Tumors Small & Large Intestine

**Non-neoplastic Polyps**
- Hyperplastic polyps
- Hamartomatous polyps
  - Juvenile polyps/Retention polyps
  - Peutz-Jeghers polyps
- Inflammatory polyps
- Lymphoid polyps

**Neoplastic Epithelial Lesions**

**Benign**
- Adenoma

**Malignant**
- Adenocarcinoma
- Carcinoid tumor
- Anal zone carcinoma
  *Malignant Melanoma

**Mesenchymal Lesions**
- Gastrointestinal stromal tumor (GIST)
- Other benign lesions • Lipoma • Neuroma • Angioma
- Kaposi sarcoma

**Lymphoma**

**Metastatic**
NON-NEOPLASTIC POLYPS

Hyperplastic Polyps

- Small (usually <5 mm in diameter) epithelial polyps hemispheric, smooth on crests of mucosal folds
- Singly or multiple, over half found in rectosigmoid colon
- Well-formed glands and crypts lined by non-neoplastic epithelial cells, most show differentiation into mature goblet or absorptive cells.
- Delayed shedding, in folding of crowded epithelial cells and fusion of crypts creates a serrated appearance.
- No malignant potential
Hamartomatous Polyps

A-Juvenile polyps

- children younger than age 5.
- Sporadic polyps in colon of adults - retention polyps
- 80% occur in rectum, may be scattered throughout colon
- Juvenile polyps are 1 to 3 cm in diameter, rounded, smooth or slightly lobulated with stalks up to 2 cm
- Retention polyps smaller (<1 cm diameter).

- Autosomal dominant juvenile polyposis syndrome, multiple (3 to 100) juvenile polyps in gastrointestinal tract, carry risk of adenocarcinoma
- Mutations in SMAD4 account for some cases of juvenile polyposis syndrome.
Juvenile Rectal Polyp
B-Peutz-Jeghers Polyps

- Singly or multiple in Peutz-Jeghers syndrome

- Autosomal dominant syndrome characterized by multiple hamartomatous polyps scattered throughout entire gastrointestinal tract and melanotic mucosal and cutaneous pigmentation around lips, oral mucosa, face, genitalia, and palmar surfaces of hands.

- Histologically, arborizing network of connective tissue and smooth muscle extends into polyp & surrounds glands

- Patient with syndrome have increase risk of developing carcinomas of colon, pancreas, breast, lung, ovaries, uterus, and testicles.

- Underlying genetic defect is mutation of gene STK11
P-J polyps
Part 4
ADENOMATOUS POLYPS (ADENOMAS)

- Intraepithelial neoplasm
- 50% of adults in the West by the age of 50
- Male and female equally affected
- Risk for colorectal carcinoma
ADENOMATOUS POLYPS

Three subtypes of adenomas

- **Tubular**
  
  Greater than 75% tubular, most are small and pedunculated

- **Villous**
  
  Greater than 50% villous tend to large and sessile

- **Tubulovillous**
  
  25-50% villous

All adenomas arise as result of epithelial proliferation

Precursor lesion for adenocarcinomas
ADENOMATOUS POLYPS (ADENOMAS)

Malignant risk correlated with three independent features

- Polyp Size
- Histologic architecture
- Severity of epithelial dysplasia

*Cancer is rare in tubular adenomas smaller than 1cm in diameter

*Risk of cancer is high 40% in sessile villous adenomas more than 4cm in diameter

*Severe dysplasia when present is often in villous areas
TUBULAR ADENOMAS

- Site: 90% in colon
- Gross: Single or multiple, Mostly less than 1 cm, smaller are sessile, larger one stalked, uncommonly exceed 2.5 cm
- Histologically: Stalk is fibromuscular and vascular derived from submucosa, lining epithelium is neoplastic columnar.
- Low to high grade dysplasia, Intramucosal carcinomas - carcinoma limited to mucosa
- S/S: asymptomatic or bleeding, change in bowel habits or intussusception
Adenomatous polyps
Tubular Adenoma
VILLOUS ADENOMA

- **Age:** older patients
- **Site:** rectum or rectosigmoid
- **Gross:** up to 10 cm in size, single mass that may grow to encircle bowel completely, Velvety to Papillary villous projection 1 to 3 cm above surrounding normal mucosa, attached by wide base, 10% are pedunculated
- **L/M:** villous projections, papillary growth covered by dysplastic columnar epithelium, invasion occur direct to submucosa as they have no stalk
- **S/S:** fluid and electrolyte depletion
- **Treatment:** local excision or APR depending on size of tumor
Villous Adenoma
Familial Adenomatous Polyposis

