POLYPOID DISEASES OF THE GASTROINTESTINAL TRACT

R3 Pornchai Achatsachat

Introduction

- Polyps: any masses that project into the lumen of the gastrointestinal tract
- True intestinal polyps: epithelial origin
- Juvenile polyp: isolated polyp in children
- Polyposis: multiple polyps
- Polyposis syndrome: genetically related disease with features including
  - Multiple polyps in the gastrointestinal tract
  - Heritability within a family
  - An increased lifetime risk of developing a related cancer in the gastrointestinal tract or in other organ systems

TABLE 93-1

Classification of Polyposis Syndromes

Classification	
Adenomatous polyposis syndromes	1. Familial adenomatous polyposis (FAP) 2. Gardner syndrome 3. Turcot syndrome
Hamartomatous polyposis syndromes	1. Juvenile polyposis 2. Cowden disease 3. Peutz-Jeghers syndrome

Introduction

- Polyps are common during childhood (1% of preschool and school-aged children)
- Most frequent cause of rectal bleeding in toddlers and preschoolers aged 2 to 5 years of age
- Juvenile polyps are most common (80%) and are followed by lymphoid polyps (15%)
- Adenomatous polyps occur in less than 3% of all children with polyps

Juvenile Polyps

Classification of Juvenile polyps (Jass's and Sachatello's)			
Isolated Juvenile Polyps (nonmalignant)	< 5 polyps	Without a family history of juvenile polyposis	Confined to the colon
Juvenile Polyposis syndromes (malignant potential)			
Diffuse Juvenile Polyposis of infancy	< 6 months	Widespread polyposis of entire GI tract	
Diffuse Juvenile Polyposis	6 months – 5 years	Multiple polyps throughout the GI tract	Mostly in the stomach, distal colon, and rectum
Juvenile Polyposis Coli	5-15 years	Multiple juvenile polyps	Confined to the distal colon and rectum

Isolated Juvenile Polyps

- Pathology
- Etiology
- Incidence
- Clinical presentation
- Treatment

Isolated Juvenile Polyps: Pathology

- Known as retention, inflammatory or cystic polyps
- 80% of polyps in children
- Generally considered hamartomas or a malformation
  - **Normal colonic tissue** arranged in a haphazard manner

Isolated Juvenile Polyps: Pathology

- Gross
  - **Typical**: glistening, smooth, spherical, reddish head
  - **Diameter**: 2 mm to several centimeters
  - Often have an ulcerated surface → rectal bleeding
  - Cross section: cystic spaces filled with mucus
  - Typically attached by a long, narrow stalk covered by colonic mucosa
    - This stalk predisposes the polyp to torsion

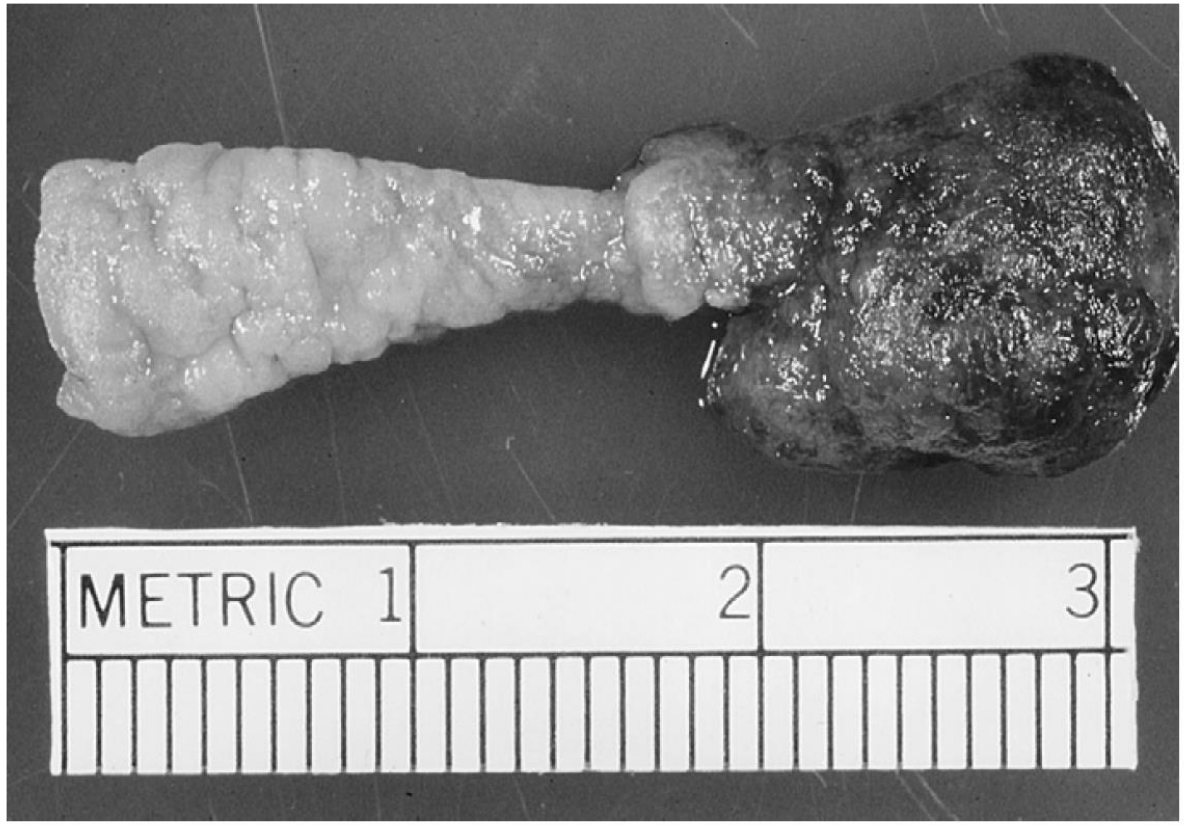


FIGURE 93-1 Typical juvenile polyp with its stalk attached.

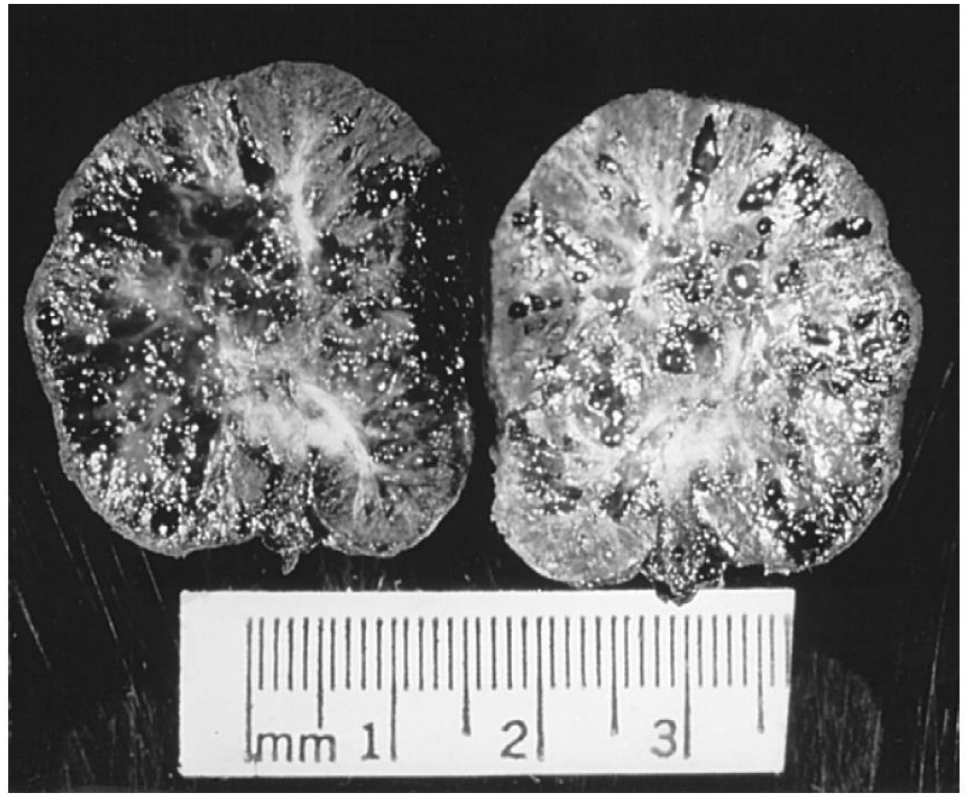


FIGURE 93-2 Gross cross section of juvenile polyp with typical cystic "lakes" filled with mucus.

