EXAMINATIONS IN GASTROENTEROLOGY

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FUNCTION OF GIT

- Digestion and nutrient uptake
- Barrier function
  - pathogens
  - toxins

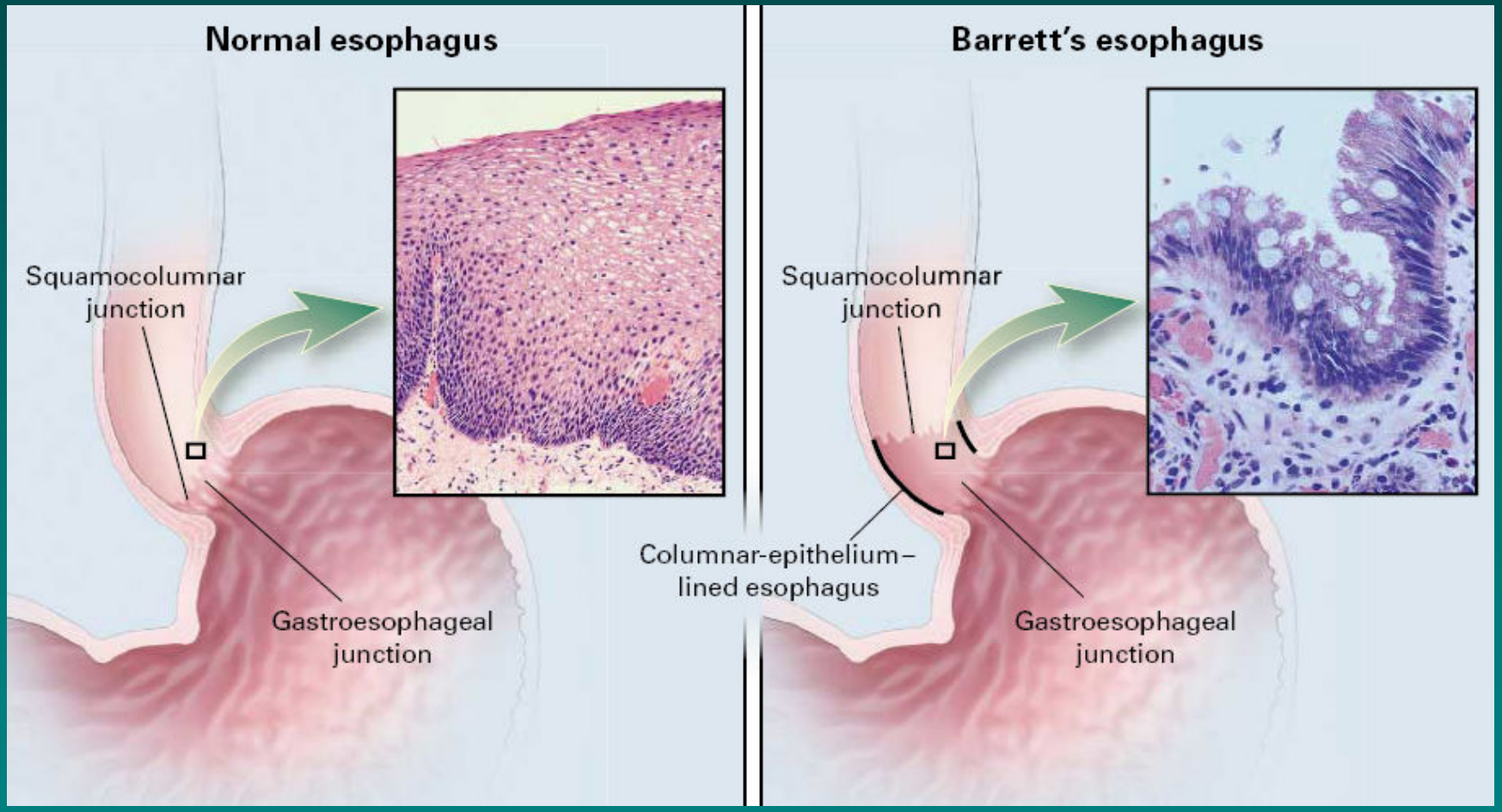
ESOPHAGUS

GASTROESOPHAGEAL REFLUX

- Squamous mucosa of esophagus is more vulnerable to peptic digestion than columnar gastric epithelium

Reflux esophagitis
Barrett's Esophagus

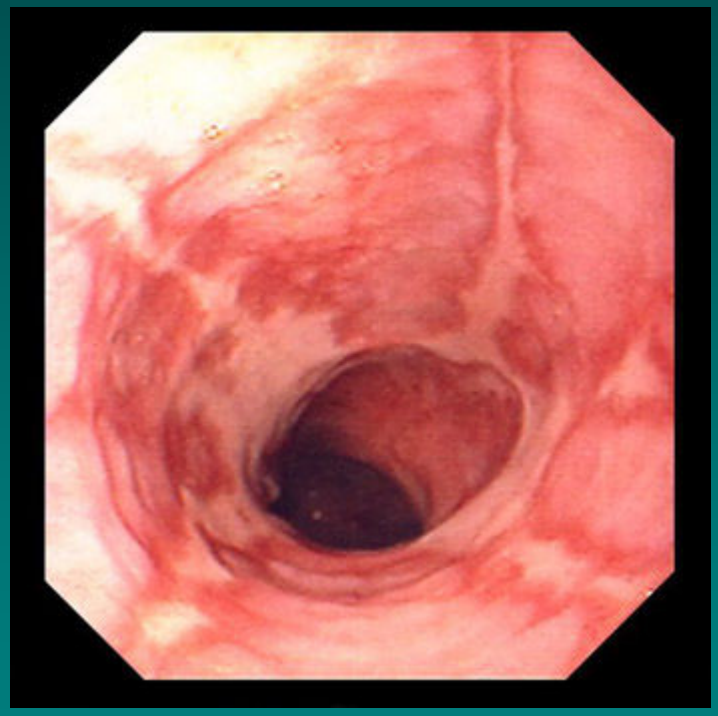
The squamocolumnar junction is proximal to the gastroesophageal junction



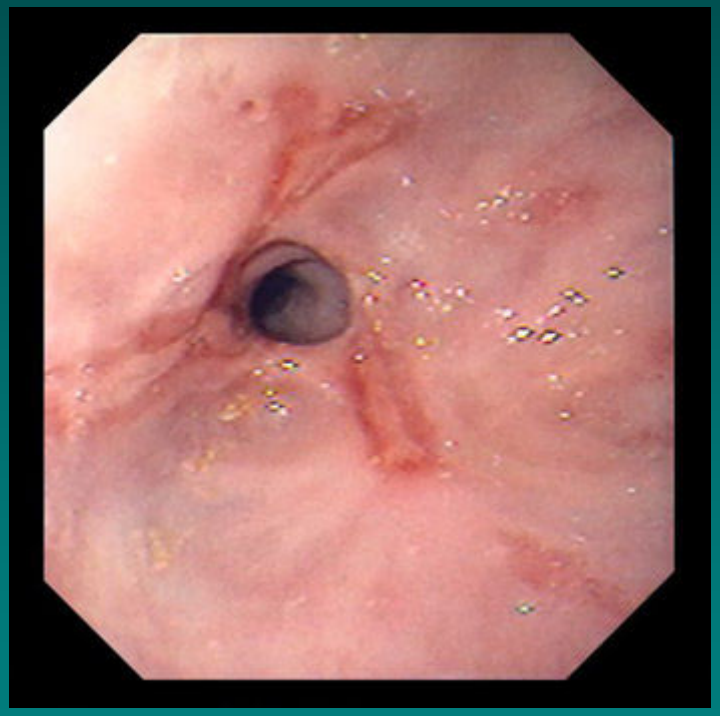
Esophagus: squamous epithelium; Stomach: columnar epithelium

Complications of Gastroesophageal Reflux Disease (GERD)

Reflux esophagitis

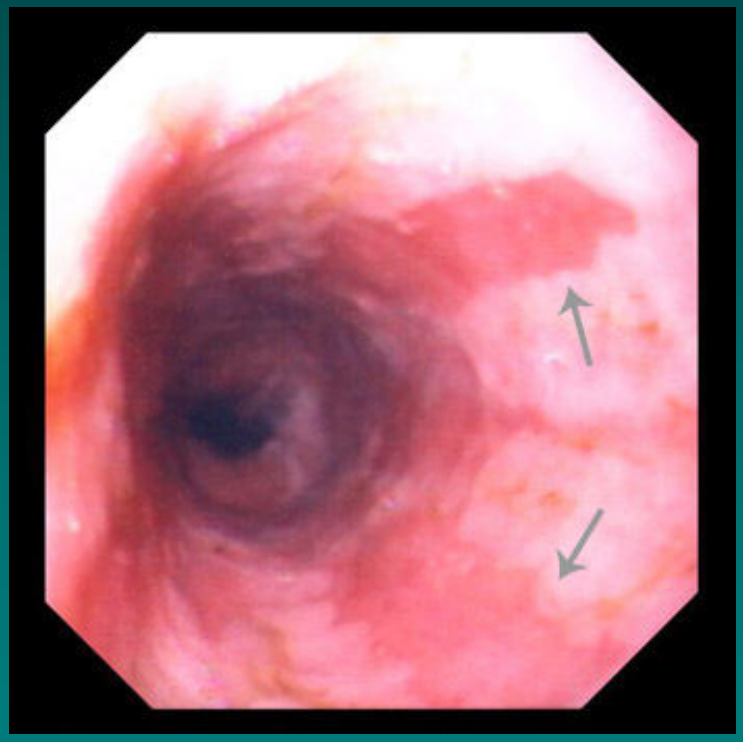


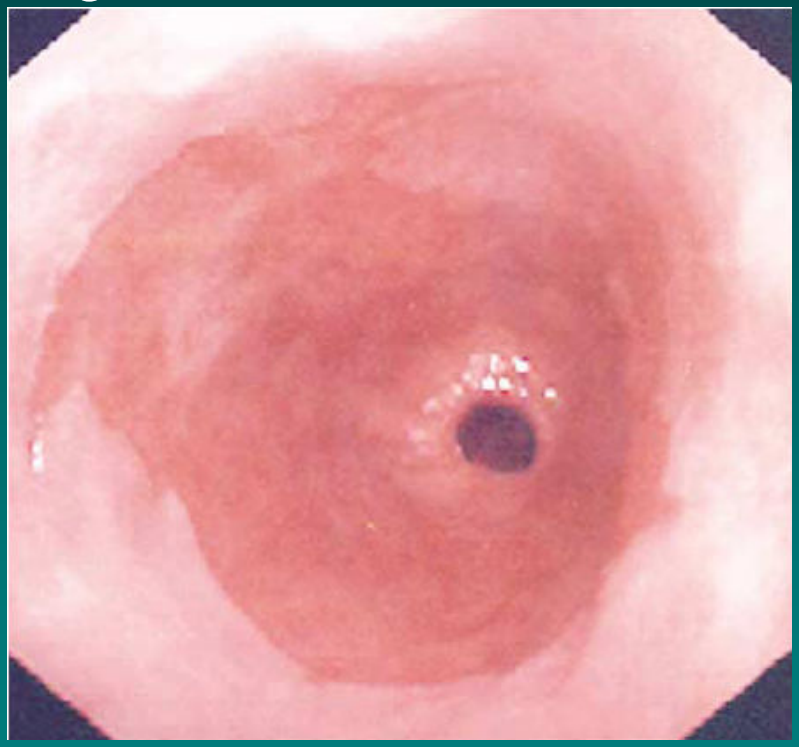
Peptic esofageal stricture



Complications of Gastroesophageal Reflux Disease (GERD)

Barrett's esophagus





Presence of columnar epithelia in the lower esophagus, replacing the normal squamous cell epithelium = Intestinal metaplasia

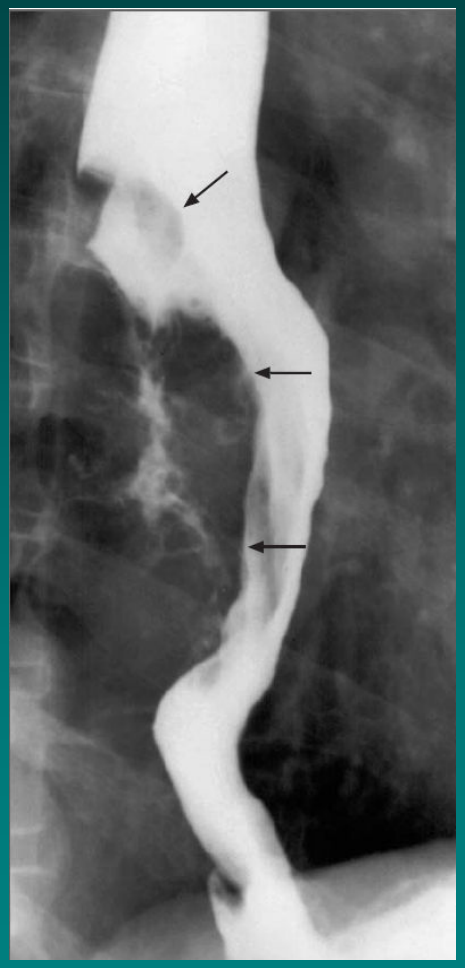
Clinical Evaluation of G-E Reflux

- Esophagoscopy
- pH monitoring (24h):
- Acid perfusion (Bernstein) test:
  - Whether the G-E acid reflux cause the pain (heartburn)
  - Perfusing the esophagus with alternating solutions of isotonic saline and 0.1 N hydrochloric acid through a nasogastric tube at a rate of 6-8 mL/min)

IMMAGING TECHNIQUES

- Native and contrast X-rays
  - foreign element, esophageal achalasia (native)
  - motility dysfunctions, lesions, tumors, strictures, membranes, hernias, spasm
  - Recording of ingestion act
    - Cineradiography, videoscopic recording
    - dysphagia, motility dysfunctions
  - Tomographic

Esophagogram
Malignant Esophageal Stricture

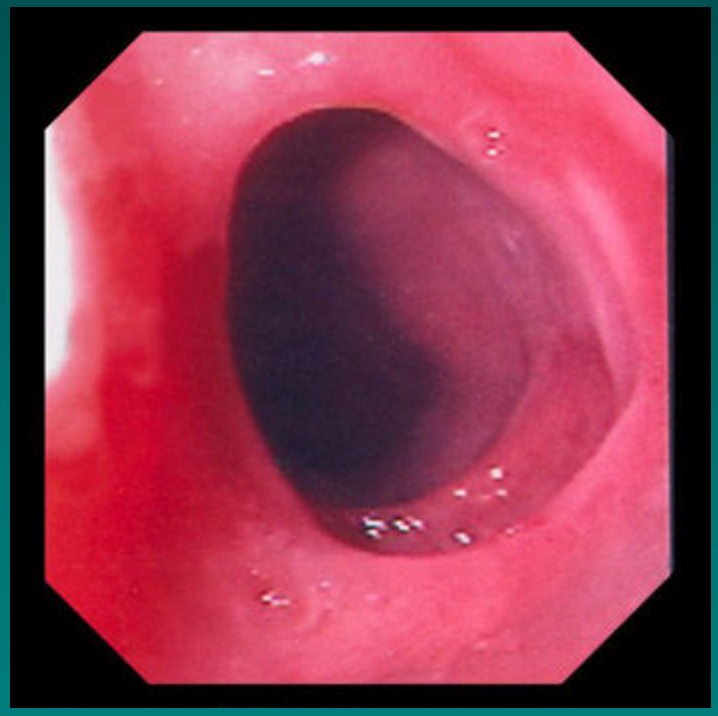


Esophagoscopy (Esophageal fibroscopy)

- Direct observation
- Biopsy (followed by histology)
- Therapy
  - Lesions
  - Acute hemorrhage
  - Foreign element ingestion
  - Tumors

