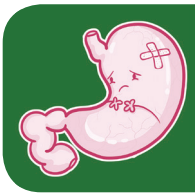

NOTES
COLORECTAL POLYP CONDITIONS

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- *Colorectal polyps:* overgrowths of epithelial cells lining colon/rectum
- Usually benign, can turn malignant

TYPES

Adenomatous polyps/colonic adenomas
- Gland-like polyps caused by tumor suppressor gene mutation in adenomatous polyposis coli (APC)
- Characterized by accelerated division of epithelial cells → epithelial dysplasia → polyp formation
- No malignant potential by itself; requires mutations in other tumor suppressants (K-RAS, p53)
- Histologic classification
  - *Tubular:* pedunculated polyp, protrudes out in lumen
  - *Villous:* sessile, cauliflower-like appearance; more often malignant
  - *Tubulovillous:* characteristics of tubular, villous polyps

Serrated polyps
- Saw-tooth appearance microscopically
- Contain methylated CpG islands → silencing of DNA-repair genes, others → more mutations → malignancy
  - *Small polyps (most common):* AKA hyperplastic polyps; rarely malignant
  - *Large polyps:* often flat, sessile, malignant

Hamartomatous polyps
- Mixture of tissues; disorganized mass containing tissue found at site of polyp
- Occur sporadically/in genetically inherited conditions (Juvenile polyposis, Peutz–Jeghers syndrome)

Inflammatory polyps
- Caused by inflammatory bowel diseases
  - Crohn's disease, ulcerative colitis
- Not malignant

CAUSES
- Genetic mutations
- Inflammatory conditions (e.g. Crohn's disease)

RISK FACTORS
- Family history
- Bowel wall injury (e.g. radiation exposure, smoking, inflammatory bowel disease)
- Risk increases with age

COMPLICATIONS
- Malignancy
  - Depends on degree of dysplasia, size of polyp

SIGNS & SYMPTOMS

- Often asymptomatic
- If ulcerating
  - Rectal bleeding, anemia symptoms (e.g. fatigue)
- If large
  - Obstruction → abdominal pain, constipation
- Malabsorption → diarrhea
- Some polyposis syndromes
  - Extracolonic symptoms

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan, MRI

- Hyperdense outpouchings of colonic wall into lumen; detection of metastases

Endoscopy (colonoscopy) with biopsy

- Type of polyp, malignant potential (degree of dysplasia)

LAB RESULTS

- Iron-deficiency anemia → decreased red blood cell (RBC) count, low mean corpuscular volume (MCV) levels
- Iron-deficiency anemia → low ferritin, serum iron, transferrin saturation
- APC, RAS, etc. mutations
- Assess asymptomatic family members for risk

OTHER DIAGNOSTICS

Digital rectal examination

- Detection of distal rectal polyps; malignant polyp, hard, irregular; benign polyps, softer, pliable

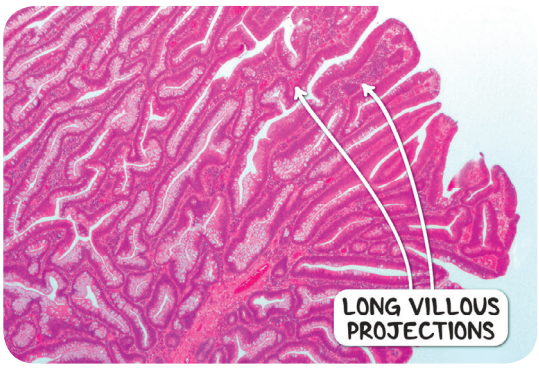

Figure 29.2 Histological appearance of a villous adenoma, characterised by a surface composed of long villous projections.