Isolated Juvenile Polyps: Pathology

- Microscopic
  - Surface: single layer of colonic epithelium
    - Often ulcerated or replaced with granulation tissue
    - Inflammation → reactive hyperplasia (can mimic dysplasia or adenomatous changes)
  - Body: dilated or cystic epithelial tubules that are lined by normal colonic epithelium
    - Tubules and cystic lakes are embedded in a lamina propria and an abundant, loose, vascular, and fibrous stroma
    - The stroma is usually heavily infiltrated with neutrophils, eosinophils, lymphocytes, and monocytes
  - Mitotic figures: rare
    - No increased risk for developing colorectal cancer

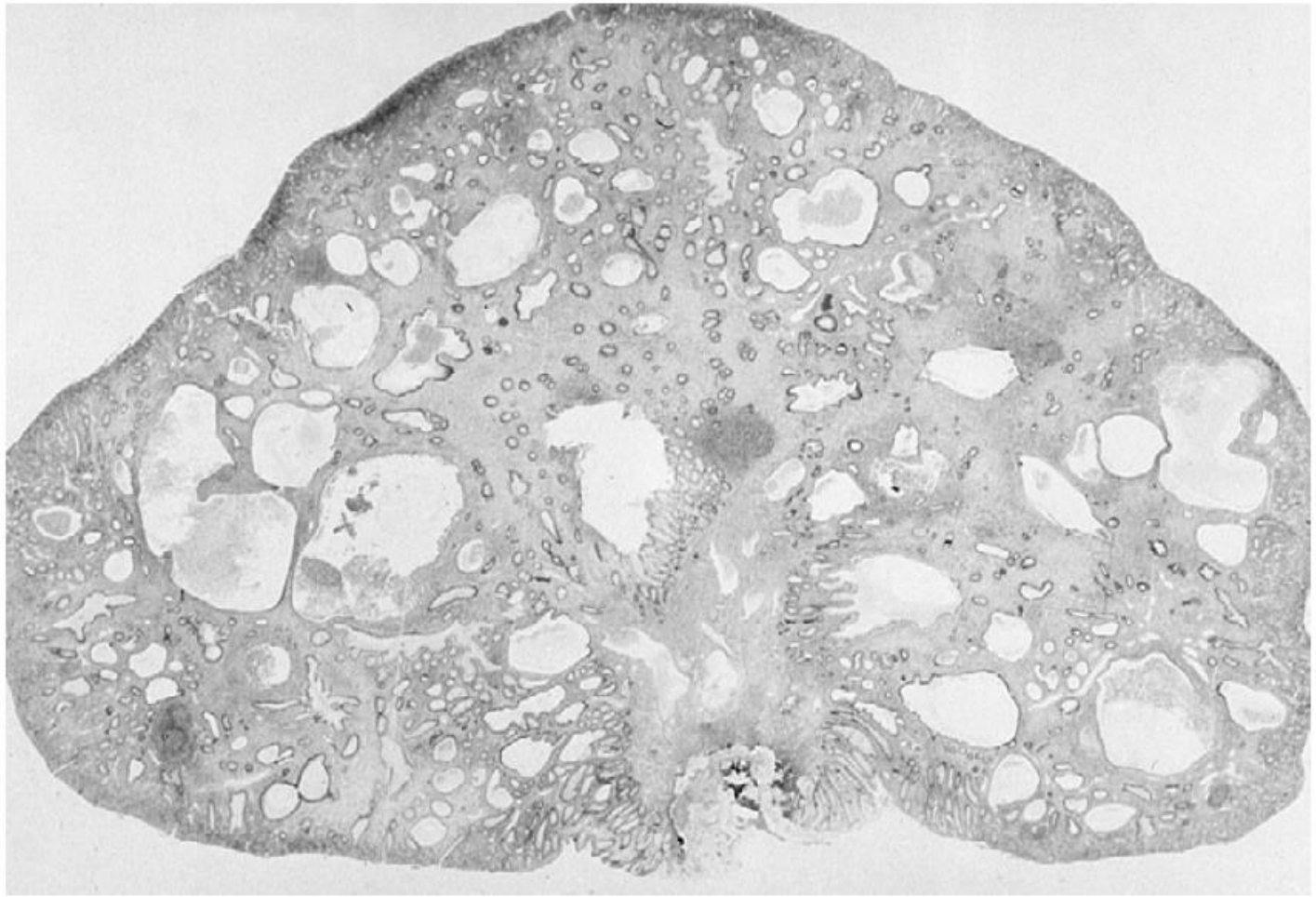
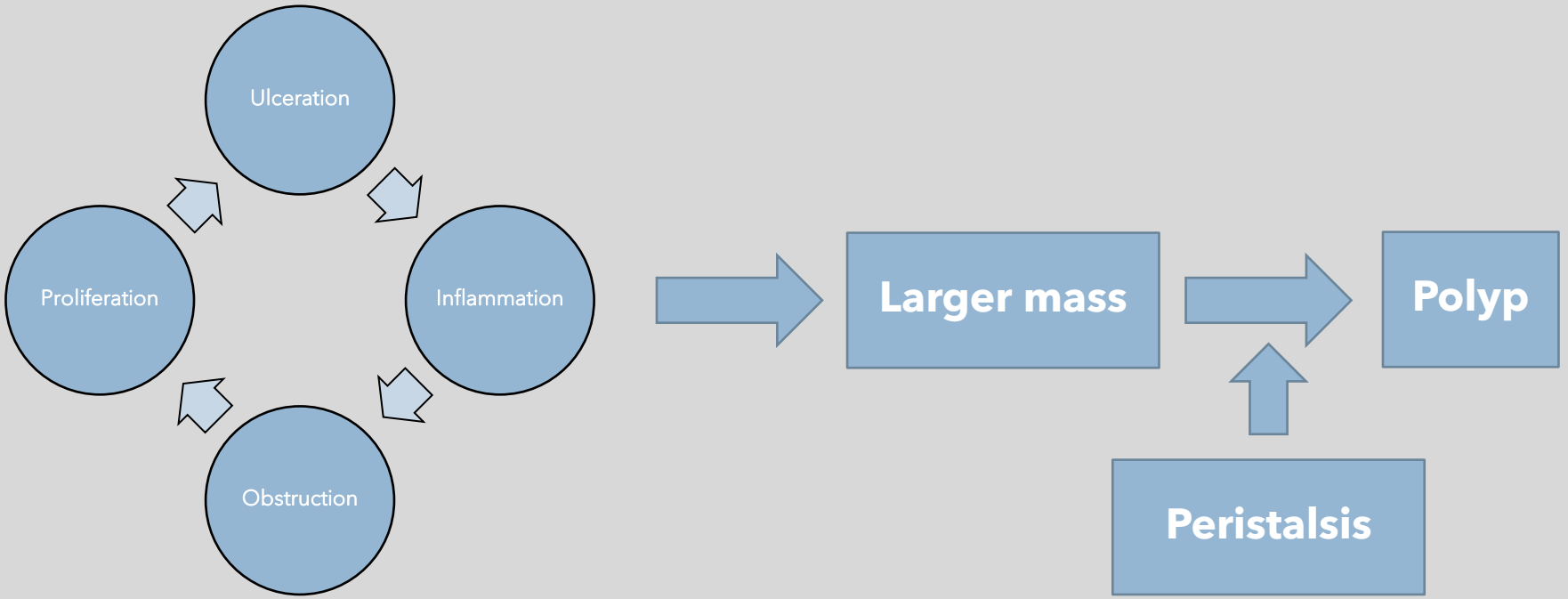


FIGURE 93-3 Photomicrograph of typical juvenile polyp. The surface shows a smooth, flattened, colonic epithelium. Large tubular and cystic lakes are present, embedded in an abundant, loose stoma.