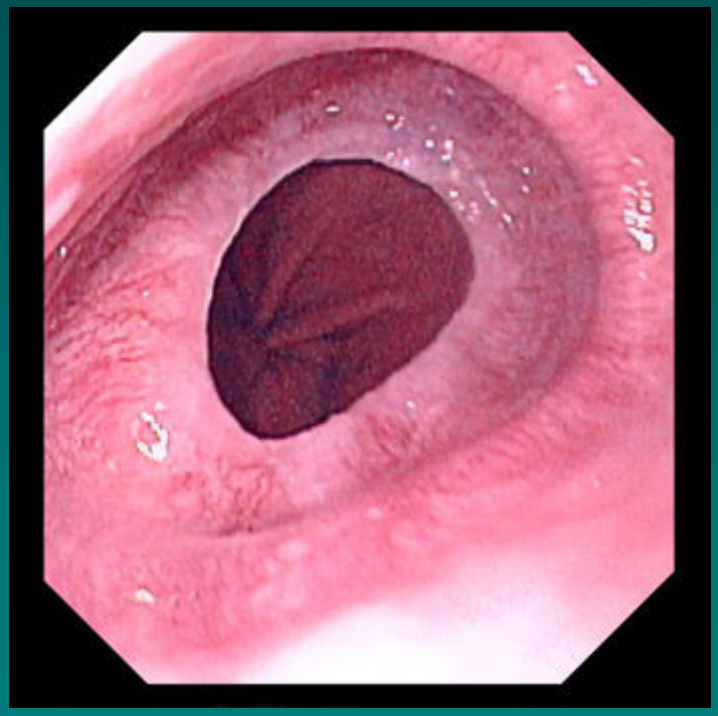
Obstructive esophageal disorders

Esophageal web



A thin mucosal membrane that grows across the lumen of the esophagus

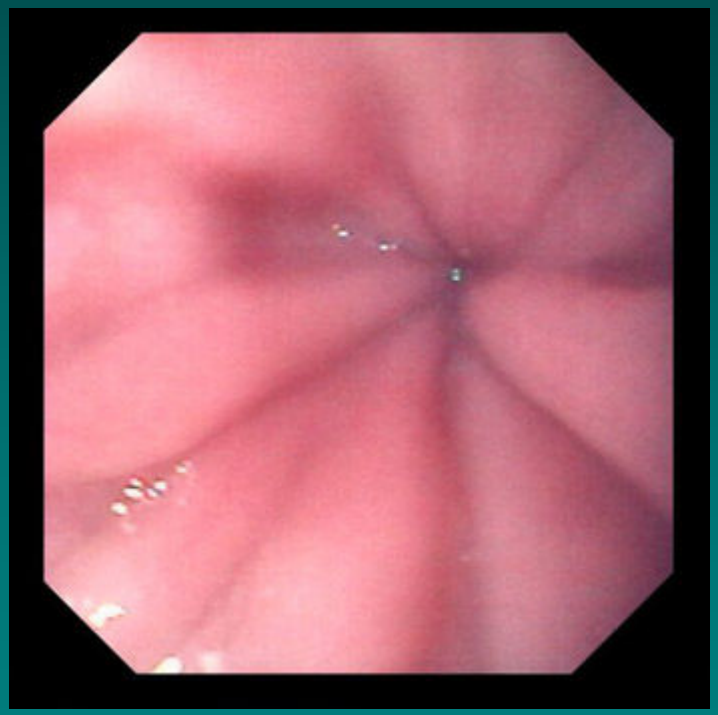
Esophageal ring



A 2- to 4-mm mucosal structure, causing a ringlike narrowing of the distal esophagus at the squamocolumnar junction

Motor esophageal disorders

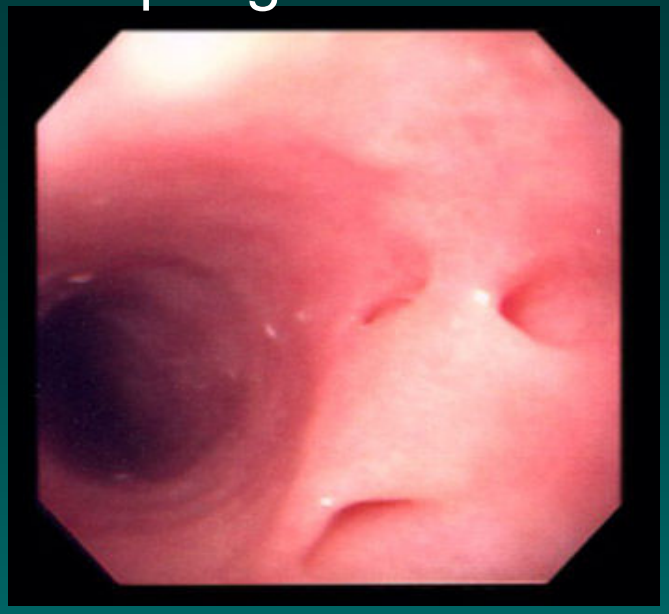
Achalasia



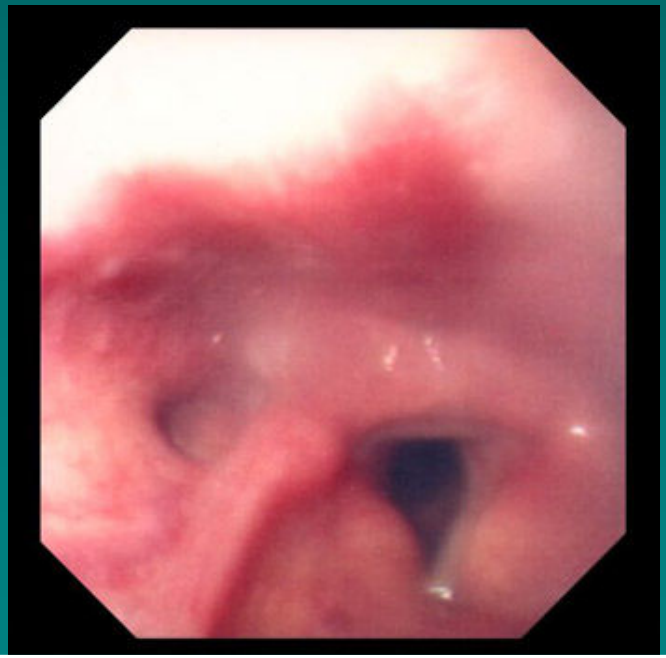
A neurogenic esophageal disorder of unknown origin characterized by impaired esophageal peristalsis and a lack of lower esophageal sphincter relaxation.

Diverticula

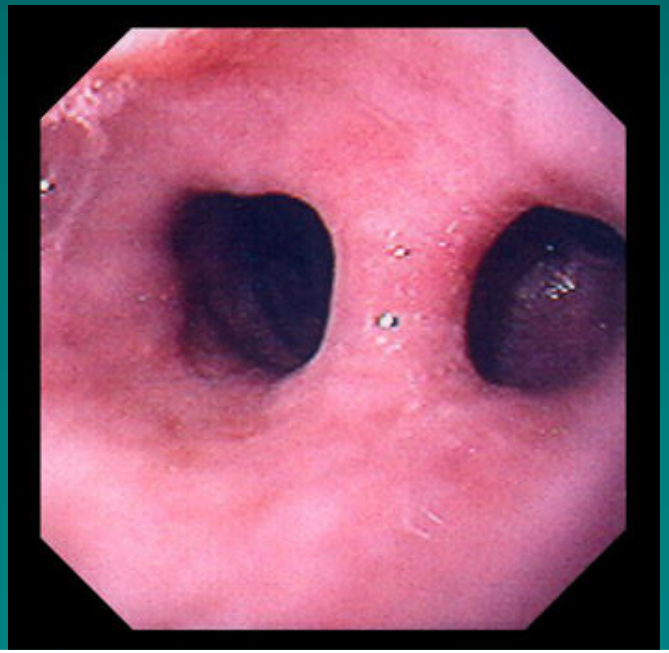
Esophageal diverticula



Zenker's diverticulum

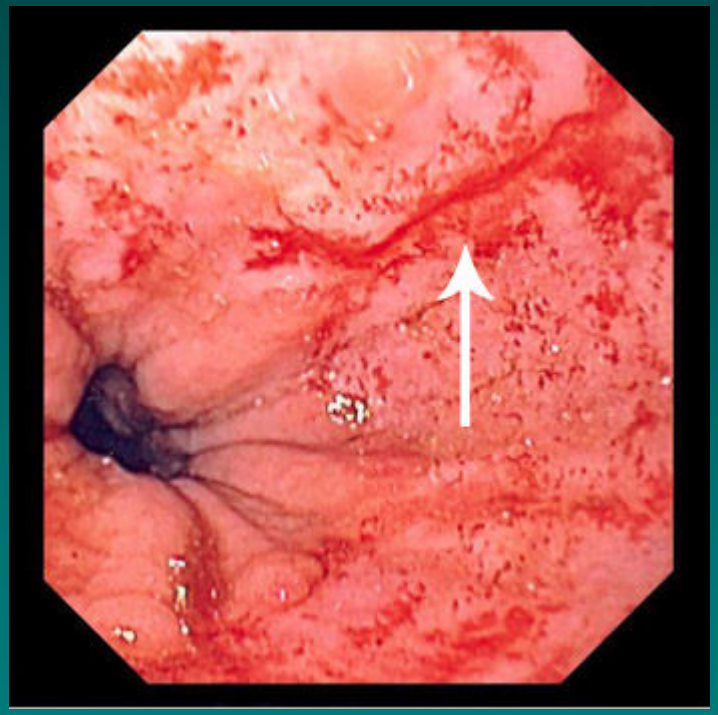


Traction diverticulum

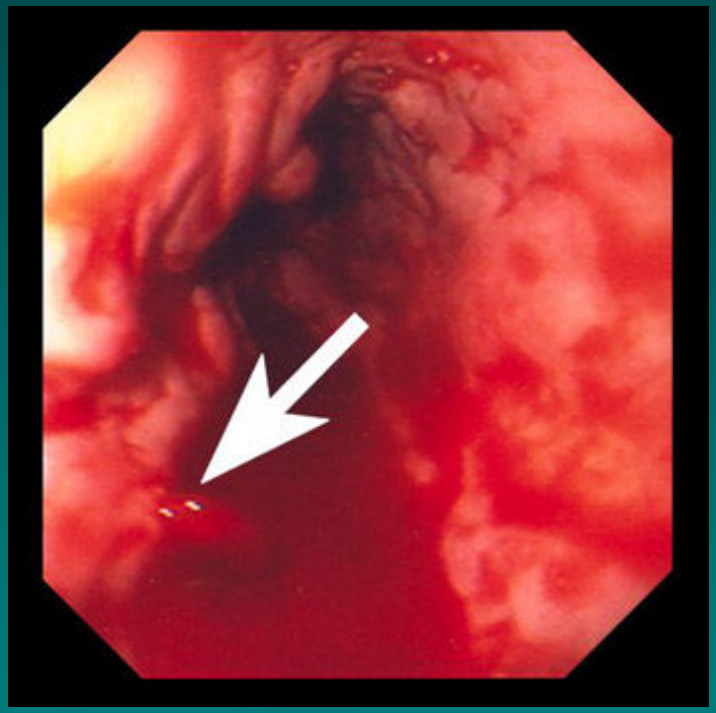


Esophageal bleeding

Mallory-Weiss tear



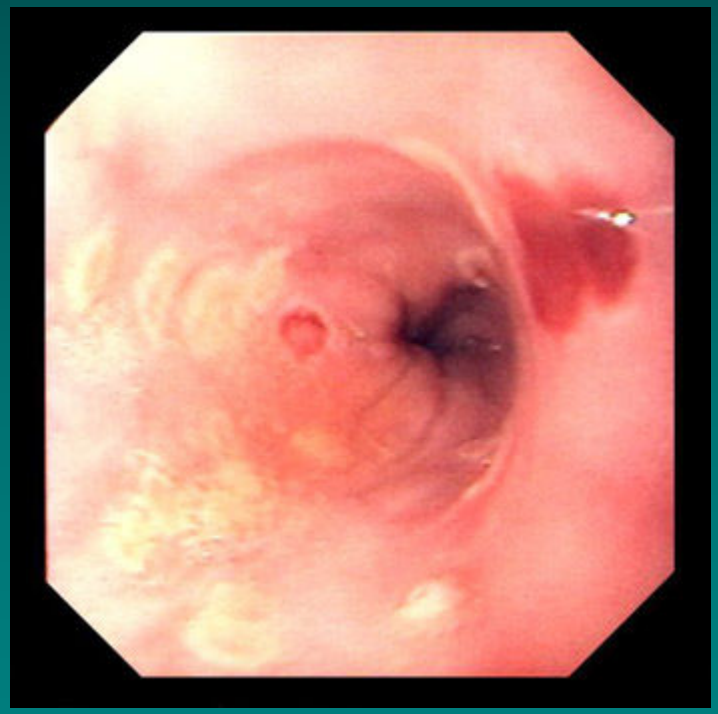
Acute varicose hemorrhage



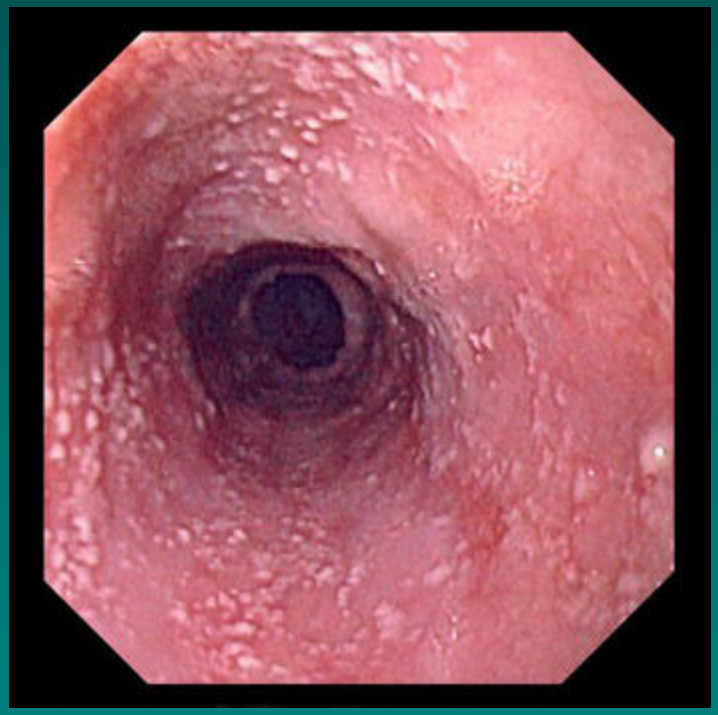
Laceration of the distal esophagus and proximal stomach during vomiting, retching, or hiccuping

