# Gastrointestinal Tract/Hepatobiliary/Nutrition

## Large bowel and anal malignancies

<table>
<thead>
<tr>
<th>Disease</th>
<th>Pathology, aetiology and epidemiology</th>
<th>Signs and symptoms</th>
<th>Diagnosis, management and prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diverticular disease</td>
<td>Acquired pseudodiverticula outputting of mucosa and submucosa</td>
<td>Clinical features:</td>
<td>Macroscopic</td>
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<tr>
<td></td>
<td>prevalence increases with age, 60% over age 70 years</td>
<td>most patients are asymptomatic</td>
<td>diverticula tend to form in two rows between anti-</td>
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<tr>
<td></td>
<td>sigmoid colon affected in 95% cases; can extend to more proximal in some cases</td>
<td>symptoms: alternating constipation, and diarrhoea,</td>
<td>mesenteric taenia and mesenteric taenia (three separate</td>
</tr>
<tr>
<td></td>
<td>western nations &gt; Asia, Africa, developing countries</td>
<td>mimic IBS intermittent cramping, continuous lower</td>
<td>longitudinal ribbons of smooth muscle on the outside</td>
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<tr>
<td></td>
<td>Aetiology and pathogenesis</td>
<td>abdominal discomfort, diarrhoea, tenses fever</td>
<td>of the ATDS colon</td>
</tr>
<tr>
<td></td>
<td>diet common in western nations</td>
<td>chronic or intermittent blood loss</td>
<td>chronic idiopathic inflammatory bowel disease</td>
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<tr>
<td></td>
<td>low fibre diet; small volume stools; hyper contractility and hyper-segmentation; increased intraluminal</td>
<td>massive haemorrhage</td>
<td>microscopic colitis</td>
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<td>pressure; mucosal herniation</td>
<td></td>
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<td>primary abnormality in the muscular layer of the bowel; increased elastic layer of the muscularis</td>
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<td>propria resulting in a muscular layer that is less pliable</td>
<td>Aetiology and pathogenesis</td>
<td></td>
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<td></td>
<td>leading to shortening of colon, and concertina effect, leading to redundant mucosa and prolapse</td>
<td>Diet common in western nations</td>
<td></td>
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<tr>
<td></td>
<td>diverticula Low fibre diet —&gt; uptake of a protein —&gt; deposition in elastic layer?</td>
<td>low fibre diet; small volume stools; hyper contractility</td>
<td></td>
</tr>
<tr>
<td>Angiodysplasia</td>
<td>Acquired condition characterised by clusters of malformed submucosal and mucosal blood vessels</td>
<td>GI bleeding in elderly recurrent/chronic massive</td>
<td>Macroscopic</td>
</tr>
<tr>
<td></td>
<td>associated with aging, most common after 6th decade</td>
<td>haemorrhage</td>
<td>angiodysplasia</td>
</tr>
<tr>
<td></td>
<td>most often in caecum/right colon (tension is high due to larger diameter)</td>
<td>Microscopically - collection if dilated torsion’ed</td>
<td></td>
</tr>
<tr>
<td></td>
<td>prevalence &lt;1% but is 2nd most common cause of lower GI bleeding in the elderly</td>
<td>vessels</td>
<td></td>
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<td>Pathogenesis intermittent occlusion of veins penetrating muscular propria due to normal distension</td>
<td></td>
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<tr>
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<td>and contraction, leading to focal dilation and tortuosity of overlying submucosal and mucosal vessels</td>
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<td>overtime degenerative changes in the composition and structure of the extracellular matrix of the</td>
<td></td>
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<td></td>
<td>bowel wall with age — contributes to loss of structural integrity</td>
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</tbody>
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| Acute infectious colitis | Inflammation of the colon secondary to an infectious organism
GI infections important cause of morbidity and mortality worldwide
More than 2000 deaths/day among children in developing countries and >10% of all deaths <5 years old worldwide
Many infections transmitted through contaminated food and water
Aetiology
Bacteria — campylobacter, salmonella, shigella, E.coli, clostridia, Yersinia, aeromonas
Pathogenesis
Host defence — gastric acidity, intestinal motility, mucus, intestinal microflora, systemic and local immune mechanisms
Bacterial virulence — adherence, enterotoxin production, cytotoxin production, mucosal invasion, others (evasion of phagocytosis, altering intestinal motility, mucolytic enzymes which disrupt mucus layer etc)
Other causes:
Parasites: entamoeba histolytica (amoebiasis)
Viruses - CMV
Fungal |
| Clinical features: Abdominal pain, nausea, vomiting, tenesmus (needing to pass stools), urgency, diarrhoea, fevers/chills, malaise, arthralgia/myalgia |
| Microscopic: Mucosal and intraepithelial neutrophil infiltrates, particularly within the superficial mucosa +/- cryptitis/crypt abscesses
Normal architecture |
| Outcome/complications:
Self-limiting (vast majority), supportive treatment, specific antimicrobial therapy
Dehydration, sepsis and shock, toxic megacolon, death, extra intestinal infections (haemolytic-uremic syndrome, Gullian-Barre syndrome) |
| CMV colitis | macroscopically - congested haemorrhage mucosa with ulceration
Microscopically - viral inclusions in stromal and endothelial cells |
| Entamoeba Histolytica | macroscopically - patchy erosion and ulceration
Microscopically - amoebic organisms in ulcer slough (resemble macrophages) |
| Pseudomembranous colitis | Inflammatory condition of the colon characterised by pseudomembranes
Generally caused by clostridium difficile |
| Presents with diarrhoea (may be blood), abdominal pain and fever |
| May be complicated by fulminating colitis with toxic megacolon or perforation
Macroscopically: yellow-white pseudomembranes that bleed when scraped off |
Associated with use of antibiotics — disrupt normal colonic microbiota allowing C. difficile overgrowth; disease caused by exotoxin production which can be detected in stool