Isolated Juvenile Polyps: Etiology

- **Unknown**: hereditary, genetic, hamartomatous malformation, inflammation
  - Structural rearrangement of the mucosa secondary to an inflammatory process



Isolated Juvenile Polyps: Incidence

- Unknown, approximately 1% of all preschool children
  - Mostly first decade of life
  - Peak incidence: 3-5 years of age
- Solitary in 50% of cases, with the remainder having 2 to 10 polyps
- Location
  - Rectum or sigmoid colon: 40%
  - Proximal colon: 60%

Isolated Juvenile Polyps: Clinical presentation

- Bleeding (93%)
  - Bright red streaks of blood over the surface of the stool
  - Autoamputate → spontaneous cessation
- Abdominal pain (10%)
  - Caused by traction on the polyp from peristaltic activity
- Prolapse of the polyp (4%)

Isolated Juvenile Polyps: Clinical presentation

- Differential diagnosis (rectal bleeding in toddlers through children)
  - **Anal fissures and rectal prolapse**: physical examination
  - **Meckel diverticulum or duplication of the intestine**
    - More substantial blood loss
    - Blood usually commingles with the stool
  - **Intussusception**: worse abdominal pain
  - **Inflammatory bowel disease**: diarrhea
  - **Henoch-Schonlein purpura**

Isolated Juvenile Polyps: Treatment

- Increased risk of malignancy
  - Shift of juvenile polyps to the more proximal colon
  - Juvenile polyposis (>5 polyps)
- Polyps in the rectum can be easily removed during **anoscopy**
- **Pancolonoscopy** in a well-prepared bowel
- Children with juvenile polyposis and adenomatous changes are more likely to have right-sided polyps
- **All polyps should be removed** and undergo histologic evaluation

Polyposis Syndromes

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Adenomatous Polyposis Syndromes

- Familial adenomatous polyposis (FAP)
- Gardner syndrome
- Turcot syndrome

Adenomatous Polyposis Syndromes

TABLE 93-2

Extracolonic Features in Familial Adenomatous Polyposis

Cancer (Lifetime Risk)	*Other Lesions*
Duodenal (1%-5%)	CHRPE
Pancreatic (2%)	Nasopharyngeal angiofibromas
Thyroid (2%)	Osteomas
Brain (medulloblastoma) (<1%)	Radiopaque jaw lesions
Hepatoblastoma (0.7% of children < 5 yr old)	Dental abnormalities
	Lipomas, fibromas, epidermoid cysts
	Desmoid tumors
	Gastric adenomas/fundic gland polyps
	Duodenal, jejunal, ileal adenomas

CHRPE, congenital hypertrophy of the retinal pigment epithelium.
Modified from Cruz-Correa M, Giardello FM: Diagnosis and management of hereditary colon cancer. Gasroenterol Clin North Am 2002;31:537-549.

Familial Adenomatous Polyposis (FAP)

- Pathology
- Etiology
- Clinical presentation
- Treatment
- Follow-up

Familial Adenomatous Polyposis (FAP)

- Hundreds to thousands of adenomatous polyps in the colon
- By 15 years of age 50% of those that carry the FAP gene will have polyps
- The lifetime risk for developing a colorectal cancer is 100%
  - Average age for developing an adenoma: 16 years
  - Average age for developing a colorectal cancer: 39 years

FAP: Pathology

- FAP is defined as the presence of **at least 100** visible adenomatous polyps in the large intestine
- Hallmark: Colorectal polyps
  - **Sparse type**: hundreds of polyps
  - **Profuse type**: thousands of polyps
    - Tend to develop adenocarcinoma at an earlier age

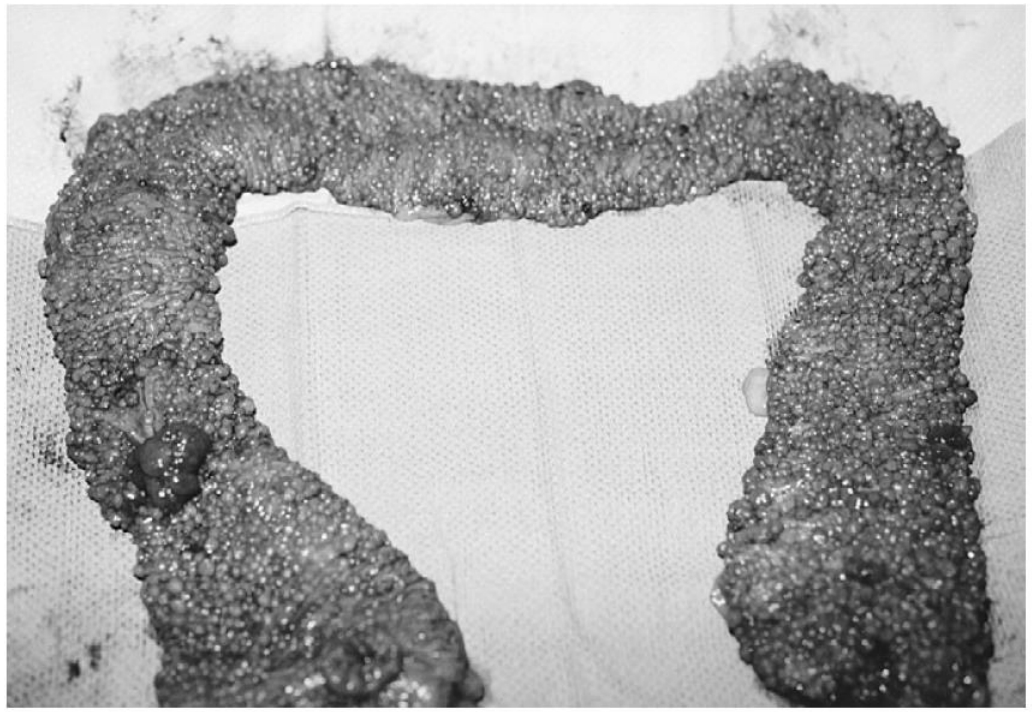


FIGURE 93-4 Gross specimen of the total colon in a patient with familial adenomatous polyposis demonstrating thousands of adenomatous polyps. Note the large adenoma in the ascending portion of the colon.

FAP: Pathology

- Polyps are typically scattered throughout the colon >> **sigmoidoscopy**
  - Size: 1-2 mm in diameter
  - Pedunculated polyps can be 1 cm in diameter or larger
  - **Duodenoscopy**: biopsy of normal-appearing duodenal mucosa may reveal microscopic adenomas

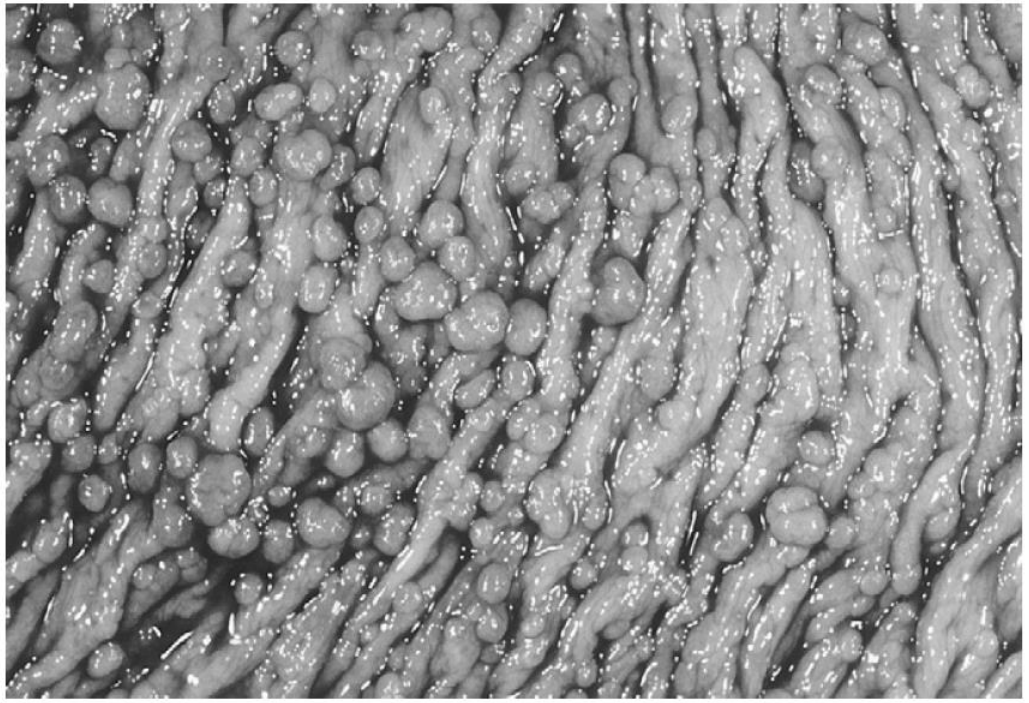


FIGURE 93-5 Close-up view of colonic mucosa demonstrating a "carpet" of small 1- to 2-mm adenomas in a patient with familial adenomatous polyposis.