- Autosomal dominant
- **Gene:** mutations of APC gene localized to 5q21
- Variants:
  - Gardner syndrome
  - Turcot syndrome
- **Age:** 2nd decade of life
- **Gross:** 500 to 2500 colonic adenomas, minimum of 100 adenomas are necessary to make diagnosis of classic FAP
- May involve other parts of GIT: stomach and small bowel, ampulla of Vater
- Majority are tubular adenomas
- Untreated cases develop Carcinoma
- Early detection and prophylactic colectomy recommended
Familial Adenomatous Polyposis FAP
Gardner syndrome

Classic FAP combined with multiple osteomas, epidermal cysts, desmoid tumour, thyroid tumours, dental abnormalities

Turcot syndrome

FAP and tumours of CNS- Medulloblastoma, Gioblastomas
Hereditary Nonpolyposis Colorectal Cancer (HNPCC)

Autosomal dominant familial syndrome

Risk of colorectal cancer and cancer of endometrium, stomach, ovary, brain, skin

Mutations in DNA repair genes MSH2, MLH1
Colorectal Carcinogenesis
**Adenoma- carcinoma sequence** postulated that loss of one normal copy of tumor suppressor gatekeeper gene *APC* occurs early. Indeed, individuals may be born with one mutant allele of APC, rendering them extremely likely to develop colon cancer. This is "first hit," according to Knudsen's hypothesis loss of normal copy of *APC* gene follows ("second hit"). Mutations of oncogene *K-RAS* seem to occur next. Additional mutations or losses of heterozygosity inactivate tumor suppressor gene *p53* and *SMAD2* and *SMAD4* leading finally to emergence of carcinoma, in which additional mutations occur.
COLORECTAL CARCINOMA

Epidemiology:
- **Age:** peak age 60 to 70yrs, **Sex:** ♂=♀
- In young patient preexisting U.C or Polyposis syndrome

Etiology:
- Dietary factors, physical inactivity and obesity

Dietary Factors predisposing to higher incidence of cancer includes
- low content of vegetable fibres,
- high contents of refined carbohydrates
- intake of high fat diet
- decrease intake of protective micronutrients
- Protective effect of NSAID
CARCINOMA

Gross:

- Proximal colon; polypoid exophytic masses
- Distal colon; annular, napkin ring constriction of bowel wall margins are beaded center is ulcerated
- Infiltrative; palpable as firm mass
- Mucinous Ca—gelatinous or glaring
Adenocarcinoma colon
HISTOPATHOLOGY

- Begin as adenocarcinoma-in-situ lesions
- Well, Moderately, Poorly, Un-differentiated
  Mucin variable, extra or intracellular mucin
- Cells- Columnar, Mucin containing, Signet ring, Neuroendocrine features
- Inflammatory and desmoplastic reaction
- Invasion of all layers of bowel
- Pericolic extension, perineural and lympho vascular invasion
Adenocarcinoma Colon
Colorectal Carcinoma

Clinical presentation:

- Change in bowel habit, rectal bleeding, anemia, vague abdominal pain
- Intestinal obstruction—left sided tumor
- Perforation
- **Serum CEA**—detected in 72-97% cases of colorectal Ca, disappears after tumor resection, reappears after recurrence or metastasis
- CEA used for monitoring therapy
- Can be detected in tissues as well
- Detection of mutations of ras and APC genes in stool
SPREAD AND METASTASIS

- **Most common sites of colonic mets:** Regional lymph nodes and liver
- **Minimum number of nodes recovered from surgical specimen of colorectal Ca should be 14-15**
- Pericolic tumor deposits
- **Other metastatic site:** peritoneum, lung, ovaries rare CNS, bone, testis, uterus and oral cavity
PROGNOSIS

- 5 yr survival rate after curative resection—40-60%
- Local recurrence and regional lymph node mets → 90% of failure cases
GRADING OF CARCINOMA

GRADING:

- I  Well differentiated
- II Moderately differentiated
- III Poorly differentiated
- IV Undifferentiated

Grading should be determined by worst pattern rather than the predominant one.
GRADING & STAGING

- **Dukes staging system—1973:**
  - A: tumor involve wall of bowel only
  - B: tumor extend through wall into peritoneum
  - C1: tumors mets in regional lymph node
  - C2: tumors mets in lymph nodes at point of mesenteric blood vessel
  - D: distant metastases

