Pathology of the gastrointestinal tract

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Pathological basis of gastrointestinal signs and symptoms

Sign or symptom	Pathological basis
Dysphagia (difficulty swallowing)	Impaired neuromuscular function (e.g. multiple sclerosis) Obstruction (intrinsic or extrinsic)
Indigestions/epigastric pain (heartburn)	Oesophageal/gastric mucosal irritation, often with inflammation and ulceration
Abdominal pain - **Visceral** - **Peritoneal**	 Spasm (colic) of muscular layer in gut wall Irritation or inflammation of peritoneum
Diarrhoea	Excessive secretion or impaired absorption of fluid within lumen of GIT
Steatorrhea (fatty stool)	Impaired absorption of fat due to reduced lipase secretion or reduced mucosal surface area for absorption
Blood loss - **In vomit (haematemesis)** - **Through anus**	 Ruptured blood vessels in oesophagus (e.g. varices) or stomach (e.g. erosion/ulcer) Ulceration or inflammation of colorectal mucosa, from tumors or ruptured blood vessels (e.g. Haemorrhoids)
Weight loss	Impaired food intake, malabsorption of food, catabolic state
Anaemia	Blood loss or ↓absorption of Fe, folate or B12
Vomiting	Gastroenteritis, apendicitis, pyloric stenosis, intestinal obstruction, stenosing gastric cancer.

Diseases of salivary glands

Sialoadenitis

- acute bacterial sialoadenitis (uncommon)
- viral infection (parotitis epidemica)
- autoimmune sialoadenitis→xerostomia (dryness of the mouth); Sjögren´s syndrome

Tumors

- Pleomorphic adenoma: benign mixed tumor
- Warthin´s tumor (adenolymphoma): benign
- Mucoepidermoid tumor (low, intermediate and high grade malignancy)
- Adenoid cystic carcinoma (perineural invasion common)

Diseases of the oesophagus

Congenital and mechanical disorders

- **Atresia:** failure of embryological canalisation, often assoc. with oesophagotracheal fistula→development of aspiration bronchopneumonia (urgent surgery necessary)

- **Hiatus hernia:** part of the stomach above the diaphragmatic orifice→gastrooesophageal reflux disease (GORD)

- **Achalazia:** failure of relaxation at the sphincter (cardiospasm)

- **Oesophageal varices:** site for portocaval shunting in portal hypertension (e.g. in cirrhosis)→rupture, life-threatening bleeding

Diseases of the oesophagus

Inflammatory disorders

- **Oesophagitis:** acute - viral (CMV) and mycotic (Candida albicans) in immunosuppressed patient, in diabetes; chronic – nonspecific or specific (tbc, Crohn´s d.)
- **Reflux oesopha**gitis: in GORD

Barrett´s oesophagus

- Long term consequence of reflux
- Metaplasia of squamous to columnar glandular epithelium
- Increased risk of oesophageal adenocarcinoma

Diseases of the oesophagus

Tumors

Benign

- Papillomas (often assoc. with HPV infection)
- Leiomyomas,…

Malignant

- Adenocarcinomas (in Barrett´s oesophagus)
- Squamous carcinoma

…wide geographic variation in incidence, links to environmental factors….

Diseases of the stomach

Congenital disorders

- **Diaphragmatic hernia:** maldevelopment of diaphragm→part of the stomach in thorax→respiratory failure

- **Pyloric stenosis:** abnormal hypertrophy of the circular muscle coat at the pylorus caused by abnormal inervation →projectile vomiting

Diseases of the stomach

Inflammatory disorders - gastritis

- **Acute gastritis:** chemical injury (alcohol, drugs)

- **Chronic gastritis:**
  - caused by *Helicobacter pylori* infection
  - autommune, causing vitamin B12 deficiency

* ***Increased risk of adenocarcinoma and lymphoma in chronic gastritis!***

- **Chemical (reactive gastritis):** due to biliary regurgitation or drug induced damage

Diseases of the stomach

Peptic ulceration

- **Major sites:** first part of duodenum, junction of antral and body mucosa in stomach, distal oesophagus, gastro-enterostomy stoma

- **Main etiology:** hyperacidity, Helicobacter gastritis, duodeno-gastric reflux, NSAIDs abuse, smoking, hyperproduction of gastrin and genetic factors

- **Ulcers acute or chronic**

- **Complications:** haemorrhage, penetratio to adjacent organs, perforation, anaemia, obstruction due to fibrous strictures, malignancy

Diseases of the stomach

Tumours

- **Benign** (epithelial adenomas, mesenchymal leiomyomas and others….)

- **Malignant**

  - majority are adenocarcinomas (intestinal type or diffuse)
  - arise on a background of chronic gastritis and intestinal metaplasia
  - often diagnosed in clinically advanced stage
  - other malignant tumours: lymphomas (H.P. gastritis), gastrointestinal stromal tumors (from low grade to high grade malignancy)

Diseases of the intestine

Congenital disorders

- **Atresia, stenosis** (failure of luminisation)
- **Malrotation** (causing obstruction)
- **Duplication, diverticula**
- **Meconium ileus** in cystic fibrosis
- **Hirschsprung disease** (aganglionosis of the large intestine, =megacolon congenitum, clinically from obstipation to total obstruction)

Diseases of the intestine

Malabsorption

Malabsorption is a state arising from abnormality in absorption of food nutrients across GIT.

Clinically: diarrhea, weight loss, flatulance, abdominal bloating, cramps, pain, anaemia, Steatorrhea

- **Coeliac disease**

(Sensitivity to gluten components in cereals, pathologic immune reaction results in villous atrophy, malabsorption, anaemia and increased risk of lymphoma).

- **Pancreatogenic**
- **Enzyme dificiences (e.g. lactase deficiency)**
- **Extensive surgical resection (e.g. in Crohn´s disease)**
- **Lymphatic obstruction (protein loosing status)**

Infection of the intestine

- **Bacterial**

(salmonellosis, typhoid fever, bacillary dysentery (*Shigella*), cholera (*Vibrio cholerae*), neonatal diarrhoea (*E. coli*), staphylococcal enterokolitis, tbc, *Clostridium difficile* enteritis (post ATB),….)

- **Viral**
- **Fungal**
- **Parasitic**

(Giardiasis, Amoebiasis, Cryptosporidiosis, Balantidiasis,…)

*Fungal, parasitic and some viral infections often in immunocompromised patients.