FAP: Pathology

- Adenomatous polyps result from a neoplastic transformation of at least one epithelial cell that is in the proliferative portion of a crypt
  - Dysplasia: atypical morphologic characteristics, with nuclear enlargement and stratification
  - Carcinoma in situ: extension into the basement membrane
  - Microscopically invasive: extend beyond the basement membrane
  - Metastasis: invades through the muscularis mucosa into the submucosa

FAP: Pathology

- Small intestinal mucosa can also be involved with adenomatous polyps
  - Frequently found around the orifice of the common bile duct
  - Variable in size, often microscopic, involve only a few crypts
  - Adenocarcinoma of the duodenal papilla and periampullary regions 2.9%
- Gastric polyps
  - Usually benign polyps of the fundic gland
  - Result from cystic dilation of specialized gastric glands
  - No evidence that neoplastic transformation

FAP: Etiology

- Incidence: 1/6000 – 1/12,000 births
- Autosomal dominant trait with 10% of new mutations
- Mutation in the APC gene on the long arm of chromosome 5
  - Gene deletion → the probability of cancer by 25 years of age is 90%
- TP53 gene on chromosome 17p
- Deleted colorectal cancer gene (DCC) on chromosome 18q

FAP: Clinical Presentation

- Most frequently identified in early adolescence
- Most patients are asymptomatic
  - 90% are identified by routine surveillance
- Increased frequency of defecation
- Rectal bleeding
- Anemia
- Abdominal pain

FAP: Clinical Presentation

- **Diagnosis**: sigmoidoscopy, occasionally by air contrast barium enema
- **Confirm diagnosis**: Biopsy of at least 10 polyps
- In some patients, most of the polyps will be located in the proximal colon

- **Gastric polyps**: up to 50%
  - Only 6%: adenomatous
- **Duodenal polyps**
  - Less often than in the stomach
  - Much more likely to be adenomatous → upper endoscopy

FAP: Treatment

- The average age for developing cancer is 39
  - 7% developing cancer by age 20
  - 15% developing cancer by age 25
- Most patients who present with symptomatic polyps already have a malignant condition
  - Colectomy is recommended at any age, if the child is symptomatic

FAP: Treatment

- Total abdominal colectomy with an ileorectal anastomosis and continued surveillance of the retained rectum
  - Immediate post-operative complications
    - Prolonged ileus (7%)
    - Anastomotic breakdown (2%),
    - Bleeding (<1%)
  - Frequency of defecation at late follow-up: 3 stools/day
  - Nighttime soiling <10%
  - Normal continence 72%
  - Subsequent treatment for their rectal polyps 44%

FAP: Treatment

- Total abdominal colectomy with an ileorectal anastomosis and continued surveillance of the retained rectum
  - Sigmoidoscopy: every 3 to 6 months
  - Fulguration of any polyps greater than 5mm in diameter
  - 10% developed carcinoma in their rectal stump
  - Cumulative risk for rectal cancer
    - 10% at 50 years of age
    - 29% at 60 years of age

FAP: Treatment

- Total colectomy with a rectal mucosectomy and an ileoanal pouch procedure
  - The J pouch is the preferred technique because of simplicity of construction and sparsity of complications
  - Larger reservoirs allow less frequent defecation but tend to be associated with more frequent bouts of inflammation of the reservoir ("pouchitis")
  - Frequency of defecation: 3.3-7.2 stools/day (average 5.8 stools/day)
  - Pouchitis 23%
  - Pelvic sepsis 8%

FAP: Other Treatments

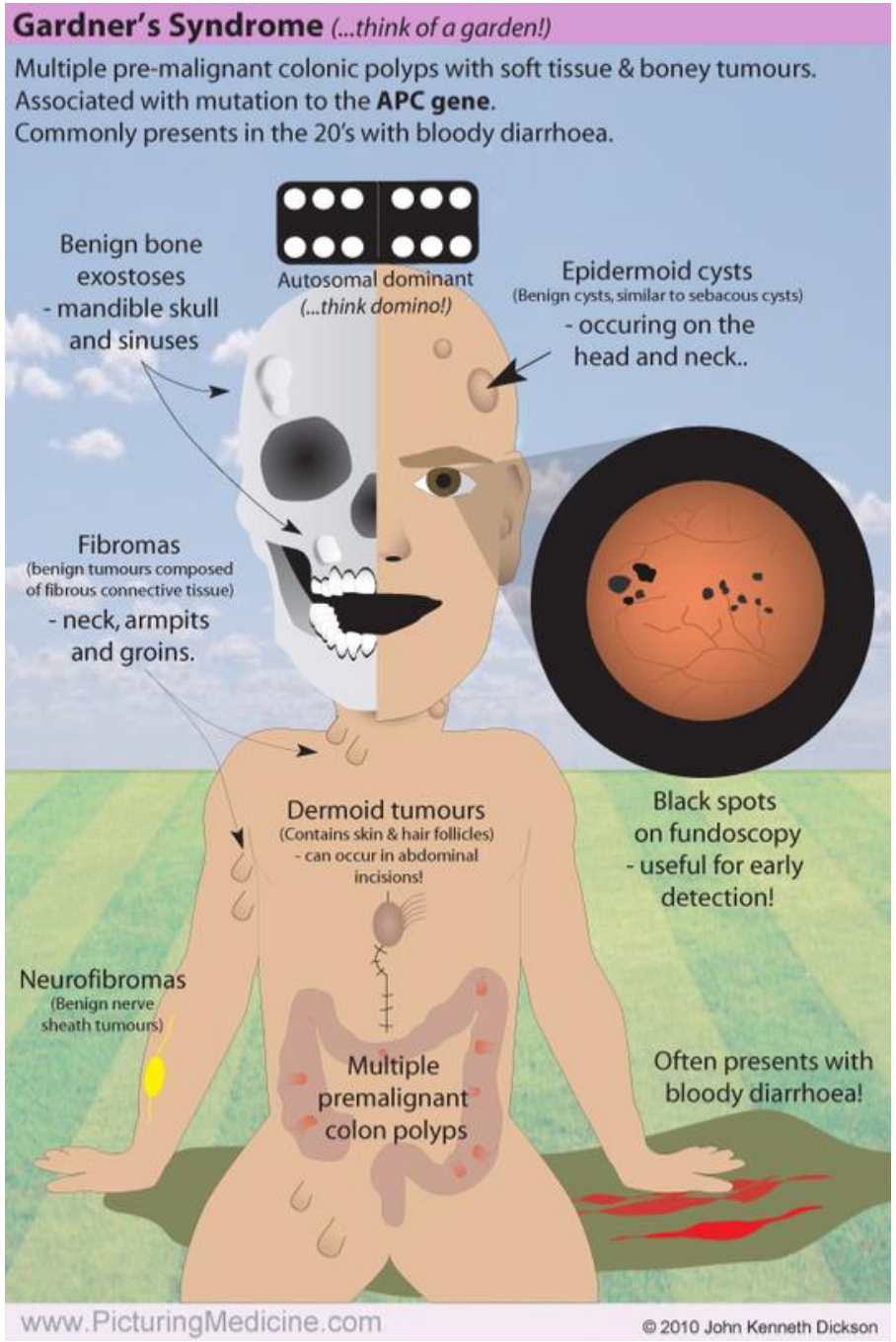
- Vitamin C
- Sulindac
- Dietary fiber
- Calcium

FAP: Follow-up

- **EGD and sigmoidoscopy**: annually
- **Duodenal polyps**: remove by endoscopic snaring or by open duodenotomy
- More aggressive intervention
  - Size larger than 1 cm in diameter
  - Rapid growth
  - Polyp induration
  - Severe dysplasia
  - Villous change
- Incidence of duodenal cancer: 1-5%

