**Oral Cavity**

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| **LEUKOPLAKIA**  |

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| * ***Definition*** *:* a clinical term  *refers to a whitish, well-defined mucosal patch or plaque caused by epidermal thickening or hyperkeratosis.* The term is not applied to other white lesions, such as those caused by candidiasis, lichen planus, or many other disorders.
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| * **Microscopy:**  vary from banal hyperkeratosis without underlying epithelial dysplasia to mild to severe dysplasia bordering on carcinoma in situ.
* **Etiology** : The lesions are of unknown cause except that there is a *strong association with the use of tobacco*, particularly pipe smoking and smokeless tobacco . Less strongly implicated are *chronic friction,* as from ill-fitting dentures or jagged teeth;
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| * **Prognosis** : Oral leukoplakia is an important finding because 3% to 6% undergo transformation to squamous cell carcinoma. The transformation rate is greatest with lip and tongue lesions and lowest with those on the floor of the mouth. Persistent leukoplakia should therefore be biopsied.
* **Three** somewhat related **lesions** must be differentiated from the usual oral leukoplakia.
1. **Hairy leukoplakia** EBV-induced epithelial hyperplasia seen mostly in patients with AIDS or other immunosuppressed patients. It has a corrugated or "hairy" surface rather than the white, opaque thickening of oral leukoplakia and has not been related to the development of oral cancer. Mostly it involves the lateral border of the tongue
2. **Verrucous leukoplakia** exhibits a corrugated surface caused by excessive hyperkeratosis. This seemingly innocuous form of leukoplakia recurs and insidiously spreads over time, resulting in a diffuse warty-type of oral lesion that may yet harbor squamous cell carcinoma.
3. **Erythroplakia** refers to red, velvety, often granular, circumscribed areas. Histologically, erythroplasia almost invariably reveals marked epithelial dysplasia (the malignant transformation rate is more than 50%), so recognition of this lesion becomes even more important than identification of oral leukoplakia.

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| **SALIVARY GLANDS** |

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| **Sialadenitis**  |

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| Inflammation of the major salivary glands may be of viral, bacterial, or autoimmune origin. Dominant among these causations is the infectious **viral** disease *mumps*, which may produce enlargement of all the major salivary glands but predominantly the parotids.  |

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| ***Bacterial*** *sialadenitis* most often occurs secondary to ductal obstruction resulting from stone formation *(sialolithiasis).****Autoimmune sialadenitis*** |

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| * seen in Sjögren syndrome
* salivary glands ………dry mouth *(xerostomia)*
* lacrimal glands, ……..dry eyes *(keratoconjunctivitis sicca)*.

**Salivary Gland Tumors*** 80% of tumors occur within the parotid glands and most of the others in the submandibular glands
* In the parotids 70% to 80% of these tumors are benign, whereas in the submaxillary glands only half are benign. Thus, it is evident that *a neoplasm in the submaxillary glands is more ominous than one in the parotids.*
* The most common *benign tumor of the salivary gland is pleomorphic adenoma*.
* The most common *malignant tumor of the salivary gland is mucoepidermoid carcinoma*.
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**Pleomorphic Adenoma (Mixed Tumor of Salivary Glands)**

* slow-growing, well-demarcated, apparently encapsulated lesion rarely exceeding 6 cm in greatest dimension
* Although they are encapsulated, in some locations the capsule is not fully developed,
* On average, about 10% of excisions are followed by recurrence.
* Histologic features: *mixed* …..epithelial and Connective tissue
* Epithelial component: ducts, acini, strands or sheets.
* Connective tmissue: myxoid stroma with islands of cartilage and bone.
* Cells are of myoepithelial origin.
* If present for many years, malignant transformation may occur (more common at submandibular glands – 40%).

 ***Mucoepidermoid carcinoma***

* The most common *malignant tumor of the salivary gland*
* composed of variable mixtures of squamous cells, mucus-secreting cells, and intermediate cells.
* subclassified into low, intermediate, or high grade.
* The clinical course and prognosis of this tumor depend on the grade of the neoplasm.

