intestinal pathology

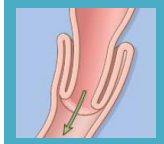
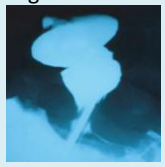
1-Intestinal obstruction

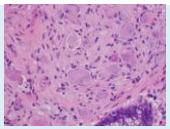
***mechanical obstruction**

-80% Intussusception, hernias, adhesions, Volvulus.
- 20% Tumors, Diverticulitis, Infarction

***non-mechanical obstruction**

Hirschsprung disease, Neurological disorders, drugs

Disease	Age group	site	Causes /factors	pathogenesis	morphology	Clinical features	treatment	Compli-cations	notes
Intussception 	Most common in Children <2 yrs		**In <2yrs:** -Idiopathic in most cases -Peyer patches hyperplasia (rotavirus vaccine, viral infections) -Meckles diverticulum (ileum). **Old children & adults:** Intraluminal mass or tumors	Segment of the intestine constricted by a wave of peristalsis telescopes into the immediately distal segment> Once trapped, invaginated segment is propelled by peristalsis, and pulls mesentery with it.		**Children>>** -abdominal swelling -distention -vomiting -currant jelly stool (stool+ blood+ mucus) -pain expressed by crying. **Adults>>** Complain from pain	-Contrast enemas in uncomplicated idiopathic cases. -Surgery if complicated or if masses are the leading point.	infarction	
Hirschsprung Disease (Congenital aganglionic megacolon)	neonates	-Rectum always involved. -Most cases are rectosigmoid.	-Mutations in **RET** in familial cases and 15% of sporadic -Other genes and environmental factors play role.	**During embryogenesis:** Disrupted migration of neural crest cells from cecum to rectum> lack of Meissner submucosal plexus and the Auerbach myenteric plexus> Failure of coordinated peristaltic contractions which will result in constipation.	**Macroscopically** by barium enema> contracted rectum(affected area)& dilated proximal normal segment  **Microscopically [Gold standard]** Absence of ganglion cells in myenteric and submucosal plexuses	-Neonatal failure to pass **meconium** (first stool that is passed after delivery of fetus). -Later, it is followed by chronic obstructive constipation.	-Surgical resection of Aganglionic segment and anastomosis of normal segments	-Enterocolitis -fluid and electrolyte disturbances (dehydration). -perforation >peritonitis.	-More common in males -More severe in females -Risk increases in siblings. -severity depends on the length. - normal ganglion cells: abundant eosinophilic cytoplasm and eccentrically (peripherally) located nucleus with prominent nucleolus.



2-vascular disorders:

-ischemic bowel disease: seen in elderly **-Hemorrhoids: can be external or internal.**

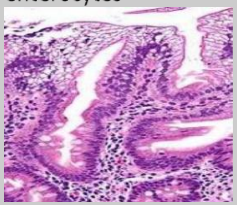
Disease	Site	Causes/ factors	Symptoms	Notes
Hemorrhoids	Hemorrhoids is subdivided according to the location into: § Internal: above the anorectal line (in the rectal mucosa). § External: below the anorectal line.	-Constipation and straining>> increase intraluminal pressure. -Venous stasis of pregnancy. -Portal hypertension (due to liver cirrhosis and schistosomiasis).	-Bleeding (fresh blood) - pain -thrombosis -inflammation	-dilated anal and perianal collateral vessels (that connect portal & caval venous systems) in submucosa of anal or rectal area -thin walled, beneath mucosa.