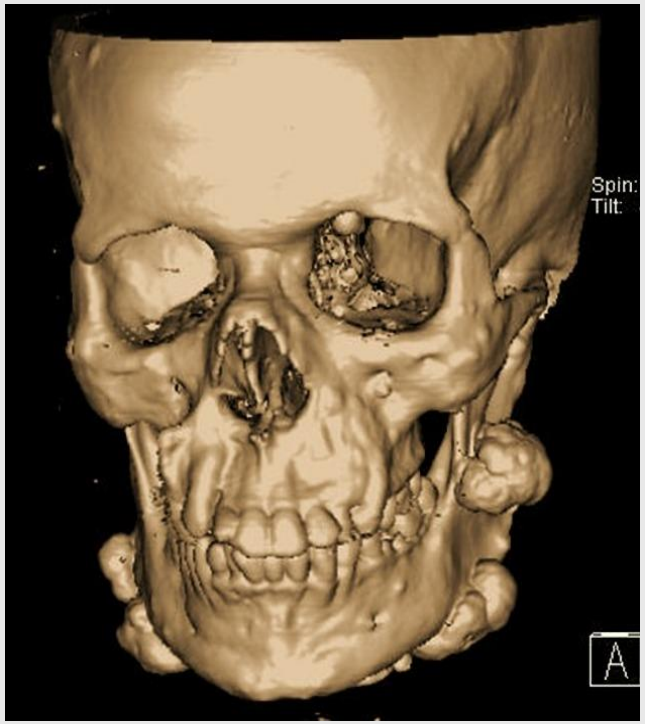
Gardner syndrome

- Colonic familial adenomatous polyposis
- Multiple osteomas, fibromas, and epidermoid cysts



Gardner syndrome

- Autosomal dominant
- The natural history and treatment of the colonic polyps is the same as FAP
- Osteomas:
  - Skull
  - Facial bones
  - Abnormal dentition with impaction and early tooth decay and supernumerary teeth
- Sebaceous cysts: legs > face > scalp > arms
- Lipomas and fibromas



Gardner syndrome

- **Periampullary cancer**: more prevalent than FAP

- **Desmoid tumors of the abdominal wall and mesentery of the small intestine**: 20%
  - Leading cause of death in those who have undergone a prophylactic colectomy
  - All stages of fibrous dysplasia including fibrosarcoma have been seen
  - Most appear after surgery, usually within 6 to 30 months

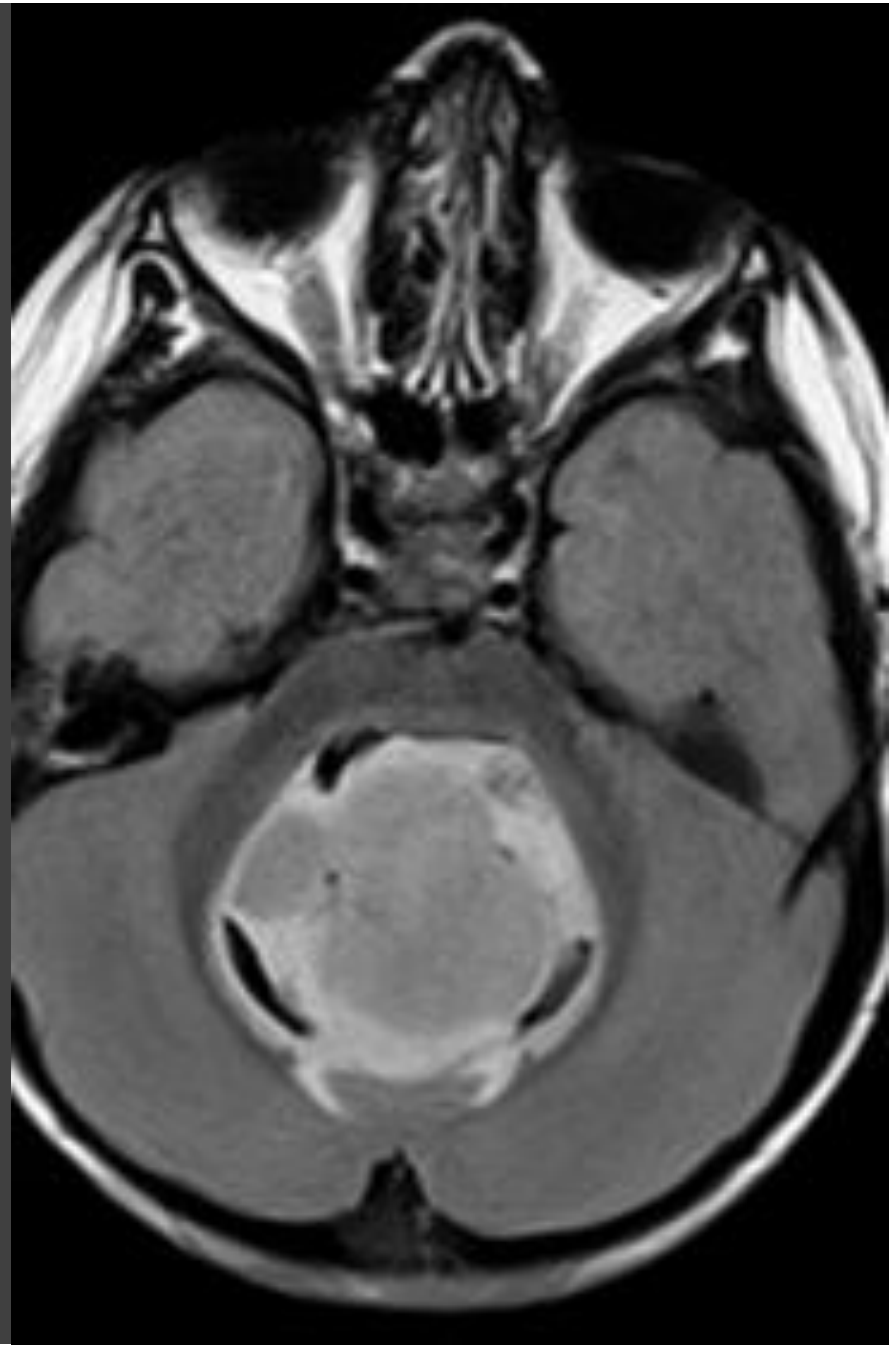
Gardner syndrome

- Desmoid tumors of the abdominal wall
  - Many of them remain static or even regress over several years
  - Growing or reach 10 cm in diameter
    - Complete local excision is met with a recurrence rate of less than 10%

- Intraabdominal desmoid tumors
  - Difficulty in resecting
  - Several drugs have been tried: steroids, antiestrogen agents, NSAIDS

Turcot syndrome

- Colonic familial adenomatous polyposis
- Intracranial brain tumors (glioblastoma and medulloblastoma)
- Ependymomas
- Carcinoma of the thyroid (usually papillary in origin)



Hamartomatous Polyposis Syndrome

Juvenile polyposis syndrome

Peutz-Jegher syndrome

Cowden disease

Overgrowth of cells that are native to the area

Not considered to have malignant potential

Juvenile Polyposis Syndrome

Diffuse juvenile polyposis of infancy

Diffuse juvenile polyposis

Juvenile polyposis coli

Diffuse juvenile polyposis of infancy

- Within the first few months of life
- Usually without any family history
- Presenting signs
  - Diarrhea
  - Rectal bleeding
  - Intussusception
  - Protein-losing enteropathy
  - Macrocephaly
  - Clubbing of fingers and toes
  - Hypotonia

Diffuse juvenile polyposis of infancy

- Treatment: usually aggressive
  - Total parenteral nutrition
  - Intestinal rest
  - Portions of the intestine with the most polyps are removed
- Despite appropriate treatment, this disease is almost universally fatal
  - Only 2 of 12 patients are reported as surviving beyond 2 years of age

Diffuse juvenile polyposis

- Usually 6 months to 5 years of age
- Presenting signs
  - Mild rectal bleeding and prolapse
  - Protein-losing enteropathy
  - Intussusception
  - Malnutrition
- Polyps associated with diffuse polyposis are found throughout the bowel, most often in the stomach, distal colon, and rectum
- Treatment: endoscopic polypectomies and segmental bowel resection
- Usually do well, although the need for recurrent therapy is common

Juvenile polyposis coli

- 5 and 15 years of age
- Presenting signs
  - Bleeding of bright red blood from the rectum
  - Anemia
  - Rectal prolapse
- Polyps are usually limited to the distal colon and rectum
- 50% have a family history → autosomal dominant

Juvenile polyposis coli

- Associated congenital defects
  - Cleft palate
  - Malrotation
  - Polydactyly
  - Abnormalities of the heart and cranium

Juvenile Polyposis Syndrome: Pathology

- Family history → juvenile polyposis syndrome
- Approximately 50 to 100 colorectal polyps
- Diffuse juvenile polyposis of infancy and diffuse juvenile polyposis
  - Also have polyps in the stomach, small intestine, or both
- Long-term surveillance due to the high risk of carcinoma (17%) occurring at an early age

Juvenile Polyposis Syndrome: Pathology

- Gross appearance
  - Same as isolated juvenile polyps
  - 20% of the polyps present grossly as a multilobular mass resembling a cluster of polyps attached to a stalk

FIGURE 93-6 Gross specimen of colon in a patient with juvenile polyposis syndrome. Note small adenomas and multilobular clusters of polyps attached to stalks.