***Adenoid cystic carcinoma***

ESOPHAGUS

**Achalasia**

* means "failure to relax."
* Incomplete relaxation of lower sphincter in response to swallowing with functional obstruction.
* It could be **primary or secondary** achalasia (Chaga’s disease due to infection by Trypanosoma cruzi or due to tumor in this area ) .
* **Complications** Progressive dilatation of the esophagus., Dysphagia, and carcinoma in 5%.

**Esophageal Varices**

* Increased blood pressure in the esophageal plexus produces dilated tortuous vessels in submucosa.
* Occur in 2/3 of cirrhotic patients
* Symptoms occur after rupture ………..massive hemorrhage ( 20% to 30% death rate).

**Esophagitis**

Common condition worldwide:

 In China extremely high.

 In Iran - 80%.

 In USA - 10-20%.

**REFLUX ESOPHAGITIS (GASTROESOPHAGEAL REFLUX DISEASE ( GERD) )**

* Reflux of gastric contents into the lower esophagus.
* The action of gastric juices is critical to the development of esophageal mucosal injury
* Conditions that decrease lower esophageal sphincter tone or increase abdominal pressure contribute to GERD and include:
1. alcohol and tobacco use,
2. obesity,
3. central nervous system depressants,
4. pregnancy,
5. hiatal hernia
6. delayed gastric emptying,
* In many cases, no definitive cause is identified.
* **Clinical Features.** The most common clinical symptoms are dysphagia, heartburn, and, less frequently, noticeable regurgitation of sour-tasting gastric contents. Rarely, chronic GERD is punctuated by attacks of severe chest pain that may be mistaken for heart disease.
* Histologic features:

 1. Eosinophils and neutrophil infiltration.

 2. Basal zone hyperplasia.

 3. Lamina propria papillae elongation.

* **Endoscopy** . Simple hyperemia, [ redness].
* **Complications** include esophageal ulceration, hematemesis, melena, stricture development, and Barrett esophagus.

**BARRETT ESOPHAGUS**

* is a complication of chronic GERD that is characterized by *intestinal metaplasia within the esophageal squamous mucosa* in the Distal esophagus
* 10% of individuals with symptomatic GERD.
* Barrett esophagus is a **pre-malignant** condition……… adenocarcinoma
* **Upper endoscopy:**  red, velvety mucosa
* Subclassified as **long segment**, in which 3 cm or more of esophagus is involved, or **short segment,** in which less than 3 cm is involved.
* **Histology**: intestinal metaplasia…….**Goblet cells**,
* Foveolar mucus cells, which do not have distinct mucous vacuoles are insufficient for diagnosis.
* When **dysplasia** is present, it is classified as low grade or high grade.

**Esophageal carcinomas**

* Two types: *squamous cell carcinomas and adenocarcinomas*
* Worldwide, squamous cell carcinomas constitute 90% of esophageal cancers
* Risk factors to **squamous cell carcinomas** are alcohol and tobacco use
* Other risk factor: Plummer-Vinson (Paterson-Kelly) syndrome ((esophageal webs, atrophic glossitis, microcytic anemia, and other abnormalities associated with iron and vitamin deficiencies)
* Half of all esophageal cancer reported in USA is *adenocarcinomas*
* ***Barrett esophagus*** *is the only recognized precursor of esophageal* ***adenocarcinoma****.* The development of adenocarcinomas from Barrett esophagus is a multistep process that unfolds over many years. The degree of dysplasia is the strongest predictor of the progression to cancer.

**STOMACH**

**Congenital Pyloric Stenosis**

* is concentric enlargement of the pyloric sphincter and narrowing of the pyloric canal that obstructs the gastric outlet.
* This disorder is the most common indication for abdominal surgery in the initial 6 months of life.
* It is four times more common in boys than in girls
* Causes *Projectile Vomiting* within the first month of life.