3-Malabsorptive diseases

Disease	causes	Mechanism	General symptoms	Specific manifestations	Notes
Malabsorptive diarhea	-Pancreatic insufficiency. -Celiac disease -Crohn disease -Cystic Fibrosis -Lactase (Disaccharidase) deficiency -Abetalipoproteinemia	***Intraluminal digestion:** Malabsorption of macromolecules (fats, carbs & proteins) due to main enzymes deficiency. ***Terminal digestion:** Malabsorption of end products due to deficiency in disaccharidases/ peptidases at the intestinal brush border. ***Transepithelial transport:** defect in the transport across the epithelial cells (nutrients can't reach vascular side). ***Lymphatic transport:** defect in transport of absorbed lipids by lymphatics to reach circulation.	-Weight loss -anorexia -Flatus -abdominal distention -Borborygmi -Muscle wasting	-Anemia and mucositis (iron, pyridoxine (VB6), folate, or vitamin B12 deficiency). -Bleeding (vitamin K deficiency). -Osteopenia and tetany (calcium, magnesium, or vitamin D deficiency). -Neuropathy (vitamin A or B12 deficiency). -Skin and endocrine disorders (Iodine results in thyroid hormone deficiency).	-It is a chronic defect in the absorption of fats, fat- or water-soluble vitamins, proteins, carbohydrates, electrolytes, minerals and water. -Its hallmark is ***Steatorrhea*** which is greasy, fatty, bulky yellow to clay colored stool (and this is due to the malabsorped nutrients in it).

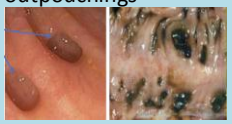
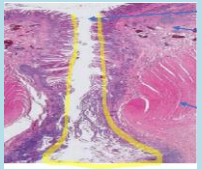
The next table will discuss the causes of malabsorptive diarrhea, let's start😊

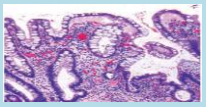
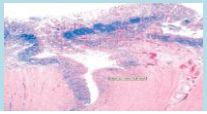
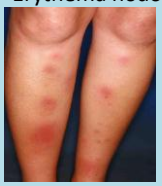
Disease	site	causes	pathogenesis	Diagnosis	Clinical features	treatment	complications	notes
Cystic fibrosis		Genetic mutations in cystic fibrosis transmembrane conductance regulator **(CFTR)** which is involved in ion transport.	Mutation in CTFR> Defects in ion transport across intestinal and pancreatic epithelium> which causes the pancreatic secretions to be thick and viscous (less ions > less water >more viscous secretions> Mucus secretions plugs pancreatic ducts causing pancreatic insufficiency in 80% of patients>Defect in **intraluminal digestion**.					-multi-organ system disease (can affect lungs, pancreas,...)
Celiac disease	Affects Small intestines	Patients carry the HLA-DQ2 or HLA-DQ8 alleles on the surface of their antigen presenting cells APCs ~ genetic predisposition.	gluten reaches the small intestine, it gets digested by its enzymes to a shorter peptide **~Gliadin~** > enters the lamina propria and gets deamidated by **tissue transglutaminase**> Deamidated gliadin reacts with **HLA-DQ2 or HLA-DQ8 on APCs** surface and this activates CD4+ T helper cells in the lamina propria causing tissue damage by multiple ways: 1) they release cytokines which damage the epithelial cells. 2) they attract intraepithelial lymphocytes (CD8+ Cytotoxic T Cells). 3) they activate B cells to produce the following antibodies: * **Anti-tissue transglutaminase antibodies** * **Anti-gliadin antibodies** ***Anti-endomysial antibodies** **All together cause tissue damage by the loss of villus architecture and loss of epithelial cells lining the mucosa, decreasing the surface area exposed for absorption leading to malabsorption> affects the terminal digestion.**	Combination between clinical, serological & histological. ***invasive: (histologic)** -multiple biopsies from second portion of the duodenum or proximal jejunum and we look for triad: 1) Intraepithelial lymphocytosis (CD8+ T cells) ~IEL~ which is the earliest manifestation. 2) Crypt hyperplasia. 3) Villous atrophy. In lamina propria: lymphocytes, plasma cells, eosinophils. ***non-invasive: (serologic)** *-Most sensitive but less specific->* Anti-tissue transglutaminase Abs, IgA. Anti-deamidated gliadin Abs, IgA & IgG. *-Most specific but less sensitive->* Anti-endomysial Abs.	***Children (6- 24) months :** Classical>> Irritability, abdominal distention, anorexia , diarrhea, failure to thrive, weight loss, or muscle wasting. non-classical>> abdominal pain, nausea, vomiting, bloating, or constipation. *Blistering skin lesion, dermatitis herpetiformis, in 10% of Pnts. ***Adults (30 60 years)** -Anemia (iron deficiency),B12 and folate deficiency (less common),Diarrhea , bloating, and fatigue.	*gluten free diet.	Increased risk of enteropathy **associated T cell lymphoma & Small intestinal adenocarcinoma**	-Gluten sensitive enteropathy -Immune mediated enteropathy -Association with: type 1 diabetes, thyroiditis, and Sjogren syndrome -IEL & villous atrophy are not pathognomonic, seen in viral enteritis -celiac disease that is missed during diagnosis: *silent celiac> +serology +histology -clinical symptoms *latent celiac> +serology -histology -clinical symptoms