Infectious Esophageal Disorders

Herpes simplex virus esophagitis

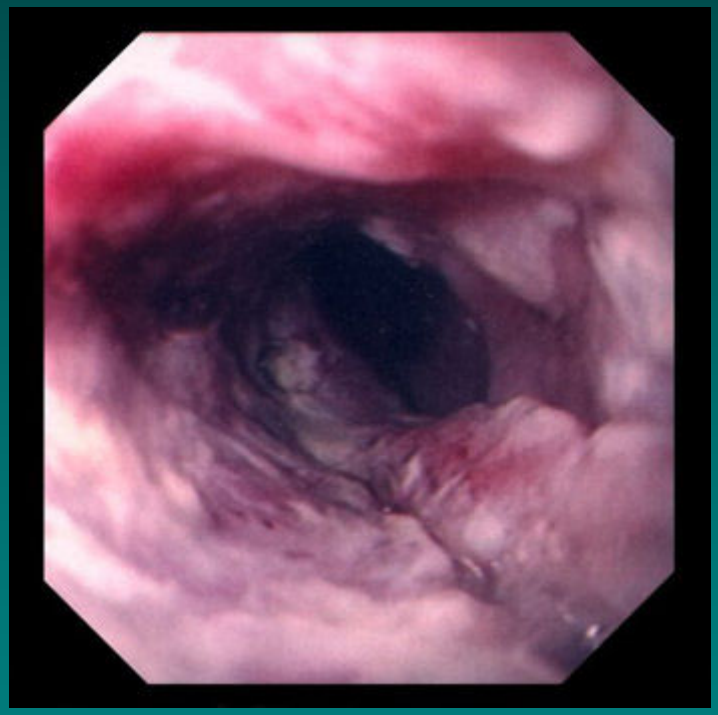


Candidal esophagitis

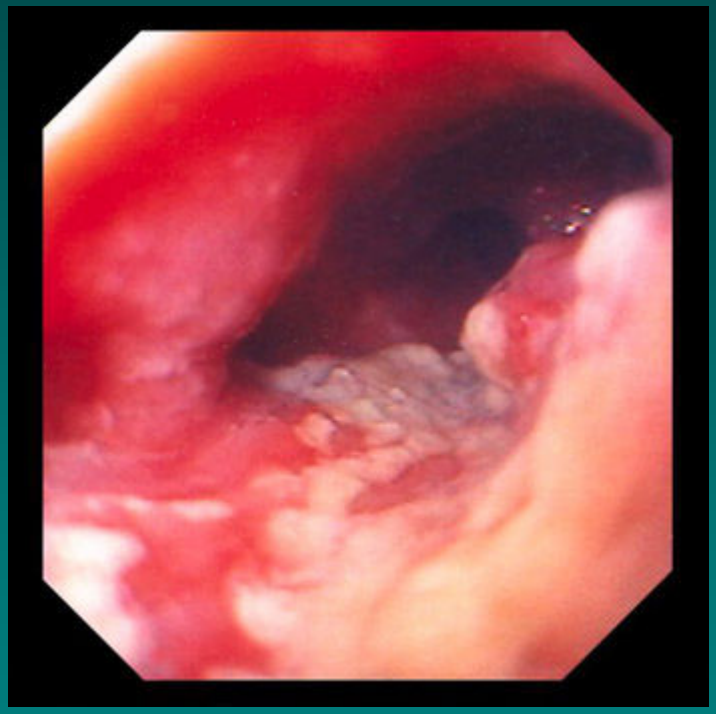


Esophageal Tumors

Squamous cell carcinoma of the esophagus

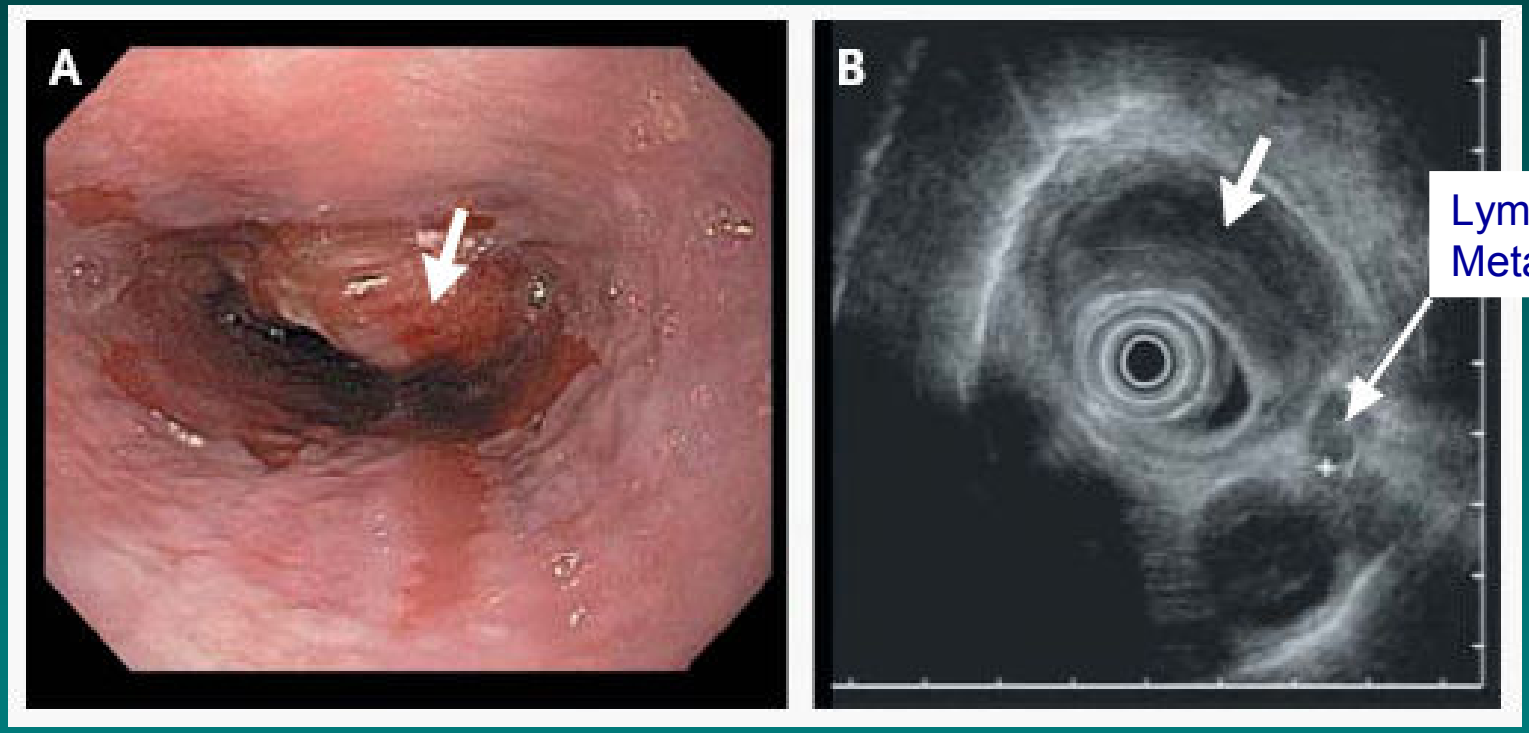


Adenocarcinoma of the esophagus



Nearly all patients with primary adenocarcinoma of the distal esophagus first have **Barrett's esophagus,** which results from chronic gastroesophageal reflux disease and reflux esophagitis.

Transmural Adenocarcinoma of the Barrett's Esophagus



Fibroscopy (Endoscopy)

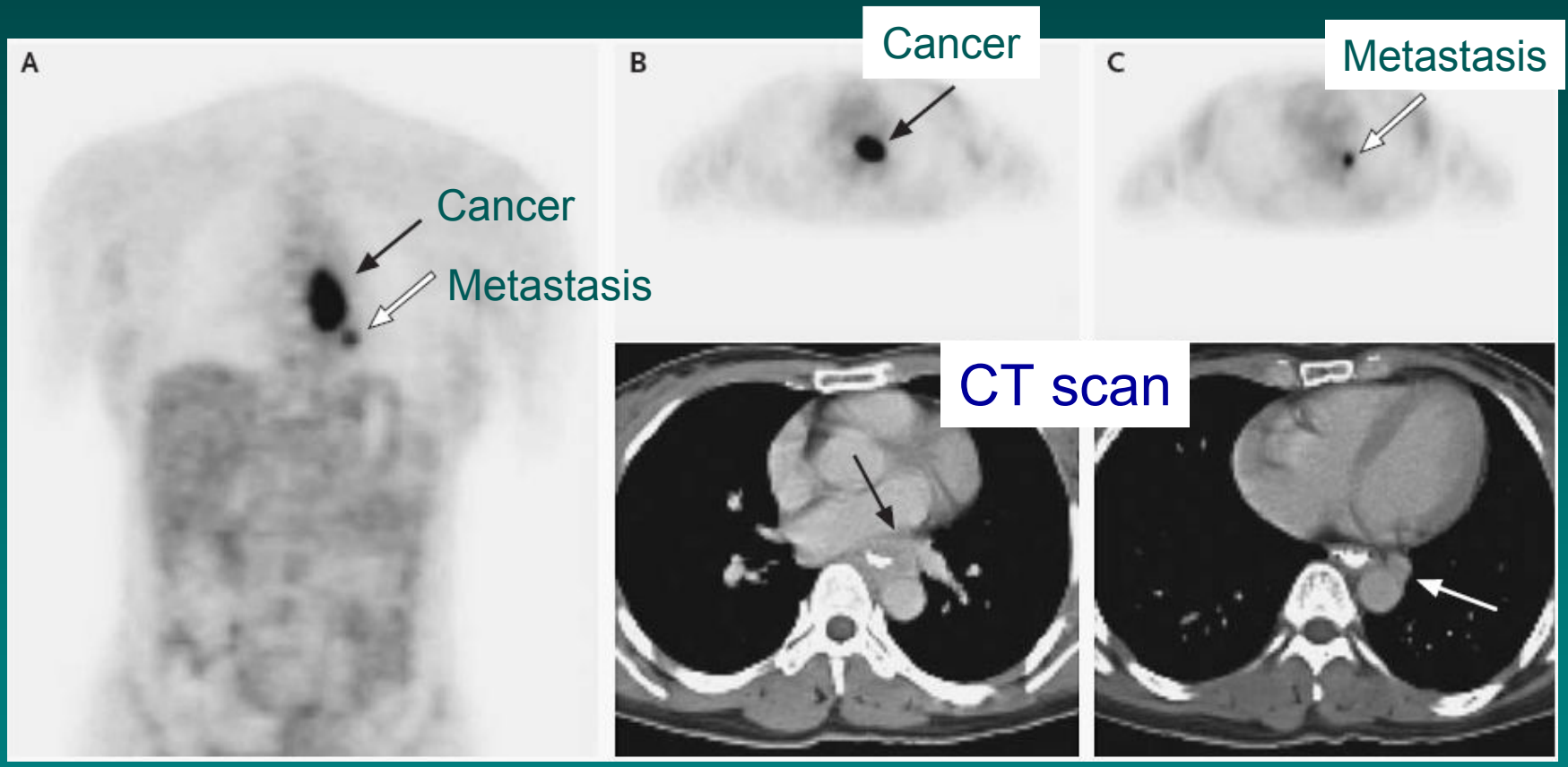
Endoscopic Ultrasonogram

OTHER IMMAGING METHODS

- Radioisotope scintigraphy
- Positron emission tomography (PET)
- Computer tomography (CT)

Positron-emission tomography

(eg. Fluorodeoxyglucose ^{18}F; ^{18}F-FDG)



Cancer of the distal esophagus with metastasis to a paraesophageal lymph node

STOMACH AND DUODENUM

Peptic ulcer disease (PUD)

- 5-10% of population (50% relapse within 5 years)
- Pathophysiology of peptic ulcer:
  - Ulcer:
    - mucosal defect reaching under the lamina muscularis mucosae
  - Localization:
    - stomach (malignant in about 5% of cases)
    - duodenum (usually non-malignant)
    - other:
      - esophagus
      - small intestine (gastro-enteroanastomosis or ectopic gastric mucosa in Meckel's diverticle)

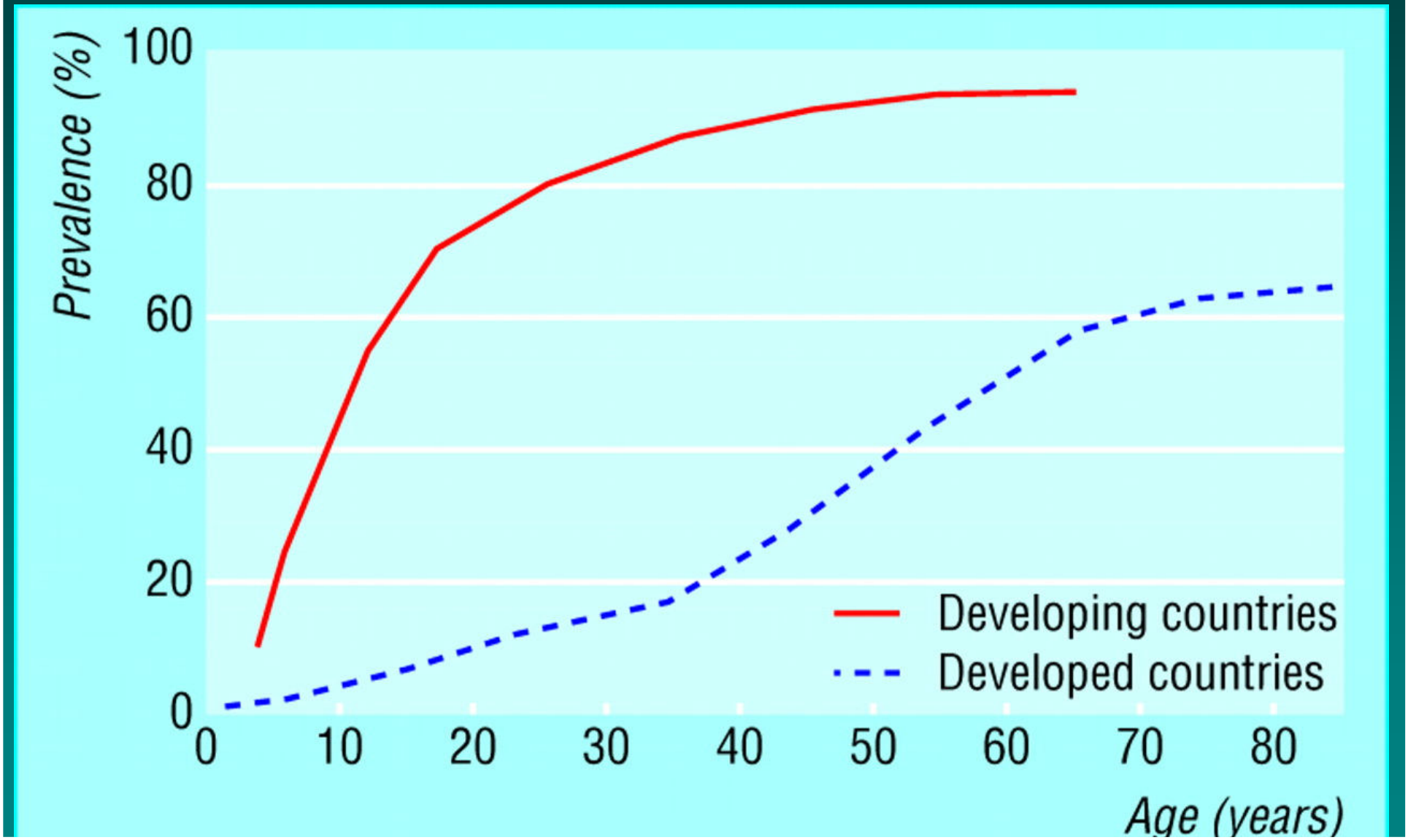
Causes of peptic ulcer disease (PUD)

Etiology:

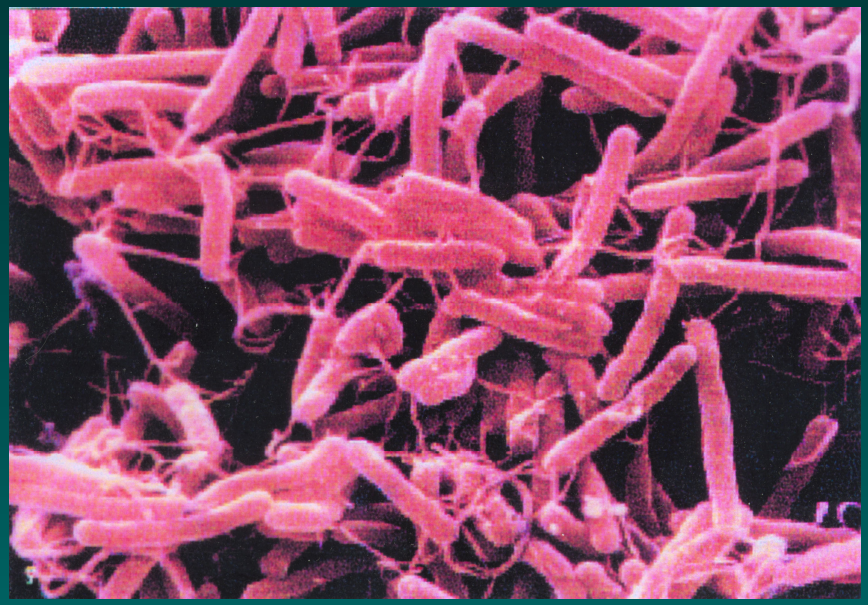
- Helicobacter Pylori (Gr- bacillus, urease production,)
- Drug therapy:
  - corticoids, nonsteroidal anti-inflammatory drugs (NSAIDS)
- Endocrine
  - Zollinger-Ellison sy. (gastrin), hyperparathyreosis
- Stress
- Hepatic failure associated
  - disordered metabolism and circulation
- Smoking?