**Gastritis**

**Acute gastritis**

* Clinical features : Depending on the severity of the anatomic changes, acute gastritis may be entirely asymptomatic, may cause variable epigastric pain with nausea and vomiting, or may present as overt hematemesis, melena, and potentially fatal blood loss. Overall, *it is one of the major causes of hematemesis*, *particularly in alcoholics.*

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| * frequently associated with Heavy use of nonsteroidal anti-inflammatory drugs (NSAIDs), particularly aspirin, Excessive alcohol consumption, and Heavy smoking
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| **Chronic Gastritis** ***H. pylori* Gastritis ( type B Chronic Gastritis )*** 90% of patient with chronic gastritis.
* *Most individuals with the infection also have the associated gastritis but are asymptomatic*.
* Helicobacter pylori, nonsporing, curvilinear gram negative rod, motile organisms. It elaborate urease and attach itself to gastric epithelial cells. It Preduce cytotoxin and endotoxin.
* gastritis develops as a result of the combined influence of bacterial enzymes and toxins and release of noxious chemicals by the recruited neutrophils.
* Interestingly, the organism is found only on gastric epithelium and does not colonise duodenal (or any other intestinal) epithelium. With this in mind, one explanation for intestinal metaplasia in the stomach is that it is a defence against bacterial colonisation.
* After initial exposure to *H. pylori*, gastritis may develop in two patterns:

(1) antral-type with high acid production and higher risk for the development of duodenal ulcer, (2) a pangastritis with multifocal mucosal atrophy, with low acid secretion and increased risk for adenocarcinoma. ***Autoimmune gastritis (*type A Chronic Gastritis)** * Antibodies against gastric parietal cells and intrinsic factor binding sites.
* hypochlorhydria and macrocytic anaemia resulting from vitamin B12 deficiency.
* Autoimmune gastritis + macrocytic anaemia = *pernicious anaemia*.
* Histologically, the body of the stomach is maximally affected: there is glandular atrophy and together with an infiltrate of lymphocytes and plasma cells. In addition, the surface and pit-lining epithelium may show *intestinal metaplasia* (IM).

**Peptic ulcer disease****Ulcer** is a breach in the mucosa of the alimentary tract extending through muscularis mucosa into submucosa or deeper.* is a breach in the mucosa lining the alimentary tract as a result of acid and pepsin attack.
* Favored sites are the anterior and posterior walls of the first portion of the duodenum and the lesser curvature of the stomach.
* Gastric and duodenal ulcers differ in their epidemiology, incidence and pathogenesis
* Two conditions are key for the development of peptic ulcers: (1) *H. pylori* infection, which has a strong causal relationship with peptic ulcer development, and (2) mucosal exposure to gastric acid and pepsin.
* peptic ulcers are created by an **imbalance** between the gastroduodenal mucosal defenses and the damaging forces that overcome such defenses
* ***H. pylori*** infection is the most important condition in the pathogenesis of peptic ulcer. The infection is present in 70% to 90% of persons with duodenal ulcers and in about 70% of those with gastric ulcers.
* Only 10% to 20% of individuals worldwide who are infected with *H. pylori* actually develop peptic ulcer.
* ***NSAIDs*** *are the major cause of peptic ulcer disease in persons who do not have H. pylori infection.* Suppression of mucosal prostaglandin synthesis, which increases secretion of hydrochloric acid and reduces bicarbonate and mucin production, is the key to NSAID-induced peptic ulceration.
* Other events may act alone or in concert with *H. pylori* and NSAIDs to promote peptic ulceration :
1. Gastric *hyperacidity* ….. *Zollinger-Ellison syndrome*
2. *Cigarette smoking*
3. Alcohol
4. *Corticosteroids*
5. psychological stress
* **microscopy see: lecture**
* **complications**
1. *Bleeding is the chief complication*, occurring in as many as one-third of patients, and may be life-threatening.
2. Perforation occurs in about 5% of patients but accounts for two-thirds of deaths from this disease in the United States.
3. Obstruction of the pyloric channel is rare.
4. Malignant transformation occurs in about 2% of patients,