TREATMENT

SURGERY

Polyp removal (polypectomy)

Colonic resection (colectomy)

- If multiple polyps associated with polyposis syndromes/polyps with high-grade dysplasia

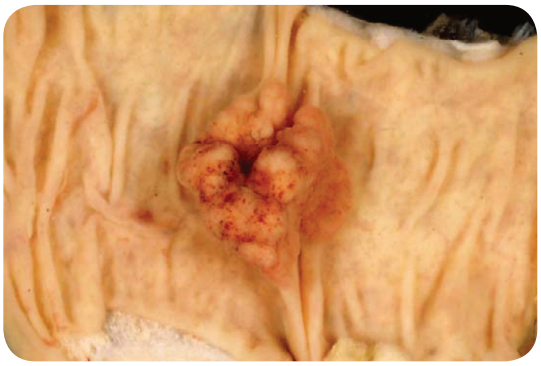

Figure 29.1 The gross pathological appearance of a sessile colorectal polyp.

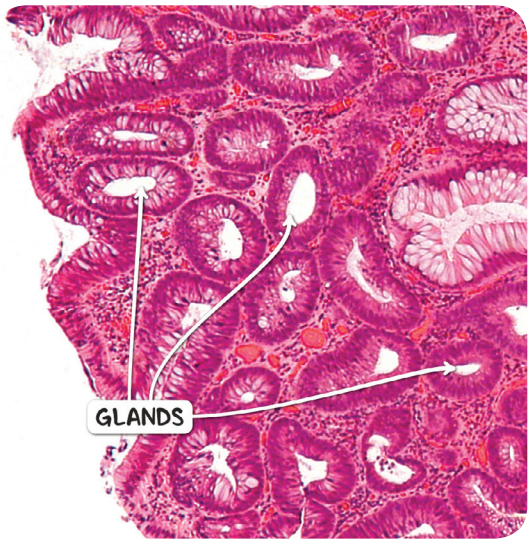

Figure 29.3 The histological appearance of a tubular adenoma composed of compact glands with variable levels of dysplasia.

FAMILIAL ADENOMATOUS POLYPOSIS (FAP)

osms.it/familial-adenomatous-polyposis

PATHOLOGY & CAUSES

- Inherited condition; hundreds/thousands adenomatous polyps in colon
- Autosomal dominant inheritance; 100% penetrance; de novo mutations may occur

TYPES

Classic FAP
- Most aggressive, frequent; > 100 polyps at diagnosis; early onset

Attenuated FAP (AFAP)
- < 100 polyps at diagnosis (oligopolyposis); later onset

Autosomal recessive FAP

CAUSES

- Germline mutation in APC gene (tumor suppressor) → prevention of apoptosis → cell overgrowth → polyps
- APC gene nonfunctional in FAP; slightly impaired in AFAP
- Autosomal recessive FAP
  - Mutations of *MUTYH* gene on chromosome 1

RISK FACTORS

- Family history

COMPLICATIONS

- Malignancy if untreated
- Extracolonic manifestations
  - Congenital hypertrophy of retinal pigment epithelium (CHRPE)
  - *Fundic gland polyps:* sessile polyps in stomach, usually not malignant
  - *Duodenal adenomas:* malignant potential
  - *Abdominal mesenchymal desmoid tumors:* compress adjacent structures → obstruction/vascular impairment
  - *Other potential malignancies:* thyroid, pancreas, brain (glioma), liver (hepatoblastoma)

SIGNS & SYMPTOMS

- Usually asymptomatic until malignancy
- Colonic manifestations
  - Palpable abdominal mass; hematochezia (rectal bleeding); pain (esp. abdomen); diarrhea

DIAGNOSIS

DIAGNOSTIC IMAGING

Endoscopy with biopsy

Colonoscopy, flexible sigmoidoscopy:
- Detection of ≥ 100 polyps; ~30 polys, AFAP

Esophagogastroduodenoscopy (EGD)
- Gastric, duodenal adenomas

Barium enema (with double contrast)
- Filling defects

Abdominal CT scan
- Hyperdense outpouchings of colonic wall into lumen

LAB RESULTS

- Iron-deficiency anemia
- ↓ RBC, ↓ MCV
- ↓ ferritin, ↓ serum iron, ↓ transferrin saturation
- APC mutations