Inflammatory bowel diseases (IBD)

- **Crohn´s disease**

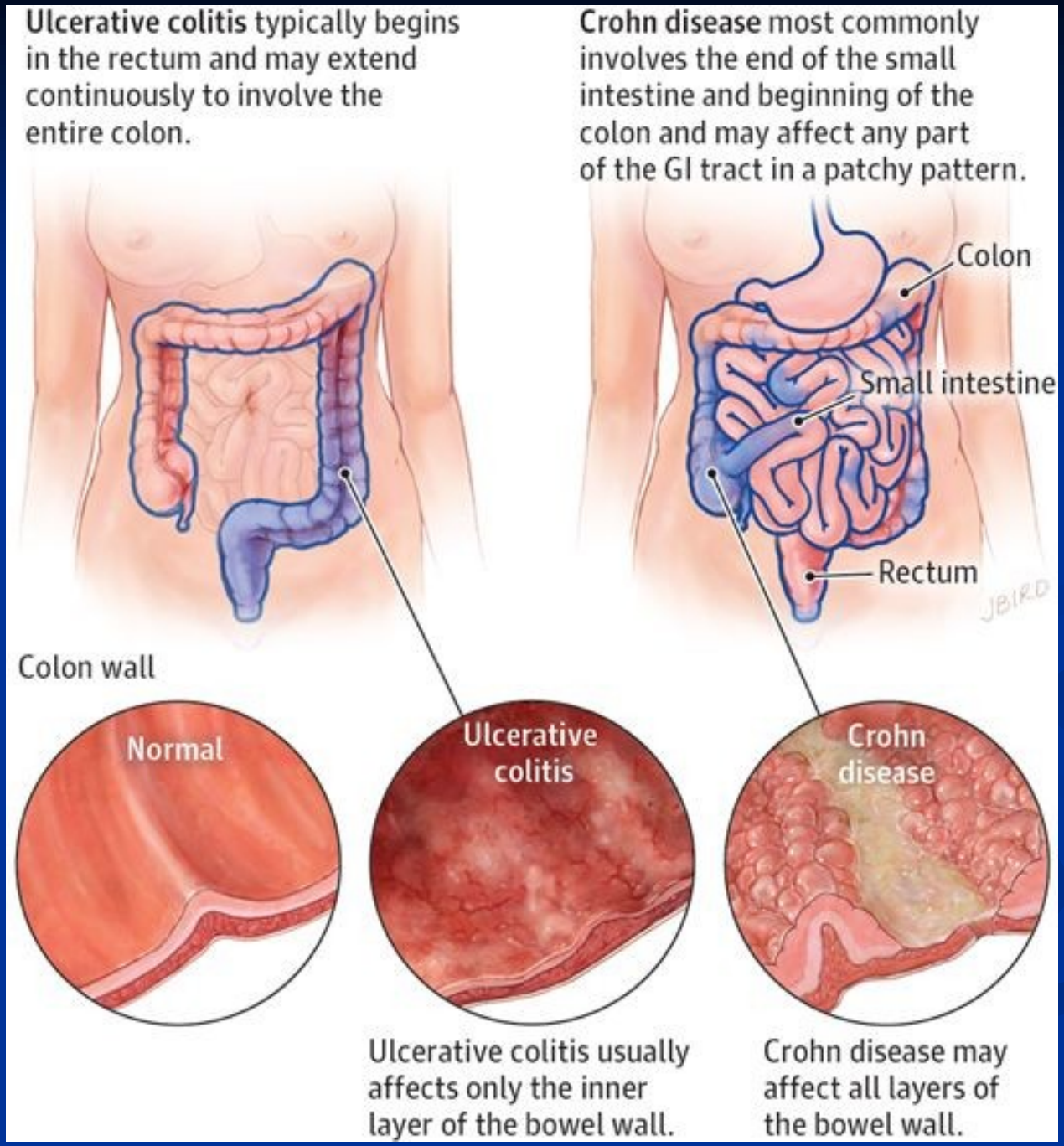
- Chronic transmural inflammation with granulomas, small bowel commonly affected, any part of gut may be involved, segmental involvement („skip lesions“)
- Thickened and fissured bowel leads to intestinal obstruction and fistulation (needs surgery)

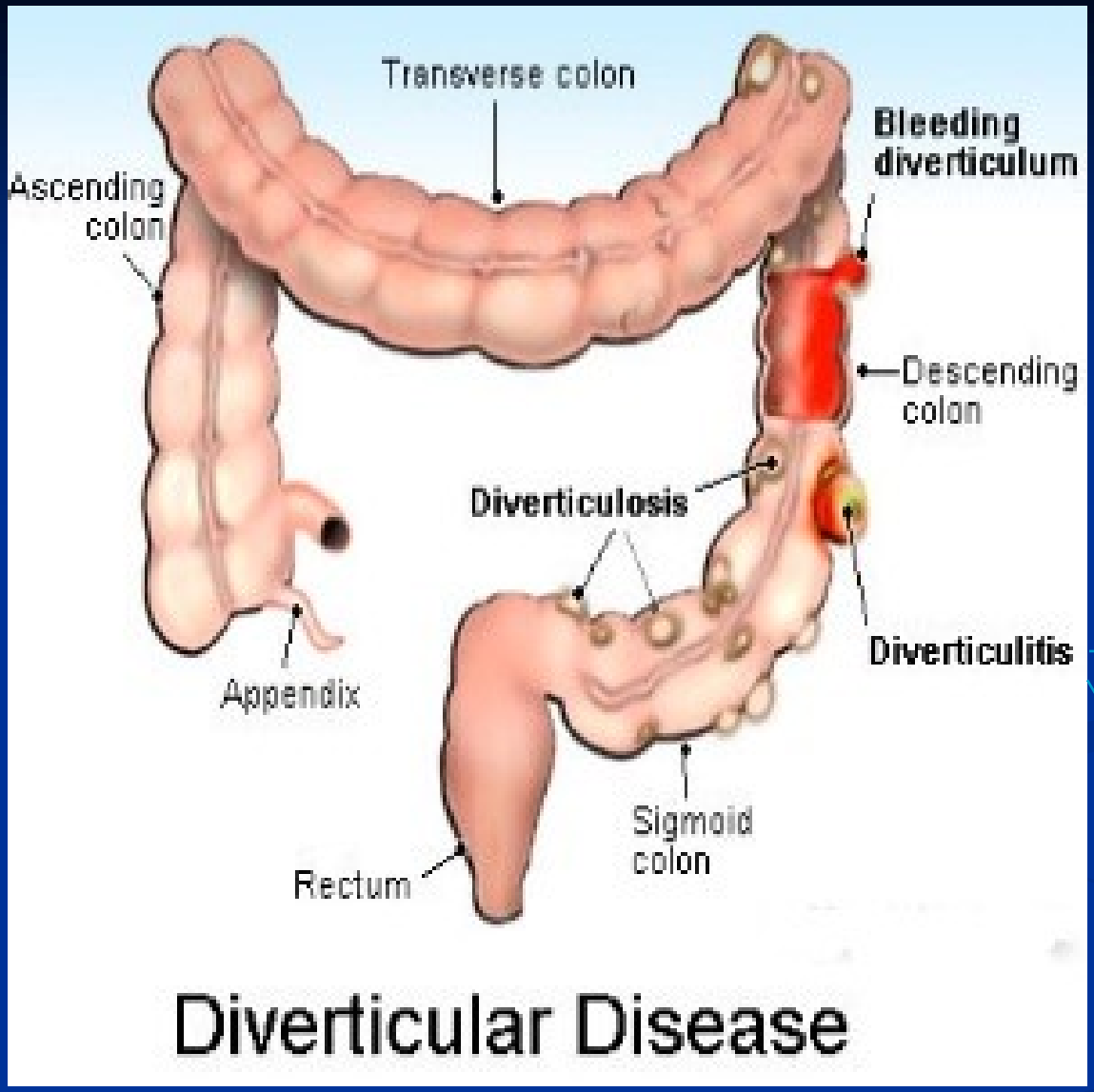
- **Ulcerative colitis**

- Chronic inflmmation, diffuse superficial, affects colon and rectum
- Complications: toxic dilatation, perforation, haemorrhage, anaemia, liver disease (primary sclerosing cholangitis often in UC patients) and **cancer!**

