MALABSORPTION

Mechanisms

1. Failure of intraluminal digestion (↓ peptic digestion, ↓ pancreatic enzymes, ↓ bile, bacterial overgrowth

2. Failure of absorption (celiac sprue, tropical sprue, Whipple's disease)

3. Failure of transport (abetalipoproteinemia, lymphangiectasia)

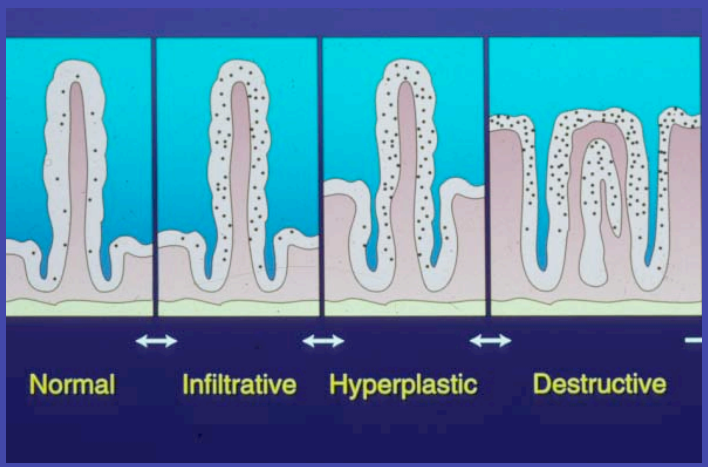
Malabsorptive disorders with specific histopathologic changes

- Celiac disease
- Tropical sprue (postinfectious sprue)
- Whipple's disease
- A-beta-lipoproteinemia
- Lymphangiectasia

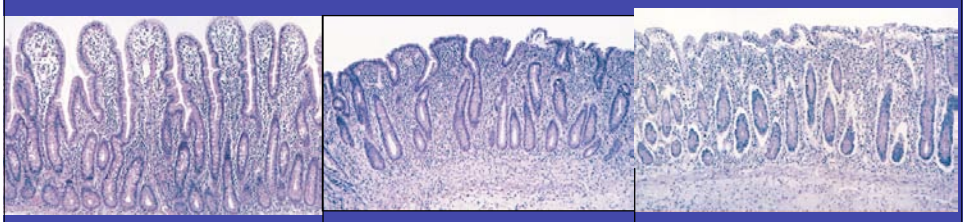
Celiac Disease: Diagnosis

- Documentation of malabsorption
- Demonstration of villous atrophy and/or intraepithelial lymphocytosis by small bowel biopsy
- Improvement of symptoms and mucosal histology after gluten withdrawal

Celiac Disease Histologic Spectrum



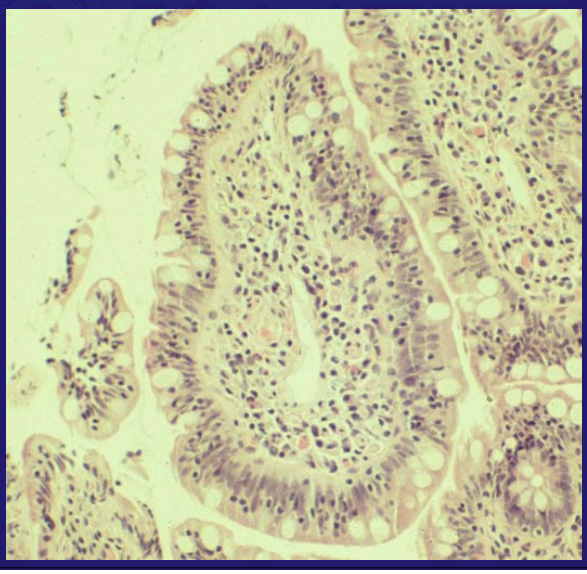
Celiac Disease



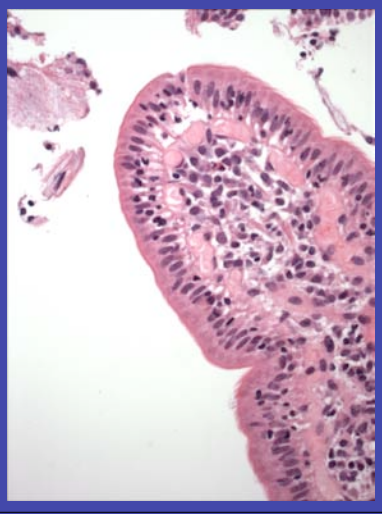
MILD	MODERATE	SEVERE
(partial villous atrophy)	(subtotal villous atrophy)	(total villous atrophy)

Lamina propria inflammation

- **Plasma cells**
- Lymphocytes
- Eosinophils
- Neutrophils



Celiac Disease–
Intraepithelial lymphocytosis



IELs increased
>5 lymph/10 enterocytes
(NL: 2 lymph/10 enterocytes)

CD3 (T-cell immunostain)

CELIAC SPRUE

Pathology

Villous atrophy
Crypt hyperplasia
Chronic inflammation
Intraepithelial lymphocytes ⬆