| (Chronic) idiopathic inflammatory bowel disease (IBD) | 1. Ulcerative colitis  
2. Crohn's disease |
|-----------------------------------------------------|--------------------------------------------------|
| Chronic illness; punctuated by exacerbations/remissions typically teens or early adulthood  
UC peak 3rd to 4th decade  
CD peak 2nd to 3rd decade (smaller peak 6th to 7th decade)  
males and females affected, CD slightly more common in females  
geographic and ethnic variation (more common amongst industrialised countries; N. America, N. Europe, Australia; less common in Asia, Africa; Ashkenazi Jews 3-5x risk) |
| Aetiology and pathogenesis  
Precise cause is unknown (environment, abnormal immune response, genetics)  
immunologic attack is cause of tissue injury  
*Crohn's disease*: predominantly TH1 and TH17 mediated process; macrophage/neutrophil  
*Ulcerative colitis*: atypical TH2 disorder |

<table>
<thead>
<tr>
<th>Crohn's disease</th>
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<tbody>
<tr>
<td>Abdominal pain, diarrhoea, constitutional symptoms (anorexia, weight loss, fever, lassitude), rectal bleeding and mucus, growth retardation (children), perianal fistula/abscess, malabsorption and deficiency (e.g. vitamin B12). Fibrosis, from mucosa out to lining of gut to lymph nodes and manifestations outside of gut.</td>
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<td>Diarrhoea, rectal bleeding and mucus, urgency, tenesmus, abdominal pain, constitutional symptoms (fever, weight loss, anorexia) superficial ulcers</td>
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</table>

Morphology  
*Abdominal pain, distension, and tenderness.  
Subcutaneous fat and omental fat reduced.  
Immunologic attack on mesenteric lymph nodes.  
Nodular mesenteric lymph nodes.  
Fibrosis, thickened bowel, loss of haustration.*

**Morphology**  
*Distinction of UC from CD  
distribution morphologic expression of disease  
Crohn's disease*  
sharp demarcation, skip lesions  
aphtous ulcers, linear ulcers, deep fissuring ulceration - fistula formation  
mucosal “cobblestone” appearance  
transmural oedema, inflammation, fibrosis and muscle hypertrophy leading to intestinal wall thickening/stricture  
mucosal inflammation, ulceration, architectural distorsion, paneth cell metaplasia  
non-caseating granulomas  
transmural inflammation, ulceration - classically “rose thorn”  
submucosal fibrosis, muscularis hypertrophy

