males	Females	Children
Barret's disease (40-60yrs)	Autoimmune gastritis	Intussusception→intestinal obstruction
Esophageal adenocarcinoma(7:1)		Juvenile polyp
Squamous cell carcinoma (4:1)		Peutz-Jeghers syndrome(10-15 yrs)
Gastric adenoma (3:1)		
Intestinal type gastric cancer (2:1)		
Hirschsprung disease		

Esophagus:
*reflux esophagitis→most common <40 (may occur in infants)
*esophageal adenocarcinoma→chromosomal abnormalities and tp53 mutation.
* esophageal adenocarcinoma→developed countries
* Squamous cell carcinoma→underdeveloped countries*squamous cell carcinoma→ Lymph node metastases : Upper 1/3: cervical LNs ,Middle 1/3: mediastinalparatracheal, and tracheobronchial LNs. ,Lower 1/3: gastric and celiac LNs.

Stomach:
*most common cause of chronic gastritis→helicobacter pylori
*hematemesis isn't common in chronic gastritis.
*H.pylori→non invasive , motile by flagella.
→ urease: split urea to ammonia ,protect the bacteria from the acidic environment.
→toxins:cagA

*autoimmune gastritis→reduced serum pepsinogen I level.
→vit. B12 deficiency

*acute gastric ulcers→
1- stress ulcers: ill patients with shock, sepsis, severe trauma.
2-cushing ulcers: intra cranial disease ,high risk of perforation. Duodenum ,stomach ,esophagus.
Direct vagal stimulation→acid hypersecretion.
3-curling ulcers: severe burn or trauma . proximal duodenum.
Ulcers are rounded ,shallow to deep, base brown to black.

*PUD hyperacidity→ Hypergastrinemia as in Zollinger-Ellison syndrome.

* Zollinger-Ellison syndrome→stomach duodenum and jejunum.(4:1 proximal duodenum:stomach).
Caused by uncontrolled secretion of gastrin by a tumor (gastrinoma) resulting massive acid production.
Ulcers are round to oval sharply punched out defect, granulation tissue.
Epigastric burning and aching pain.
Pain 1-3 hours after meals at daytime worsens at night.

*gastric polyps arise from chronic gastritis and regress after H.pylori eradication.
*Gastric adenoma→background of chronic gastritis atrophy and intestinal metaplasia. Dysplasia in all cases. Risk of adenocarcinoma higher than colonic adenoma.

*Gastric adenocarcinoma→ Japan, Costa Rica, Chile.
Background of mucosal atrophy and intestinal metaplasia.
-signet ring.
Two main types: intestinal and diffuse.
Mutations in CDH1 (E-cadherin)→familial diffuse type.
CDH1 mutations→sporadic diffuse type.
FAP: APC gene mutation→ intestinal type cancer.
B catenin mutation→sporadic intestinal type Ca.
P54 mutation in sporadic cancer of both types.

*** diffuse type gastric cancer M: F =1:1

*Lymphoma→stomach is the most common site.
Most common type: indolent extra nodal marginal zone B-lymphomas (MALToma)
Second most common: diffuse large B cell lymphoma.

*Neuroendocrine (carcinoid) tumor→>40% in small intestine.
Associated with endocrine cell hyperplasia, chronic atrophic gastritis and Zollinger- Ellison syndrome.
-slower growing than carcinomas.

*Carcinoid syndrome: due to vasoactive substances. Cutaneous flushing, sweating, bronchospasm, colicky abdominal pain, diarrhea, right-sided valvular fibrosis.

Intestines:

*Intussusception→segment of the intestine constricted by a wave of peristalsis →telescopes into the immediately distal segment.
-abdominal swelling

*Hirschsprung disease: congenital defects in colonic innervation
Congenital aganglionic megacolon.
-more common in males while it is more severe in females.
-risk increases in siblings.
-disrupted migration of neural crest from cecum to rectum.
-lack of Meissner submucosal plexus and the Auerbach myenteric plexus.
-mutations in RET.

*Hemorrhoids: dilated anal and perianal collateral vessels that connects the portal and caval venous system.
-bleeding, pain, thrombosis and inflammation.

*diarrheal disease: (*dysentery: painful bloody small volume diarrhea)
*malabsorptive diarrhea: chronic, defective absorption of fats , lipid and water soluble vits, proteins, carbs, electrolytes, minerals and water.
→hallmark: **steatorrhea**

*cystic fibrosis→mutations in cystic fibrosis transmembrane conductance regulator (CFTR)
-defects in ion transport across intestinal and pancreatic epithelium.
-thick viscous secretions
-mucus plugs in pancreatic ducts→pancreatic insufficiency.
-meconium ileus in neonates.
-defect in intraluminal digestion.

*celiac disease→gluten sensitive enteropathy, immune mediated enteropathy.
-wheat, rye or barley.
-**genetically predisposition→HLA-DQ2 or HLA-DQ8.**
-association with type 1 diabetes, thyroiditis, Sjogren syndrome.
-gluten>gliadin>reacting with **HLA-DQ2 or HLA-DQ8** on antigen-presenting cells>CD4+ T cells activation>cytokines>tissue damage.
-anti-tissue transglutaminase antibodies, anti- gliadin antibodies, anti-endomysial antibodies.
-happens in the second portion of the duodenum or proximal jejunum.