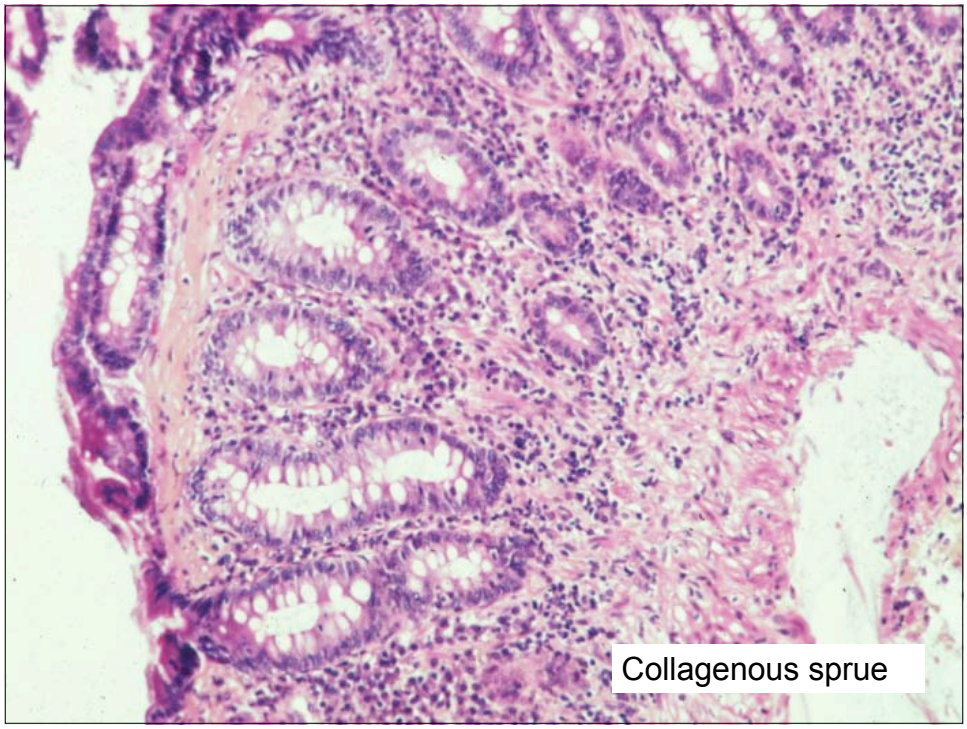
Malabsorption: Definition

- Suboptimal absorption of fats, vitamins, proteins, carbohydrates, electrolytes, minerals and water

CELIAC SPRUE

Complications

Collagenous sprue
Refractory sprue
Lymphoma
Gastrointestinal carcinoma



Enteropathy-Associated T-Cell Lymphoma

- Celiac sprue-associated in most but not all cases
- Malabsorption unresponsive to gluten-free diet
- Variable gross and microscopic appearance
- Poor prognosis

TROPICAL SPRUE

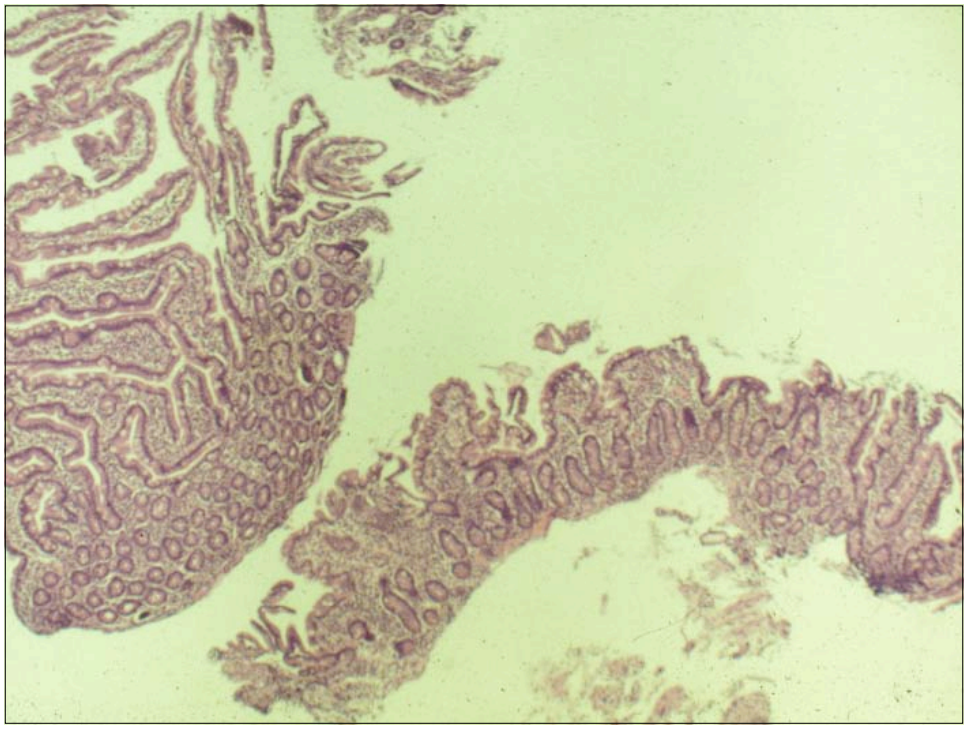
Post-infectious sprue
Enterotoxic bacteria
(E. coli, hemophilus)
Response to antibiotics
Carribean
Central + South America
Central + South Africa
India

TROPICAL SPRUE

Pathology

Subtotal villous atrophy
Distal and proximal small bowel
Patchy

Macrocytic anemia and megalocytosis due to B_{12} malabsorption



Whipple's Disease

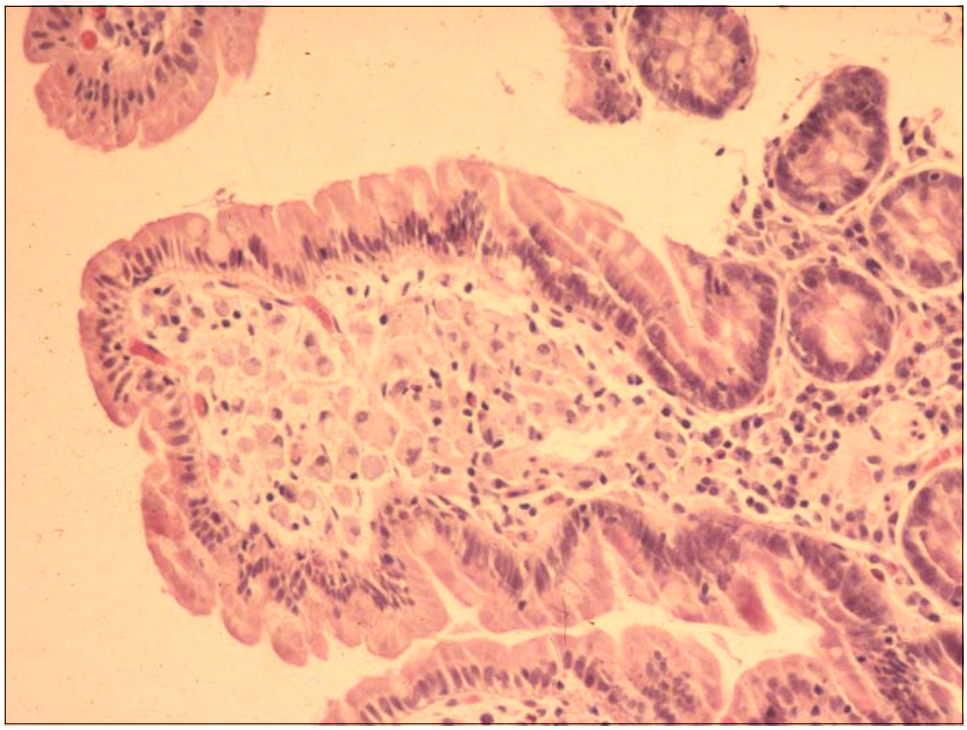
- Rare systemic disease: about 1000 cases reported up to 2007
- Small intestine, CNS and joints are preferentially affected
- Cause: *Tropheryma whipplei,* discovered in 1992, cultured in 2000

