Tumors of the Intestines

Non-Neoplastic Polyps
  - Hyperplastic, Hamartomatous, Juvenile, Peutz-Jeghers, Inflammatory and Lymphoid Polyps

Neoplastic Epithelial Polyps
  - Benign Polyps
    - Adenoma
      - Tubular Adenoma
      - Villous Adenoma
      - Tubulovillous Adenoma
    - sessile Serrated Adenomas
  - Malignant Lesion
    - Adenocarcinoma
    - Squamous Cells Carcinoma of the Anus

Other Tumors
  - Gastrointestinal Stomal Tumor (GIST)
  - Carcinoid Tumor
  - Lymphoma
<table>
<thead>
<tr>
<th>Diseases</th>
<th>Epidemiology</th>
<th>Morphology</th>
<th>Microscopic</th>
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</thead>
</table>
| **Hyperplastic Polyps** | • Most are sporadic  
  • Increase in age  
  • 90% happens in the Colon  
  • Half of people over the age of 60 are having polyps | • Small  
  • Nipple like  
  • Hemispherical  
  • Smooth protrusion of Mucosa into the lumen  
  • Can be either  
  o Solitary  
    ▪ Have no malignant potential  
  o Multiple /Hyperplastic Polyposis  
    ▪ Hyperplastic Serrated Adenomas have malignant potential; may evolve into Colorectal Carcinoma | • Abundant crypts lined by  
  o Well-differentiated Goblet cells  
  o Absorptive cells  
  • Separated by scant Lamina Propria |
| **Juvenile Polyps (children) Retention Polyps (adult)** | • **Incidence**  
  o Juvenile Polyps  
    ▪ Children <5 years old  
  o Retention Polyps  
    ▪ Adults at any age  
  • Hamartomatous proliferations; no malignant transformation | • Rounded  
  • Smooth  
  • Slightly lobulated  
  • Sometimes Pedunculated  
  • Size  
  o Children – large  
  o Adult – smaller | • Hamartomatous proliferation of mainly the Lamina Propria  
  • Enclosing a wide spaced and dialted Cystic gland  
  • Not a premalignant lesion |
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<tr>
<td>**Familial Polyposis</td>
<td>• <strong>Autosomal Dominant Disorder</strong></td>
<td>• 500-2500 colonic Adenomas</td>
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<tr>
<td>Syndrome</td>
<td>o Defect on APC gene on chromosome 5q21</td>
<td>• Most polyps are Tubular Adenoma</td>
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<td></td>
<td>• High risk in developing Colorectal Carcinoma</td>
<td>• Occasionally may present with Villous Adenoma</td>
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<td></td>
<td>• Minimum of 100 polyps for diagnosis</td>
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<td></td>
<td>• <strong>Gardner and Turcot Syndrome</strong></td>
<td>• May affect other part of GIT especially the Duodenum (Duodenal Adenoma)</td>
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<td></td>
<td>o Just a variant of FPS</td>
<td>• May have signs of Haemorrhage and may pass through the faeces</td>
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<td></td>
<td>o Have occurrence of extraintestinal tumors</td>
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<td></td>
<td>▪ Osteomas</td>
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<td>▪ Fibromas</td>
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<td>▪ Gliomas</td>
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<td>• <strong>Autosomal Dominant Disorder</strong></td>
<td>• Most polyps are Tubular Adenoma</td>
</tr>
<tr>
<td></td>
<td>o Defect on LKB1 gene encoding for Threonine Kinase</td>
<td>• Occasionally may present with Villous Adenoma</td>
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<td></td>
<td>• <strong>Characterized by</strong></td>
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<tr>
<td></td>
<td>o Mucocutaneous lesion</td>
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<td>▪ Hyperpigmented macules on</td>
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<td>• Lips</td>
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<td>• Oral mucosa</td>
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<td>o Benign hamartomatous lesion on the GIT</td>
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<td><strong>Cowden Syndrome</strong></td>
<td>• <strong>Autosomal Dominant Disorder</strong></td>
<td>• Most polyps are Tubular Adenoma</td>
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<tr>
<td></td>
<td>o Defect in PTEN (Phosphatase and Tensin Homologue) Tumor Suppressor gene</td>
<td>• Occasionally may present with Villous Adenoma</td>
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<tr>
<td></td>
<td>o Encodes for Phosphatase</td>
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<td></td>
<td>• <strong>Characterized by</strong></td>
