macrocephaly, Lhermitte-Duclos disease, trichelemmomas, oral papillomas, cutaneous lipomas, macular pigmentation of the glans penis, autism spectrum disorder, esophageal glycogenic acanthosis, multinodular goiter, vascular anomalies	Breast 85%, thyroid 35%, kidney 34%, endometrium 28%, melanoma 6%

[1]FAP, familial adenomatous polyposis, includes Gardner syndrome, 2/3rds of Turcot syndrome cases and AFAP
[2]AFAP, attenuated familial adenomatous polyposis
[3]CHRPE, congenital hypertrophy of the retinal pigment epithelium
[4]CNS, central nervous system
[5]Includes Cowden syndrome, Bannayan-Riley-Ruvalcaba syndrome and adult Lhermitte-Duclos disease

Additional conditions that exhibit gastrointestinal polyposis

Category	Condition	Cause	Histology of polyps	GI areas affected	Other disease manifestations	
					Benign	Malignant
Syndromes where polyps contain neural elements	Neurofibromatosis type I (NFI)	Mutations of NF1 gene, autosomal dominantly inherited	Neurofibromas and ganglioneuromas	Small bowel> stomach>colon	Café-au-lait spots Cutaneous neurofibromas	Ampullary carcinoid, phenochromocytoma, GISTS[1]
	Multiple endocrine neoplasia type IIB (MEN2B)	Mutation of RET proto-oncogene, autosomal dominantly inherited	ganglioneuromas	Lips to anus, but most common in colon and rectum	Pheochromocytoma parathyroid adenoma	Medullary thyroid carcinoma
Syndromes of uncertain etiology	Cronkhite-Canada syndrome	Possibly infectious	Juvenile polyps	Stomach to anus	Skin hyperpigmentation, hair loss, nail atrophy, hypogeusia	12% to 15% colon cancer
	Serrated polyposis	Possibly inherited	Serrated	Colon	None known	Colon cancer risk probably increased
Conditions with inflammatory polyps	Inflammatory bowel disease	Crohn's disease and ulcerative colitis	Pseudopolyps	Colon	As in inflammatory bowel disease	
	Devon polyposis	Inherited	Fibroid polyps	Ileum, stomach	None	None
	Cap polyposis	Unknown, possibly internal prolapse	Similar to solitary rectal ulcer	Rectosigmoid	Rectal bleeding	None
Polyposis conditions arising from lymphoid tissue	Nodular lymphoid hyperplasia	Isolated>immuno-deficiency>lymphoma	Hyperplasia of lymphoid nodules	Small bowel, stomach, colon	Related to underlying disease	
	Multiple lymphomatous polyposis	A type of mantle cell lymphoma	Multiple malignant lymphomatous polyps	Small bowel and colon >stomach	None known	
	Immunoproliferative small intestinal disease (a MALT[2] lymphoma)	Most cases from Camyplobacter jujuni infection	Plasma cell proliferation	Small bowel	Malabsorption, progression to lymphoplasmacytic and immunoblastic lymphoma if not treated in early stages	
Miscellaneous non-inherited polyposis conditions	Leiomyomatosis	Not known	Leiomyoma	Colon, other	None known	
	Lipomatous polyposis	Not known	Lipoma	Colon, other	None known	
	Multiple lymphangiomas	Not known	Lymphiangoma	Colon	None known	
	Pneumatosis cystoides intestinalis	Not known	Inflammatory and air spaces	Colon and other GI locations	None known	

[1]GISTS, gastrointestinal stromal tumors
[2]MALT, mucosa-associated lymphoid-tissue

Questions

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