- **IBD etiology**

- Genetically determined immune over-reaction to gut bacterial components and also to some endogenous antigens

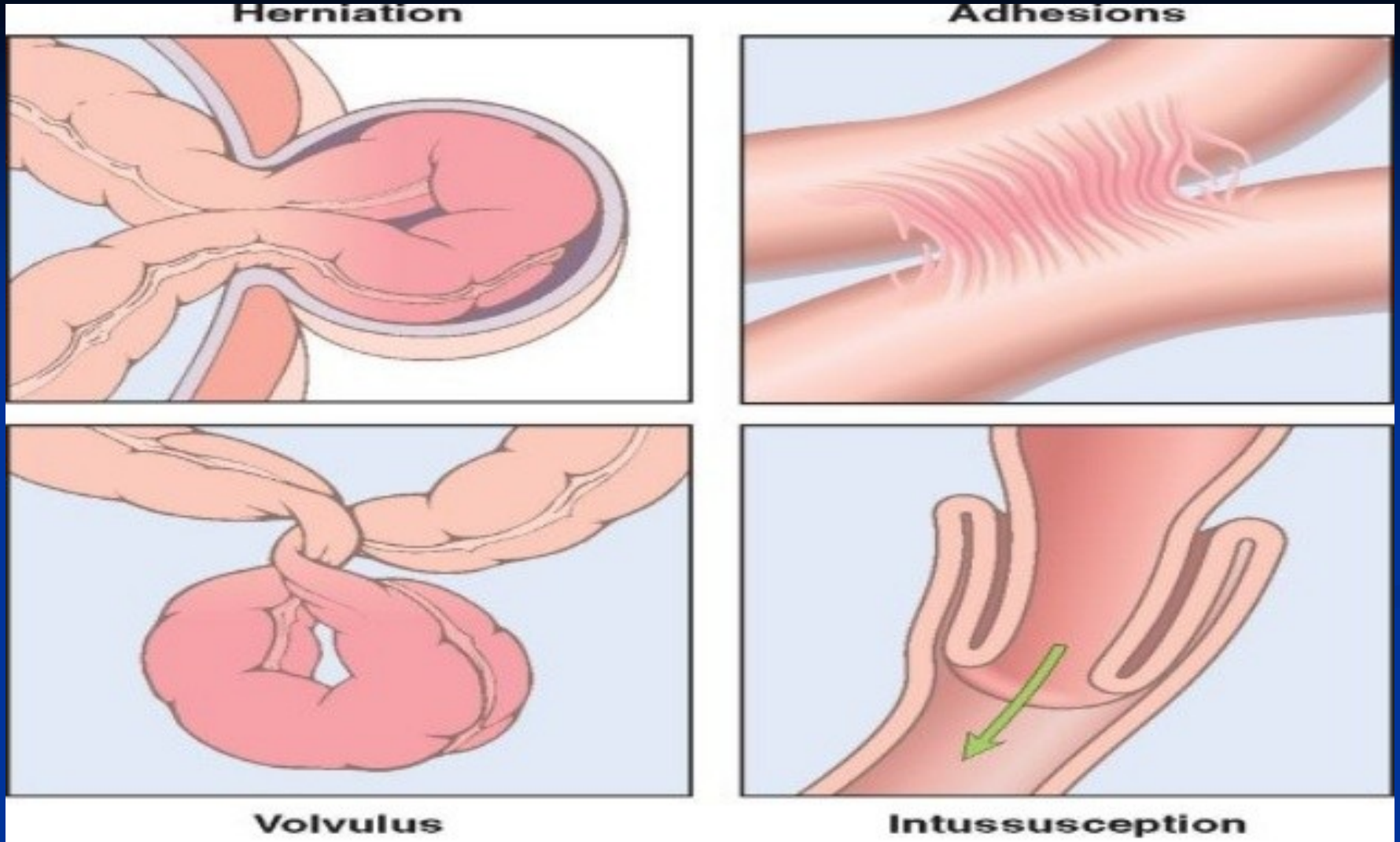

Ulcerative colitis typically begins in the rectum and may extend continuously to involve the entire colon.
Crohn disease most commonly involves the end of the small intestine and beginning of the colon and may affect any part of the GI tract in a patchy pattern.
Colon
Small intestine
Rectum
JBIRD
Colon wall
Normal
Ulcerative colitis
Crohn disease
Ulcerative colitis usually affects only the inner layer of the bowel wall.
Crohn disease may affect all layers of the bowel wall.