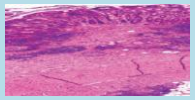
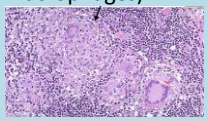
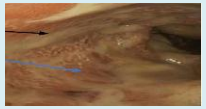
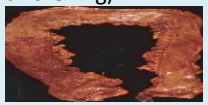
Lactase Deficiency	Apical brush border membrane where lactase exists	***congenital:** Due to autosomal recessive (AR) genetic mutation. ***acquired:** -Following viral or bacterial enteritis> which damage the apical brush border >>loss of lactase. -Or due to downregulation of the lactase gene after childhood as the need for milk decreases.	Deficient lactase>> lactose accumulates in the gut lumen absorbing water and causing **osmotic diarrhea.** ***Affects the Terminal digestion**	-biochemical test *Biopsies are normal*	***-osmotic diarrhea*** -watery , frothy stools . -abdominal distention after milk ingestion.	Stop milk & dietary products.		
Abeta lipoprotei nemia		Autosomal recessive, rare.	inability to secrete triglyceride-rich lipoproteins due to a transepithelial transport defect of triglycerides, monoglycerides and fatty acids in which they enter the epithelial cells but don't reach the blood (accumulate) So, there is a lack of absorption of fat and fat-soluble vitamins + decreased synthesis of lipoproteins which are an important part of the plasma membrane.	Microscopically: clear cytoplasm due to fat globules and lipid accumulation in enterocytes 	**In infats:** -failure to thrive - diarrhea - steatorrhea			Absence of B-lipoprotien in blood

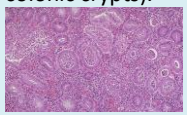
4-Inflammatory bowel diseases

- Sidmoid diverticulitis
- CIBD
  - Crohn disease
  - ulcerative colitis

Disease	Age group	site	Causes /factors	pathogenesis	Morphology	Clinical features	treatment	Complicati-ons	notes
Sigmoid diverticulitis	Older adults	**Sigmoid colon**(the most common site) and **rectum**	Constipation due to low fiber diet	Constipation> increase intraluminal pressure in sigmoid colon& Exaggerated peristaltic contractions(due to low fiber diet) > outpouching of mucosa& submucosa> Pseudodiverticulae (diverticulosis) > obstruction by fecalith material> diverticulitis	**Macroscopically**: Flasklike outpouchings  **Microscopically:** Atrophic mucosa and compressed submucosa, abscent muscularis in the wall of diverticula 	-Mostly asymptomatic. -Intermittent lower abdominal pain(The main complaint of diverticulitis) -Constipation or diarrhea(if it is inflamed)	-High fiber diet. -Antibiotics in diverticulitis -Surgery (stenosis& strictures)	-Recurrent diverticulitis leads to strictures& stenosis>> intestinal obstruction -perforationof inflamed diverticulum> peritonitis and severe abdominal pain.	-acquired