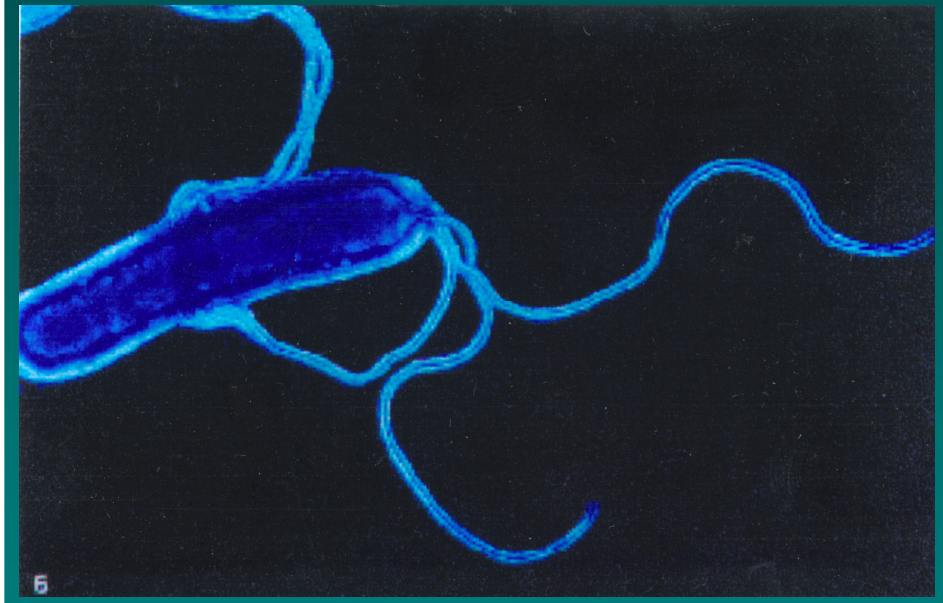
Helicobacter Pylori

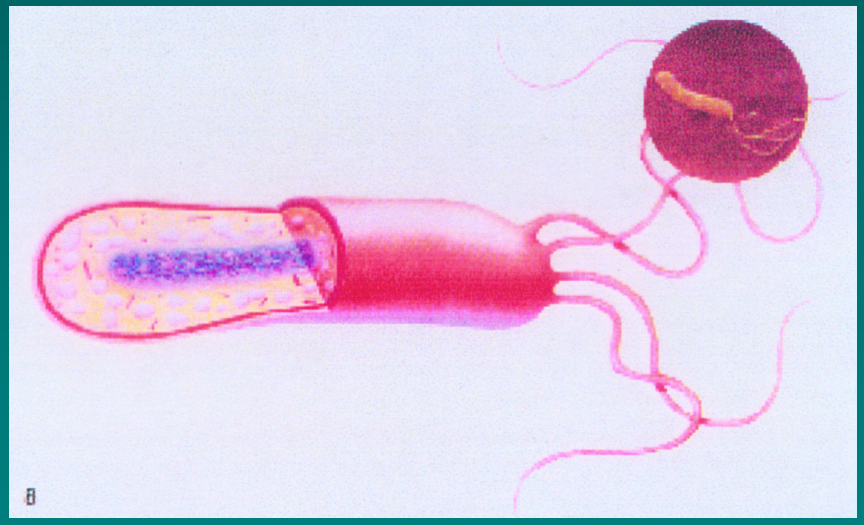
The most common human infection (increase with age)



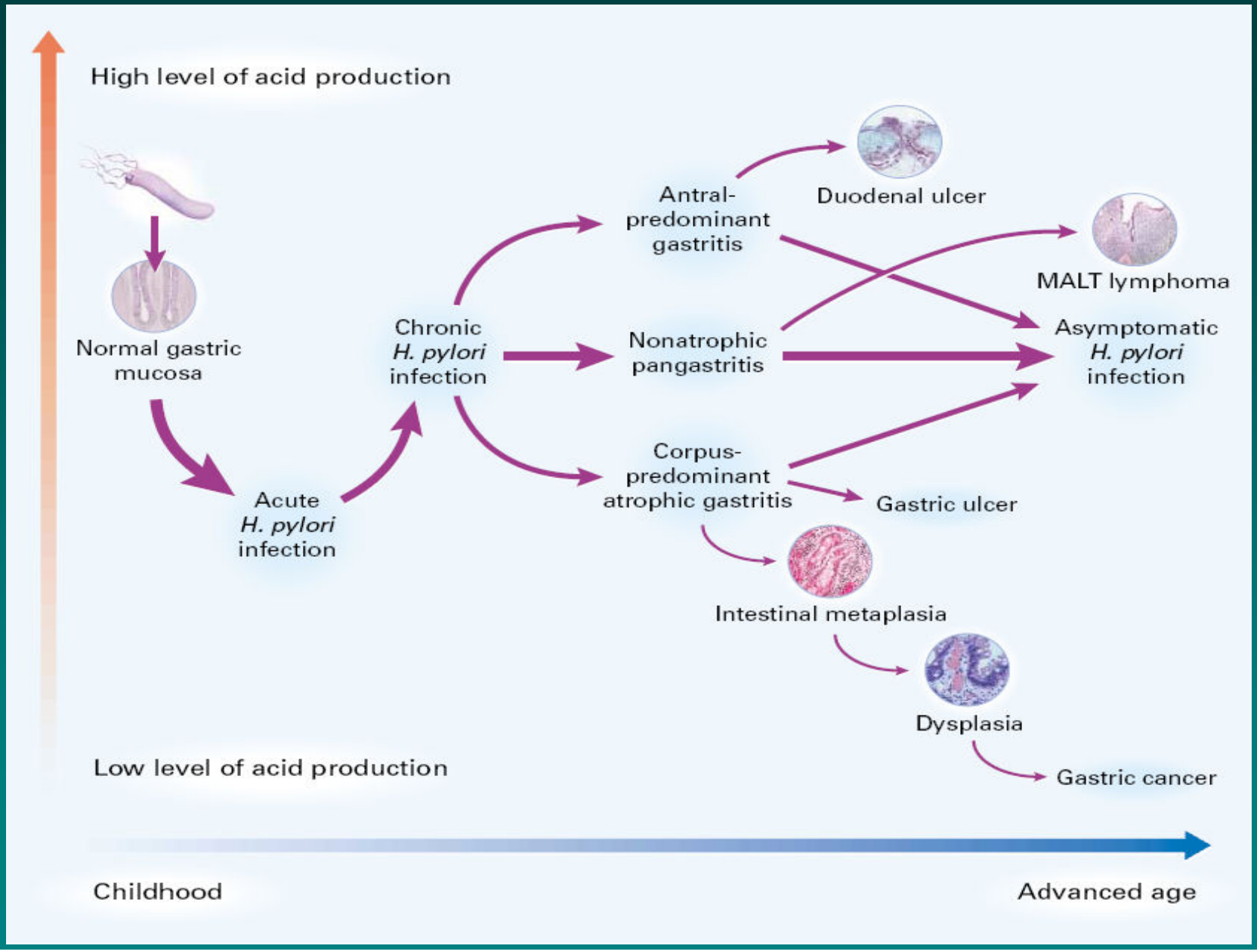
Helicobacter Pylori







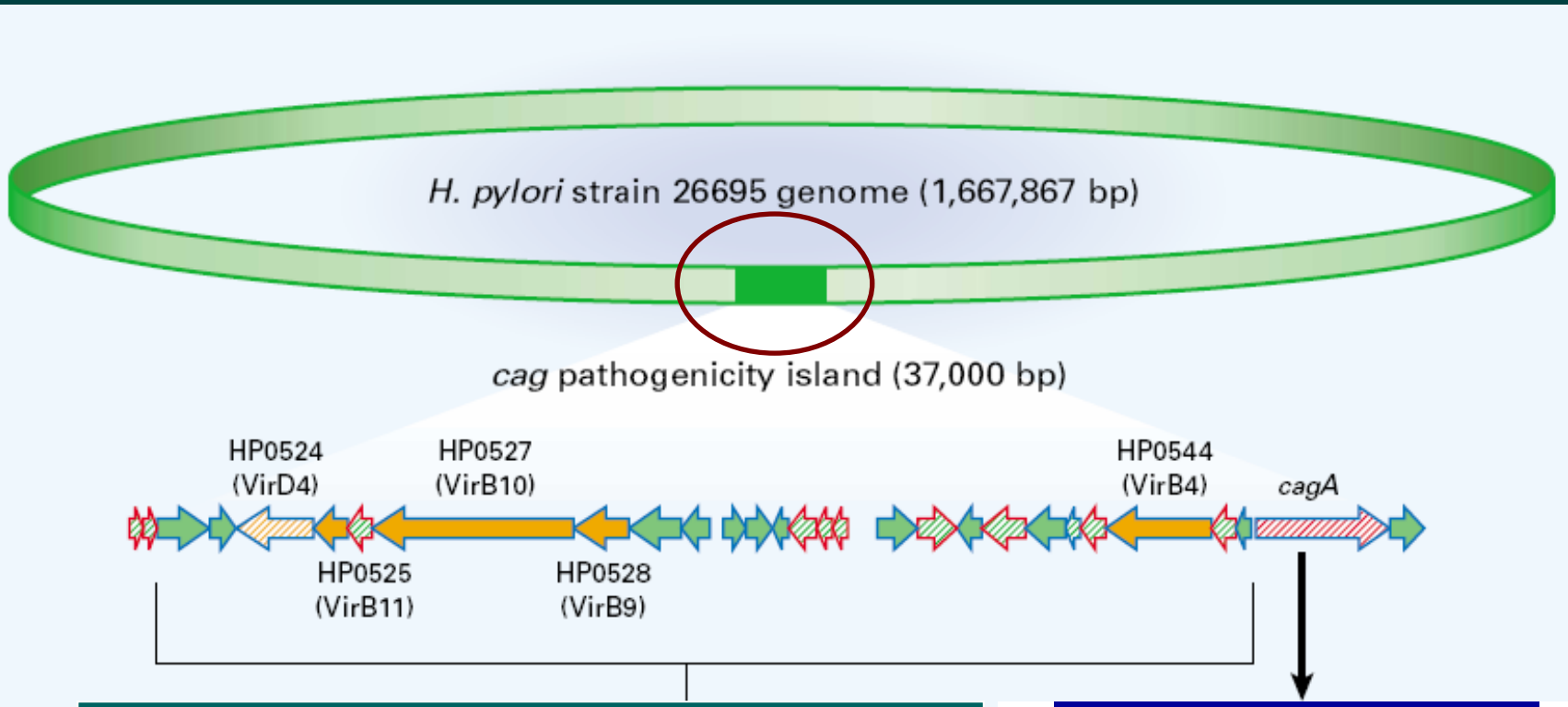
Natural History of *Helicobacter pylori* Infection



Helicobacter Pylori

- ”Discovered” 1982 Warren and Marshall
- Not all infected individuals have disease manifestation (15-20% HP positive have PUD)
- Virulence associated genes
  - vac A gene = vacuolising cytotoxin gene
  - cag A gene = cytotoxin associated gene
  - Urease (allow to survive extremely low pH ~ 1.0)
    - Cleaves urea to ammonium (which protects bacteria from HCl) and CO_2

The *cag* Pathogenicity Island



Encodes proteins which form secretion apparatus capable of delivering CagA from bacterium into the host cells

Translocation of CagA into the host cells

Phosphorylation of CagA by host kinases

Activation of intracellular signaling pathways

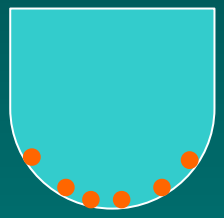
Diagnosis of *H. pylori* infection

- Noninvasive:
  - serologic testing (serum IgG to H. pylori antigens)
  - breath test with isotype-labeled urea

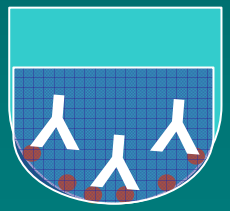
- Invasive: Endoscopy + biopsy +
  + histological analysis of bioptic material
  + confirmation of urease activity (Clotest)
  + cultivation of H. pylori from the sample
  + PCR detection of H. pylori DNA in the sample

IgG to *H. pylori antigens* (ELISA)