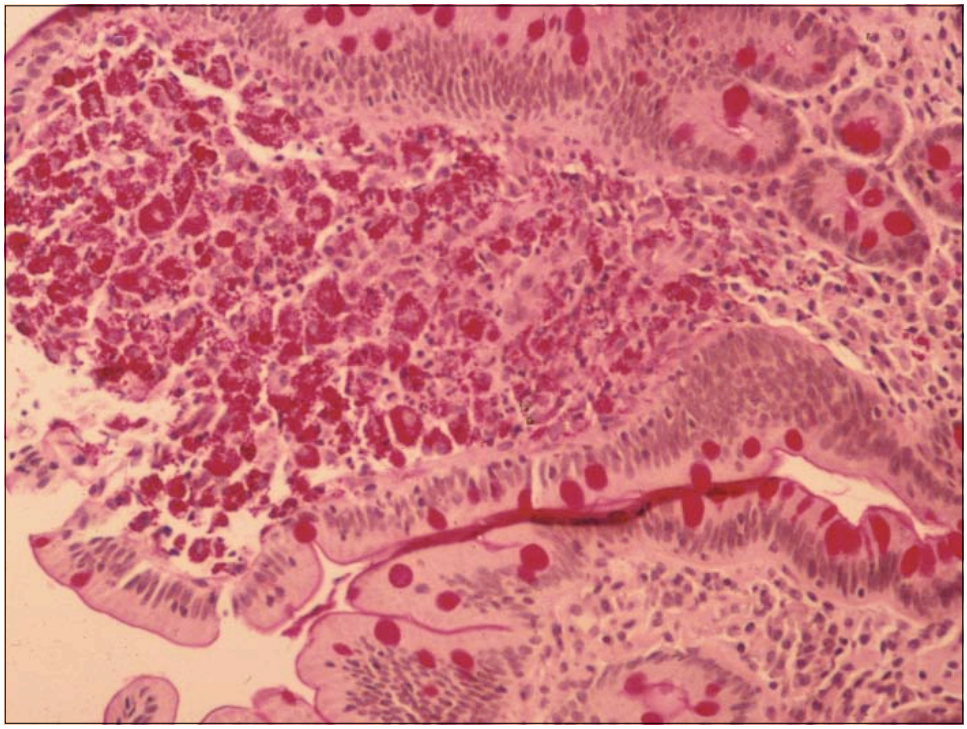
WHIPPLE'S DISEASE

Pathology

Villous flattening
Foamy macrophages in lamina propria
PAS + ("Whipple" macrophages)
EM: rod-shaped bacteria