Disease	Age group	site	Causes /factors	pathogenesis	Morphology	Clinical features	treatment	Complications	notes
Crohn disease	Adolescence& young adults -2nd peak in fifth decade	-Can affect any area in GIT (from the mouth to the anus). *Most common sites: terminal ileum, ileocecal valve, and cecum *transmural -Regional enteritis, It does not involve the bowel in a continuous fashion. Small intestine alone 40%. Small intestine and colon 30%. Colon only 30%.	**Multi factorial>>** -Genetic factors. -Alterations in host interactions with intestinal Microbiota. -Intestinal epithelial dysfunction. -Aberrant mucosal immune responses. -Altered composition of the gut microbiome. -Hygiene hypothesis.	**Aggravated immune response (the main pathology of the disease).** -Trans epithelial flux of bacteria >Activation of innate and adaptive immune responses > Release of TNF and immune signals> Increase tight junction permeability> More flux of luminal bacteria> Self amplifying cycle (stimulus at any site is sufficient to initiate IBD).	**Macroscopically:** -Regional enteritis. -Skip lesions -strictures common  -Earliest lesion: aphthous ulcer (shallow). -Elongated, serpentine ulcers. -Edema, loss of bowel folds. -Cobblestone Appearance  -creeping fat -fissures, fistulas, Perforations. **Microscopically:** ***active phase**: -Neutrophils -Crypt abscesses. -Ulceration. ***chronic phase**: -Distortion of mucosal architecture.  -Paneth cell metaplasia in left colon. -Mucosal atrophy. -fissures 	-Intermittent attacks (on&off disease) of mild diarrhea, fever, and abdominal pain. -Acute right lower-quadrant pain and fever (20%) – Due to terminal ileitis or ileocecal valve inflammation. -Bloody diarrhea and abdominal pain (colonic involvement). -may complain from constipation if strictures occur. -Asymptomatic intervals (weeks to months of no symptoms) between attacks. ***Extra intestinal Manifestations:** -Uveitis -Migratory polyarthritis -Sacroiliitis -Ankylosing spondylitis -Erythema nodosum  -Clubbing of the fingertips  -Primary sclerosing cholangitis (more with UC).	Immunosuppressive and immunomodulatory agents are mainstays of IBD therapy. -Probiotic (or beneficial) bacteria may benefit IBD patients.	-Iron-deficiency anemia -Hypoproteinemia and hypoalbuminemia, malabsorption of nutrients, vitamin B12 and bile salts. -Fistulas, peritoneal abscesses (complication of rupture and resultant peritonitis), and strictures due to fibrosis. **-Risk of colonic adenocarcinoma**	-immune- mediated disease. -Genetic predisposition. -> 200 genes associated with IBD, all with CD. -susceptibility gene: NOD2. -Autophagy genes. -defective immune regulation of T cells. -TH1 mainly in CD. - Concordance rate for monozygotic twins: 20%. -Triggers of the attacks: physical or emotional stress, specific dietary items, NSAID use, and cigarette smoking.