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<tr>
<td></td>
<td>o Hamartomatous polyps of GIT</td>
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<td></td>
<td>o Increase risk of developing Neoplasms in</td>
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<td></td>
<td>▪ Thyroid</td>
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<td></td>
<td>▪ Breast</td>
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<td>▪ Uterus</td>
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<tr>
<td></td>
<td>▪ Skin</td>
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<td></td>
<td>▷ Hyperpigmented macules on</td>
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<td><strong>Premalignant Polyps</strong></td>
<td>▷ Hyperpigmented macules on</td>
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<td>▷ Lips</td>
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<td></td>
<td>▷ Oral mucosa</td>
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<td></td>
<td>▷ Benign hamartomatous lesion on the GIT</td>
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<tr>
<td>Diseases</td>
<td>Epidemiology</td>
<td>Gross</td>
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<td>-----------------------</td>
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<tr>
<td><strong>Tubular Adenomas</strong></td>
<td>• Incidence</td>
<td>• May arise anywhere in the colon but commonly at the Rectosigmoid</td>
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<tr>
<td></td>
<td>o Before the age of 40</td>
<td>junction</td>
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<tr>
<td></td>
<td>• 20-30%</td>
<td>• Can be either</td>
</tr>
<tr>
<td></td>
<td>o After the age of 60</td>
<td>o Small Adenomas</td>
</tr>
<tr>
<td></td>
<td>• 40-50%</td>
<td>o Larger Adenomas</td>
</tr>
<tr>
<td></td>
<td>• Male and female are equally affected</td>
<td>• Pedunculated with Raspberry like head</td>
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<td></td>
<td>• Increase the risk of developing Colonic Carcinoma</td>
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<tr>
<td></td>
<td>Clinical Manifestations</td>
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<tr>
<td></td>
<td>• Sized of Adenomas</td>
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<tr>
<td></td>
<td>o Smaller remain asymptomatic</td>
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<td></td>
<td>o Larger may cause severe bleeding leading to</td>
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<tr>
<td></td>
<td>• Iron Deficiency Anemia</td>
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<td></td>
<td>• Occult and overt Rectal bleeding</td>
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<td></td>
<td>• Villous Adenoma is often symptomatic</td>
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<tr>
<td></td>
<td>o Occult and overt Rectal bleeding</td>
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<td>o Secrete mucoid material rich in K+ and protein leading to</td>
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<td></td>
<td>• Hypoproteinaemia</td>
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<td></td>
<td>• Hypokalaemia</td>
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<td></td>
<td>• All mandatory to be excised</td>
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<td></td>
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<tr>
<td></td>
<td>o Rectum</td>
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<tr>
<td></td>
<td>o Rectosigmoid junction</td>
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</tr>
<tr>
<td></td>
<td>• The polyps tend to be larger in size</td>
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<tr>
<td></td>
<td>• Generally can be either</td>
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<tr>
<td></td>
<td>o Sessile</td>
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<td></td>
<td>o Cauliflower like</td>
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<td></td>
<td>o Velvety</td>
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<tr>
<td><strong>Tubulovillous</strong></td>
<td>• Can be either</td>
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<tr>
<td>Adenomas</td>
<td>o Pedunculated</td>
<td></td>
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<tr>
<td></td>
<td>o Sessile</td>
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</tr>
<tr>
<td></td>
<td>o Or both</td>
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## Malignant Tumor of the Intestine