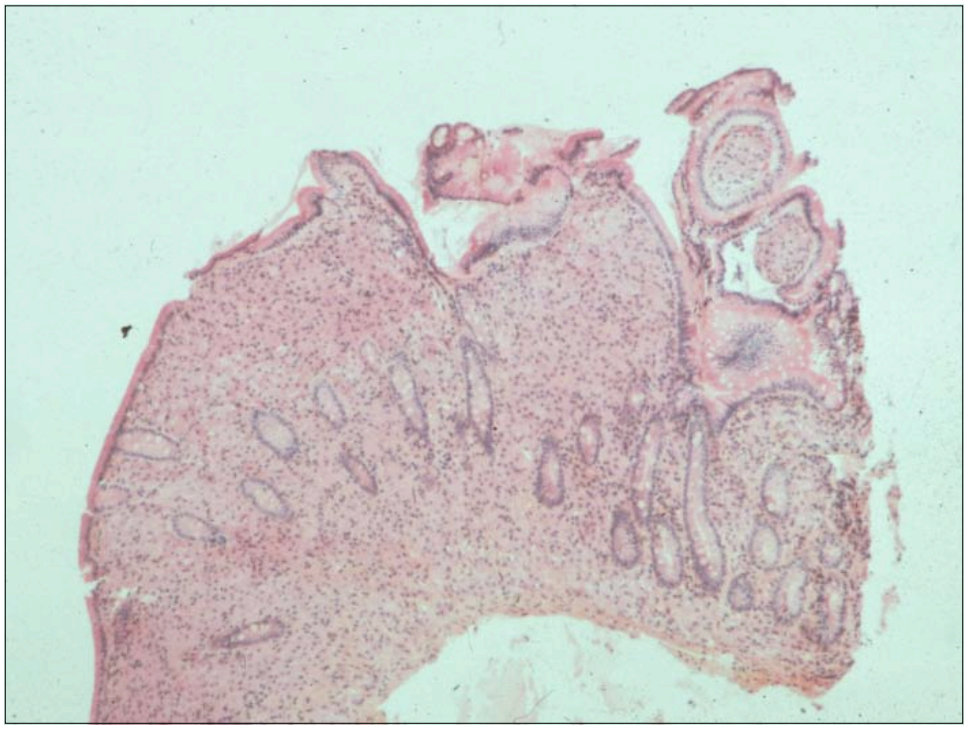
DD: MAI

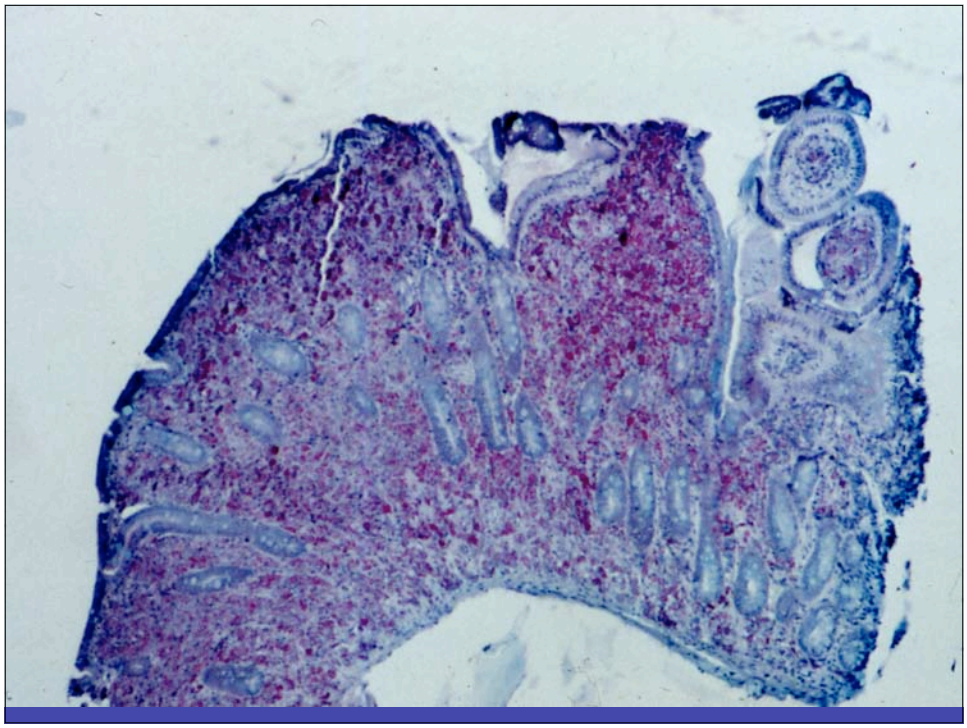


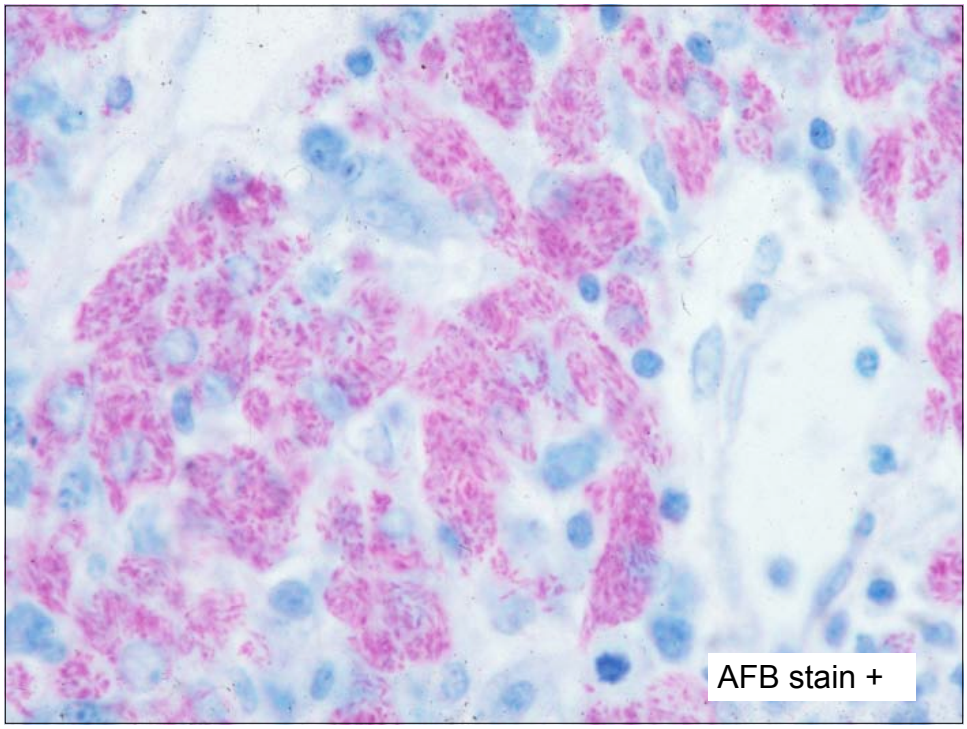


Whipple Disease: Differential Diagnosis (MAI)

- Infection with *Mycobacterium avium intracellulare (*MAI *or* MAC*)*
  - *– MAI (AFB +); Whipple (AFB-)*
- Common in patients with AIDS
- Decreasing incidence since new antiviral medications







MAC Infection in AIDS

Frequency

- 15-24% during lifetime (adults)
- 50% at autopsy
- Late in the course of HIV infection
- Rare in Africa

MAC Infection in AIDS

Natural History

- Primary infection (not reactivation)
- Ingestion or inhalation
- Multiple strains -- environmental source
- Asymptomatic colonization
- Disseminated infection (CD4 < 60)
- Life expectancy: 4-11 months
- New antiretroviral therapy may change natural history

ABETALIPOPROTEINEMIA

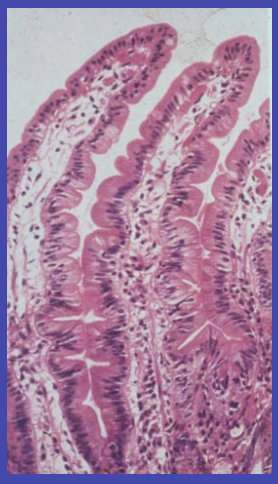
Rare inborn error of metabolism
Autosomal recessive
Failure to synthesize apolipoprotein B
Failure to assemble chylomicrons, VLDL, LDL
Abnormal red blood cells ("burr cells")

ABETALIPOPROTEINEMIA

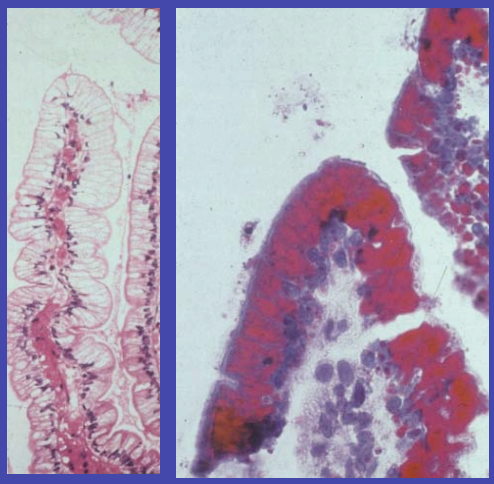
Pathology

Normal villous architecture
Normal absorptive surface
Lipid vacuoles in absorptive cells
Lipid staining
Electron microscopy