					-transmural inflammation  ***Hallmark> noncaseating granuloma** (combinations of multi-nucleated giant cells and epithelioid macrophages) 				
Ulcerative colitis	Adolescence& young adults -2nd peak in fifth decade	**colon** and **rectum**, extends only into mucosa and submucosa. *Extends proximally in continuous pattern.	**Multi factorial>>** -Genetic factors. -Alterations in host interactions with intestinal Microbiota -Intestinal epithelial dysfunction. -Aberrant mucosal immune responses. -Altered composition of the gut microbiome. -Hygiene hypothesis.	**Aggravated immune response (the main pathology of the disease).** Trans epithelial flux of bacteria >Activation of innate and adaptive immune responses > Release of TNF and immune signals> Increase tight junction permeability> More flux of luminal bacteria> Self amplifying cycle (stimulus at any site is sufficient to initiate IBD).	**Macroscopically:** -Broad-based ulcers  -Pseudopolyps  -Mucosal atrophy in long standing disease. - Thin wall (no mural thickening).  -Serosal surface is normal (no transmural inflammation). -No strictures. **Microscopically:** -Inflammatory infiltrate (whether it	-Relapsing remitting disorder. -Attacks of bloody mucoid diarrhea +lower abdominal cramps. -Temporarily relieved by defecation. -Attacks last for days, weeks, or months. -Asymptomatic intervals. -Infectious enteritis may trigger disease onset, or cessation of smoking. Also in UC we can see **extra- intestinal maifestations** such as: -Uveitis -Migratory polyarthritis -Sacroiliitis -Ankylosing spondylitis -Erythema nodosum -Clubbing of the fingertips -Primary sclerosing cholangitis (more with UC)	-Colectomy cures intestinal disease only, extra-intestinal manifestations are not cured by colectomy. - Immunosuppressive and immunomodulatory agents are mainstays of IBD therapy. -Probiotic (or beneficial) bacteria may benefit IBD patient.	-toxic megacolon  -The risk of adenocarcinoma	-Genetic predisposition. -Autophagy genes. -defective immune regulation of T cells. -TH2 mainly in UC. -Pan colitis : The entire large intestine up to the cecum is affected (the most severe form). -Occasionally focal appendiceal or cecal inflammation-In a dis continuous fashion (not typical scenario). -small bowel is normal. -Concordance rate for monozygotic twins: 16%

					is active or chronic inflammation). -Crypt abscesses (Seen in the active phase). -Crypt distortion (a chronic feature with haphazard arrangement of colonic crypts).  -Epithelial metaplasia (Another chronic feature) -Submucosal fibrosis (due to inflammation). -Inflammation is limited to mucosa and submucosa. -No skip lesions. -No granulomas.				

5-colonic polyps &neoplastic diseases

***colonic polyps:**

-neoplastic>>colonic adenomas

-non-neoplastic>>1-inflammatory polyps → Juvenile polyps

2-hamartomatous polyps

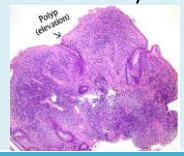
3-hyperplastic polyps → Peutz-Jeghers syndrome

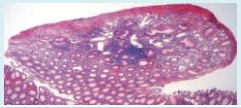
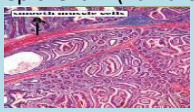
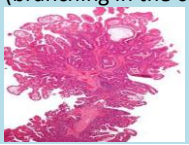
***familial syndromes:**

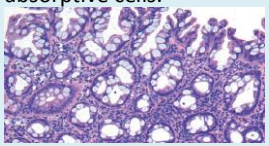
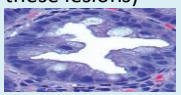
1) Familial Adenomatous Polyposis (FAP)

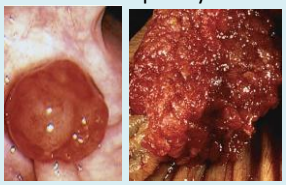
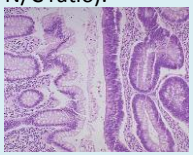
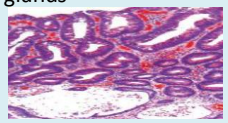
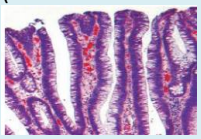
2)Hereditary Non-Polyposis Colorectal Cancer (HNPCC)

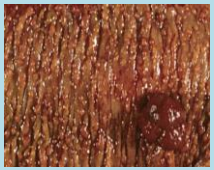
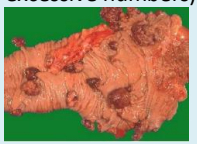
***colonic adenocarcinoma**