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<th>Microscopic</th>
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</table>
| Colorectal Carcinoma      | • 98% are Adenocarcinoma  
  - Anus usually Squamous Cell Carcinoma  
  • Peak incidence during  
    - 60-70 years old  
    - Below 50 years old <20%  
  • Affecting male more than female  
  • If develop during early life, should suspect  
    - Familial Polyposis Syndrome  
    - Ulcerative Colitis  
  • Multifactorial Disorder  
    - Genetic  
      - Adenoma-carcinoma Pathway  
        - Familial  
          - APC inactivation  
        - Sporadic  
          - Inactivation of multiple genes  
      - Microsatellite Instability Pathway  
        - Familial  
          - Inactivation of DNA repair gene  
            - MLH1  
            - MSH2  
        - Sporadic  
          - Inactivation of DNA repair gene  
            - MLH1  
            - MSH2  
    - Environmental (Dietary)  
      - Low content fiber diet  
      - High content refined carbohydrate diet  
      - High fat content diet  
      - Decreased intake of protective micronutrients  
      - Vitamin A, C and E  
|                           | • Sites  
  - 25% - Caecum and Asc  
  - 25% - Dsc and Prox Sigmoid  
  - 25% - Dist Sigmoid and Rectum  
  - 25% - scattered elsewhere  
  • Often lesion appears solitary, frequently destroy the earlier Adenomatous lesion  
  • If multiple, deform the colonic structure  
  • Morphological patterns  
    - If happen in Proximal Colon  
      - Polypoid  
      - Exophytic growth  
      - Extend along the wall of Caecum and Asc Colon  
    - If happen in Distal Colon  
      - Annular (ring shape)  
      - Encircling the lesion  
      - Napkin-ring constrictions  
      - Narrowing of the lumen  
      - Both patterns may infiltrate the whole wall of intestine and leading to firm masses on the Serosa  
|                           | • Most of the cases are Adenocarcinoma  
  • Ranging from well-differentiated to poorly differentiated  
  • All are Anaplastic  
  • Most produce Mucin  
    - Since Mucin is secreted inside the wall of the Intestine rather into the Lumen, the secretion may “dissect” through the wall and enable invasion  

### Sites

- 25% - Caecum and Asc
- 25% - Dsc and Prox Sigmoid
- 25% - Dist Sigmoid and Rectum
- 25% - scattered elsewhere

### Gross

- Often lesion appears solitary, frequently destroy the earlier Adenomatous lesion
- If multiple, deform the colonic structure
- Morphological patterns
  - If happen in Proximal Colon
    - Polypoid
    - Exophytic growth
    - Extend along the wall of Caecum and Asc Colon
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    - Napkin-ring constrictions
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    - Both patterns may infiltrate the whole wall of intestine and leading to firm masses on the Serosa

### Clinical Manifestations

- Remain asymptomatic for years
- Pattern
  - If happens at the Proximal Colon
    - Iron Deficiency Anemia
    - Fatigue
    - Weakness
  - If happens at the Distal Colon
    - Occult bleeding
    - Changes in bowel habit
- Crampy pain on the Left Lower Quadrant
- All Colorectal Carcinoma will metastasize to distant tissue, in order of preference
  - Pericolic Lymph Nodes
  - Lungs
  - Bones
  - Serosal membrane of Peritoneum

### Diagnosis

- Screening
  - Digital Rectal examination
  - Fecal testing for occult blood
  - Barium enema
  - Sigmoidoscopy and Colonoscopy
  - Serum markers
    - Carcinembryogenic antigen
    - Non-specific
    - False positive results in
      - Various kind of tumor
        - Lungs, ovary, breast
      - Non-cancerous condition
        - Liver cirrhosis, UC, pancreatitis

- Diagnostic
  - Biopsy
  - Metastasize study
    - CT scan and X-ray
### Neoplasms of the Small Intestine

- **Adenoma**
- **Adenocarcinoma**

#### Clinical Manifestations

- **Adenomas**
  - Anemia
  - Rarely cause
    - Intussusception
    - Obstruction
  - If happen near to Ampulla of Vater may cause biliary obstruction leading to Jaundice
- **Adenocarcinoma**
  - Cramping pain
  - Nausea
  - Vomiting
  - Weight loss
  - At the time of diagnosis, distant metastasize is common