**Ulcerative colitis**  
left sided disease but extends proximally continuous - no skip lesions  
hyperaemia, granularity, friability  
broad based ulceration (not linear) with pseudopolyps/islands of regenerating mucosa; muscular and serosa are normal. No transmural inflammation  
architectural distorsion with gland disarray/atrophy, Paneth cell metaplasia -persists between attacks  
Lymphoplasma cytic inflammation (granulomas); acute inflammation - crepitates, crypt abscess  
Extraintestinal manifestations  
skin — erythema nodosum, pyoderma grangrenosum  
eyes — episcleritis, uveitis, iritis, conjunctivitis  
mouth - oral aphthous ulcers  
joints - seronegative arthropathy (pauciarticular; polyarticular); axial arthropathy (ankylosing spondylitis, sacroileitis)  
hepatobiliary - primary sclerosing cholangitis
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<tr>
<th>Condition</th>
<th>Description</th>
<th>Associated Features</th>
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<tr>
<td><strong>Outcome and clinical course</strong></td>
<td>Chronic illness; exacerbations and remission smoking is a risk factor for CD, protective in UC stress may precipitate flares in UC</td>
<td>Treatment: supportive therapy, immunosuppressive therapy, surgery, surveillance for malignancy surgery curative for UC, disease often recurs at anastomotic or other sites in CD</td>
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<td><strong>Crohn’s disease</strong></td>
<td>Perforation, abscess, strictures, fistula, malabsorption, nutritional deficiency (B12, iron deficiency), neoplasia (intraepithelial neoplasia, and carcinoma)</td>
<td>Ulcerative colitis Toxic megacolon, perforation, neoplasia: intraepithelial neoplasia and carcinoma</td>
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<td>Toxic megacolon, perforation, neoplasia: intraepithelial neoplasia and carcinoma</td>
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<td><strong>(Chronic) microscopic colitis</strong></td>
<td>Encompasses two entities collagenous colitis; thickened sub-epithelial collagen band lymphocytic colitis; intraepithelial lymphocytes (&gt;20/100 epithelial cells) and epithelial injury, chronic inflammation, normal architecture. No thickened sub-epithelial collagen band middle age to older; F&gt;M radiologically and colonoscopy are normal associated with autoimmune diseases (e.g., Grave disease, RA, autoimmune or lymphocytic gastritis), drugs (e.g., NSAID), coeliac disease</td>
<td>Chronic non-bloody diarrhoea Microscopically Intraepithelial lymphocytes and epithelial injury, thickened sub epithelial collagen band, chronic inflammation, normal architecture Outcome and prognosis course of microscopic colitis is benign and prognosis is excellent. Most patients respond to cessation of potential risk factors (e.g. NSAID) and symptomatic measures. Anti-inflammatory measures if needed (e.g. mesalamine, budesonide, corticosteroids) &gt;70% of patients experience long-term cessation of diarrhoea, others experience relapse and require repeated therapy following period of remission</td>
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<td><strong>Ischaemic colitis</strong></td>
<td>Inflammatory disease of colon due to reduced blood flow, leading to ischaemic injury and secondary inflammation Aetiology occlusive arterial (thromboemboli; cholesterol emboli) venous (strangulated hernia, volvulus, obstruction, venous thrombosis, external compression) non-occlusive</td>
<td>Macroscopic — mucosal, mural, transmural infarction Complications: perforations, massive haemorrhage, sepsis, stricture (fibrosis which closes off the lumen)</td>
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<td>Iatrogenic colitis</td>
<td>Diversion colitis, drug-induced colitis, radiation, GVHD (post bone marrow transplantation)</td>
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<td>Polyp</td>
<td>Mass that protrudes to the lumen of the gut:</td>
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### Polyp
- Mass that protrudes to the lumen of the gut:
  - sessile
  - tubular (more common, more benign)/villous
  - pedunculated
  - abnormal mucosal proliferation
  - abnormal connective tissue proliferation
  - adenomas, hyperplastic polyps, hamartomatous polyps, non-epithelial polyps

### Colorectal adenocarcinoma
#### Diagnosis
- Clinical, endoscopic and radiological features
- Confirmation of malignancy: pathological features of endoscopic biopsies (pre-treatment)