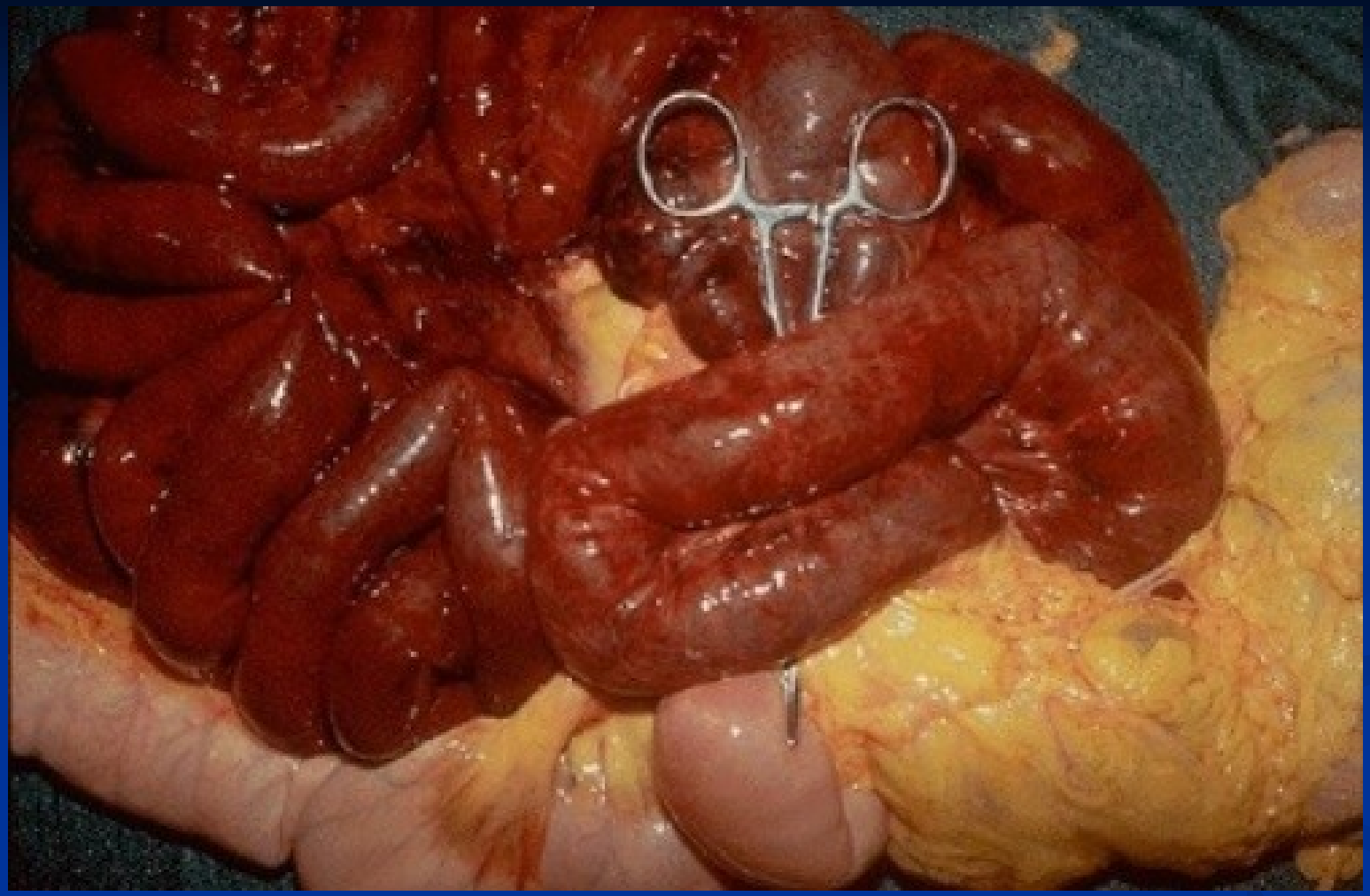
Perforation, abscess, peritonitis, sepsis

Fistula into bladder, vagina, small intestine

Diverticula = herniation of mucosa into intestinal wall

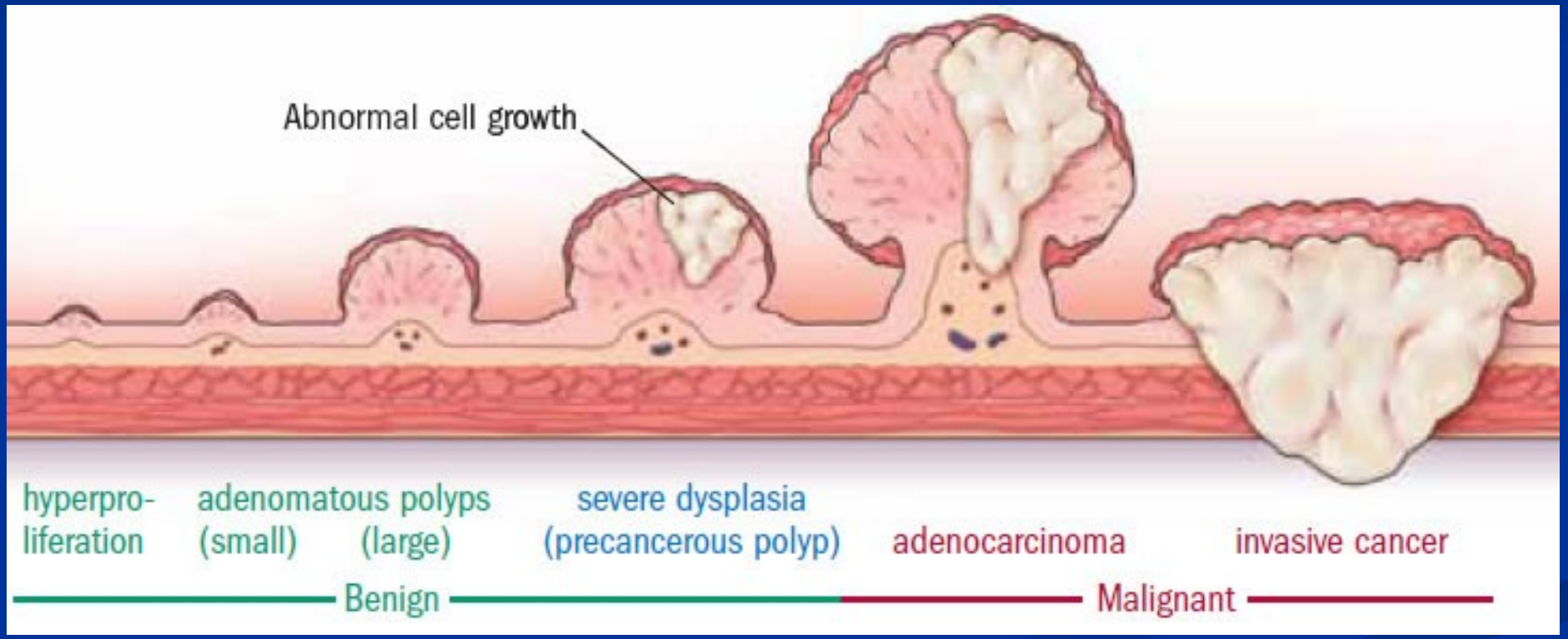


Intestinal obstruction. The four major causes of intestinal obstruction are (1) herniation of a segment in the umbilical or inguinal regions, (2) adhesion between loops of intestine, (3) volvulus, and (4) intussusception.



Haemorrhagic infarction of the small bowel = ischaemic necrosis (caused by thrombosis, thrombembolisation,..).