**Malignant neoplasm of stomach*** **Carcinoma – 90-95%**
* **Lymphoma – 4%**
* **Carcinoids – 3%**
* **Malignant spindle cell – 2%**

**Gastric adenocarcinoma*** is the second leading cause of cancer-related deaths in the world,
* favored location is the lesser curvature of the antropyloric region
* show two morphologic types, called *intestinal* and *diffuse*.
* Both intestinal-type and diffuse gastric carcinoma are generally asymptomatic and can be discovered only by repeated endoscopic examinations in persons at high risk.
* For obscure reasons, the earliest lymph node metastasis may sometimes involve a supraclavicular lymph node (**Virchow node**). Another somewhat unusual mode of intraperitoneal spread in females is to both the ovaries, giving rise to the so-called **Krukenberg tumor**

***intestinal type*** * Arise from gastric mucous cells that have undergone intestinal metaplasia in the setting of chronic gastritis.
* better differentiated
* chronic gastritis associated with *H. pylori* infection constitutes a major risk factor for this type

***diffuse type*** * arise de novo from native gastric mucous cells,
* not associated with chronic gastritis
* No true tumor mass is seen; instead, the wall of the stomach is thickened and firm. If the entire stomach is involved, it is called a linitis plastica tumor.
* Histology : poorly differentiated ( do not form glands but rather permeate the mucosa and wall as scattered individual **"signet-ring" cells)**
* Mutations in *E-cadherin* are present in 50% of diffuse cancers.

***Gastric lymphoma*****Low-grade B cell lymphoma** * Arise in mucosa associated lymphoid tissue (MALT lymphoma).
* *H. pylori infection*
* Can be cured by surgical resection

**High-grade B cell lymphomas** * Aggressive
* respond to chemotherapy

**SMALL AND LARGE INTESTINES****Hirschsprung Disease*** Absence of the Ganglia are from the submucosa (Meissner plexuses )and muscle wall (Auerbach plexuses) of the intestine
* This will lead to functional obstruction and progressive distention of the colon proximal to the affected segment.
* rectum and distal colon are usually involved
* The effects of the aganglionosis vary from life-threatening total obstruction to mild cases causing chronic constipation

**Diverticular disease** * Diverticulum is an Outpouching of the mucosa of the intestine.
* **True diverticula** have all the layers( mucosa, submucosa, and muscularis) of the intestine; congenital diverticula such as Meckel's diverticula are true diverticula.
* **False diverticula** mucosal herniations through a weakened intestinal wall, often at a point of deficiency in the muscularis externa, are lined by mucosa and fibrous tissue and do not have muscle
* Most acquired diverticula are false diverticula

***Meckel diverticulum**** The most common congenital anomaly of the gastrointestinal tract (2% of the population )
* It results from failure of involution of the omphalomesenteric duct.
* Found within 2 feet (1 m) of the ileocecal valve, and is usually 2 inches (5 cm) long.
* 40% of cases have heterotopic gastric mucosa or pancreatic tissue
* **Complications**:
1. Peptic ulceration may occur when there is gastric mucosa
2. Bleeding is an important cause of chronic intestinal blood loss, resulting in iron deficiency anemia.
3. Infection ……a clinical picture very similar to that of acute appendicitis

***Colonic Diverticulosis**** common in developed countries ( 50% of patients over the age of 60 years).
* The sigmoid colon is most commonly involved.
* It is a result of a diet deficient in fiber
* Most cases of sigmoid diverticulosis are asymptomatic,
* **Complications**
1. Infection (diverticulitis) left-lower-quadrant abdominal pain (left-sided appendicitis).
2. Intestinal obstruction
3. Fistulas occur most commonly between the sigmoid colon and the urinary bladder.
4. Hemorrhage may occur as a result of erosion of blood vessels in the wall of the diverticulum,