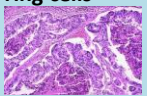
Colonic polyps						
Disease	**Age group**	**site**	**cause**	**morphology**	**Risk to develop cancer**	**notes**
1-Inflammatory polyps		Anywhere in the GIT, The most common site is **rectum** >>called "solitary rectal ulcers".	Chronic cycles of injury and healing give a polypoid mass of inflamed and reactive mucosal tissue	**Microscopically:** composed of dense inflammatory cells 	-	***Non-neoplastic polyps***
2- Hamartomatous polyps: **- disorganized, tumor-like growths composed of mature cell types normally present at the site at which the polyp develops.** **- Sporadic or syndromic** **-We will mention 2 types of hamartomatous polyps>>**						
A-Juvenile polyps **[Sporadic and familial (juvenile polyposis syndrome)]**	Children younger than 5 years of age (either sporadic or familial).	In sporadic (acquired) cases> usually **rectum.**	**Familial:** Transforming growth factor-β (TGF-β) mutation>> Affects the Pathways that regulate cellular growth.	**Macroscopically:** they appear as large polyps with cystic spaces in between **Sporadic:** solitary (one single polyp) in the rectum usually. **familial:** juvenile polyposis syndrome is characterized by multiple polyps 3-100 polyps. **Microscopically:** -Pedunculated (has stalk) -Reddish lesions (due to inflammation). -Cystic spaces on cut sections.	**-increase the risk of adenocarcinoma** just in familial cases **(juvenile polyposis syndrome).**	***Non -neoplastic polyps*** - the **most common** type of hamartomatous polyps. - sporadic juvenile polyps are **not** associated with development of Adenocarcinoma. -we can distinguish between familial& sporadic juvenile polyps by the number of polyps, can't distinguish by morphology. - juvenile polyposis syndrome is **autosomal dominant** syndrome.

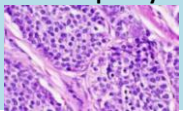
				-Dilated glands filled with mucin and inflammatory debris. -Granulation tissue on surface. 		
B-Peutz-Jeghers syndrome	Mean age: 10-15 yrs	most common in the **small intestine.**	Germ line loss of-function mutations in the LKB1/STK11 gene	**In syndromic cases**>> multiple gastrointestinal hamartomatous polyps and **mucocutaneous hyperpigmentation** **Macroscopically:** the polyps are large and pedunculated with a lobulated contour. **Microscopically:** -Arborizing network of connective tissue, smooth muscle, lamina propria. -glands lined by normal-appearing intestinal epithelium (hamartomatous).  -Christmas tree pattern (branching in the center) 	-increase risk for development of **several malignancies**, including cancers of the colon, pancreas, breast, lung, ovaries, uterus, and testes.	***Non -neoplastic polyps*** - Peutz-Jeghers syndrome is a **rare autosomal dominant** disorder. -usually appears as syndromic.
3-Hyperplastic polyps	in the fifth to sixth decade of life **(old age).**	the left colon (specifically; in the **rectosigmoidal area)**	**Decreased epithelial turnover** and delayed shedding of surface epithelium (long turnover time). >>> pileup of goblet cells & epithelial overcrowding.	**Macroscopically:** -Small < 5 mm - polyps appear as smooth, nodular protrusions of the mucosa, often on the crests of mucosal folds. - They may occur singly but are <u>multiple more frequently</u>. **Microscopically**: (gold standard)	no malignant potential (devoid of dysplasia, totally benign)	***Non-neoplastic polyps***

				-Crowding of goblet & absorptive cells.  -Serrated surface (hallmark of these lesions) 		