→in children (6-24 months):classical (irritability, abdominal distention, anorexia, diarrhea, failure to thrive, wight loss, muscle wasting.) or non classical symptoms (abdominal pain, nausea, vomiting, bloating, constipation.)

→in adults: anemia, B12 +folate deficiency, diarrhea, bloating and fatigue.
Silent celiac or latent celiac
Increases risk of enteropathy associated T cell lymphoma and small intestine adenocarcinomas.

-noninvasive.

*lactase (disaccharidase) deficiency: osmotic diarrhea.
Lactose remains in gut lumen.
Lactase found at apical brush border membrane.
-acquired: viral or bacterial enteritis, downregulation of gene.
-congenital AR, genetic mutation, rare, explosive diarrhea watery frothy stools and abdominal distention after milk congestion.

*abetalipoprpteinemia: autosomal recessive and rare
-Infants with failure to thrive, diarrhea, steatorrhea
-lack of absorption a fat and fat-soluble vitamins.
-In ability to synthesize, triglyceride-rich lipoproteins.
-transepithelial, transport effect of TG and FAs.
-monoglycerides and triglycerides accumulate epithelial cells.

*inflammatory intestinal disease:-sigmoid diverticulitis
-chronic inflammatory bowel disease (CIBD)
-Crohn disease
-ulcerative colitis

*Inflammatory bowel disease→chronic IBD.
Genetic predisposition, inappropriate mucosal damage.
-ulcerative colitis: limited to the colon and rectum and extends only into mucosa and submucosa.

-Crohn disease: regional enteritis, frequent ileal involvement, affect any area in GIT(most common sites→ terminal ileum, ileocecal valve and cecum), **frequently transmural.**
Earliest lesions→aphthous ulcer
Elongated→serpentine ulcers
Edema→loss of bowel folds.
--**cobblestone appearance**
Thick bowel wall (fibrosis, hypertrophic MP).
Creeping fat.
-crypt abscesses.
-fissures, fistulas, perforations.

-**hallmark→noncaseating granulomas**.
-neutrophils in active disease.
-mild diarrhea.
-acute right lower quadrant abdominal pain and fever.
Triggers: physical or emotional stress, specific dietary items, NSAID use and tobacco smoking.
-**Iron deficiency anemia(because it cause problems in absorption)**, **hypo**proteinaemia and **hypo**albuminaemia malabsorption of nutrients, vitamin B12 and bile salts.
-fistulas, peritoneal abscesses.
-risk of colonic adenocarcinoma.
-erythema nodosum, clubbing of the fingertips, primary sclerosing cholangitis.

*ulcerative colitis:
- Always involves the rectum.
-Extends proximally in continuous pattern.
- Pan colitis.
- Occasionally focal appendiceal or cecal inflammation.
-Ulcerative proctitis or ulcerative proctosigmoiditis
-Small intestine is normal (except in backwash ileitis)
-pseudopolyps
-serosa is not involved, the ulcers are superficial, no thickening in the mucosa.
-toxic megacolon.
-inflammation **limited to mucosa** and submucosa.
-no granulomas.
-no skip lesions.
-attacks of bloody mucoid diarrhea+ lower abdominal cramps.
-triggers: cessation of smoking.
-erythema nodosum, clubbing of the fingertips, primary sclerosing cholangitis.
-colectomy cures intestinal disease only.

*sigmoid diverticulitis:
-acquired→pressure in the sigmoid colon or exaggerated peristaltic contractions or low fiber diet and constipation.
-pseudodiveticulae.
-outpouchings of colonic mucosa and submucosa.
-thin wall.
-risk of perforation, recurrent diverticulitis leads to strictures.

colonic polyps and neoplastic disease:

most common site→colon
sessile polyp→no stalk
pedunculated polyp→stalk

*inflammatory Polyps→solitary rectal ulcer syndrome.
-recurrent abrasion and ulceration of the overlying mucosa.
-chronic cycles of. Injury and healing give a polypoid mass.

Hemartomatous polyps:
1.Juvenile polyps
2.Peutz-Jeghers syndrome

1.Juvenile polyps: most common
Sporadic or solitary.
-rectum
-syndromic→multiple
Autosomal dominant
-TGF-B mutation
-increased risk of colonic adenocarcinoma.
- pedunculated
-reddish lesions, cystic spaces.
-granulation tissue on surface.
-dilated glands

2.Peutz-Jeghers syndrome:
Autosomal dominant
-multiple gastrointestinal hmartomatous polyps
-most common site→small intestine.
-**mucocutaneous hyperpigmentation**.
-**LKB1/STK11 gene mutation.**
-the polyp is large (Christmas tree pattern)
-glands lined normal-appearing intestinal epithelium.

*hyperplastic polyps:
-generation more than degradation
Decreased epithelial turnover and delayed shedding of surface epithelium > pileup of goblet cells & epithelial overcrowding.
-no malignant potential.
-left colon
-rectosigmoid
Multiple
Crowding of goblet and absorptive cells.

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