Tumours of the intestine – carcinogenesis of colorectal cancer



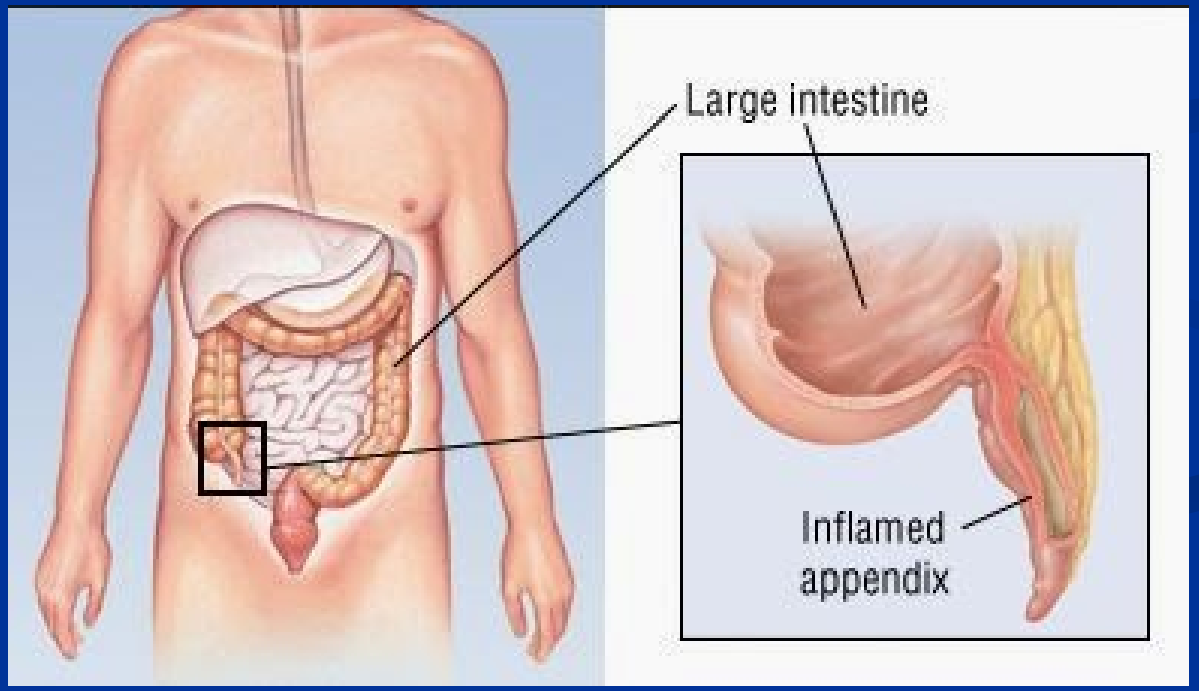
Colorectal cancer (CRC)

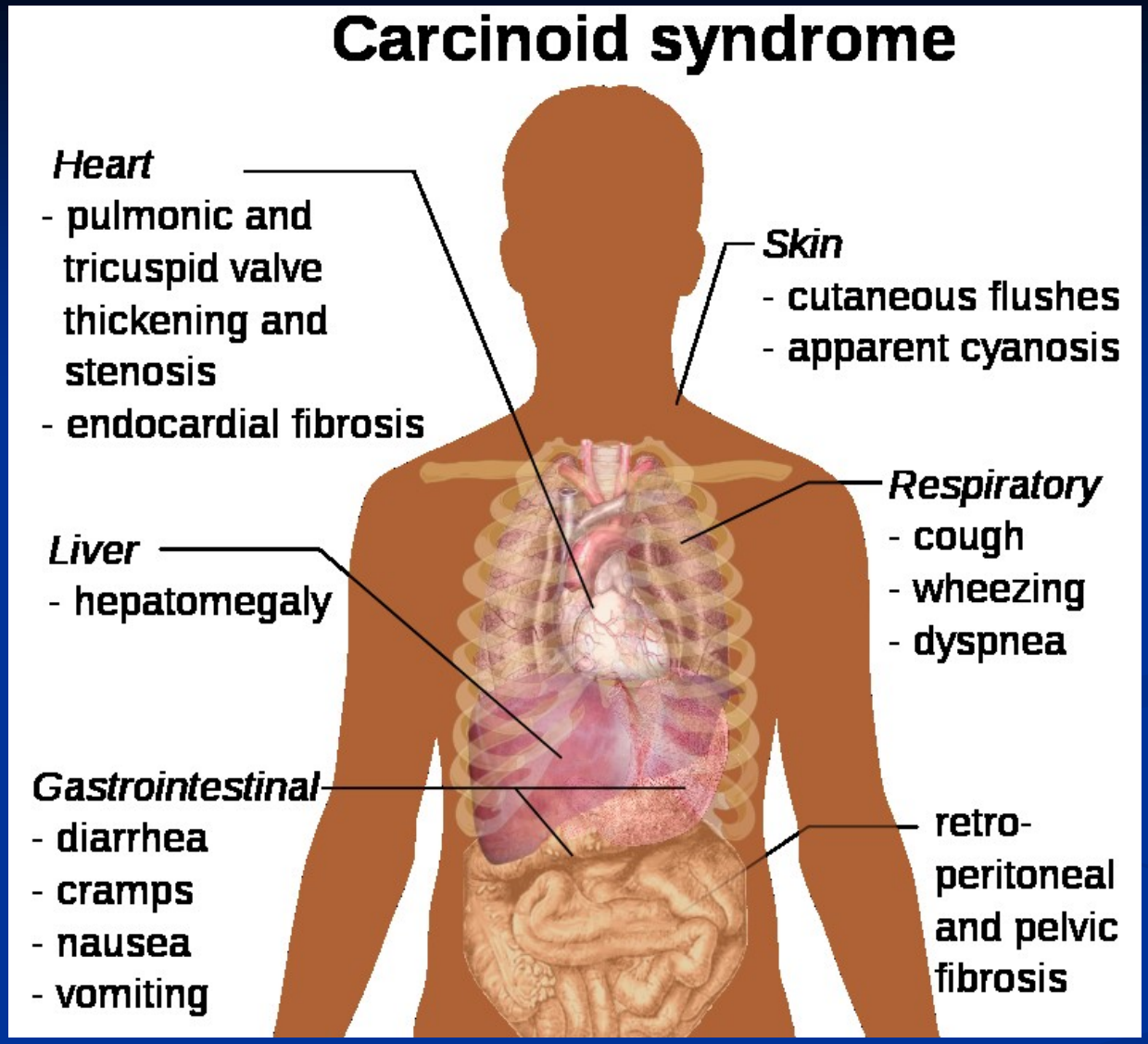
- Common malignancy in developed countries
- Adenocarcinomas
- Increased risk in patients with adenomatous polyps and longstanding ulcerative colitis
- Hereditary increased risk in patients with familial adenomatous polyposis and Lynch syndrome
- In early stages good prognosis

+ other malignant tumors: neuroendocrine carcinomas (=carcinoids), lymphomas (often in small intestine)

Appendicitis

- Common cause of acute abdomen, needs surgery
- Inflammation often precipitated by obstruction due to faecolith, lymphoid hyperplasia or tumor
- **Complications:** peritonitis, portal pyaemia and hepatic abscesses





Due to production of serotonine by neuroendocrine carcinoma=carcinoid tumor.