**Malabsorption Syndrome*** There is increased fecal excretion of fat (steatorrhea) and the systemic effects of deficiency of vitamins, minerals, protein and carbohydrates.
* Steatorrhea is passage of soft, yellowish, greasy stools containing an increased amount of fat.
* Fat excretion exceeding 6 g/d is demonstrated in a 72-hour stool sample.
* ***Malabosortion affect many organs***
* Hematopiotic system, …………anemia and bleeding
* Musculoskeletal system, ……………osteopenia
* Endocrine system, …………………….amenorrhea, infertility, hyperparathyridism
* Skin, ………………………………………….purpura dermatitis hyperkeratosis
* Nervous system, ………………………neuropathy

***Celiac disease**** immune reaction to gliadin fraction of the wheat protein gluten
* Usually diagnosed in childhood – mid adult.
* 80–90% of patients have the histocompatibility antigen human leukocyte antigen (HLA)-B8 or HLA-DR3.
* Patients have raised antibodies to gluten and IgA antiendomysial autoantibodies
* Celiac disease is associated with dermatitis herpetiformis
* ***Clinical features***
* Infants : Failure to thrive, diarrhea.
* Adults : Diarrhea, flatulence, weight loss and fatigue.
* ***Histology***
* Mucosa is flattened with marked villous atrophy.
* Crypts are elongated and hyperplastic.
* Lamina propria shows increase in chronic inflammatory cells.
* **Diagnosis**
1. Clinical documentations of malabsorption.
2. Small intestine biopsy to demonstrate villous atrophy
3. Improvement of symptom and mucosal histology on gluten withdrawal from diet.
* **Complications**
* 10 to 15% risk of developing GI lymphoma.

***Tropical Sprue (post-infectious sprue)**** An acquired disease that is commonly seen in the Caribbean, Far East, and India.
* It is thought to result from chronic bacterial infection of the small intestine because treatment with broad-spectrum antibiotics is often successful.
* Tropical sprue occurs in adults and is characterized by a severe malabsorption syndrome in which folic acid and vit. B12 deficiency is often a dominant feature……… megaloblastic changes
* ***Histology***
* Jejunal biopsy shows villous atrophy that is usually partial.
* Total villous atrophy is rare.
* Unlike celiac disease, injury of small intestine occur at all levels.

**Idiopathic Inflammatory Bowel Disease*** Although their causes are still not clear, the two diseases probably have an immunologic hypersensitivity basis.

**Crohn's disease*** is a chronic inflammatory disorder that most commonly affects the ileum and colon but has the potential to involve any part of the gastrointestinal tract from the mouth to the anus.
* **Etiology:**
* The cause of Crohn's disease is unknown. Antibodies against intestinal epithelial cells have been identified in the serum and lymphocytes of patients with Crohn's disease
* **Clinical Features**
* Any age but has its highest incidence in young adults
* Extremely variable. In Acute phase: fever, diarrhea, and right lower quadrant pain may mimic acute appendicitis. In Chronic disease : remissions and relapses over a long period of time. Thickening of the intestine may produce an ill-defined mass in the abdomen.
* **Sites of Involvement:**
* Any part of the GIT from the mouth to the anus. Involve ileum in 30% and colon in 20%. Most commonly involve terminal ileum. Commonly (75%) have perianal lesions such as abscesses, fistulas, and skin tags.
* **Gross Appearance:**
* Involvement is typically segmental, with skip areas of normal intestine between areas of involved bowel.
* Marked fibrosis causing luminal narrowing with intestinal obstruction.
* MUCOSA: longitudinal serpiginous ulcers separated by irregular islands of edematous mucosa. This results in the typical cobblestone effect.
* Fissures (deep and narrow ulcers that look like stabs with a knife that penetrate deeply into the wall of the affected intestine)
* fistulas (communications with other viscera).
* FAT : In involved ileal segments, the mesenteric fat creeps from the mesentery to surround the bowel wall (creeping fat)
* **Microscopic Features**
* Crohn's disease is characterized by distortion of mucosal crypt architecture, transmural inflammation, and the presence of epithelioid granulomas. granulomas are present in about 60% of patients.
* Fissure-ulcers and fistulas can be seen microscopically.
* **Complications**
1. intestinal obstruction
2. fistula formation between involved loops of bowel and adjacent viscera. Fistulas between the ileum and the colon result in malabsorption as a result of colonization of the ileum with colonic bacteria; Enterovesical fistulas lead to urinary infections and passage of gas and feces with urine. Enterovaginal fistulas produce a fecal vaginal discharge.
3. Malabsorption syndrome may also follow disease in the terminal ileum, in which there may be failure of absorption of vitamin B12 and bile acids, resulting in megaloblastic anemia and fat malabsorption. Iron deficiency anemia may occur as a result of chronic occult bleeding, and protein-losing enteropathy as a result of loss of protein from the inflamed mucosa.
4. Extraintestinal manifestations are common ( arthritis and uveitis).
5. Slight increased risk of development of carcinoma of the colon—much less than in ulcerative colitis.