OTHER DIAGNOSTICS

Family history

- Cancers, gastrointestinal (GI) tract diseases

Digital rectal examination

- Palpable mass

Ophthalmic examination

- CHRPE

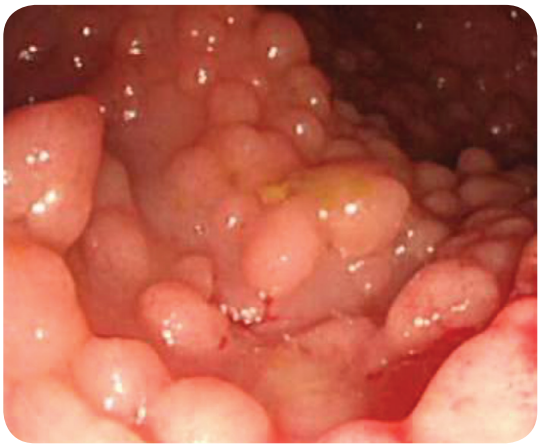

Figure 29.4 Endoscopic appearannce of the colon in a case of familial adenomatous polyposis.

TREATMENT

MEDICATIONS

- Cyclooxygenase 2 inhibitors, other nonsteroidal anti-inflammatory drugs (NSAIDs)
- *Epidermal growth factor receptor inhibitor:* erlotinib
- Chemotherapy, if colon cancer

SURGERY

- Frequent endoscopic check-ups to detect onset of polyposis every 1–2 years
  - If polyps detected → surgical removal (colectomy; proctocolectomy)

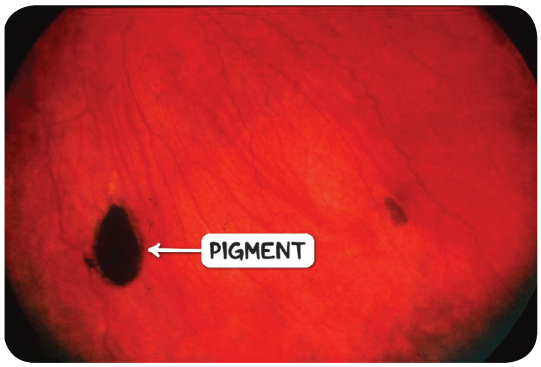

Figure 29.5 A retinal photograph demonstrating hypertrophy of the retinal pigment epithelium in a case of familial adenomatous polyposis.

GARDNER'S SYNDROME (GS)

osms.it/gardners-syndrome

PATHOLOGY & CAUSES

- Variant of FAP with prominent extracolonic manifestations
- Inherited condition; numerous adenomatous polyps in colon; extracolonic polyps, tumors
- Tumors outside colon
  - Fibromas, lipomas, epidermoid cysts, thyroid neoplasms, osteomas, desmoid
- Extracolonic polyps can arise in stomach, duodenum, spleen, kidneys, liver, mesentery, small bowel; CHRPE lesions

CAUSES

- *APC*, *RAS*, *TP53* mutation; *DCC* deletion → furthers carcinogenesis
- Autosomal dominant inheritance

COMPLICATIONS

- Malignancy in colon, thyroid, liver, kidneys

SIGNS & SYMPTOMS

- Colonic manifestations
  - Rectal bleeding, diarrhea
- Extracolonic manifestations
  - Desmoid tumors (parietal bumps, bleeding)
  - Dental problems
  - Epidermoid cysts
  - Epigastric pain, bleeding, jaundice
  - Malnutrition → malaise, lethargy, fatigue