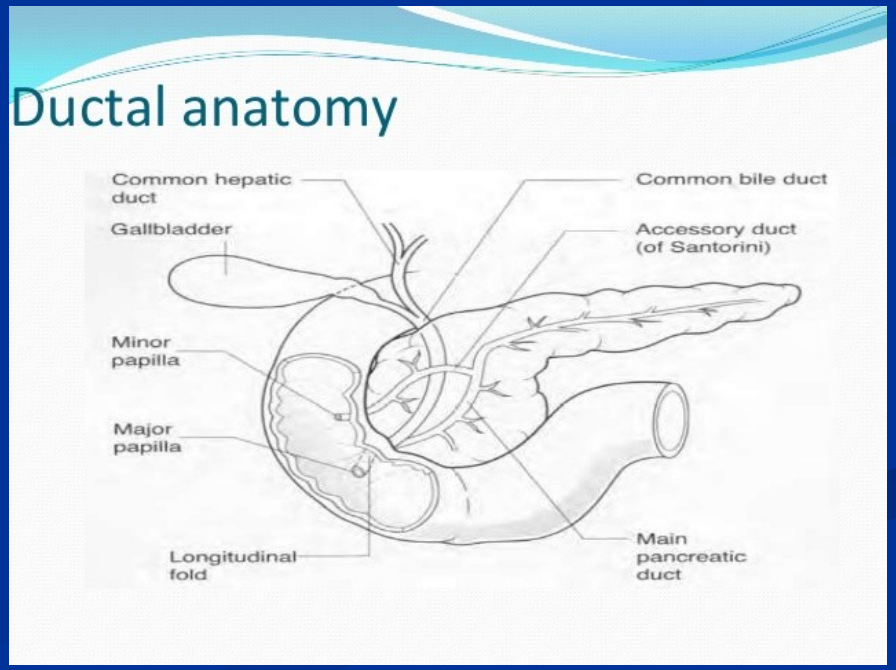
Pathology of the exocrine pancreas

(exocrine gland producing trypsin, lipase, phospholipase, amylase, elastase…enzymes normally activated in duodenum)

Congenital abnormalities

(causing obstruction of duodenum, increases risk of pancreatitis)

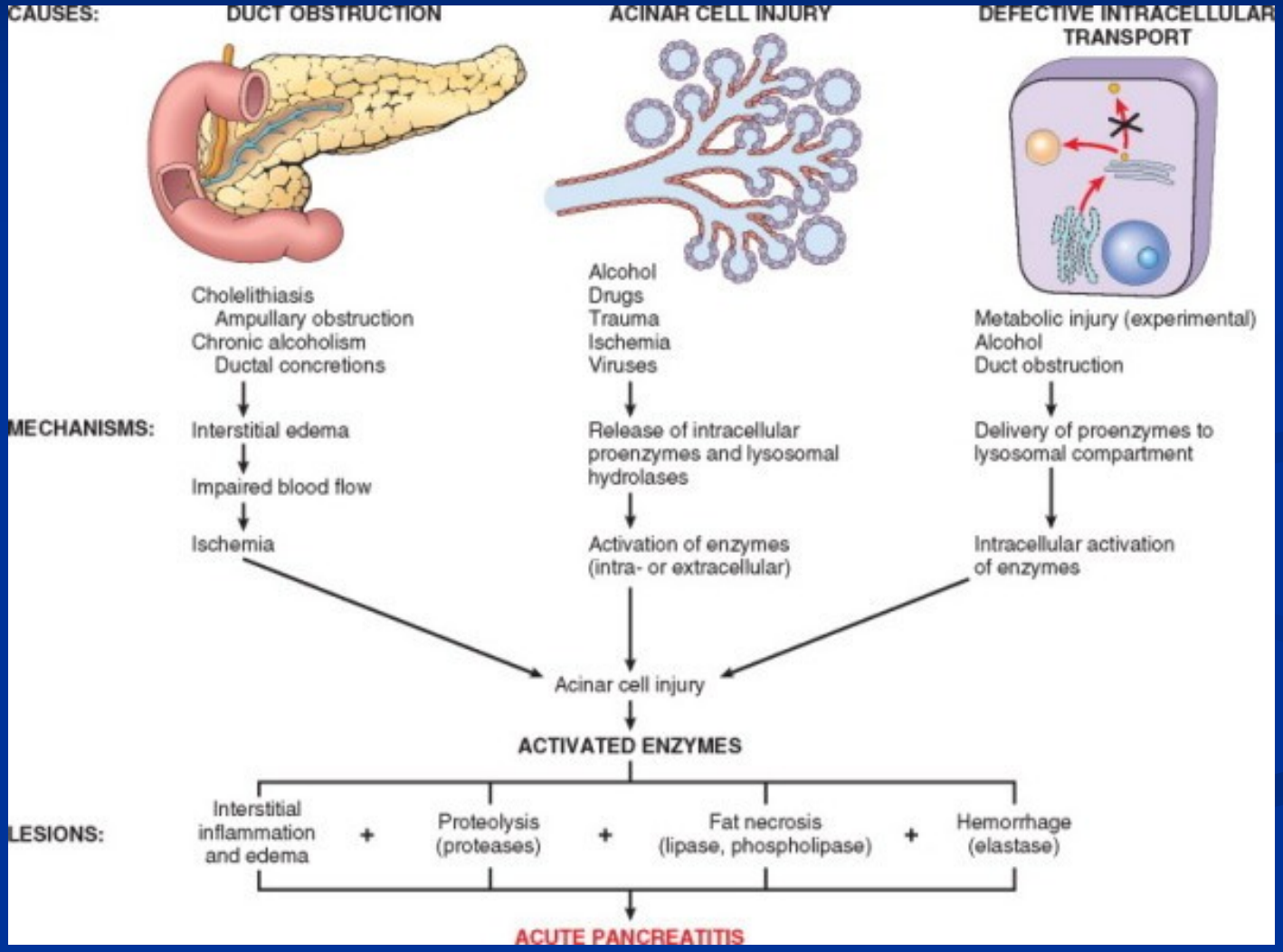
- Annular pancreas
- Pancreas divisum
- Ectopic pancreatic tissue (in stomach,..)
- Cysts



Acute pancreatitis

- Autodigestion of the pancreatic substance by inappropriately activated pancreatic enzymes
- Aetiological factors include: duct obstuction, shock, alcohol,….
- Amylase released into blood (used diagnostically)
- Often haemorrhagic
- Fat necrosis, binds calcium
- Clinically severe abdominal pain, nauzea, vomiting, clinical deterioration may be rapid - shock.