**Ulcerative Colitis**Ulcerative colitis is an inflammatory disease of uncertain cause. It has a chronic course characterized by remissions and relapses.common in the 20- to 30-year age group but may occur at any age. **Etiology**The cause is unknown; Antibodies that cross-react with intestinal epithelial cells and certain serotypes of *Escherichia coli* have been demonstrated in the serum of some patients with ulcerative colitis. **Clinical Features*** In the acute phase and during relapse, the patient has fever, leukocytosis, lower abdominal pain, and diarrhea with blood and mucus in the stool.
* The disease usually has a chronic course, with remissions and exacerbations; in some cases, the patient has chronic continuous disease with mild diarrhea and bleeding.

**Diagnosis*** Mucosal biopsies taken at endoscopy are useful in diagnosis. The presence of crypt atrophy, distortion of crypt architecture, and an increased number of lymphocytes and plasma cells in the lamina propria are helpful in differentiating ulcerative colitis from other causes of acute colitis. However, these mucosal changes can be seen in both ulcerative colitis and Crohn's disease .
* The only finding on mucosal biopsy that reliably differentiates ulcerative colitis and Crohn's disease is the presence of noncaseating epithelioid granulomas in the latter

**Sites of Involvement*** Ulcerative colitis is a disease of the rectum, which is involved in almost all cases and in some patients remains the only site of disease, and the colon.
* The disease extends proximally from the rectum in a continuous manner without skip areas.
* The ileum is not involved as a rule; 10% of cases show mild nonspecific mucosal inflammation for a few centimeters proximal to the ileocecal valve (backwash ileitis).

**Gross Appearance*** involves mainly the mucosa. Even in severe disease, the external appearance of the affected colon shows nothing other than mild hyperemia.
* The mucosal surface shows diffuse hyperemia with numerous superficial ulcerations in the acute phase. The rough, red, velvety appearance on colonoscopy is characteristic but not specific
* The regenerated or nonulcerated mucosa may appear polypoid (inflammatory pseudopolyps) in contrast with the atrophic areas or ulcers.

**Microscopic Appearance (active and chronic)*** The inflammation is usually restricted to the mucosa.
* In the active phase, the mucosa shows marked inflammation with neutrophils, lymphocytes, and plasma cells. Neutrophils are present in both lamina propria and in glands (crypt abscesses).
* In the chronic phase, the crypts are decreased in number (crypt atrophy) and show distorted architecture due to abnormal branching .
* Active inflammation correlates well with the severity of symptoms.