Juvenile Polyposis Syndrome: Pathology

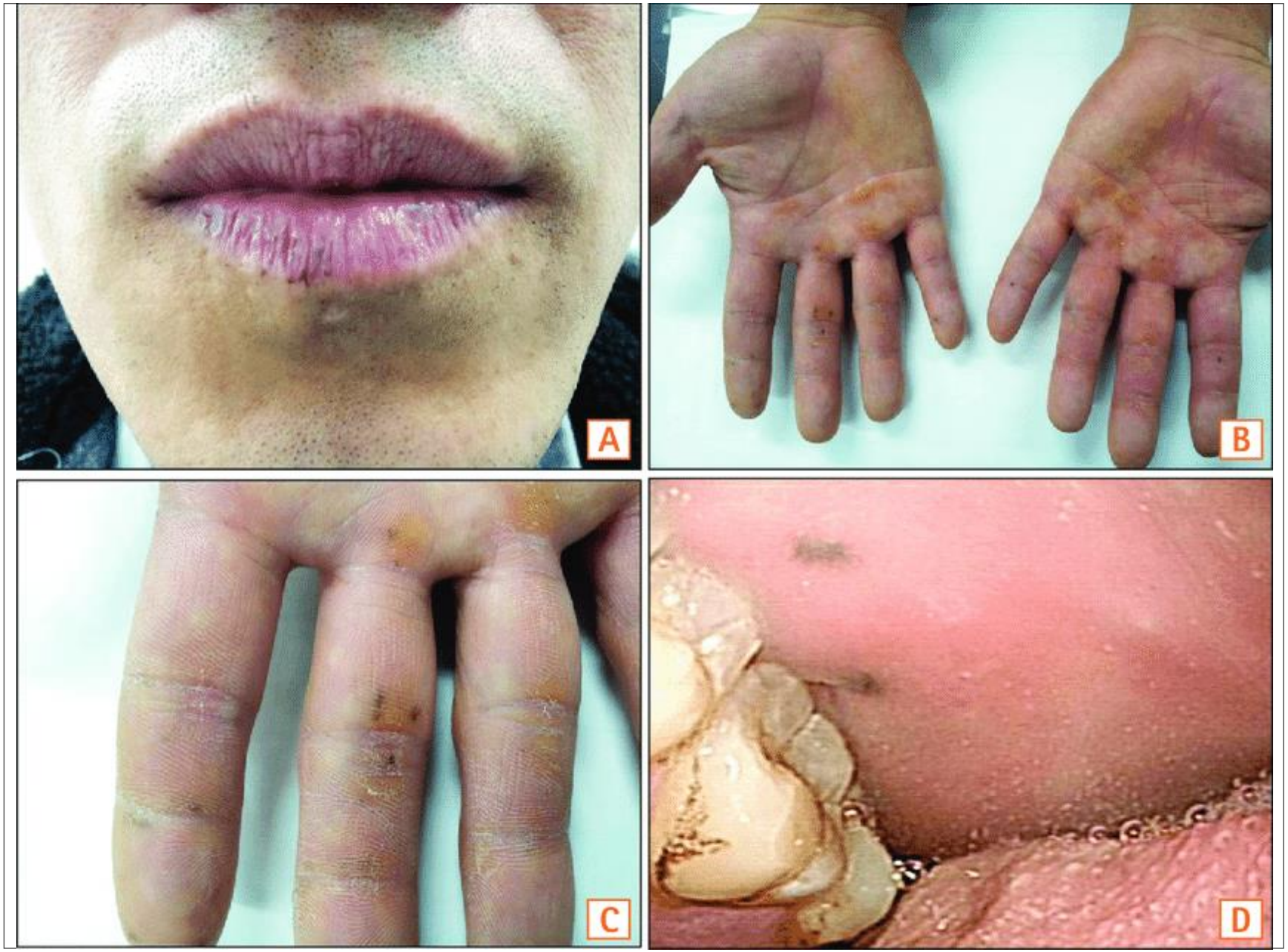
- Histologic appearance
  - More epithelium with a villous or papillary configuration
  - Epithelial dysplasia can occur in juvenile polyps and in coexisting adenomas found in conjunction with juvenile polyps
  - Carcinoma in situ has been found
  - Lobular polyps have a higher propensity for more severe dysplasia (47%) than the nonlobular polyps (10%)
- Cumulative risk for cancer by age 60 is 68%

Juvenile Polyposis Syndrome: Treatment

- Long-term follow-up of patients and their family members
- Some advocate prophylactic colectomy and rectal mucosectomy with endorectal ileal pull-through as a primary treatment
- Others recommend regular screening (every 2 years) with colonoscopy and random biopsy and subsequent colectomy if severe dysplasia, rapid polyp formation, or bleeding occurs
- The approach to patients with juvenile polyposis should be similar to that taken for patients with familial adenomatous polyposis

Peutz-Jegher Syndrome

- Pathology
- Etiology/Incidence
- Clinical presentation
- Treatment



Peutz-Jegher Syndrome: Pathology

- Melanotic spots
  - Brown to black
  - Lips, mouth, Buccal mucosa
  - Hands, feet, nasal mucosa, conjunctivae, rectum
  - Usually present at infancy
  - Usually fade at puberty

Peutz-Jegher Syndrome: Pathology

- Polyps: anywhere from the stomach to the rectum
  - Small intestine (55%)
  - Stomach and duodenum (30%)
  - Colon and rectum (15%)
- Gross
  - Few millimeters to several centimeters
  - Smooth, firm, pedunculated lesions that are lobulated

Peutz-Jegher Syndrome: Pathology

- Histologic
  - Hamartomas of the muscularis mucosa
  - Strands of smooth muscle fibers that divide the polyp into sectors
  - Adenomas can occur concurrently with Peutz-Jeghers polyps

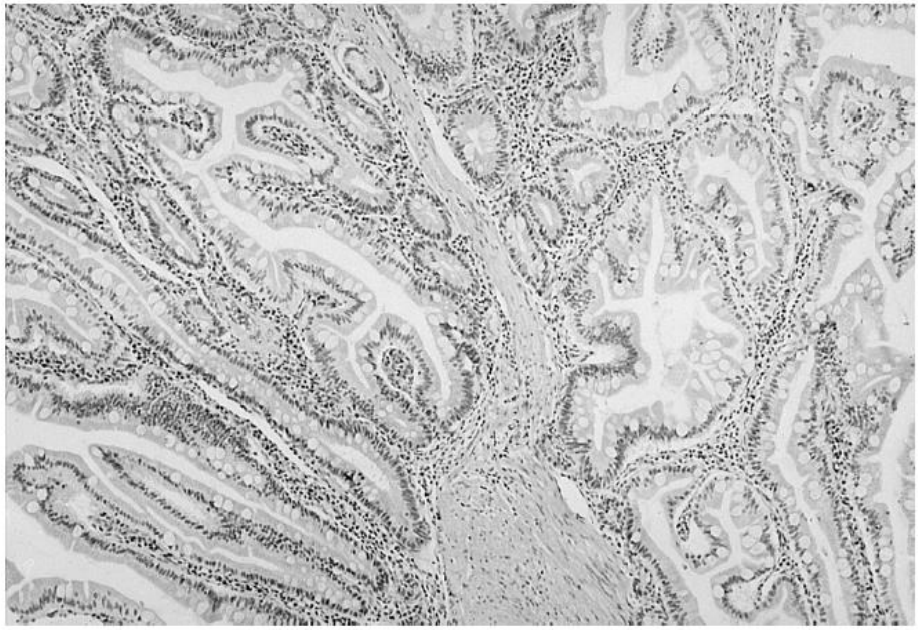


FIGURE 93-7 Photomicrograph of a Peutz-Jeghers polyp demonstrating a hamartomatous alteration of the muscularis mucosa. Smooth muscle fibers divide the polyp into sectors.