Etiology of acute pancreatitis



Chronic pancreatitis – classification TIGARO

- **T**oxic (alcohol, drugs, uremia,…)
- **I**diopathic
- **G**enetic (hereditary pancreatitis, AD, increased risk of cancer!)
- **A**utoimmune
- **R**ecurrent
- **O**bstructive (e.g. by tumor)

Pancreas shows fibrosis and exocrine atrophy.
Patient develops malabsorption due to loss of pancretic secretion

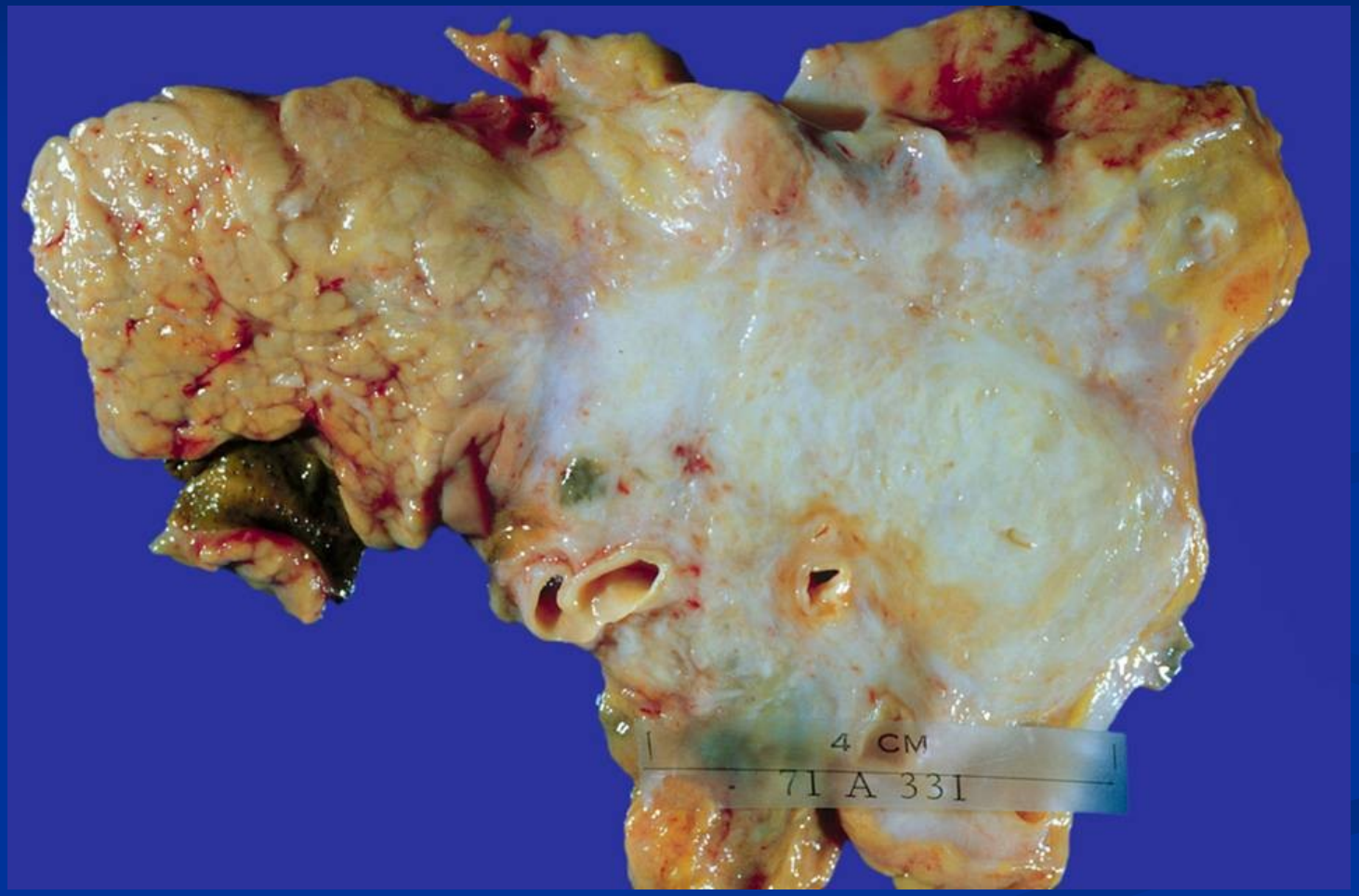
Cystic fibrosis (mucoviscidosis)

- **Hereditary disorder, AR (CFTR gene mutated)**
- **Channelopathy causing abnormal water and electrolyte transport across cell membranes**
- **Mucous secretion of abnormally high viscosity obstructiong th ducts of exocrine glands**
- **Clinicopathological features:**
  - Meconium ileus in neonates
  - Recurrent bronchopulmonary infectios (especially with *Pseudomonas aeruginosa*)
  - Bronchiectasis
  - Chronic panreatitis
  - Malabsroption
  - Infertility in males

Carcinoma of the pancreas

- Usually adenocarcinoma (=ductal adenocarcinoma in 90 % of all pancreatic tumors)
- May present with obstructive jaundice
- Very poor prognosis (absence of effective screening, late diagnosis in majority cases)
- Metastases in lymph nodes and liver

Ductal adenocarcinoma (head of the pancreas)



Other pancreatic tumors

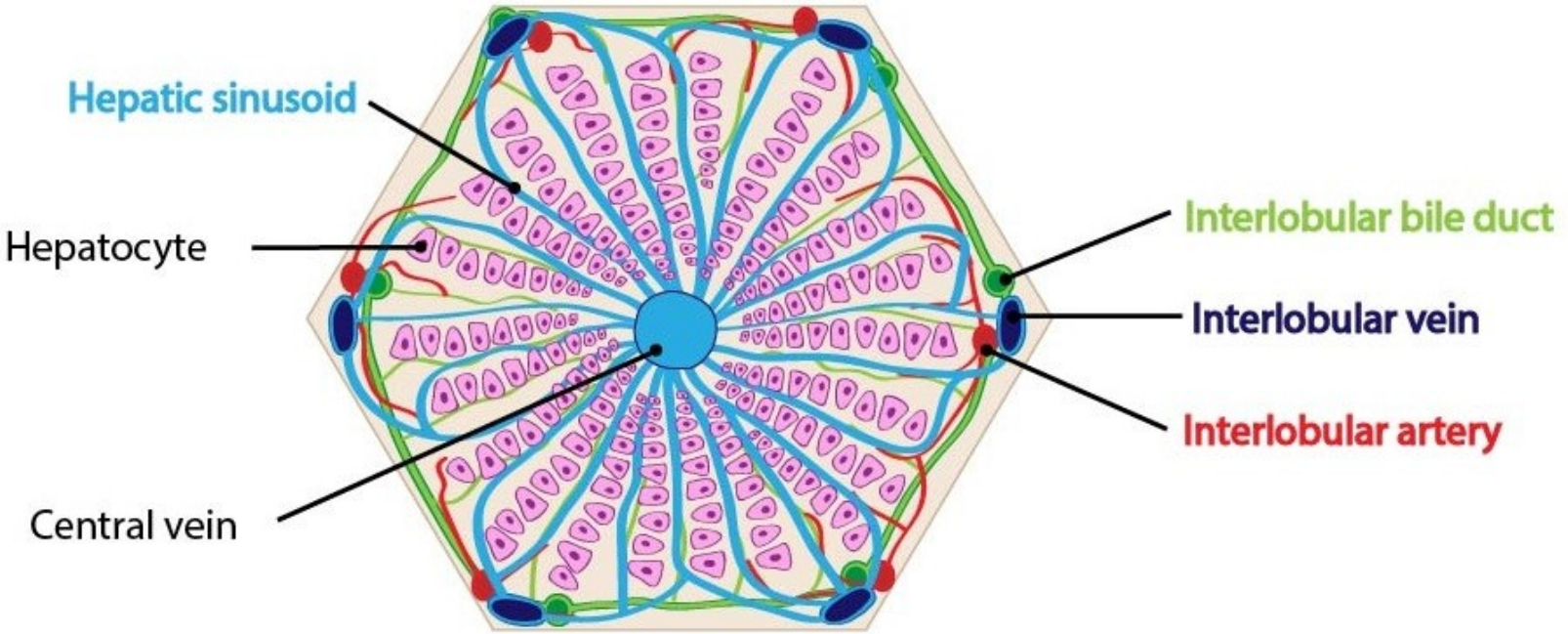
- Cystic neoplasms of the pancreas (mucinous cystic neoplasm, intraductal papillary mucinous neoplasm, serous cystadenoma)
- Acinar cell carcinoma
- Solid pseudopapillary tumor (in young females)
- Neuroendocrine carcinomas (often hormone producing)