**Complications*** Acute phase.
1. Severe bleeding
2. Toxic megacolon ( dilation of the colon, with functional obstruction
* Chronic ulcerative colitis
* increased risk of developing colon carcinoma.
* The presence of high-grade dysplasia in a mucosal biopsy imposes a high risk of cancer and is an indication for colectomy.
* Extraintestinal manifestations
* occur more commonly in ulcerative colitis than in Crohn's disease.
* include ***arthritis***, uveitis, skin lesions (a necrotic skin lesion in the extremities known as pyoderma gangrenosum is typical), and sclerosing pericholangitis (fibrosis around bile ducts), leading to obstructive jaundice.

**Tumors of the intestines*****Polyps**** **Polyp** is a mucosal growth that protrude into the lumen of gut. It could be sessile or pedunculated
* Polyps may be formed as the result of abnormal mucosal maturation, inflammation, or as epithelial proliferation with dysplasia
* **Polyposis** is multiple polyps.
* **Types**
1. ***Non-neoplastic polyps***
2. Hyperplastic polyps
3. Hamartomatous polyps (Juvenile & Peutz-Jeghers polyps)
4. Inflammatory polyps
5. Lymphoid polyp
6. ***Neoplastic polyps***
7. Adenoma

***Non-neoplastic polyps*****Hyperplastic Polyp*** Asymtomatic
* > 50% are located in the rectosigmoid
* well-formed glands and crypts lined by differentiated goblet or absorptive cells.

**Hamartomatous polyps** Juvenile Polyps (retention polyp)* Developmental malformations affecting the glands and lamina propria
* Commonly occur in children under 5 years old in the rectum.
* In adult called retention polyp.
* Juvenile polyposis syndrome. multiple hamartomatous polyps throughout the GI tract.

Peutz-Jehgers syndrome* Rare, autosomal dominant.
* Uncommon hamartomatous polyps accompanied by mucosal and cutaneous pigmentation around the lips, oral mucosa, face and genitalia.
* Polyps tend to be large and pedunculated.
* Have an increased risk of developing carcinoma of the pancreas, breast, lung, ovary and uterus.

**Inflammatory Polyps*** Occur in patients with longstanding IBD, especially in chronic ulcerative colitis.
* Usually multiple.
* Represent an exuberant reparative response to longstanding mucosal injury called pseudopolyps

**Neoplastic Polyps (Adenomas) [ *Adenomatous Polyp]**** Occur mainly in large bowel.
* Can be Sporadic or familial
* Vary from small pedunculated to large sessile
* Epithelium proliferation and *dysplastia*
* Divided into:
1. Tubular adenoma: has less than 25% villous architecture
2. Villous adenoma: villous architecture over 50%
3. Tubulovillous adenoma: villous architecture between 25 and 50%.

1] ***Tubular adenoma**** Represents 75% of all neoplastic polyps.
* 75 % occur in the distal colon and rectum.
* Size: few millimeters (sessile) to many centimeters (have stalk).
* Severe dysplasia and invasive carcinoma may supervene.

***2] Villous Adenoma**** The least common, largest and most ominous of epithelial polyps.
* Present with rectal bleeding or anemia, large ones may secrete copious amounts of mucoid material rich in protein.
* 75% located in rectosigmoid area.

**3] *Tubulovillous adenoma**** Intermmediate in size, frequency of having a stalk, degree of dysplasia and malignant potential between tubular and villous adenomas.

**Relationship of Neoplastic Polyps to Carcinoma*** Adenoma to carcinoma sequence is documented by several observations and genetic alterations.
* The probability of carcinoma occuring in a neoplastic polyp is related to:

 1. The size of the polyp. 2. The relative proportion of its villous features. 3. The presence of significant cytologic atypia (dysplasia) in the neoplastic cells.**Familial Polyposis Syndrome*** Patients have genetic tendencies to develop neoplastic polyps, most often autosomal dominant.
1. ***Familial polyposis coli (FPC)***
* Genetic defect ch5 q21.
* Innumerable neoplastic polyps in the colon (500 to 2500)
* Polyps are also found elsewhere in alimentary tract
* Most polyps are tubular adenomas
* The risk of colorectal cancer is 100% by midlife.
1. ***Gardener’s syndrome***
* Polyposis coli, multiple osteomas, epidermal cysts, and fibromatosis.
1. ***Turcot syndrome***
* Polyposis coli, glioma and fibromatosis

***Malignant Tumors of Large Intestine*** **Adenocarcinoma** * Constitutes 98% of all cancers in the large intestine.
* Causes 15% of all cancer-related death in the USA.