Peutz-Jegher Syndrome: Etiology/Incidence

- Rare, equal sex distribution
- All ethnic groups
- Autosomal dominant, some develop de novo
- In Peutz-Jeghers–affected individuals many (but not all) have a mutation of a novel serine/threonine kinase (LKB1 or STK11) with loss of kinase activity

Peutz-Jegher Syndrome: Clinical Presentation

- Screening programs
- If no family history
  - Crampy abdominal pain related to transient intussusception of a polyp
  - Anemia resulting from occult blood loss
  - Malignant conditions
- 30% of patients present with signs and symptoms in the first 10 years of life
- 50% presenting with signs and symptoms by 20 years of age

Peutz-Jegher Syndrome: Clinical Presentation

- **Malignant changes** in hamartomatous polyps have been commonly reported
- Separate adenomatous and carcinomatous changes in hamartomas have also been reported
- 22% developed cancer
- Relative risk for death
  - Gastrointestinal cancer alone: 13X
  - All cancers: 9X
- The chance of dying from cancer by the age of 60 is approximately 50%

Peutz-Jegher Syndrome: Clinical Presentation

- Extraintestinal tumors
  - Ovarian: cystadenomas, granulosa cell tumors, sex-cord tumors
  - Cervical: adenocarcinoma, usually associated with ovarian tumor
  - Testicular:
    - Sertoli cell tumors → gynecomastia
    - Malignant potential → orchiectomy
  - Breast
  - Thyroid
  - Bile duct
  - Pancreatic
  - Gallbladder

Peutz-Jegher Syndrome: Treatment

- Peutz-Jeghers syndrome should be suspected in any child who presents with colicky abdominal pain or occult anemia and melanotic pigmented spots
- Management protocol: annual evaluations:
  - (1) symptoms related to polyps
  - (2) blood count to detect anemia caused by blood loss,
  - (3) breast and pelvic examinations with cervical smears and pelvic ultrasonography in girls
  - (4) testicular examination with ultrasonography in boys
  - (5) pancreatic ultrasonography

Peutz-Jegher Syndrome: Treatment

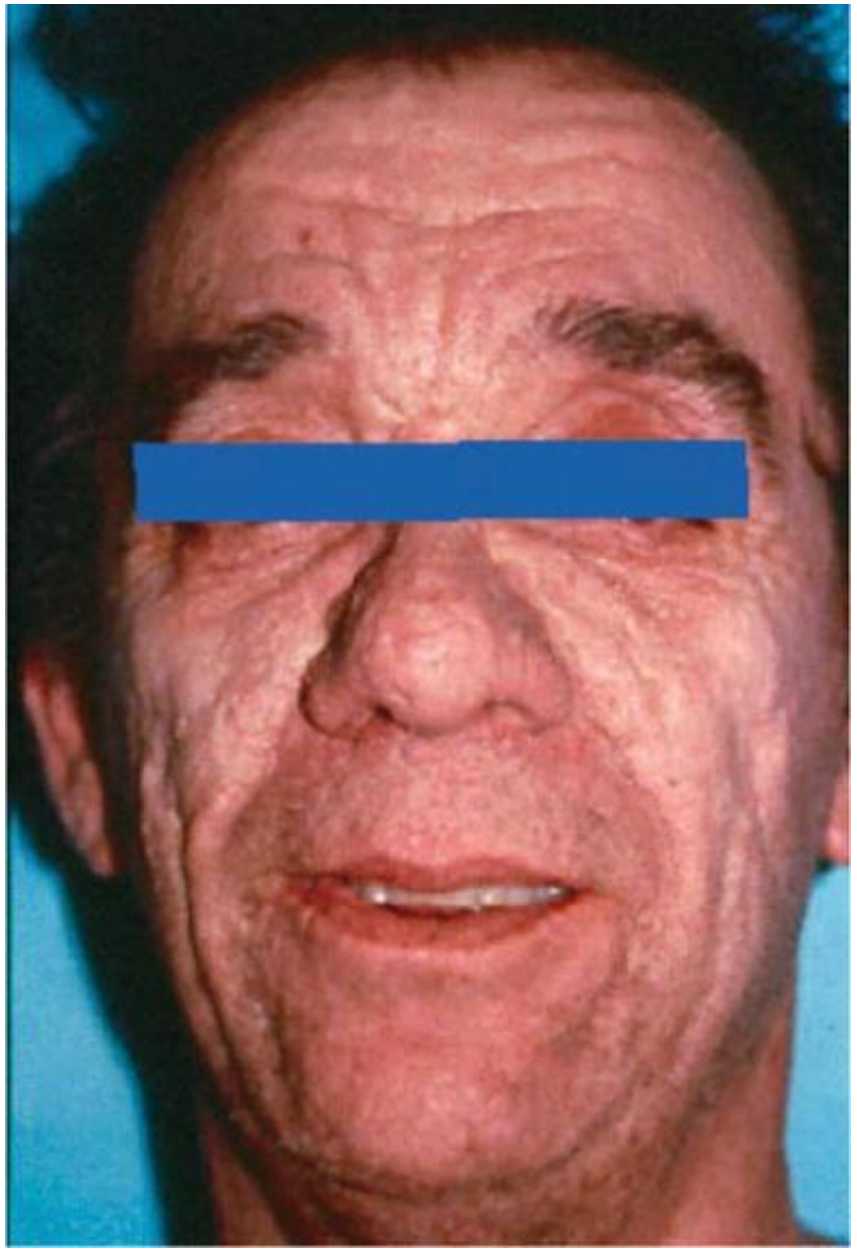
- Esophagogastroduodenoscopy and colonoscopy: biennial
- Small intestine contrast studies: biennial
- Magnetic resonance imaging (MRI):
  surveillance modality for small intestinal screening
- Mammography is recommended at 25, 30, 35, and 38 years of age,
  biennially until 50 years of age, and then annually

Peutz-Jegher Syndrome: Treatment

- All polyps larger than 5 mm found at endoscopy should be removed
- Laparotomy with intraoperative enteroscopy is recommended for removal of all small bowel polyps greater than 15 mm in diameter
- Any intestinal or extraintestinal tumors should be treated aggressively
- Dying by the age of 60 is close to 60% compared with 25% in an age-matched general population

Cowden disease

- Autosomal dominant
- Multiple hamartomas that affects all three of the germ layers
- Increased risk of developing breast, thyroid, and endometrial neoplasias
- Dermatologic lesions: 80%
  - Facial trichilemmomas
  - Acral keratoses
  - Papillomatous papules
  - Mucosal lesions



Cowden disease

- Other major but not necessarily pathognomonic criteria
  - Breast carcinoma
  - Thyroid carcinoma
  - Macrocephaly
  - Endometrial carcinoma
- Gastrointestinal polyposis: 35%
  - Typically juvenile polyps without any increased risk of developing a gastrointestinal cancer

Nonepithelial Polyps

- Lymphoid polyps
  - Pathology
  - Incidence
  - Clinical presentation
  - Treatment

Lymphoid Polyps: Pathology

- Few millimeters to 3 centimeters in diameter
- Usually sessile in form
- Caused by elevation of hyperplastic submucosa lymphoid aggregates
  - Believed to be caused by nonspecific infections of childhood
- The overlying mucosa often becomes ulcerated → volcano-like appearance
  - Leads to occult blood loss

Lymphoid Polyps: Incidence

- Tend to develop in young children within the first few years of life as a result of exposure to new bacteria and viruses
- The peak incidence is at 4 years of age and significantly diminishes by 5 years of age

Lymphoid Polyps: Clinical Presentation

- Anemia
- Rectal bleeding
- Diagnostic methods: colonoscopy, air contrast barium enema, or both
- Small elevations of otherwise-normal mucosa are seen on endoscopy, and biopsy will confirm the diagnosis
- Histologic evaluation reveals lymphoid aggregates with large germinal follicles