	Age group	site	cause	morphology	Risk to develop cancer	notes
Colonic adenomas	Usually **Old age** -Earlier with family history		-Family history -Age -Lifestyle **All play a role to develop adenoma**	**Macroscopically:** -Typical adenomas can be pedunculated or sessile. - texture resembling velvet or a raspberry  **Microscopically:** -Hallmark: epithelial **dysplasia** (nuclear hyperchromasia, elongation, stratification, high N/C ratio).  -Adenomas can be classified as tubular, tubulo-villous, or villous on the basis of their microscopic architecture. ***tubular adenomas**: tend to be small, rounded or tubular glands  ***villous adenomas:** which are often larger and sessile, are covered by slender villi (similar to intestinal villi)  ***Tubulo-villous adenomas**: have a mixture of tubular and villous elements.	**Precursor for majority of **colorectal adenocarcinomas** (sporadic& inherited) - Most adenomas DO NOT progress to carcinoma.	***neoplastic polyps*** -**Most common and clinically important** - Increase with age. - the foci of invasion are more frequent **in villous adenomas** than in tubular adenomas (due to the larger size). -**Size** : most important correlate with risk for malignancy. -**High-grade dysplasia** is the second factor.

Familial syndromes					
Disease	**Age group**	**cause**	**morphology**	**Risk to develop cancer**	**notes**
1) Familial Adenomatous Polyposis (FAP)	teenage years	Mutation in APC gene.	**Macroscopically:** Hundreds of small colonic polyps are present along with a dominant polyp (it's like a carpet covered by multiple polyps, and the intestinal mucosa is lost.  **Microscopically:** Multiple adenomas (tubular, villus or tubule-villous)	**-Colorectal adenocarcinoma** develops in **100%** of patients with untreated FAP often before 30 years of age.	-autosomal dominant disorder - no predominant site. - **Standard therapy:** prophylactic colectomy before 20 Year of age. However, patients remain at risk for extraintestinal manifestations, including neoplasia at other sites. ***Variants of FAP**: -**Gardner syndrome**: intestinal polyps + osteomas (mandible, skull, and long bones); epidermal cysts; desmoid and thyroid tumors; and dental abnormalities. -**Turcot syndrome**: intestinal adenomas and CNS tumors (medulloblastomas >> glioblastomas)
2) Hereditary non-polyposis colorectal cancer (HNPCC) "Lynch syndrome"	Young age	Inherited germ line mutations in **DNA mismatch repair genes** (MSH2 or MLH1)> accumulation of mutations in microsatellite DNA (short repeating sequences) > microsatellite instability.	**-**Adenomas are present, BUT POLYPOSIS IS NOT (not in excessive numbers)  -Right colon with excessive **mucin** production.	**Clustering of tumors**: Colorectum, endometrium, stomach, ovary, ureters, brain, small bowel, hepatobiliary tract, and skin.	-**colon cancer** often located in the right colon. -Colon cancers (e.g. cecal, colorectal) in patients with HNPCC tend to occur at younger ages than sporadic colon cancers.