Abetalipoproteinemia



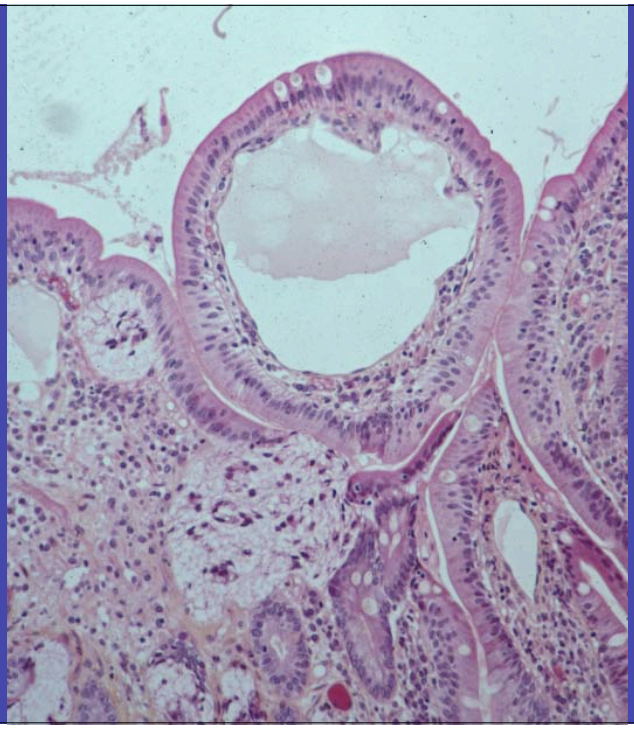
Normal



Lipid stain

Lymphangiectasia

- **Primary lymphangiectasia**: rare congenital disorder; defective lymphatics; normally absorbed nutrients reach the lymphatics but cannot be transported into the circulation.
- **Secondary lymphangiectasia**: more common; complication of any disorder that causes lymphatic obstruction: enlarged mesenteric lymph nodes (cancer or inflammatory), heart disease (constrictive pericarditis, CHF)

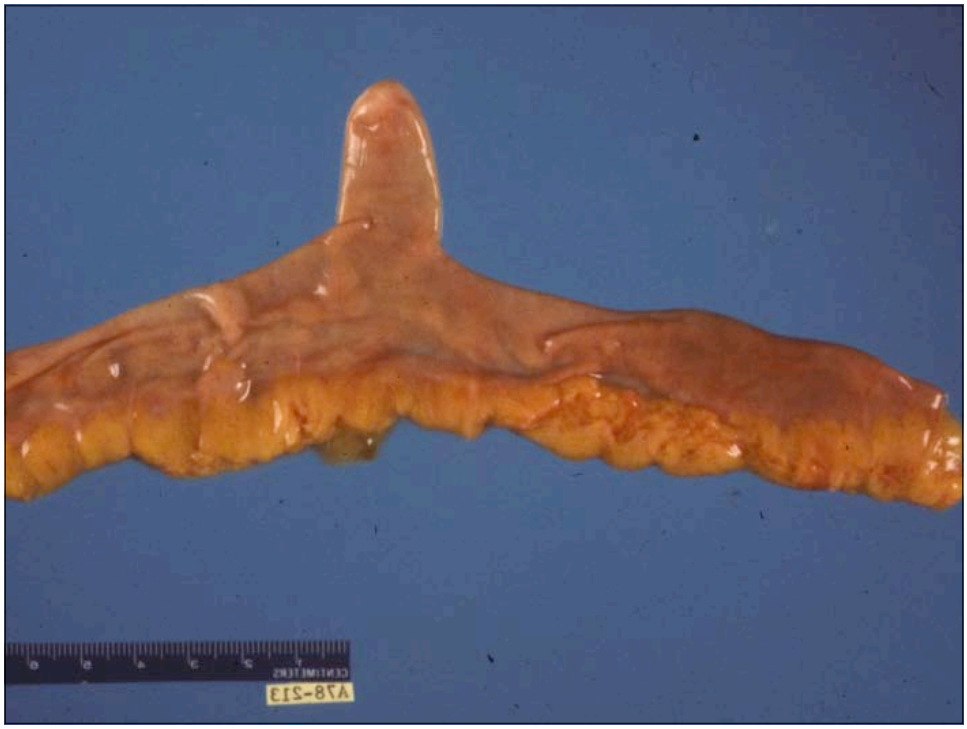


Other malabsorptive disorders with specific tissue changes

- Collagenous sprue
- Lymphoma
- AIDS enteropathy
- Infections (CMV, MAI, cryptosporidiosis, microsporidiosis, isosporiasis, giardia)
- Eosinophilic gastroenteritis
- Radiation enteritis
- Microvillus inclusion disease (rare)

Meckel's diverticulum

- Persistence of vitelline duct (connects developing gut and yolk sac)
- 2% of normal population
- 30cm proximal to ileocecal valve
- True diverticulum (all 3 layers of bowel wall)
- Heterotopic rests: gastric, pancreatic (50%)
- Complications: ulceration, bleeding, intussusception, perforation)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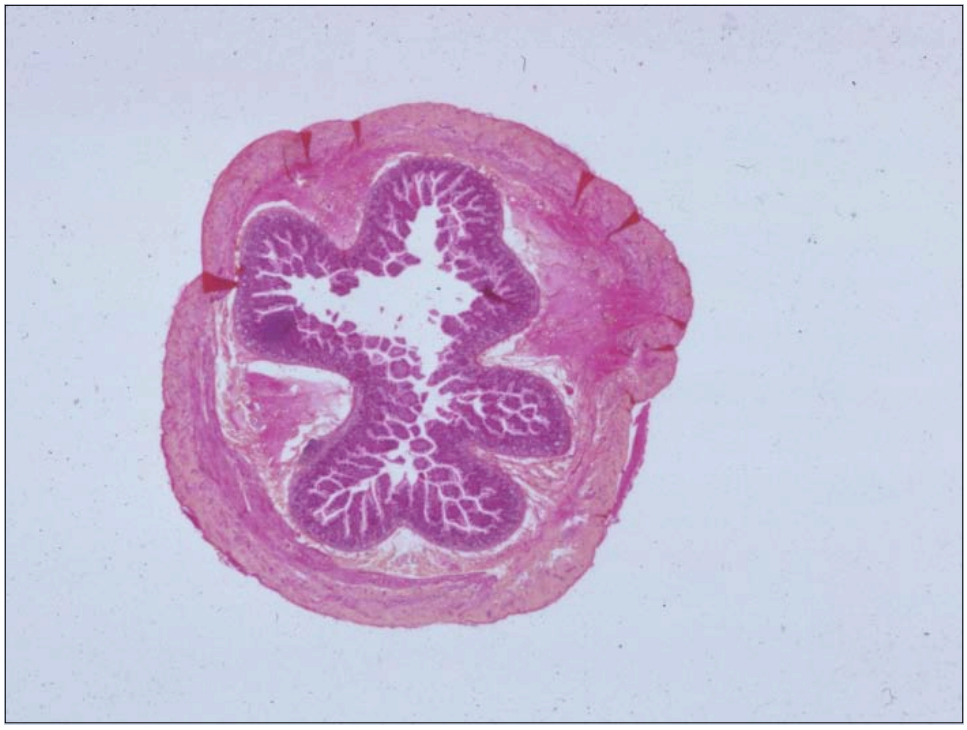