- **Astler and Coller—1954:**
  - A: limited to mucosa
  - B1: involving muscularis externa but not penetrating it
  - B2: penetrating through muscularis externa
  - C1: confined to bowel wall but with nodal mets
  - C2: penetrating through wall and with nodal mets
TNM Staging/Classification
Colorectal Carcinomas

- **Tis** Carcinoma in situ (high-grade dysplasia) or intramucosal carcinoma (lamina propria invasion)
- **T1** Tumor invades submucosa
- **T2** invades into muscularis propria but not penetrating through it
- **T3** invades through the muscularis propria into subserosa
- **T4** Tumor invades adjacent organs or visceral peritoneum
- **Nx** lymph nodes cannot be assessed
- **N0** No regional lymph node metastasis
- **N1** Metastasis in 1 to 3 regional lymph nodes
- **N2** Metastasis in 4 or more regional lymph nodes
- **Mx** Distant metastasis cannot be assessed
- **M0** No distant metastasis
- **M1** Distant metastasis or seeding of abdominal organs
Carcinoid Tumors

- Low grade neoplasm originating from diffuse neuroendocrine system outside of pancreas and thyroid C cells.
- Adults, Located in ileum mostly

GROSS:
- Intact mucosa, tumor infiltrating submucosa and extending to muscularis externa.
- Brightly yellow color

MICROSCOPY:
- Solid nests of monotonous population of cells having small round nuclei scant to moderate granular cytoplasm fine nucleoli.
- Peripheral palisading common, scanty mitotic figures, lymphatic and neural invasion common.
- Microscopic types: insular, trabecular, glandular, undifferentiated, mixed.
CARCINOID TUMORS

- HISTOCHEMISTRY - argentafin argyrophilic positive, negative for mucin
- ULTRASTRUCTURE - dense core secretory granules
- IMMUNO - CK7, CK 20 +ve, pan-endocrine markers +ve
- Blood and urine contains high levels of 5-HT, and 5-hydroxyindoleacetic acid (5-HIAA)
- SPREAD AND METASTASIS - low grade, slow growth rate, highly invasive, metastasis to regional lymph nodes and liver.
- CARCINOID SYNDROME - Develops as they secrete 5-HT, 5-HIIA, histamine, bradykinin, and prostaglandins
- Features of Carcinoid Syndrome: Cyanosis of face, chest, intermittent hypertension, palpitations, watery stools.
GASTROINTESTINAL LYMPHOMA

- About 1% to 4% of all gastrointestinal malignancies are lymphomas.

- By definition, primary gastrointestinal lymphomas exhibit no evidence of liver, spleen, mediastinal lymph node, or bone marrow involvement at the time of diagnosis—regional lymph node involvement may be present.

- Primary gastrointestinal lymphomas usually arise as sporadic neoplasms but also occur more frequently in certain patient populations:
  1. Chronic gastritis caused by H. pylori (MALT Lymphoma)
  2. chronic spruelike syndromes (T-Cell Lymphoma),
  3. natives of the Mediterranean region (IPSID)
  4. congenital immunodeficiency states,
  5. infection with human immunodeficiency virus, and
  6. following organ transplantation with immunosuppression.
MALIGNANT LYMPHOMA AND RELATED DISORDERS

T-CELL LYMPHOMA (High Grade)

B-CELL LYMPHOMA (High or Low Grade)
  - MALT-lymphoma
  - Bussrkitt Lymphoma
  - Diffuse large B-cell lymphoma

IMMUNOPROLIFERATIVE SMALL INTESTINAL DISEASE (IPSID)

- Common among Arabs, Jews, blacks of South Africa.
- Associated with diarrhea and malabsorption
- Children and young adults
- Intestinal wall shows heavy lymphoplasmacytic cell infiltrate of slightly immature appearing plasma cells synthesize abnormal monoclonal alpha heavy chains
GIT - LYMPHOMAS

Morphology

- Early lesions plaque-like expansions of mucosa and submucosa.
- Diffusely infiltrating lesions, mural thickening, with effacement of overlying mucosal folds & focal ulceration
- May be polypoid or form large, fungating, ulcerated masses.

- Atypical lymphoid cells populate superficial or glandular epithelium (lymphoepithelial lesion).
- Later the mucosa, submucosa, and even muscle wall are replaced by a monotonous infiltrate of malignant cells.
METASTATIC TUMORS

- Disk like areas with central ulceration
- Primary: Melanoma, Ca lung
- Prostatic Ca mets may simulate primary rectal Ca
- Mesothelioma as multiple colonic polyps