	Age group	site	cause	pathogenesis	Clincal features	morphology	complications	treatment	notes
Colonic adeno carcinoma	Peak: 60 to 70 yrs. -20% under 50 years (with familial syndromes)	**Colon** **If molecular defect in APC/WNT pathway:** *familial (FAP)**>any site in the colon** *sporadic (80% of cases)> **left side of colon.** **-if molecular defect in DNA mismatch repair:** *familial (HNPCC)> **right side of colon** *sporadic (10-15)% of cases> **right side of colon.** - Small intestine is **uncommonly** involved by neoplasia.	Multi-factorial and multiple genes are involved, two Genetic Pathways in both sporadic &familial cases. -Low intake of vegetable fiber and high intake of carbohydrates and Fat plays a role to develop adenocarcinoma. -Sporadic more than familial.	**1) APC/β-catenin pathway** (chromosomal instability pathway)>> increased WNT signaling. **APC gene** mutation → **Beta Catenin** accumulation → Beta Catenin enters the nucleus → Activation of **MYC and Cyclin-D1** → Proliferation will start → Additional mutations will accumulate like **KRAS** gene leading to inhibition of apoptosis → **SMAD2 & SMAD4 & TP53** mutations will take place. -Expression of telomerase also increases as the tumor advances. 2**) Microsatellite Instability pathway** Loss of mismatch repair genes > Mutations accumulate in microsatellite repeats> Microsatellite instability > Uncontrolled cell growth if located in coding or promoter regions of genes involved in cell growth and apoptosis (TGF-B and BAX genes).	-Early cancer is **Asymptomatic.** **-Right Sided cancer >** Fatigue and weakness & Iron-deficiency anemia (in an older male or postmenopausal female is gastrointestinal cancer until proven otherwise). **-Left sided carcinomas >** occult bleeding, changes in bowel habits, cramping left lower quadrant discomfort.	**Macroscopically:** -Proximal colon tumors: polypoid, exophytic masses, rarely cause obstruction.  -Distal colon: annular lesions (napkin ring)> constrictions &narrowing.  **Microscopically:** *Typical adenocarcinoma (FAP+sporadic colon cancer) >Tubular, villus architecture. *Mucinous adenocarcinoma (HNPCC+sporadic colon cancer)> sessile serrated adenoma. **-Dysplastic GLANDS** with strong **desmoplastic response**. -**Necrotic debris** are typical. -Some tumors give abundant mucin or form **signet ring cells** 	**Metastasis** usually to the **lung** and the **liver**	Endoscopic screening >> cancer prevention.	**Most common malignancy of the gastrointestinal tract.** -Aspirin or other NSAIDs have a protective effect ((COX-2) promotes epithelial proliferation). -**Both copies of APC** should be inactivated for adenoma to develop (1st and 2nd hits). -Tow important prognostic factors: 1-Depth of invasion. 2-Lymph node metastasis. -Poor differentiation and mucinous histology > poor prognosis.

Appendix									
Disease	**Age group**	**Site**	**cause**	**pathogenesis**	**Clinical features**	**morphology**	**treatment**	**complications**	**notes**
Acute appendicitis	The most common in **adolescents and young adults**, but may occur in elderly (due to colon tumor which is common in elderly).		Luminal obstruction Mainly due to **fecalith** & less commonly by **gallstone**, **worms**, **tumor** (especially in elderly).	Luminal obstruction in 50-80% of cases >> increased luminal pressure >> impaired venous drainage >> ischemic injury & stasis associated bacterial proliferation >>> inflammatory response rich in neutrophils & edema	Early acute appendicitis: periumbilical pain -Later: pain localizes to the right lower quadrant, -Nausea, vomiting, low-grade fever, mildly leukocytosis. -A classic physical finding is McBurney's sign (McBurney's point). -Signs and symptoms are often **absent**, creating difficulty in clinical diagnosis.	**Microscopically: (The gold standard diagnosis)** neutrophilic infiltration of the muscularis propria (no neutrophils> no appendicitis).	The appendectomy is performed even when the surgeon is not 100% sure that the case is truly appendicitis.	In untreated cases>> Appendix rupture then leads to peritonitis. ***Acute suppurative appendicitis** → more severe form with massive neutrophilic infiltration>> focal abscess formation. *** Acute gangrenous appendicitis** >> necrosis and ulceration of the appendix.	
Tumors of the appendix>> Carcinoid (neuroendocrine tumor)		Distal tip of the appendix is the common site				*Incidentally found during surgery (appendectomy) or on examination of a resected appendix.* **Macroscopically:** Yellowish-well circumscribed Mass in the tip of the appendix  **Microscopically:** 			-RARE -Nodal metastases & distant spread are rare → in most cases considered benign tumors.

Done by : Sajeda Alkhateeb

Corrected by : Leen Hajeer

GOOD LUCK