**Predisposing factors:** 1. Inflammatory bowel diseases,
2. polyposis syndrome.
3. *hereditary nonpolyposis colorectal cancer syndrome* (HNPCC)
4. Diet: Low content of unabsorpable vegetable fibre, High fat content, and Reduced intake of vit A, C & E.

**Carcinogenesis*** Two pathogenetically distinct pathways for the development of colon cancer, both seem to result from accumulation of multiple mutations
1. **The APC / B-*catenin pathway ( 85%)***
* chromosomal instability that results in stepwise accumulation of mutations in a series of oncogenes and tumor suppressor genes.
1. **The *DNA mismatch repair genes pathway (***15%) ***:***
* There is accumulation of mutations (as in the *APC/B-catenin schema)*
* Inherited mutations in one of five DNA mismatch repair genes (MSH2, MSH6, MLH1, PMS1, AND PMS2) give rise to the hereditary non polyposis colon carcinoma (HNPCC)
* **MLH1** gene is the one most commonly involved in sporadic colon carcinomas
* *Microsatellite instability* (MSI) is the molecular signature of defective DNA mismatch repair

***Morphology**** 70% of colorectal carcinomas are in the rectum, rectosigmoid and sigmoid colon.
* Left-sided carcinomas tend to be annular, encircling lesions with early symptoms of obstruction.
* Right-sided carcinomas tend to grow as polypoid, fungating masses, obstruction is uncommon.
* Mucinous adenocarcinoma secret abundant mucin that may dissect through cleavage planes in the wall.

***Clinical features**** Left-sided lesions tend to present earlier but also have a more infiltrative growth pattern and a poorer prognosis.
* Right-sided lesions tend to present with weakness, malaise, weight loss, unexplained anemia (secondary to early bleeding).
* Serum levels of carcinoembryonic antigen (CEA) are related to tumor size and extent of spread. They are helpful in monitoring for recurrence of tumor after resection.
* Duke classification is used for staging

**Small Intestinal Neoplasms*** In descending order of frequency: carcinoid, adenocarcinomas, lymphomas and leiomyosarcomas.
* ***Carcinoid Tumors***
* Neoplasms arising from endocrine cells Kulchitsky or enterochromaffin cells found along the length of GIT mucosa. Cells have an affinity for silver salts.
* 60 to 80% in appendix and terminal ileum, and 10 to 20% in rectum.
* Tumor cells arranged in trabecular, insular, glandular or undifferentiated patterns are monotonously similar to each other with regular round nuclei
* Ultrastructral features: neurosecretory electron dense bodies in the cytoplasm

***Clinical features**** Asymptomatic
* May cause obstruction, intussusception or bleeding.
* May elaborate hormones: Zollinger-Ellison, Cushing’s carcinoid
* 5 years survival rate is 90%, small bowel Carcinoid with liver metastasis the 5 years survival rate is better than 50%
* ***Carcinoid syndrome***
* 1% of carcinoid tumor & in 20% of those of widespread metastasis
* Paroxymal flushing, episodes of asthma-like wheezing, right-sided heart failure, attacks of watery diarrhea, abdominal pain, edema and pellagra-like lesions of the skin and oral mucosa.
* The principal chemical mediator is serotonin
* The syndrome is classically associated with ileal carcinoids with hepatic metastases.

**Lymphoma*** Most often low-grade lymphomas arising in mucosal-associated lymphoid tissue (MALT) lymphoma or high-grade non-Hodgkin's lymphomas of B cell type.
* May occur in any part of the intestine;
* the ileocecal region is a favored site for Burkitt's lymphoma.

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