- 96-well ELISA plate



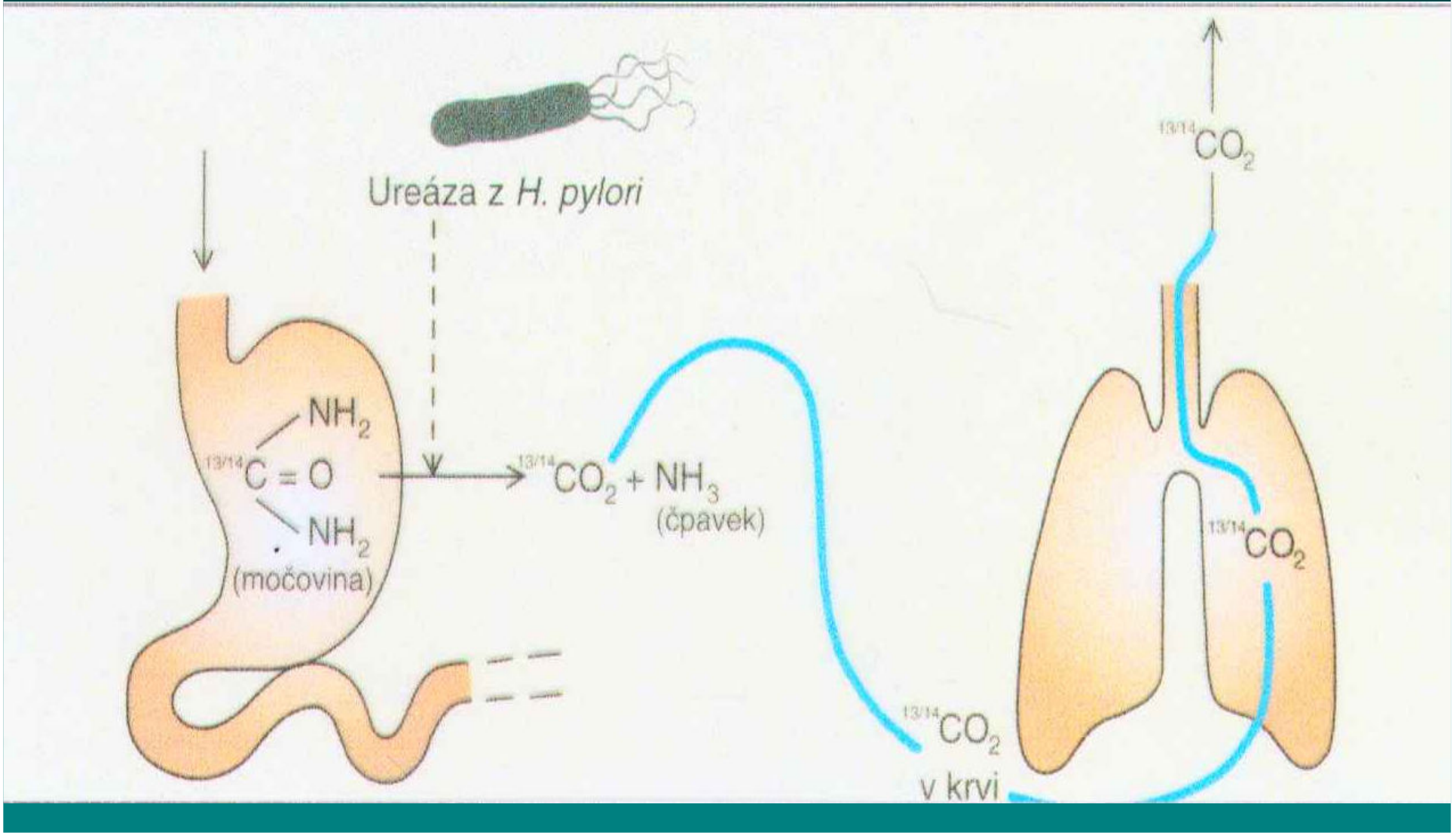
H. pyplori antigen



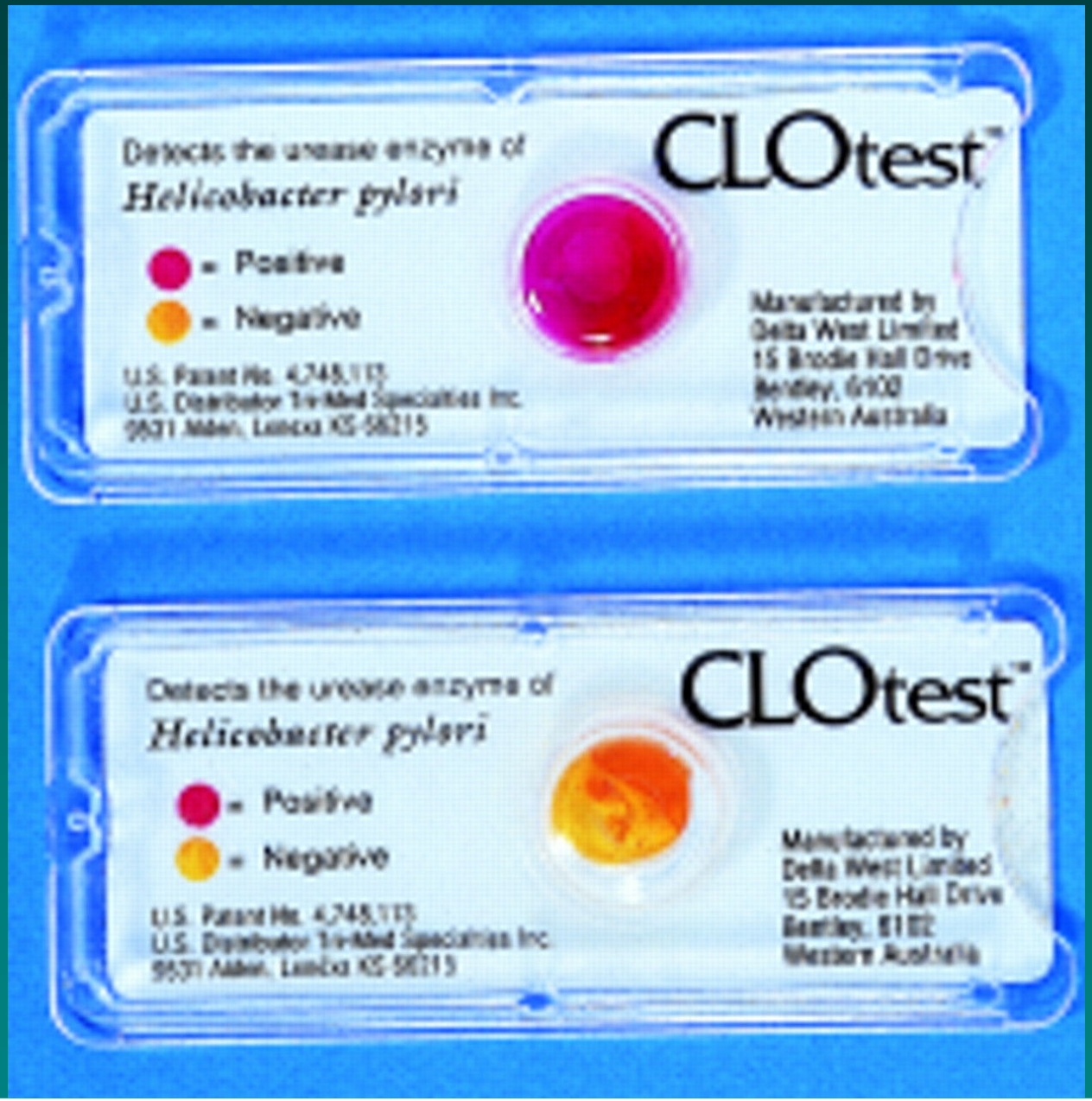
Pacient’s serum/plasma

Anti-IgG (Ig) –HRP (AP)

Breath test with isotope-labeled urea (^{13}C or ^{14}C)



Positive and negative results of CLO test for *H pylori*



X-ray Examination of Stomach and Duodenum

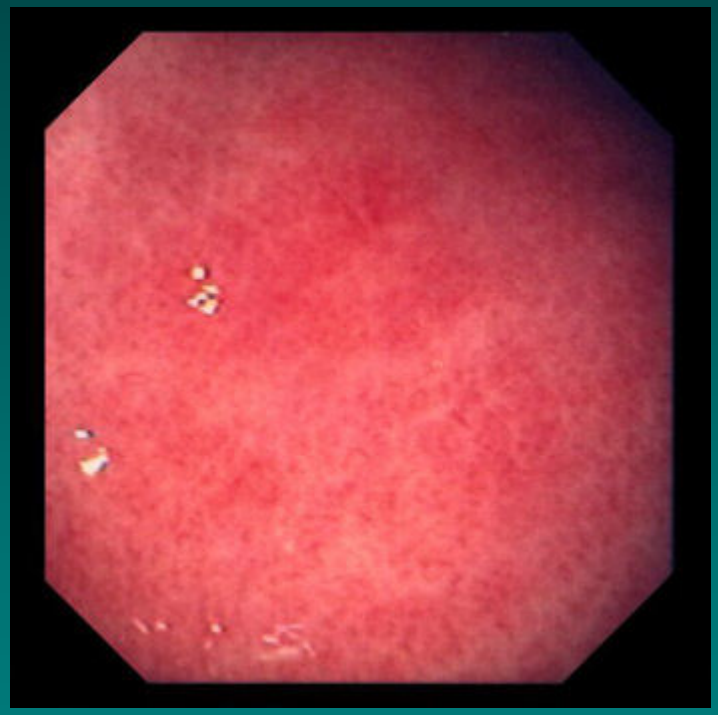
- With contrast:
  - stomach shape
  - changes in mucosal surface relief
  - peristalsis evaluation
  - emptying ability of stomach

Endoscopic Examination
(gastroscopy, fibroscopy)
(Esophagogastroduodenoscopy = EGD)

- Risk of serious complications 1:800
- Risk of patients death 1:5000
- direct observation of mucosal defects + biopsy
  - erosions
  - Ulcers
  - bleeding

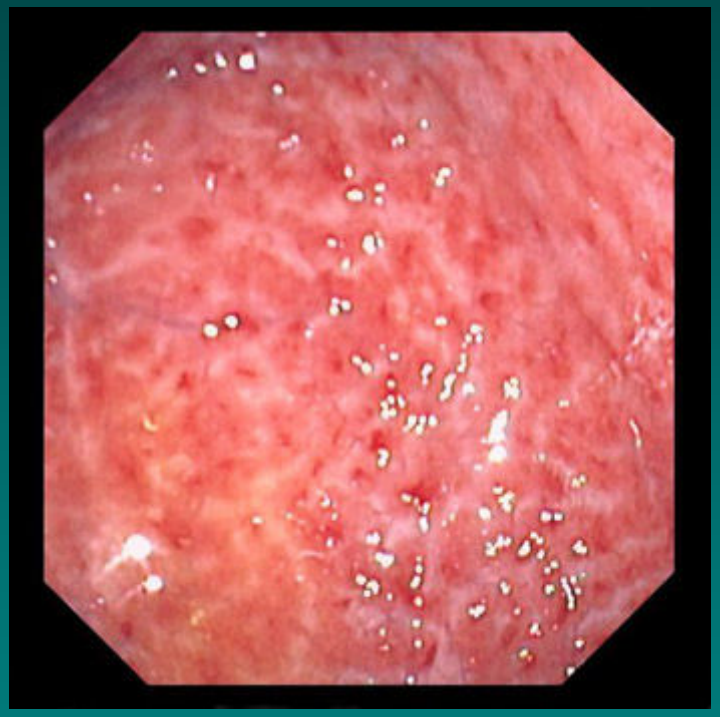
Gastritis

Acute gastritis



Patient tested positive for H. pylori

Chronic gastritis

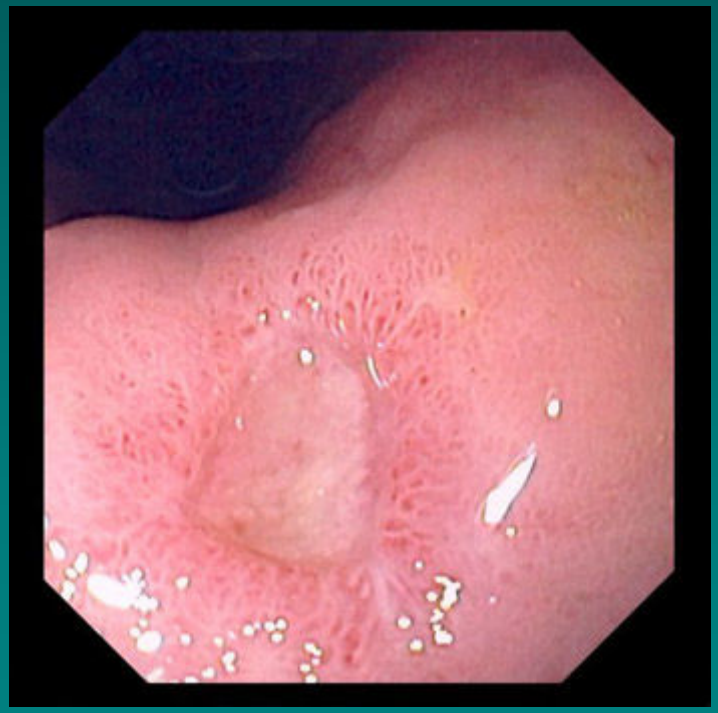


Chronic erosive gastritis may be idiopathic or caused by drugs, Crohn's disease or viral infections.
Helicobacter pylori does not appear to have a major role in the pathogenesis of this condition.

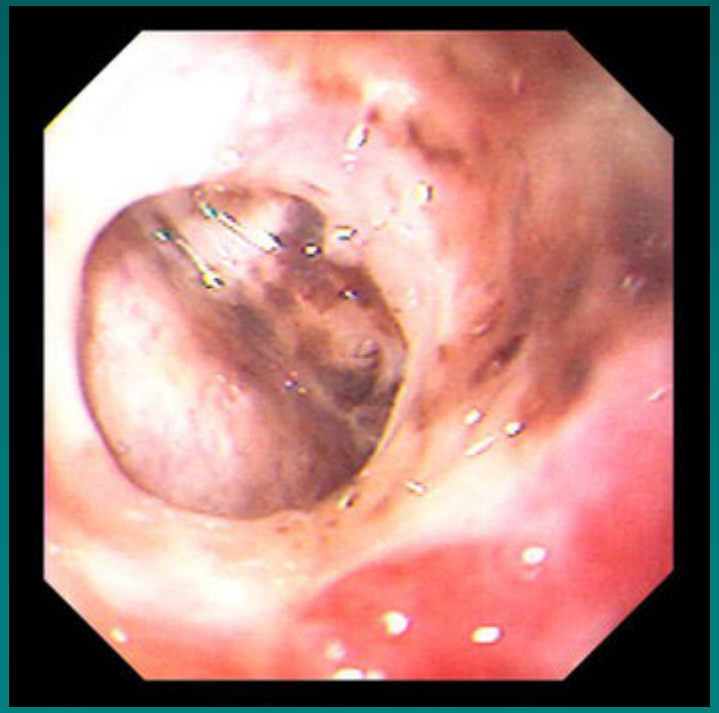
Peptic Ulcer Disease

An excoriated segment of the GI mucosa, typically in the stomach (gastric ulcer) or first few centimeters of the duodenum (duodenal ulcer), which penetrates through the muscularis mucosae

Gastric ulcer

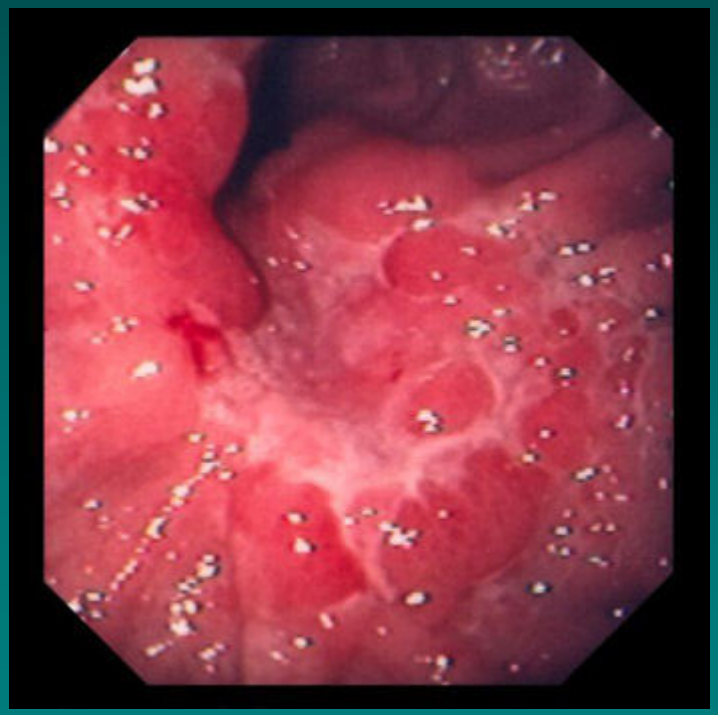


Gastric ulcer (confined perforation)



Gastric Tumors

Gastric adenocarcinoma (signet ring cell type)



Gastric adenocarcinoma (see Plate 34-3) accounts for 95% of malignant tumors of the stomach

Differential diagnosis commonly involves peptic ulcer disease

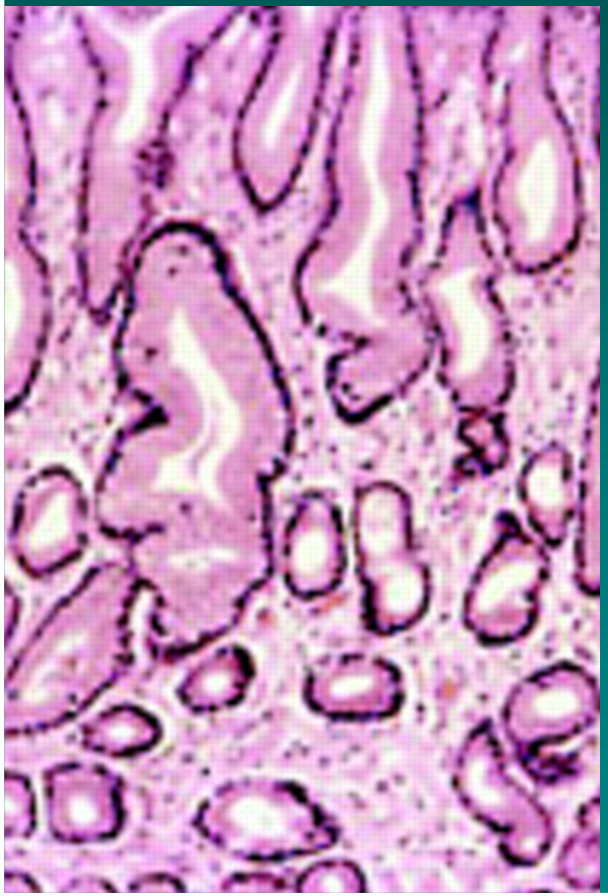
Endoscopy:
- direct inspection
- biopsy of suspicious areas

Cytology on gastric washings
- together with biopsy improves results.