DIAGNOSIS

DIAGNOSTIC IMAGING

Endoscopy with biopsy

Colonoscopy, flexible sigmoidoscopy

- Direct visualization of adenomatous polyps in colon

Abdominal CT scan

- Hyperdense outpouchings of colonic wall into lumen

Head/dental X-ray

- Dental abnormalities

LAB RESULTS

- Iron-deficiency anemia
  - ↓ RBC, ↓ MCV
  - ↓ ferritin, ↓ serum iron, ↓ transferrin saturation
- Tumoral markers (e.g. carcinoembryonic antigen)
- APC, RAS, TP53 mutations; DCC deletion

OTHER DIAGNOSTICS

Physical examination

- Supernumerary impacted teeth
- Multiple jaw osteomas, odontomas

Digital rectal examination

- Palpable mass

Ophthalmic examination

- CHRPE

ECG

- Stomach, duodenum for polyps

TREATMENT

- No cure; palliative treatment

SURGERY

- Excision of tumors/polyps with wide (8mm) margin
- Colectomy

OTHER INTERVENTIONS

- Radiotherapy, if recurrent

JUVENILE POLYPOSIS SYNDROME

osms.it/juvenile-polyposis

PATHOLOGY & CAUSES

- Numerous benign (AKA juvenile) polyps along GI tract
- Majority non-neoplastic hamartomas polyps, in colorectum

CAUSES

- *BMPR1A*, *SMAD4* mutations
- Autosomal dominant inheritance; incomplete penetrance
- De novo mutations (25%)

COMPLICATIONS

- Increased risk of colorectal/extracolonic adenocarcinoma; intestinal obstruction

SIGNS & SYMPTOMS

- Hematochezia, anemia symptoms; abdominal pain; diarrhea/constipation; rectal prolapse

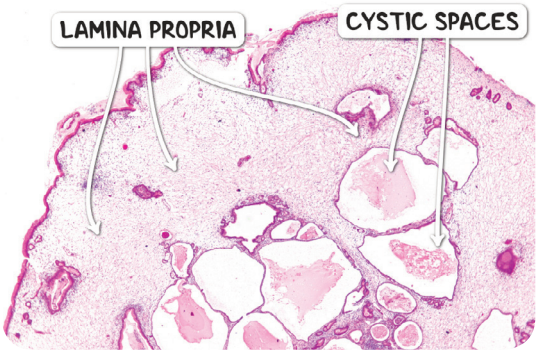

Figure 29.6 A juvenile retention polyp with abundant edematous stroma and dilated cystic spaces filled with mucin. The spaces are lined by cuboidal epithelium.

DIAGNOSIS

DIAGNOSTIC IMAGING

Endoscopic studies

- E.g. endoscopy, colonoscopy, sigmoidoscopy
- Criteria for diagnosis
  - > five juvenile polyps in colon/rectum
  - Multiple juvenile polyps in other areas of GI tract
  - Family history with any number of polyps
- Biopsy, cytology

LAB RESULTS

- Iron-deficiency anemia
  - ↓ RBC, ↓ MCV
  - ↓ ferritin, ↓ serum iron, ↓ transferrin saturation
- *BMPR1A*, *SMAD4* mutations

TREATMENT

SURGERY

- Polypectomy
- Surgical colectomy, proctocolectomy
  - Malignant, ulcerating polyps

PEUTZ-JEGHERS SYNDROME (PJS)

osms.it/peutz-jeghers

PATHOLOGY & CAUSES

- Inherited condition; benign hamartomatous polyps, in small bowel; also in colon, stomach
- Associated with hyperpigmented (melanin-containing) macules on skin, mucosa

CAUSES

- IV drug use
  - Increases likelihood of infective endocarditis
- Congenital bicuspid aortic valve
- Diabetes, high blood pressure, smoking

COMPLICATIONS

- Very high risk of extracolonic malignant transformation
  - Breast, ovarian, cervical, testicular, pancreatic, thyroid cancer
- Mild malignant potential of polyps