Intussusception

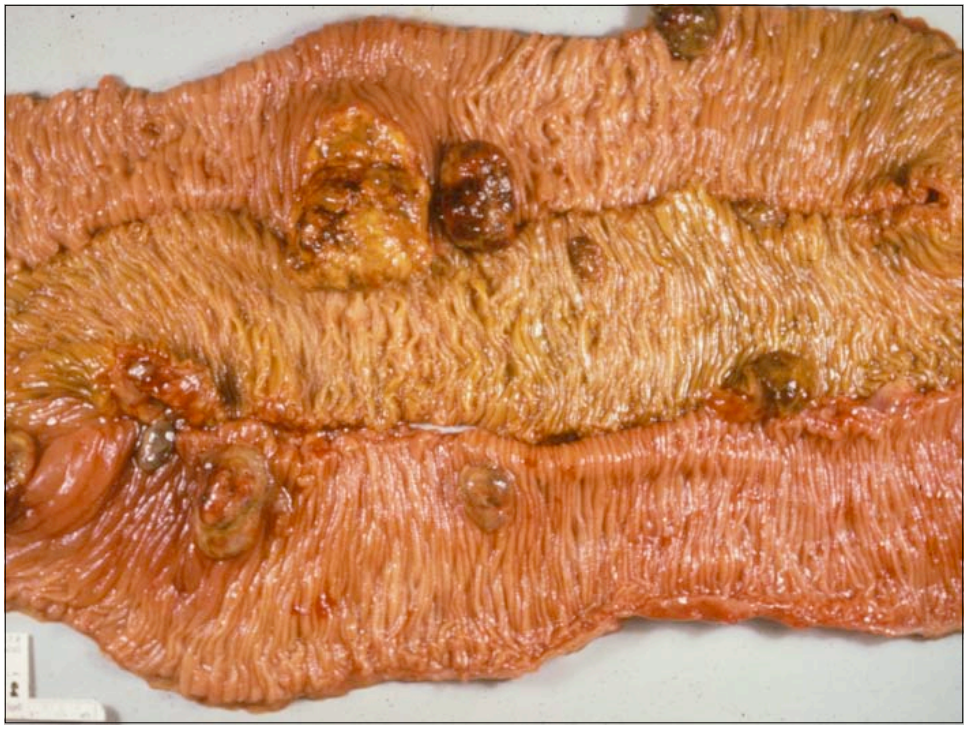
- Telescoping of one segment of bowel into another
- Peristalsis propels the invaginated proximal segment farther into the distal segment
- Spontaneous in children
- Secondary to intraluminal masses in adults
- Complications: obstruction, infarction

Volvulus

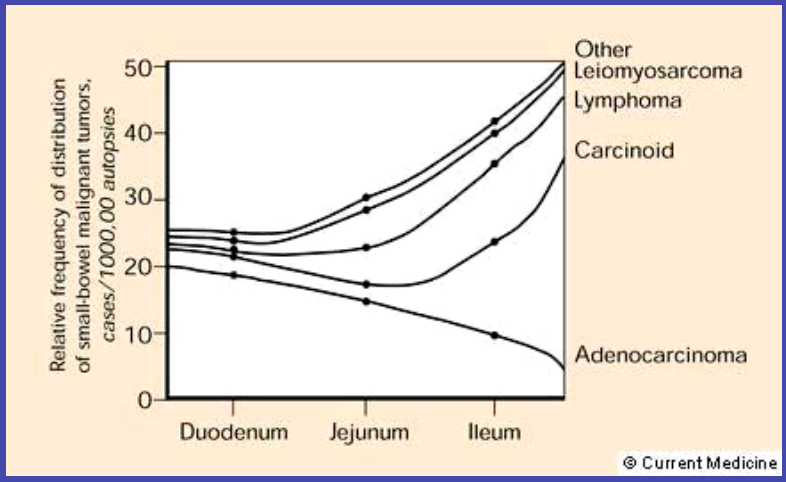
- Twisting of a loop of bowel around its mesenteric base
- Sigmoid colon, cecum, small intestine, stomach, rarely transverse colon
- Complications: obstruction, infarction

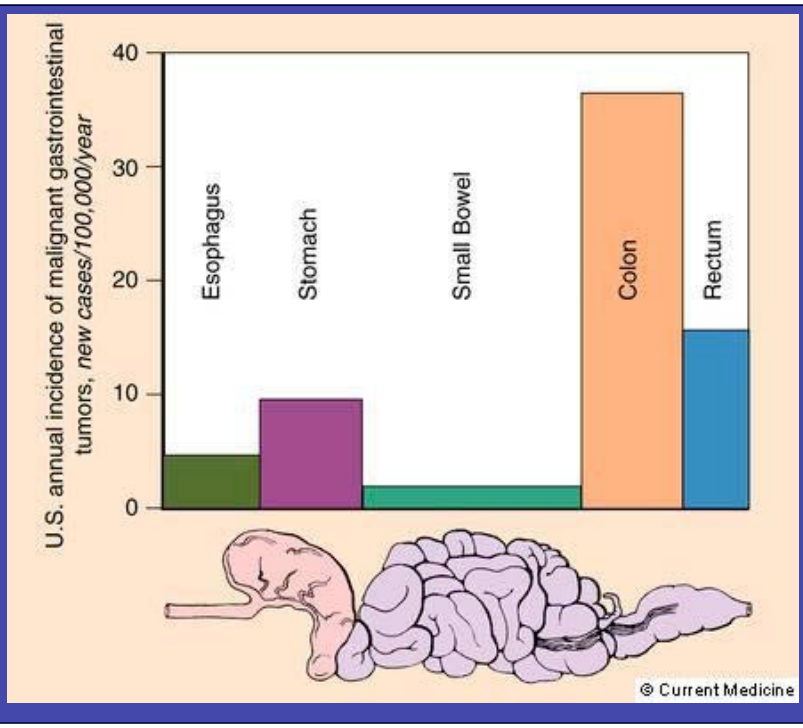
Tumors of the Small Intestine

- Least frequent of all GI tumors (3-6%)
- Secondary tumors: serosal implants, direct extension from neighboring organs, distant metastases
- Primary tumors: benign tumors (often found incidentally at autopsy or surgery); malignant tumors (intestinal obstruction and bleeding)