#### Pathological assessment in CRC
- Pre-treatment diagnosis
- Prognostication: staging, other features

#### Therapy
- Mutational analysis K-Ras, N-Ras
- Response to treatment

### Adenoma
- tubular
- villous
- tubulo-villous
- serrated

**Adenoma carcinoma sequence**
- High prevalence of adenoma and carcinoma in similar population and similar distribution in colorectum
- Early invasive carcinoma show residual adenoma
- Risk of carcinoma related to number of adenomas
- Surveillance programs that detect and remove adenomas result in reduction of the incidence of carcinoma

#### Epidemiology
- Peak incidence: 60-70 (except familial cases)
- Environment, dietary (high calorie, low fibre, refined carbs, red meat, reduced protective micronutrients)
- NSAIDs -?protective

#### Facts
- Rectosigmoid - 55%
- Caecum/ascending colon - 22%
- Transverse - 11%
- Descending colon - 6%
- Most - single

### Neoplasia of the large bowel
#### Adenoma
- Tubular
- Villous
- Tubulo-villous
- Serrated

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### Polyp
- Asymptomatic
- Screening (national bowel cancer screening program)
- Incidental
- FOBT +ve (faecal occult blood test)

#### Adenoma carcinoma
- Fatigue, anaemia, weakness
- Anaemia PR, altered bowel habits
- Screening
- Metastatic disease
**Morphology**
- proximal - polypoid, exophytic (proliferating externally)
- distal - ulcer, annular stricture — proximal dilatation
- invasion of submucosa —-> muscle ——> series

**Colorectal adenocarcinoma**
- dysplastic glands + invasion to the submucosa and beyond

**Colorectal carcinogenesis**
- most sporadic
- only 1-3% are familial and associated with predisposing conditions e.g. IBD
- stepwise accumulation of multiple mutations
- APC-beta catenin pathway; loss of APC gene
- Microsatellite instability pathway; genetic lesions in the DNA mismatch repair genes (MSH2, MSH6, MLH1, PMS1, PMS2)
- Serrated pathway

**Invasion/Spread**
- direct invasion to adjacent structures
- blood vessels - liver
- lymphatics - lymph nodes
- When the polyp breaches the muscularis mucosa.

**Dysplasia** are pre-cancerous lesions
- Disordered growth, differentiation and maturation of cellular components of tissue
- CONFINED to the epithelium; no invasion
- morphologic expression of disturbance of growth regulation
- individual dysplastic cells show features similar to malignant cells

**Benign non epithelial neoplasms** (rare):
- leiomyoma
- neuroma, schwannoma
- haemangioma
- lipoma

**Neuroendocrine tumours** (carcinoid)
<table>
<thead>
<tr>
<th>Tumour Type</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>Neuroendocrine cell lineage</td>
<td>at least low grade, a few are high grade neuroendocrine carcinoma</td>
</tr>
<tr>
<td>Appendix</td>
<td>most common site, SI (ileum), rectum, stomach, colon</td>
</tr>
<tr>
<td><strong>Gastrointestinal stromal tumours (GIST)</strong></td>
<td>spindle cell neoplasm</td>
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<td>interstitial cells of Cajal (ICC) or precursors - special cells of the GUT wall coordinating peristalsis</td>
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<td>80% CD117 (C-kit) and 10% PDGFRA (platelet derived growth factor receptor Alpha)</td>
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<td>high and low risk malignant potential</td>
</tr>
<tr>
<td><strong>Lymphomas</strong></td>
<td>1-4% of GIT malignancies</td>
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<td>Types of lymphomas</td>
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<td>B cell lymphomas: marginal zone lymphoma (MALT), Diffuse large B cell lymphoma (DLBCL), Burkitt lymphoma, mantle cell lymphoma, other - T cell lymphoma; associated with malabsorption syndromes i.e. coeliac</td>
</tr>
</tbody>
</table>

### Familial adenomatous polyposis (FAP) syndrome
Familial adenomatous polyposis (FAP) is an inherited condition in which numerous adenomatous polyps form mainly in the epithelium of the large intestine. While these polyps start out benign, malignant transformation into colon cancer occurs when they are left untreated.

### Hereditary non-polyposis colorectal carcinoma (HNPCC)
Lynch syndrome is an autosomal dominant genetic condition that has a high risk of colon cancer as well as other cancers. The increased risk for these cancers is due to inherited mutations that impair DNA mismatch repair.