### Gastrointestinal Stromal Tumors

- Based on Histochemical markers, it is divided into
  - Tumors that show Smooth Muscle differentiation
  - Tumors that show Neural differentiation
    - Often called Gastrointestinal Autonomic Nerve Tumors
  - Tumors with Smooth Muscle/Neural dual differentiation
  - Tumors that lacking are lacking of differentiation toward the two lineages
- GIST commonly occurs at the Stomach
  - But can also be at Small and Large intestine
- Due to genetic disorder
  - Somatic mutation in CD117 gene encodes for Tyrosine Kinase Receptor
  - This enable the receptor to keep on stimulated without binding to the ligand

### Epidemiology

- Less common compared to Colon Ca
- Most of the cases are benign

### Morphology

- Can grow as
  - Napkin-ring encircling pattern
  - Polypoid fungating masses like in the Colon
- Most originate from the Duodenum including the Ampulla of Vater
- A prominent mass arose from the Muscularis layer
- Exophytic growth
- Retained the covering mucosa except at the central ulcerated area
- Can be either
  - Spindle shaped cells for Smooth muscle differentiation
  - Epitheloid as for Neural differentiation
- Area of haemorrhage and ulcer

### Microscopic

- Most of the cases are Adenocarcinoma
- Ranging from well-differentiated to poorly differentiated
- All are Anaplastic
- Most produce Mucin
  - Since Mucin is secreted inside the wall of the Intestine rather into the Lumen, the secretion may “dissect” through the wall and enable invasion
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| Carcinoids of GIT | - No age exempt, peak incidence at the age of 60  
- Derived from the Neuroendocrine cells of the GIT mucosa  
- May release peptide and non-peptide hormone leading to their clinical manifestations  
- Arise from  
  - Pancreas  
  - Peripancreatic tissue  
  - Lungs  
  - Biliary tree  
  - Liver  
  - GIT  
    - Ileum  
    - Rectum  
    - Stomach  
    - Colon  
- Can be further divided depending on  
  - Growth pattern  
    - Trabecular  
    - Glandular  
    - Undifferentiated  
    - Mixed  
  - Hormone produced  
    - Bradykinin  
    - Serotonin  
    - Histamine  
    - Prostaglandin  
  - Site of origin  
    - Foregut  
      - Pancreas  
      - Stomach  
      - Duodenum  
    - Midgut  
      - Jejunum  
      - Ileum  
      - Appendix  
      - Ascending Colon  
    - Hindgut  
      - Transverse Colon  
      - Descending Colon  
      - Rectum  
| Gross | Microscopic |
| - Small  
- Button-like submucosal elevation  
- Intact or ulcerated Mucosa  
- Cut surface is solid yellow tan  
- Can be either  
  - Multiple – gastric and ileum  
  - Solitary – appendix  
- Tumor cells are  
  - Uniform  
  - Monotonous in appearance  
  - Scanty cytoplasm  
  - Nucleus is  
    - Round to oval  
    - Fined stippled chromatin  
  - Forming discrete  
    - Islands  
    - Glands  
    - Cords or  
    - Trabaculae  
- Mitoses is infrequent  
- Cellular atypia is uncommon  
- Presence of membrane bound secretory granules |

**Clinical Manifestations**

- **Cutaneous flushes and cyanosis**  
  - Due to vasomotor disturbances  
- **Diarrhea, abdominal pain, nausea and vomiting**  
  - Due to increase in GIT motility  
- **Cough, dyspnea and wheezing**  
  - Due to Bradykinin liberated to the lung leading to Asthmatic like attack  
- **Nodular liver in metastatic cases**  
- **Zollinger-Ellison syndrome**  
  - Hypersecretion of Gastrin  
- **Systemic fibrosis**  
  - Heart valve stenosis  
  - Peritoneum  
  - Pelvic fibrosis