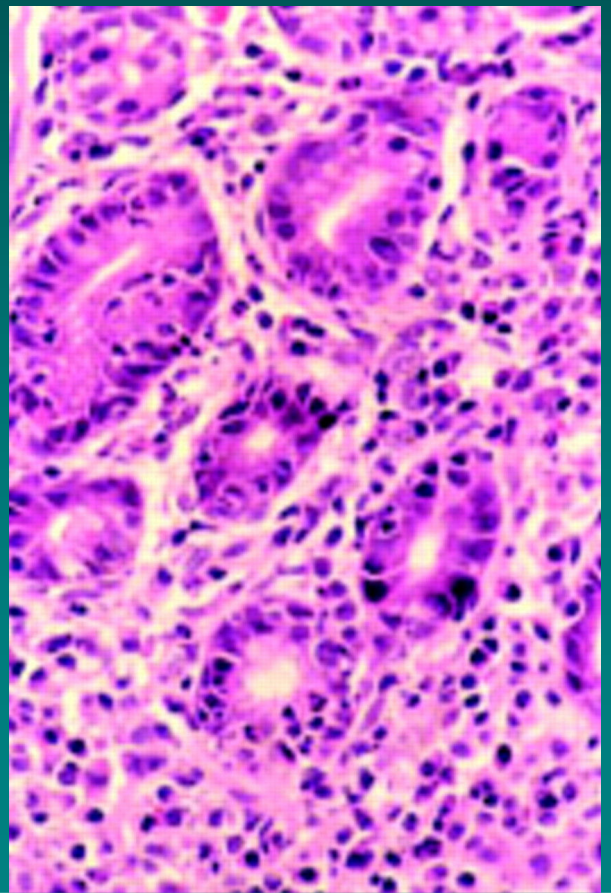
X-rays
- unreliable in finding small, early lesions (<1 cm in diameter)

Histology of gastric mucosa

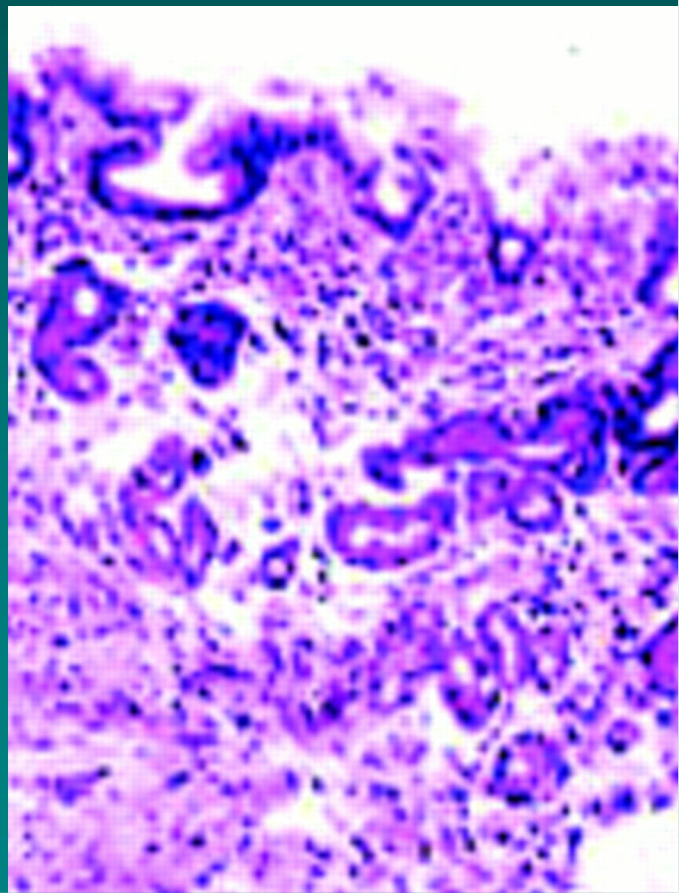
normal antral mucosa



active gastritis



atrophy of antral mucosa



Other Diagnostic Methods

- Gastric acid secretoty studies:
  - basal acid output (BAO): Four 15 min samples of stomach secretion
  - maximal (peak) acid output (MAO or PAO): collection of stomach fluid in 15 min. intervals after the s.c. administration of pentagastrin
  - Dg: Zollinger-Ellison sy
- Serum gastrin levels: Zollinger-Ellison sy

SMALL INTESTINE

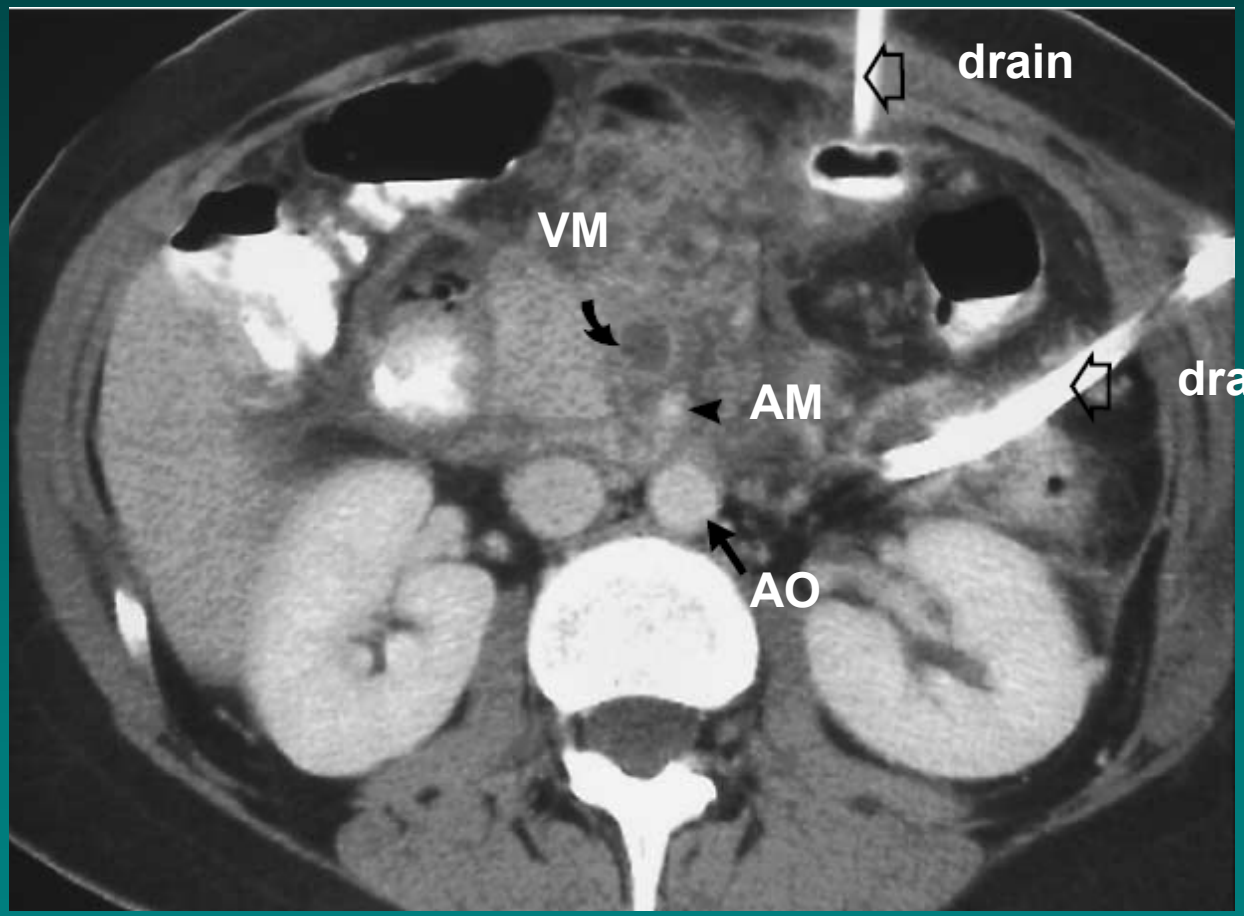
X-ray Examination

Native – ileus

Contrast – morphology and motility

- Barium radiography - intestinal passage (tumors, enteritis)
- Arteriography
  - embolization of a. mesentherica
  - arterial bleeding (limit ~0.5 mL/min)

Computer-Tomographic Scan of the Abdomen in a Patient with Acute Thrombosis of the Superior Mesenteric Vein Complicating Acute Pancreatitis



Superior mesenteric vein is enlarged as a result of the thrombosis (curved arrow)

Resorption Tests

- Direct methods
  - analysis of stool compounds (fat > 6g / day steatorhea ~ malabsorption)
- Indirect methods
  - measurement of the concentrations of p.o. administered compounds in:
    - urine
    - serum

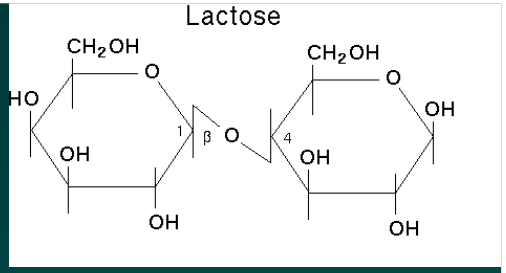
Resorption Tests

- Xylose test
  - measurement of xylose in urine or blood after p.o. administration (25 g)
  - resorption defects in proximal intestine
  - steatorhea, malabsorption sy., Crohn's disease
  - Blood 300 mg/L (2mmol/L) 2 h after p.o. xylose
  - Urine >4g in 5h
- Schilling test
  - p.o. administration of radio-labeled vitamin B12 and measurement of its activity in urine or blood
  - whether B12 deficiency is caused by intrinsic factor deficiency

Small Bowel Biopsy

- patient swallows lubricated tube with a Carey capsule
- the tube is manipulated with fluoroscopic guidance through the pylorus to the third or fourth portion of the duodenum
- biopsy specimen is obtained by producing negative pressure with a syringe while the aspiration port is open

Lactose Intolerance



- The diagnosis may be suspected when chronic or intermittent diarrhea is acidic (pH < 6)
- The lactose tolerance test:
  - Lactose 50 g p.o.
    - Diarrhea with abdominal bloating and discomfort within 20 to 30 min
    - Blood glucose flat curve with no significant peak (peak 1-2 hours)
    - The hydrogen breath test
      - Interval measurement of breath hydrogen by mass spectrometry
  - Small-bowel biopsy
    - lactase activity in a jejune biopsy specimen confirms the diagnosis

Other Tests

- Technetium-99m labeled erythrocytes:
  - patients with susceptive lower GI bleeding after an exclusion of upper GI bleeding
  - sensitivity ~ 0.1 mL/min

LARGE INTESTINE AND RECTUM

X-ray

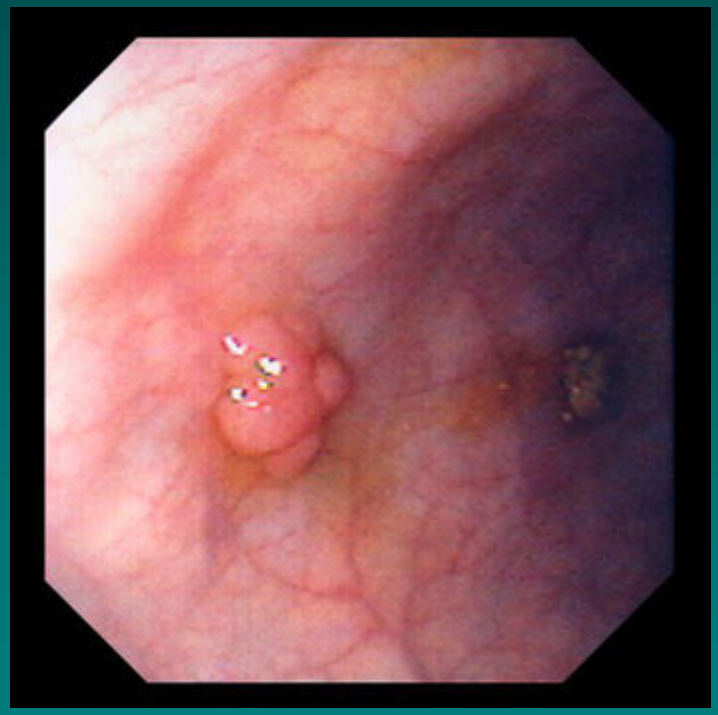
- Native
  - dg. ileus
- Contrast - irrigoscopy
  - dg. tumors, diverticulose disease, chronic obstipation, repeated diarrhea, Inflammatory Bowel Diseases (IBD; ulcerous colitis, Crohn's disease)

Colonoscopy, rectoscopy

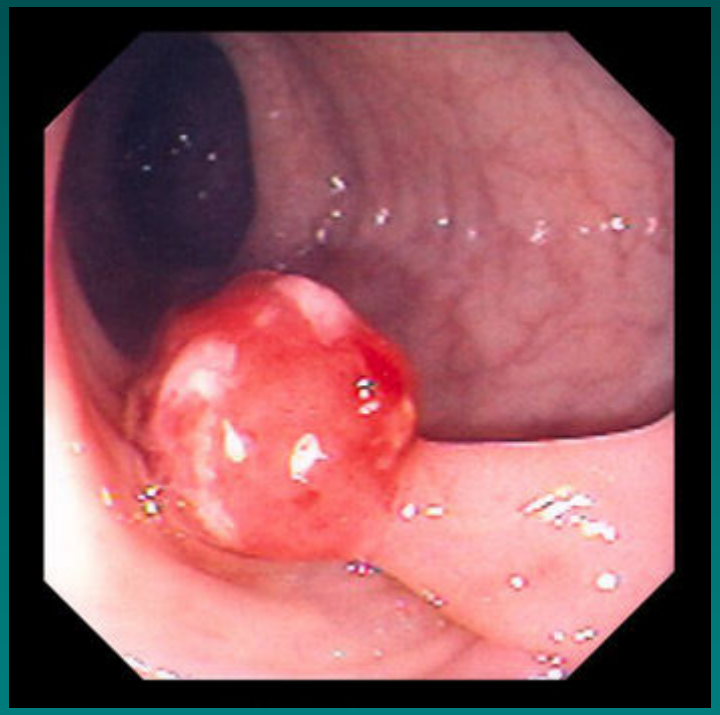
- Rigid or flexible fibroscopes
  - Direct observation
  - Biopsy and cytology
  - Therapeutical procedures

POLYPS OF THE COLON AND RECTUM

Colonic polyp (sessile)



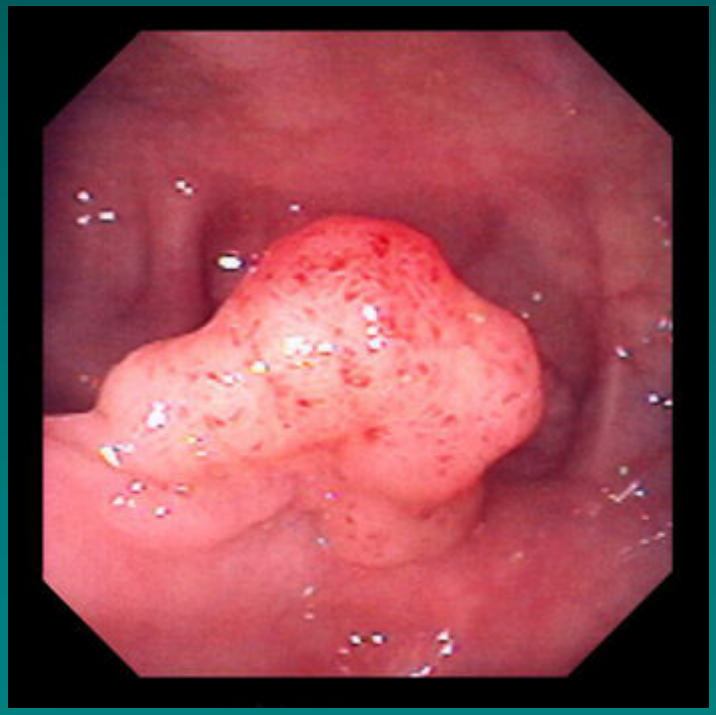
Colonic polyp (pedunculated)



Histology demonstrated benign tubular adenoma

POLYPS OF THE COLON AND RECTUM

Villous adenoma.