Primary malignant neoplasms of Small Intestine



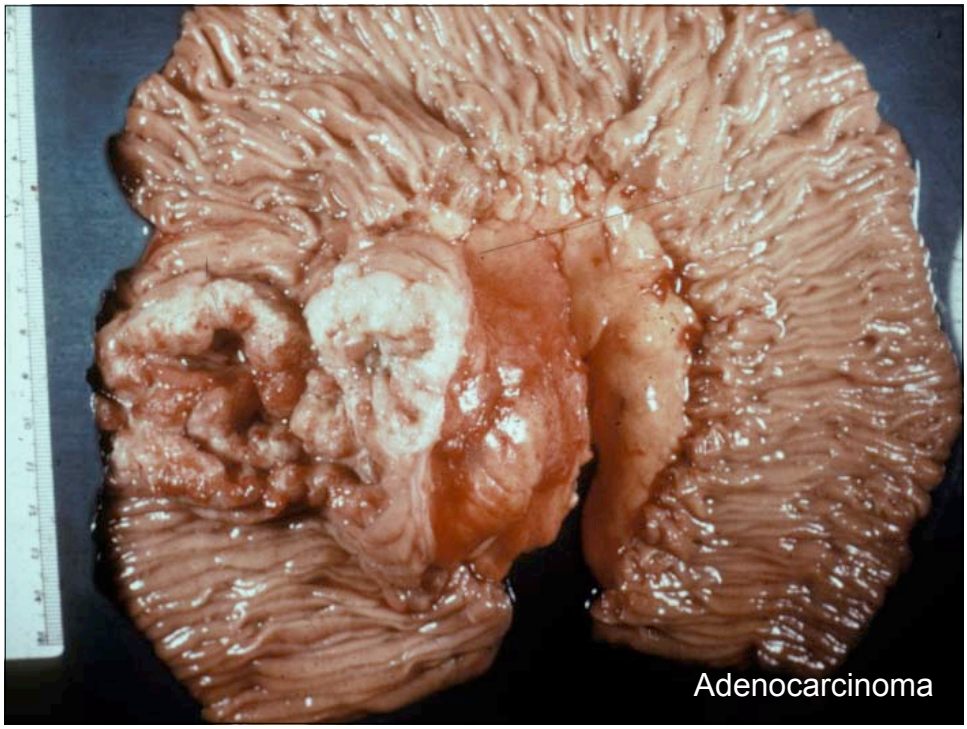


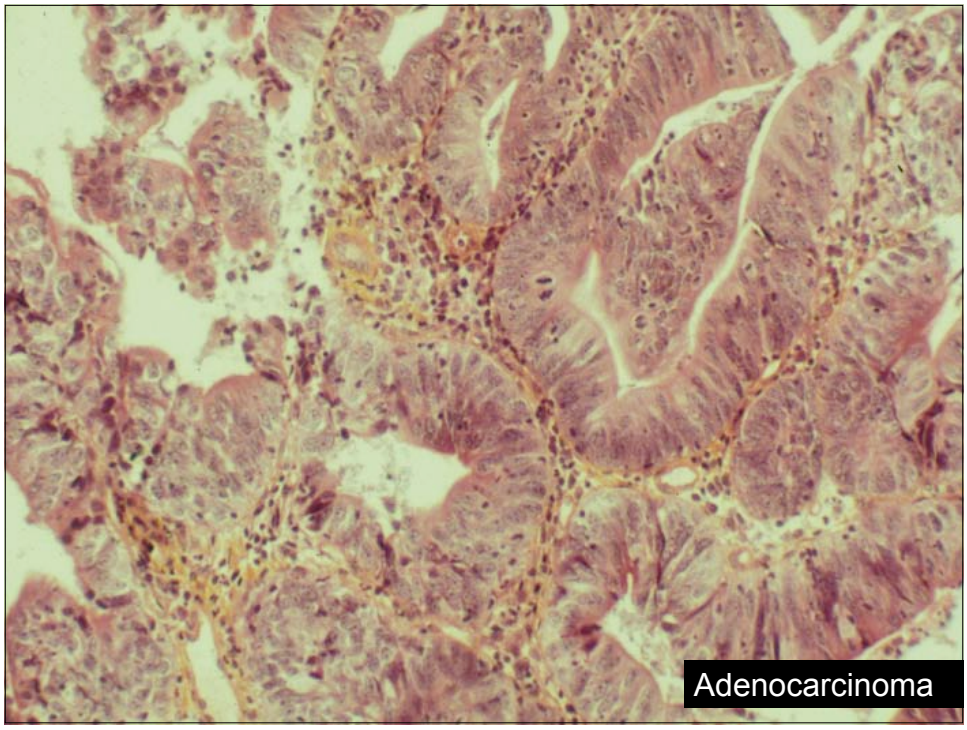
Tumors of the Small Intestine: why are they so rare?