Lymphoid Polyps: Treatment

- Benign, self-limiting, tend to regress spontaneously
- Once a histologic diagnosis is made, expectant measures substantial uncontrolled bleeding and intussusception

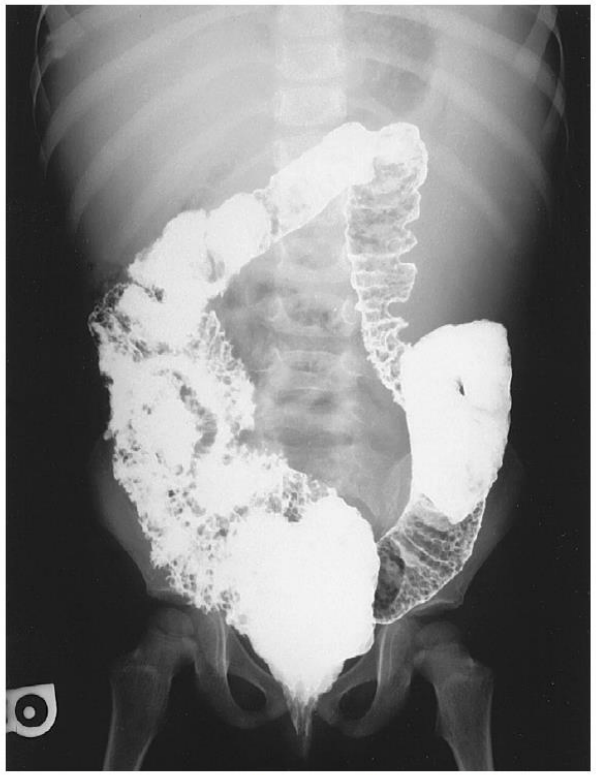


FIGURE 93-8 Barium enema showing multiple, small 1- to 2-mm mucosal nodules throughout the entire colon and terminal ileum. The central umbilication within these nodules seen on this postevacuation film is diagnostic of diffuse lymphoid hyperplasia.

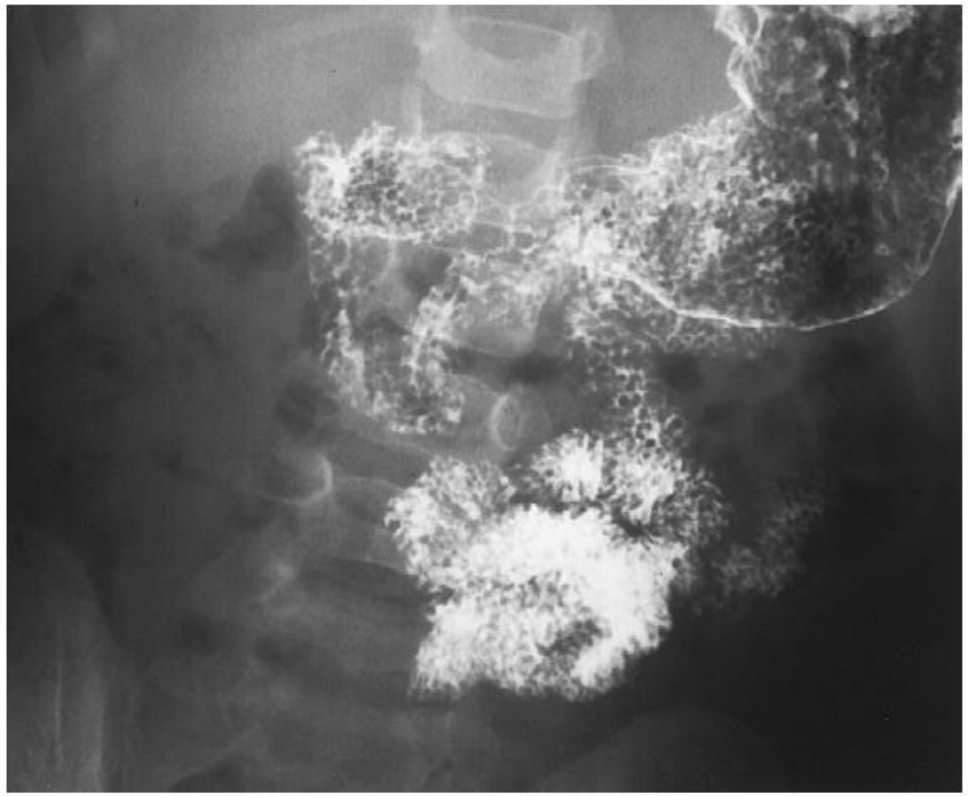
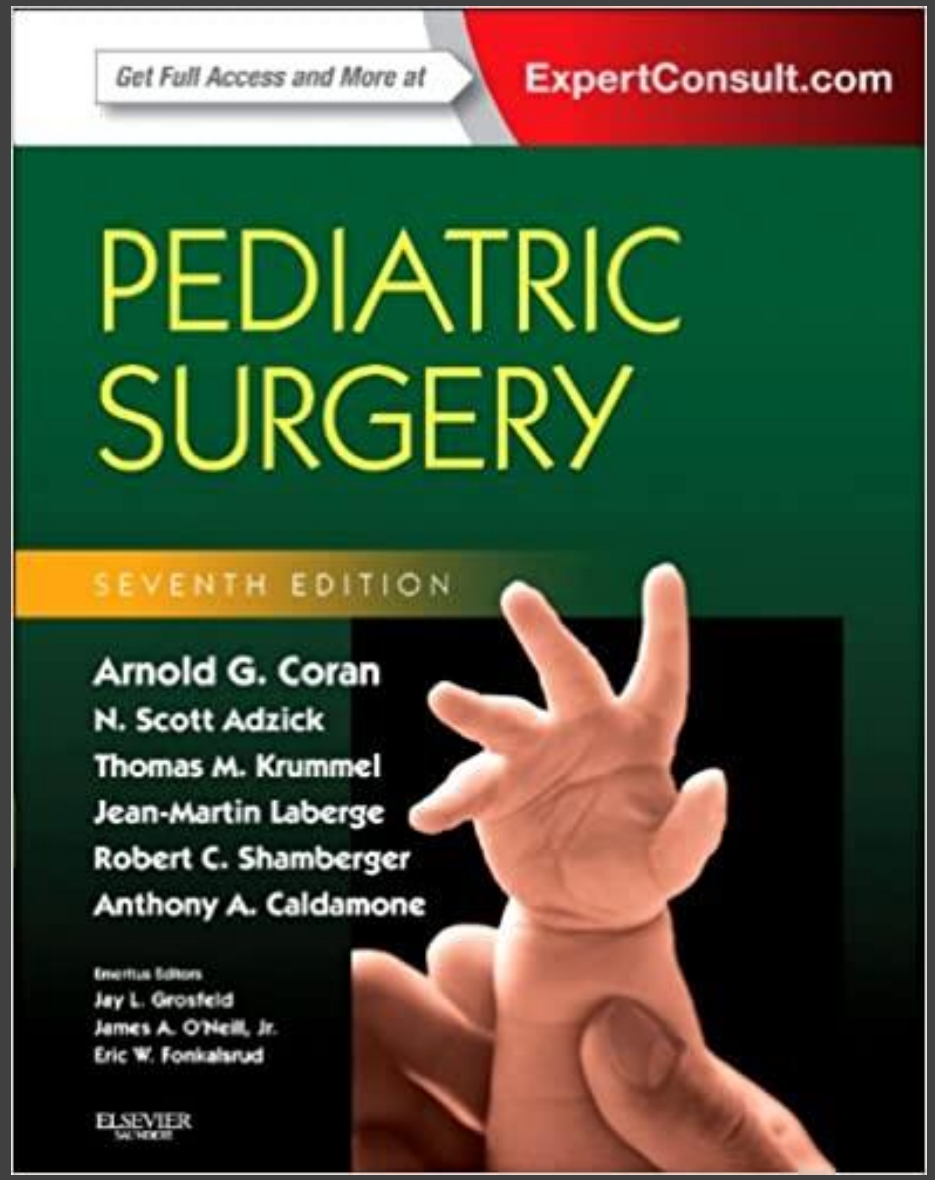


FIGURE 93-9 An upper gastrointestinal series showing diffuse lymphoid hyperplasia throughout the stomach and small intestine.

REFERENCE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