Stool Examinations

a) Microbiology
b) Parazitology
c) Occult blood
d) Fat content

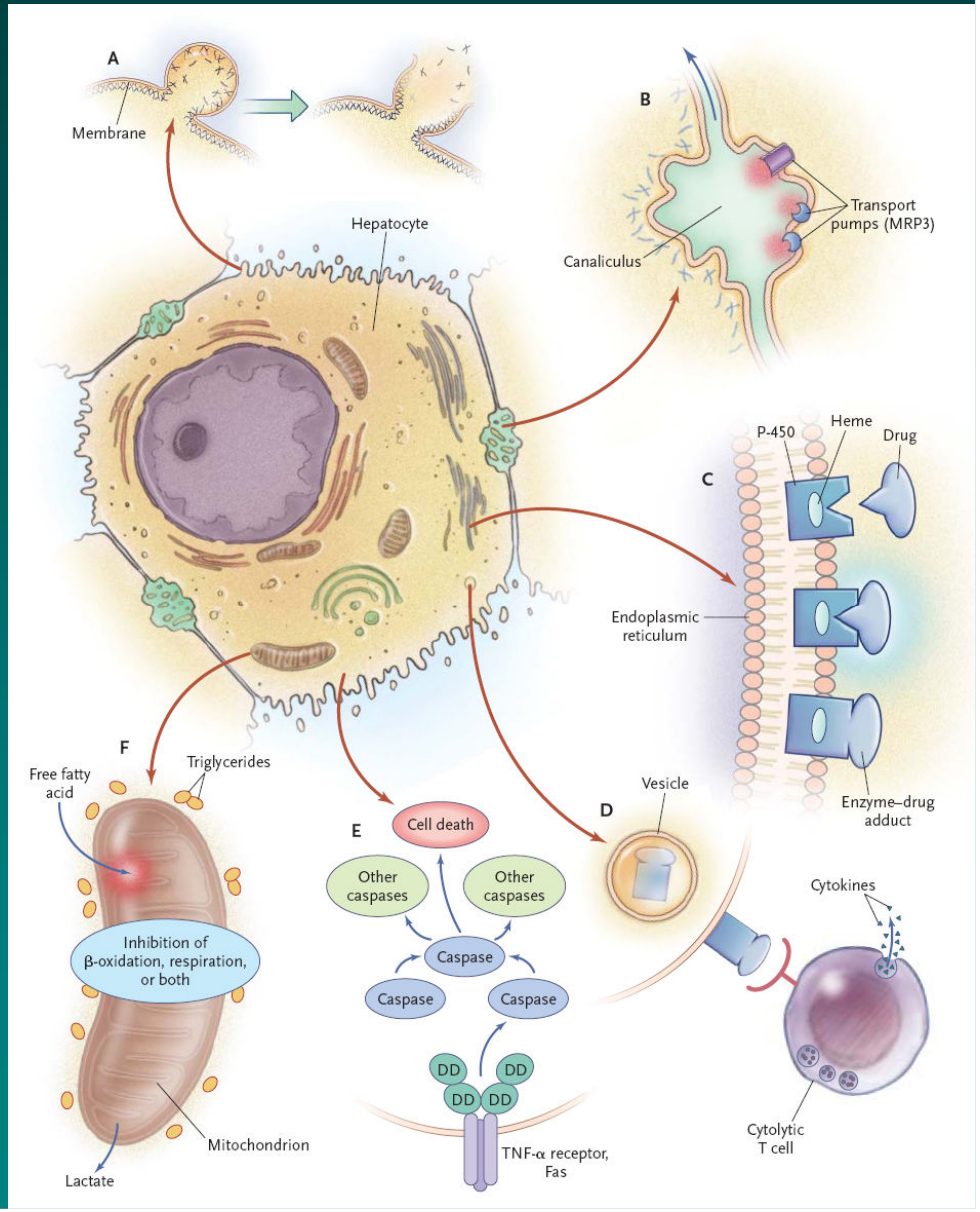
LIVER AND BILIARY SYSTEM

Causes of pathological results of liver tests

- Decrease of amount of functioning hepatic tissue
  - “liver function tests“ (decrease of synthesis of albumin and clotting factors)
- Hepatocyte damage
  - serum aminotransferases, hyperbilirubinemia
- Cholestasis
  - elevated bilirubin, elevation of alkaline phosphatase, elevated cholesterol
- Portosystemic shunts
  - Decrease in uptake of substances from blood (elevated ammonia)

Six Mechanisms of Liver Injury

A. Disruption of intracellular calcium homeostasis
B. Interruption of transport pumps (e.g. MRP3)
   - excretion of bilirubin and organic compounds
C. covalent binding of drug to P-450 enzymes
   - nonfunctioning adducts
D. Enzyme–drug adducts migrate to the cell surface
   - target immunogens
E. Activation of apoptotic pathways
   - TNF receptor family
F. Drug – induced inhibition of mitochondrial function
   - β-oxidation and respiratory-chain enzymes inhibition



LIVER PANEL

- Aspartate aminotranspherase (AST)
- Alanine aminotranspherase (ALT)
- Alkaline phosphatase (ALP)
- Bilirubin
- Albumin
- Total plasma protein

Aspartate-aminotransferase (AST)

- 0.5-0.65 μkat/L
- reliable marker with good monitoring value in liver diseases (decline to normal values are observed during regeneration)
- heart, muscles, brain, kidneys, pancreas, lungs, leukocytes, and ***liver***
- elevation – myocardial infarction, heart failure, muscle injury, CNS diseases, and other non-hepatic diseases; ***hepatocellular damage***
- severe elevation – acute viral or toxic hepatitis

Alanine-aminotransferase (ALT)

- 0.55-0.65 μkat/L
- primary in hepatocytes – more specific for liver diseases
- ratio AST/ALT < 1
  - AST/ALT >2 in alcoholic liver disease (caused by vitamine B6 deficiency - cofactor for ALT)

Alkaline phosphates (ALP, AP)

- liver, bone, placenta, and intestine
- 2.3-2.7 μkat/L
- severe elevation
  - cholestasis from intrahepatic (prim. biliarny cirrhosis) and extrahepatic causes (bile duct obstruction)
- mild elevation
  - hepatocellular damage (hepatitis, cirrhosis)
- isolated elevation
  - granulomatous or focal liver lesions (abscess, tumor)
  - nonhepatic tumors (bronchogenic ca, Hodgkin's lymph.)
  - Bone diseases (metastases, osteomalatia)
  - Pregnancy

Serum bilirubin

- 17-20 μmol/L, 0.3 - 1.9 mg/dL
- Causes of hyperbilirubinemia:
  - bilirubin overproduction (hemolysis) ~ unconjugated bilirubin (serum)
  - decreased liver uptake and conjugation ~ unconjugated bilirubin (serum)
  - decreased billiary secretion (cholestasis) ~ conjugated bilirubin (serum, urine)

Total plasma protein (65-80 g/l)

- Decrease
  - Hyperhydratation
  - Malnutrition (Prealbumin)
  - Third space escape (ascites, edema)
- Elevation
  - dehydration

Albumin

- 32-45 g/l
- Half-life about 14-20 days
- Reserve of hepatic albumin synthesis
- Decrease:
  - chronic liver diseases (cirrhosis, ascites) in combination with increase in distribution space
  - malnutrition
  - loss in urine (nephrotic syndrome)
  - loss through intestine (exsudative gastroenteropathies)
  - loss by skin (burns)

Other Laboratory tests: Enzymes

- 5’ Nukleotidase
  - more specific than ALP
  - used to confirm hepatic origin of ALP
- GMT (GGT) = gamma-glutamyl transpeptidase (transferase) (0.6-1.1 μkat/l)
  - elevation – bile ducts obstruction, drug and alcohol abuse
- Lactate-dehydrogenase = LD(H) (to 7.5 μkat/l)
  - good marker of hemolysis, myocardial infarction, malignant liver diseases
- Cholinesterase (80-190 μkat/l)
  - decreased – hepatic parenchyma damage
  - elevated – alcoholism

Other Laboratory tests: bilirubin

- Urine bilirubin
  - related to increase of conjugated bilirubin in serum
  - early symptom of acute viral hepatitis (occurs event before the onset of jaundice)
  - false-negative – bilirubin oxidation, ascorbic acid, nitrates in urine
- Urobilinogen in urine (gut-derived metabolite of bilirubin)
  - overproduction of bilirubin (hemolysis)
  - decreased uptake by liver and decreased excretion (entero-hepatic circulation exceeds liver capacity)

Other Laboratory tests: Serum Immunoglobulins

- Elevation:
  - chronic liver disease (increased antigenic stimulation of extrahepatic lymphoid tissues by GIT antigens, portal circulation dysfunction, porto-systemic blood shunting)
- mild elevation
  - acute hepatitis
- severe elevation
  - chronic active hepatitis
- IgM – elevated in primary biliary cirrhosis
- IgA – elevated in alcoholic liver disease
- IgG – elevated in chronic active hepatitis

Other Laboratory tests: coagulation

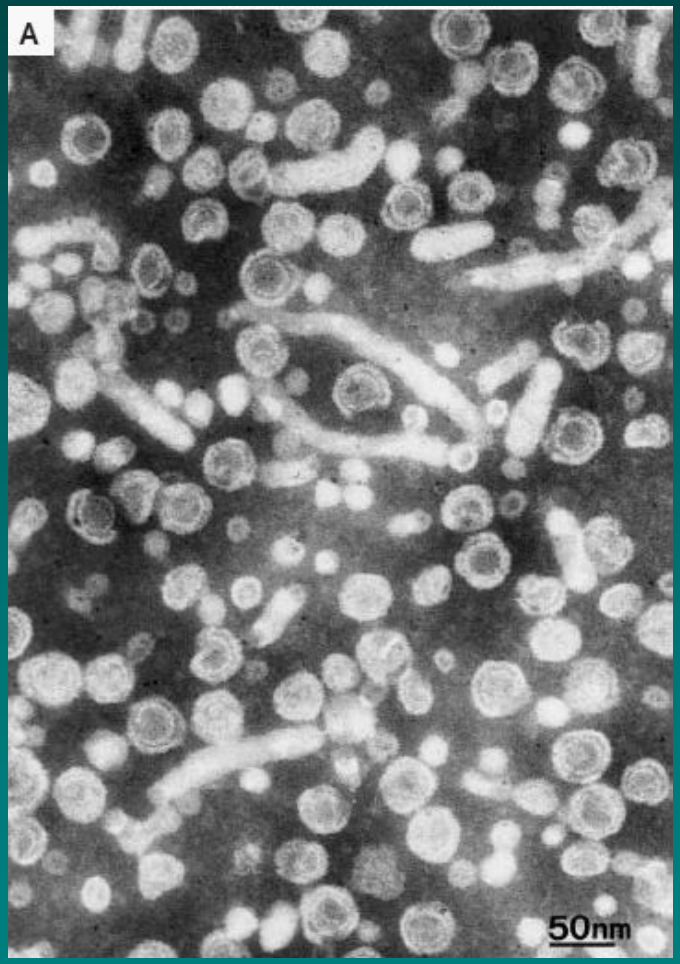
- Prothrombin time = Quick test = PT
  - F I (fibrinogen)*, II (prothrombin)*, V, VII*,IX*,X* (vit. K)
  - prognostic value in acute liver damage - half-life of clotting factors is from several hours to several days
  - required before surgery on liver disease patients

Other Laboratory tests: Specific proteins

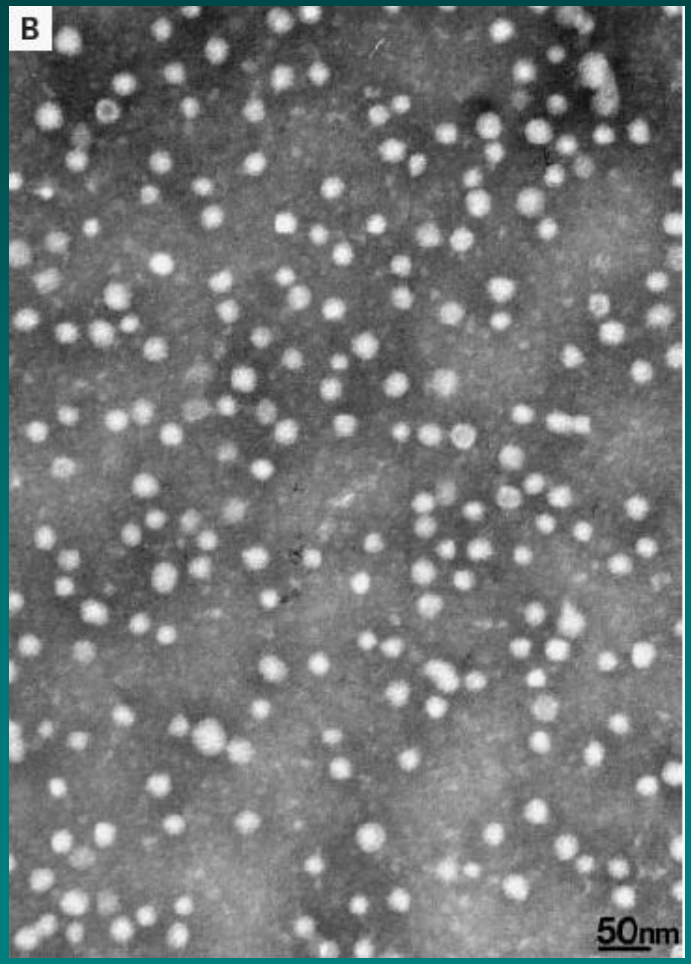
Viral antigens = Ag

- HB**s**Ag – **s**urface antigen of hepatitis B virus
  - positive 1–7 weeks before clinical manifestation of disease, during, and 1–6 weeks after and in chronic form
- HBeAg – marker of infectivity of hepatitis B
- Antigen specific antibodies (Ab):
  - antibodies IgM (acute) and IgG for hepatitis A virus
  - anti-HBs – to surface antigen
    - Positive after course of hepatitis type B and after immunization
  - anti-HBc - during acute phase of hepatitis B

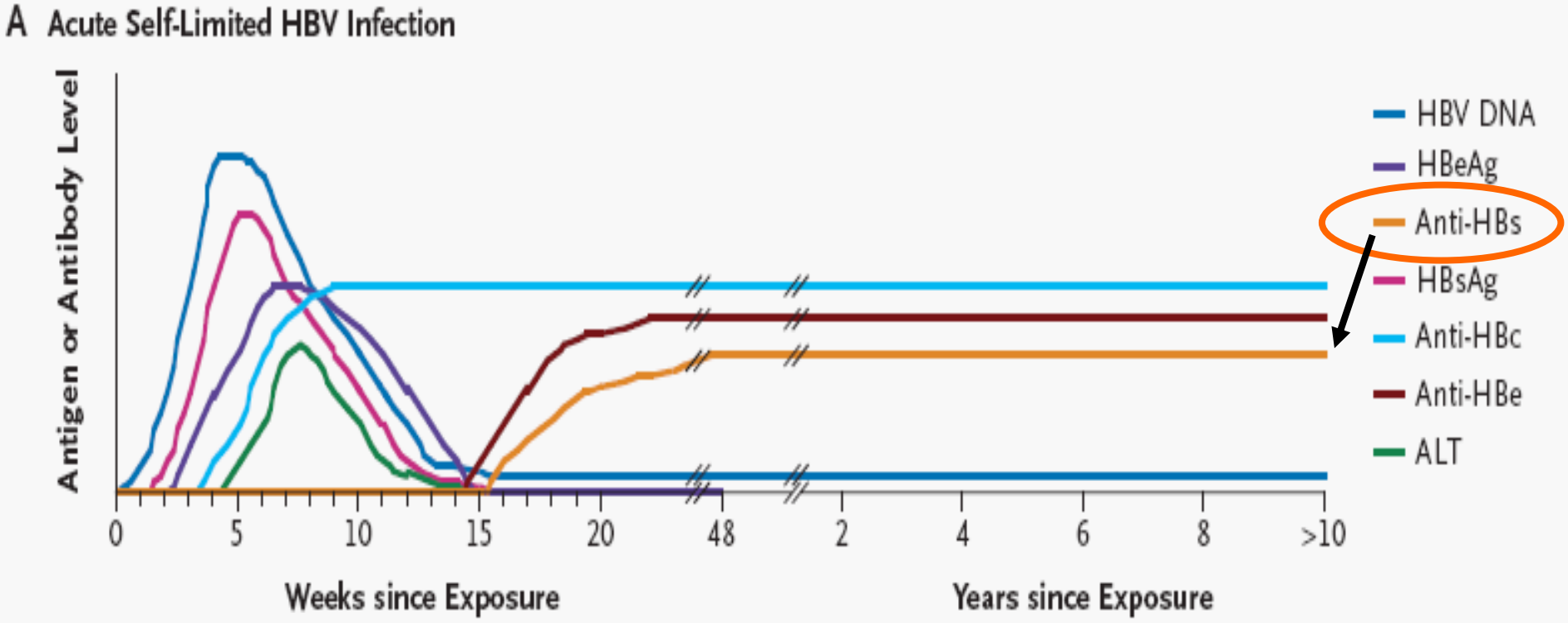
HBV virions (Dane particles) and filaments



HBsAg particles



Patterns of Serologic and Molecular Markers in HBV Infection



Prince AM, Lee D-H, Brotman B. Transfusion 2001;41: 329-32.