- Rapid transit of small bowel contents
- Smaller bacterial load
- Increased lymphoid tissue

Carcinomas of the Small Intestine

- Most common location: duodenum, periampullary, least common: ileum
- Growth patterns: annular constricting or polypoid masses
- Symptoms: Obstruction and/or bleeding
- Predisposing conditions: Celiac disease and Crohn's disease


Adenocarcinoma


Adenocarcinoma

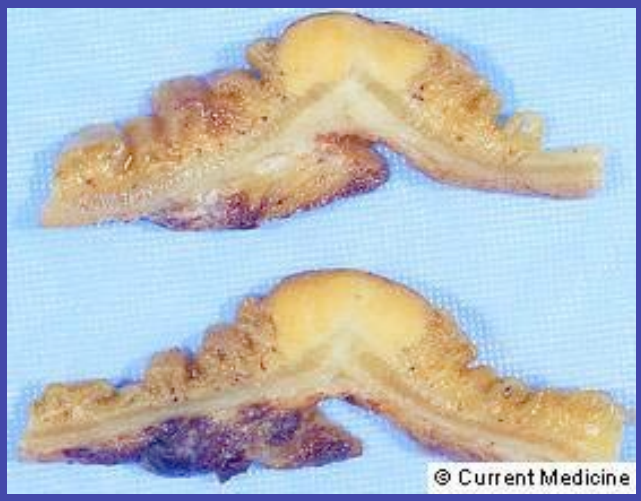
Carcinoid Tumors of the GI Tract

- GI tract is the most common site of carcinoids (67%)
- Small intestine is the most common site of GI carcinoids, followed by rectum and appendix
- Prognosis is site and size dependent

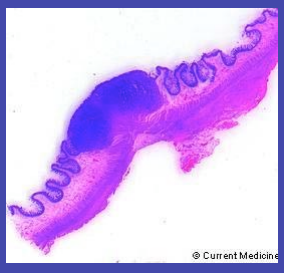
Carcinoid tumor of the small intestine

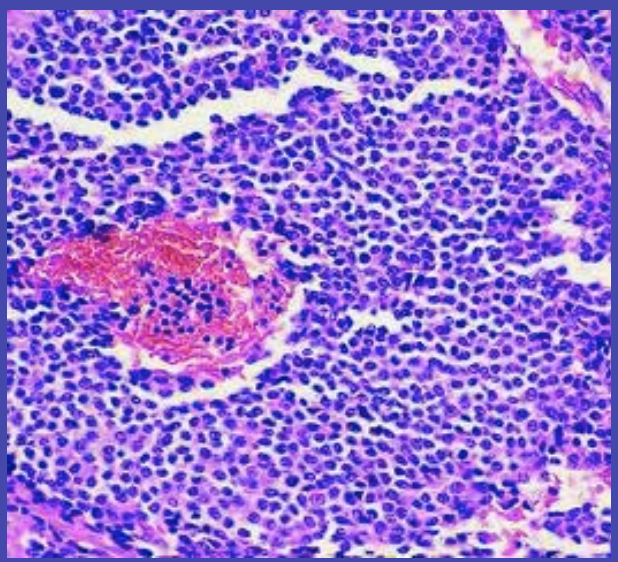
- Endocrine neoplasm of Kulchitsky cell origin
- Most common in ileum (80%)
- Mostly found incidentally (60-75%)
- Multicentric; slowly growing
- Gross appearance: yellow- tan nodules
- Prognosis: size and site dependent (<1cm:2% metastasis;1-2cm:50%; >2cm:80%; best prognosis in appendix)

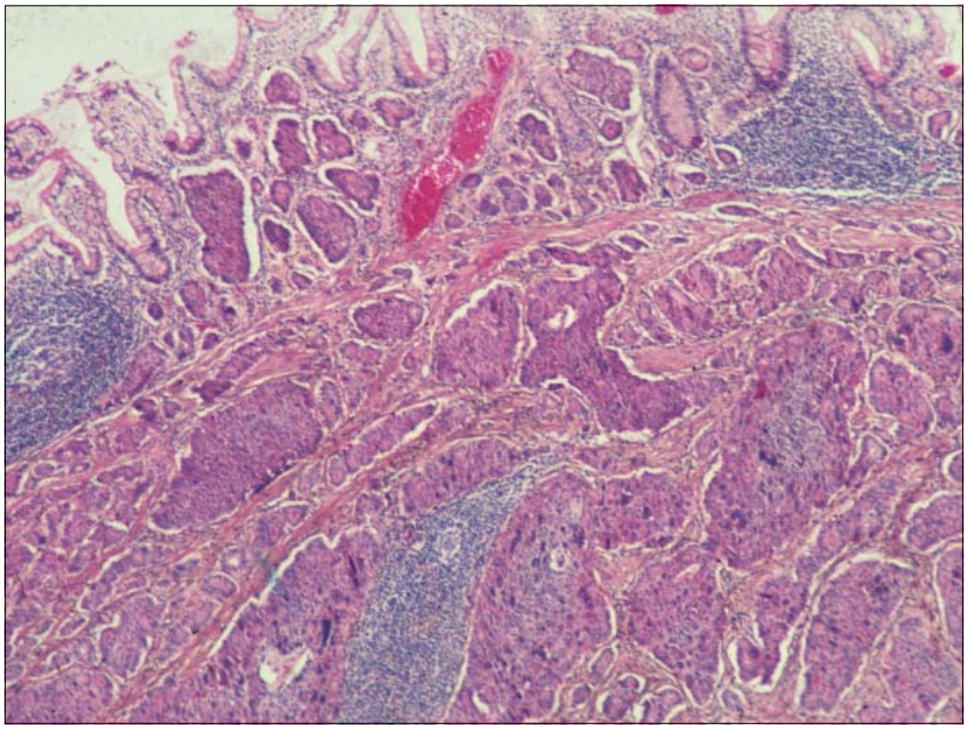
Carcinoid tumor- Ileum



Carcinoid tumor- Ileum







Carcinoid tumor: Prognosis

- Much better than ordinary adenocarcinoma
- 68% 5-year survival after resection (as compared to 25-35% for adenocarcinoma)
- 38% 5-year survival after incomplete resection
- 21% 5-year survival with liver metastasis

Carcinoid Syndrome

- Only in patients with liver metastases
- Cutaneous flushing, diarrhea, bronchospasm, right heart failure
- Serotonin, bradykinin, substance P, prostaglandins
- Elevated 5HIAA(5 hydroxy-indol-acetic acid, metabolic product of serotonin) in urin

Gastrointestinal Stromal Tumor (GIST) of the small intestine

- 2/3 arise in the stomach, most of the remainder in the small intestine
- Cell of origin: interstitial cell of Cajal (c-kit immunoreactivity)
- Prognostic factors: size (>4cm), mitotic count (>5 per 50 HPF), cellularity, mucosal invasion, necrosis