SIGNS & SYMPTOMS

- GI
  - Ulceration → GI bleeding (hematochezia/melena) → symptoms of anemia
  - Colicky abdominal pain
  - Intussusception → bowel obstruction, bowel infarction
  - Diarrhea, constipation
- Pigmented lesions around oral mucosa, nostrils, perianal area of extremities; fade after puberty

DIAGNOSIS

DIAGNOSTIC IMAGING

Endoscopy, colonoscopy, with biopsy

Capsule endoscopy

Abdominal CT scan

- Hyperdense outpouchings of colonic wall into lumen

LAB RESULTS

- Fecal occult blood test
- Iron-deficiency anemia
  - ↓ RBC, ↓ MCV
  - ↓ ferritin, ↓ serum iron, ↓ transferrin saturation
- Tumor markers
  - CEA, CA-19-9, CA-125
- *STK11* (*LKB1*) mutations

OTHER DIAGNOSTICS

Diagnostic criteria

- One of following
  - ≥ two PJ polyps confirmed histologically
  - ≥ one PJ polyp with family history
  - PJS-associated mucocutaneous pigmentations

Digital rectal examination

- Palpable mass

TREATMENT

SURGERY

- Polypectomy

MEDICATIONS

- Cyclooxygenase 2 inhibitors (celecoxib)

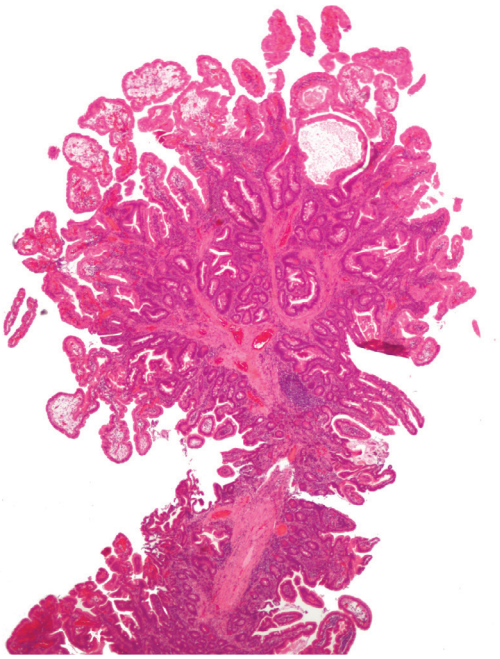

Figure 29.7 Histological appearance of a Peutz-Jegher's polyp.

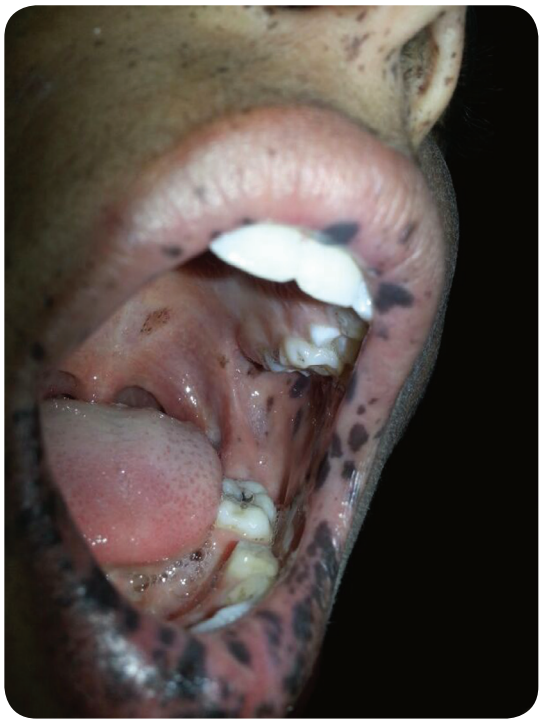

Figure 29.8 Multiple melanotic macules on the skin and oral mucosa of a young boy with Peutz-Jegher's syndrome.