…….

- Secondary (metastatic) tumors

Diseases of the liver and biliary system

Liver structure



Pathological basis of hepatic signs and symptoms

Sign and symptom	Pathological basisexcephalopathy
Jaundice/icterus (skin and mucosal yellowing due to ↑bilirubin)	**Haemolytic** (due to ↑haemolysis, increased formation of bilirubin) **Intrahepatic** (in liver diseases, impaired conjugation and/or excretion) **Post-hepatic** (due to biliary obstraction (by tumor, calculi, strictures,..) + congenital congenitl hyperbilirubinaemia caused by congenital metabolic defects
Dark urine	Conjugated hyperbilirubinaemia (water-soluble), e.g. in haemolysis
Pale faeces	Biliary obstruction causing lack of bile pigments
Spider naevi **Gynaecomastia**	Secondary to hyperoestrogenism
Oedema	Reduced plasma oncotic pressure due to hypoalbuminaemia
Xanthelasma	Cutaneous lipid deposits in hypercholesterolaemia in chronic biliary obstruction
Steatorrhoea	Malabsorption of fat due to lack of bile (e.g. in chronic biliary obstruction)
Pruritus	Biliary obstruction resulting in bile salt accumulation
Ascites	Combination of hypoalbuminaemia and portal hypertension
Bruising or bleeding	Impaired hepatic synthesis of clotting factors
Hepatomegaly	Increased size of liver due to inflammation (hepatitis), infiltration (fat) or tumor.
Encephalopathy	Failure of liver to remove exogenous or endogenous substances mimicking or altering balance of neurotransmitters
Haematemesis	Ruptured oesophageal varices due to portal hypertension

Acute liver injury

- **Clinicopathological features:**
  - Malaise
  - Jaundice
  - Raised serum bilirubin and transaminase (AST, ALT, GGT)
  - In severe cases liver failure

- **Causes include:**
  - viral infections
  - high alcohol consuption
  - adverse drug reaction
  - biliary obstruction, e.g. due to gall stones

- **Possible outcomes:**
  - complete recovery
  - chronic liver disease
  - death from liver failure

Hepatitis viruses: their characteristics and assoc. Diseases						
Virus	Type virus	Incubation period (days)	Illness	Carriers	Serological markers	Tranmisssion
HAV	RNA	15-40	Mild, very low mortality	No	IgM anti-HAV Ab	Faecal-oral
HBV	DNA	50-180	↑risk of chronic hepatitis and cirrhosis, liver cancer	Yes	HBsAg, HBeAg	Blood, blood products, needles, veneral
HCV	RNA	40-55	Fluctuating; ↑risk of chronic hepatitis and cirrhosis, liver cancer	Yes	anti-HCV Ab, HCV RNA	Blood, blood products, needles, possibly veneral
HEV	RNA	30-50	Very low risk of chronicity, full recovery usual, except in pregnancy (in pregnancy high mortality rate).	No	anti-HEV Ab	Faecal-oral

- **Alcoholic liver injury**
- Common cause of acute and chronic liver disease

- Include:
- Fatty change in liver cells
- Acute hepatitis
- Architectural damage ranging from portal fibrosis to cirrhosis

- **Drug induced liver injury**
- Cholestatic or hepatocellular
- Dose-related (predictable) or idiosyncratic (unpredictable)

- **Acute biliary obstruction**
- Usually due to gall stones
- Clinically colicky pain and jaundice
- May be complicated by infection (cholangitis, spesis)

Chronic liver diseases

- **Chronic hepatitis**
- **Iron overload and the liver**
  - Haemosiderosis (normal liver architecture)
  - Haemochromatosis

(complicated by fibrosis and cirrhosis; congenital or aquired)

- **Wilson´s disease**
  - Inherited disorder of copper metabolism, copper accumulates in liver and brain
- **Alpha-1 antitrypsin deficiency**
  - Congenital defect of synthesis, risk of emphysema and cirrhosis
- **Autoimmune liver diseases**
  - Autoimmune hepatitis
  - Primary biliary cirrhosis
  - Sclerosing cholangitis

Are able to progress into cirrhosis!

Liver cirrhosis

- **Diffuse and almost irreversible process**

- **Characterized by fibrosis and nodular regeneration**

- **Morphologically classified:**

- Micronodular
- Macronodular

- **Causes include:**

- Viral hepatitis, alcohol, haemochromatosis, autoimmune liver diseases, recurrent biliary obstruction, Wilson´s disease,….

- **Complications**

- Liver failure
- Portal hypertension
- Liver cell carcinoma

Tumors of the liver

- **Benign**
  - Liver cell adenoma
  - Angioma

- **Malignant**
  - **Primary**

Liver cell carcinoma

Cholangiocarcinoma

Angiosarcoma

Hepatoblastoma (in children)

  - **Secondary - metastatic**

Diseases of the gall bladder and bile ducts

- **Cholelithiasis**
  - ↑risks: females, obesitdy, diabetes
  - cholesterols, bile pigment or mixed stones
  - Complications: cholecystitis, obstructive jaundice, carcinoma

- **Acute and chronic cholecystitis**

- **Carcinoma of the gall bladder and bile ducts**

- **Biliary obstruction**
  - Due to gall stones, carcinoma of the common bile duct, carcinoma of the pancreatic head, inflammatory strictures of the common bile duct, primary biliary cirrhosis, sclerosing cholangitis, congenital biliary atresia

Thank you for your attention….