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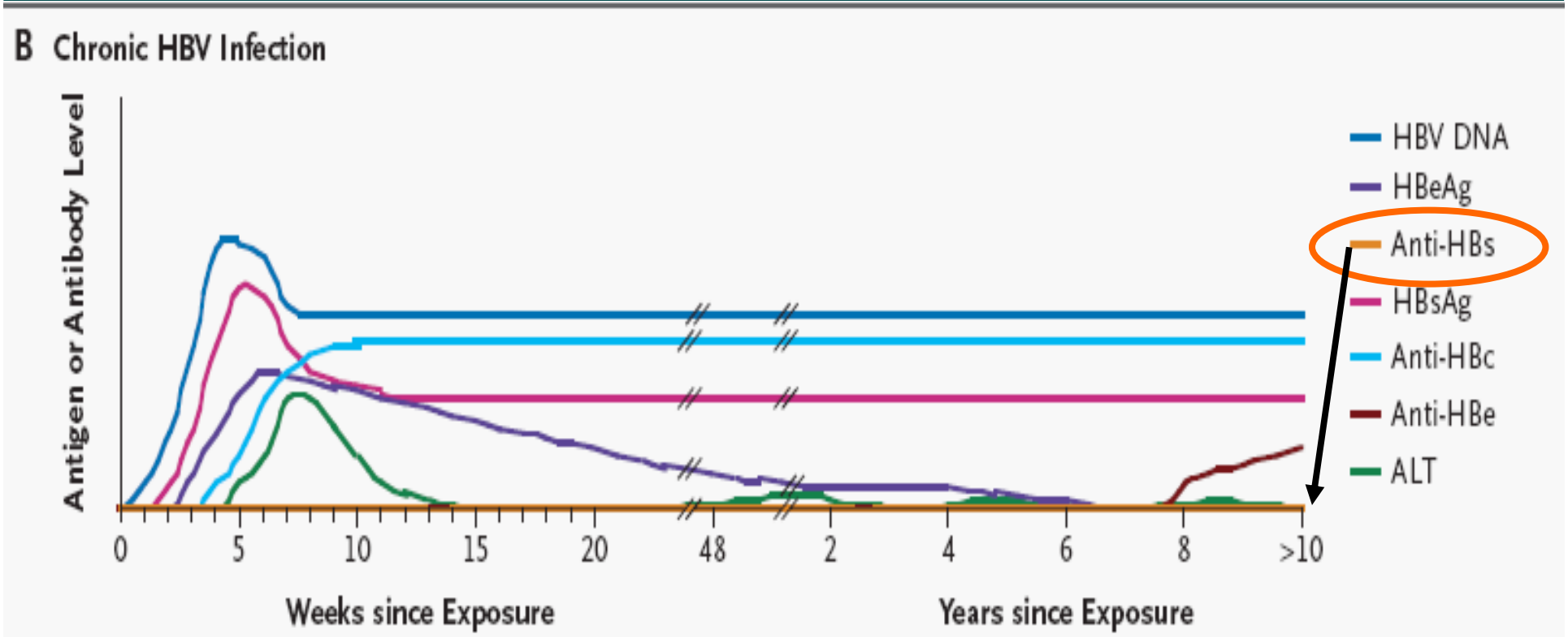


Prince AM, Lee D-H, Brotman B. Transfusion 2001;41: 329-32.

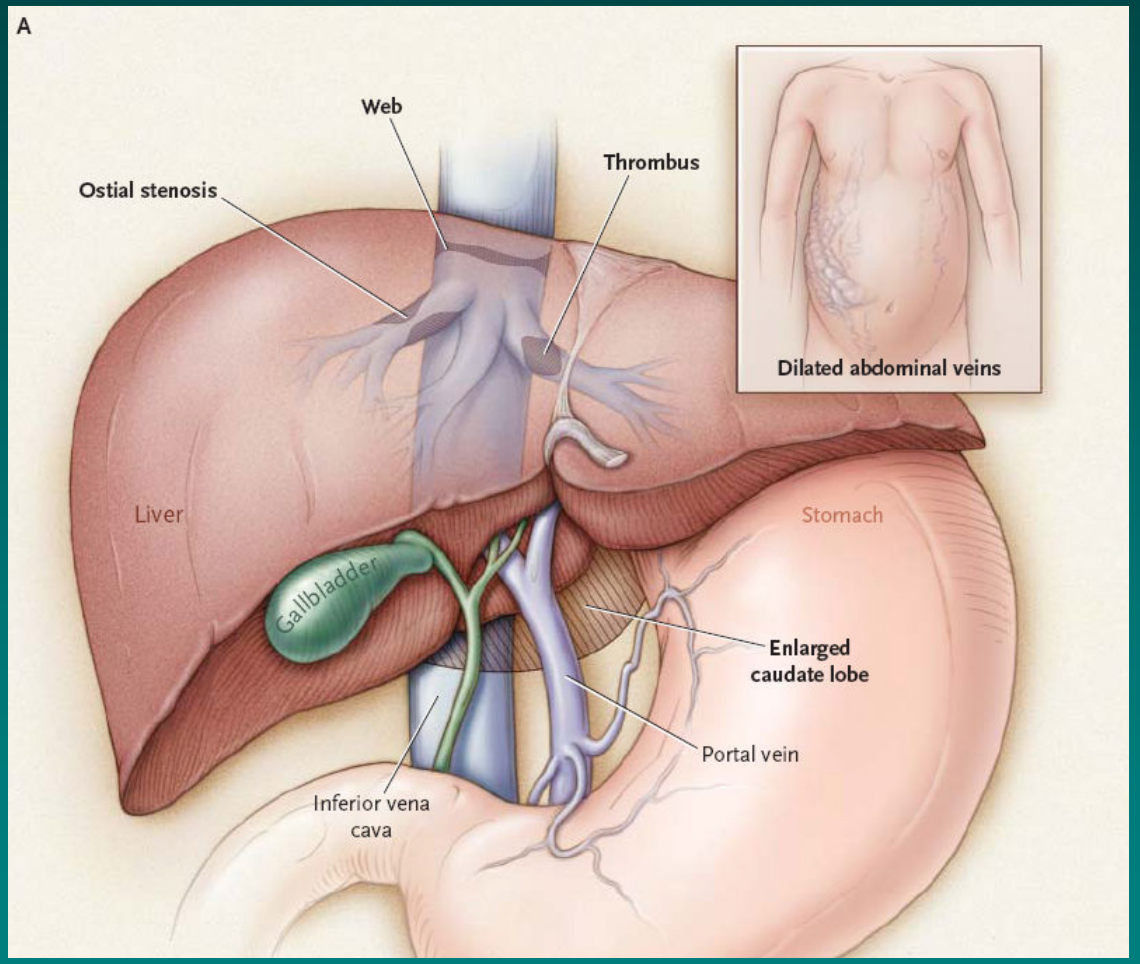
Other Laboratory tests: Tumor markers

- **AFP** = alpha-fetoprotein, normally synthesized in fetal liver
  - primary hepatocellular carcinoma (HCC)
  - mild elevation: acute and chronic hepatitis (liver regeneration)

Imaging Methods

- native X-ray
- ultrasound examination, ultrasonography = USG
- ultrasound Doppler portal blood flow examination
- CT
- MRI
- radionuclide imaging
- per oral cholecystography
- endoscopic retrograde cholangiopancreatography = ERCP
- percutanneous trans-hepatic cholangiography = PTC
- trans-venous liver biopsy
- angiographic methods

Obstruction of the Venous Outflow Tract of the Liver in the Budd–Chiari Syndrome



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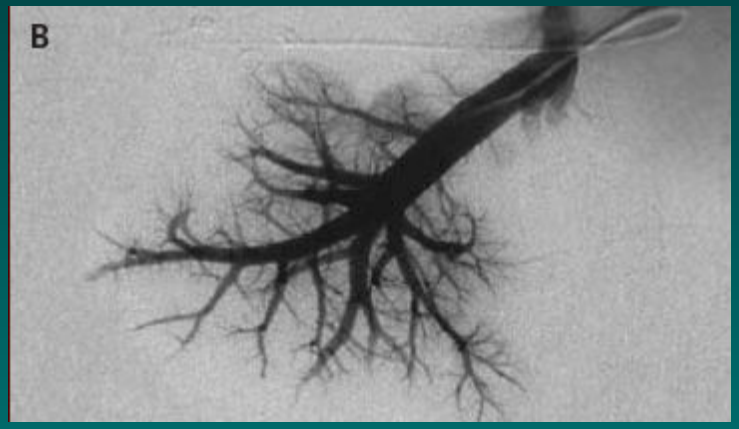
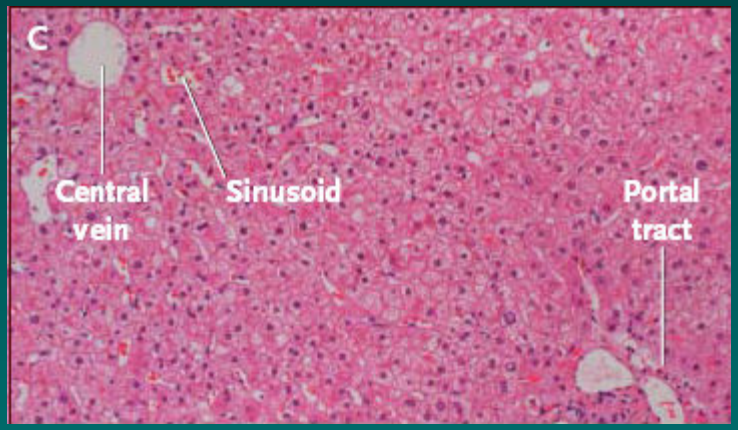
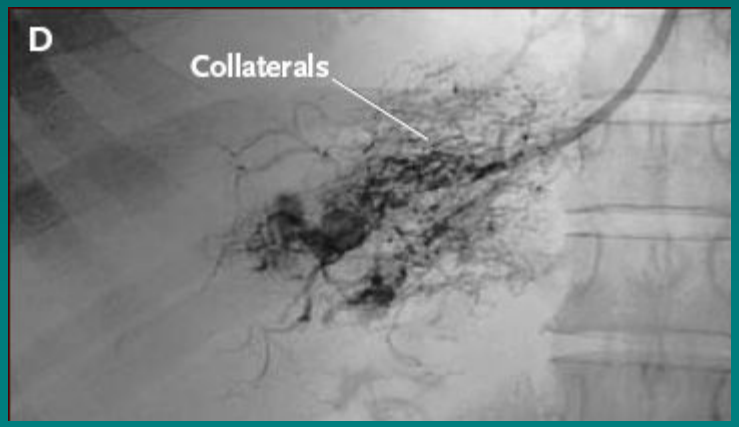
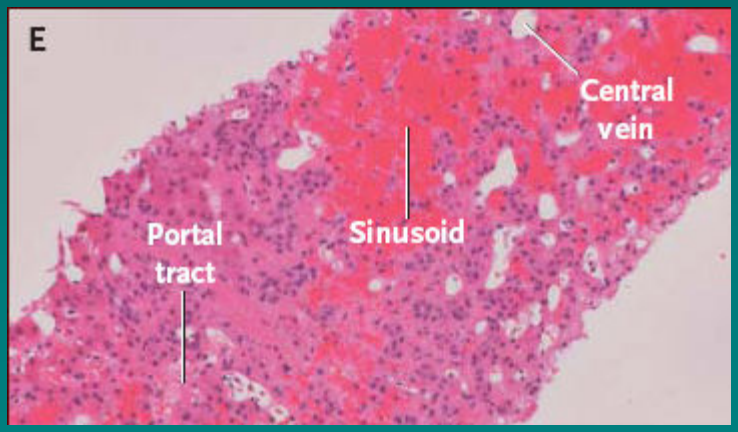


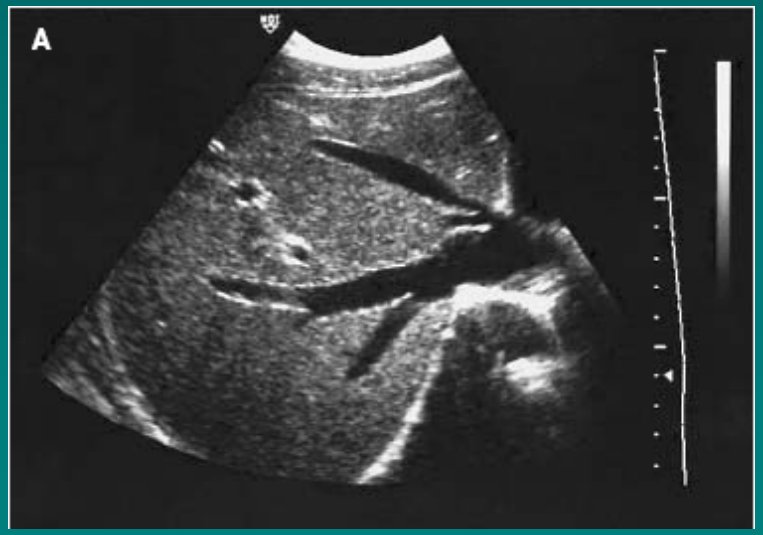




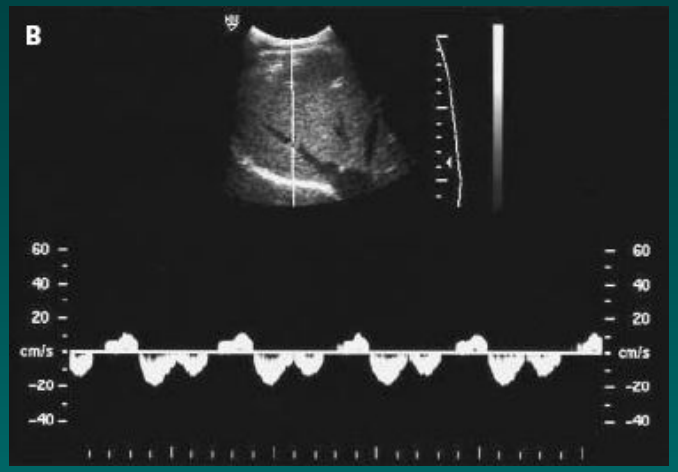


Doppler Ultrasonographic Examination of the Right Hepatic Vein

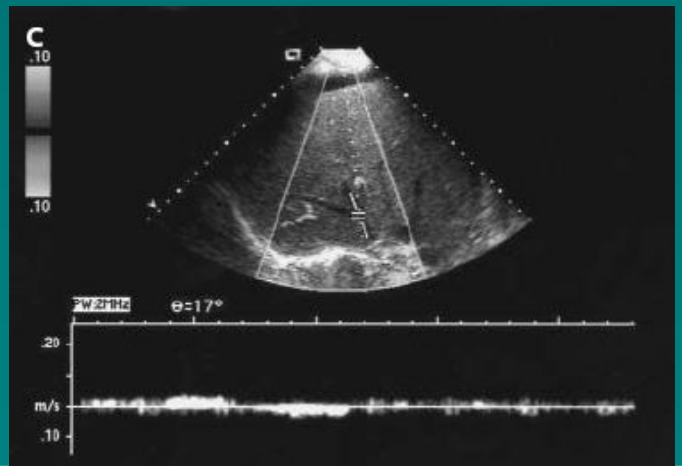
normal right hepatic vein



Doppler evaluation of the right hepatic vein reveals a biphasic wave form



No flow in the right hepatic vein in a patient with the Budd–Chiari syndrome

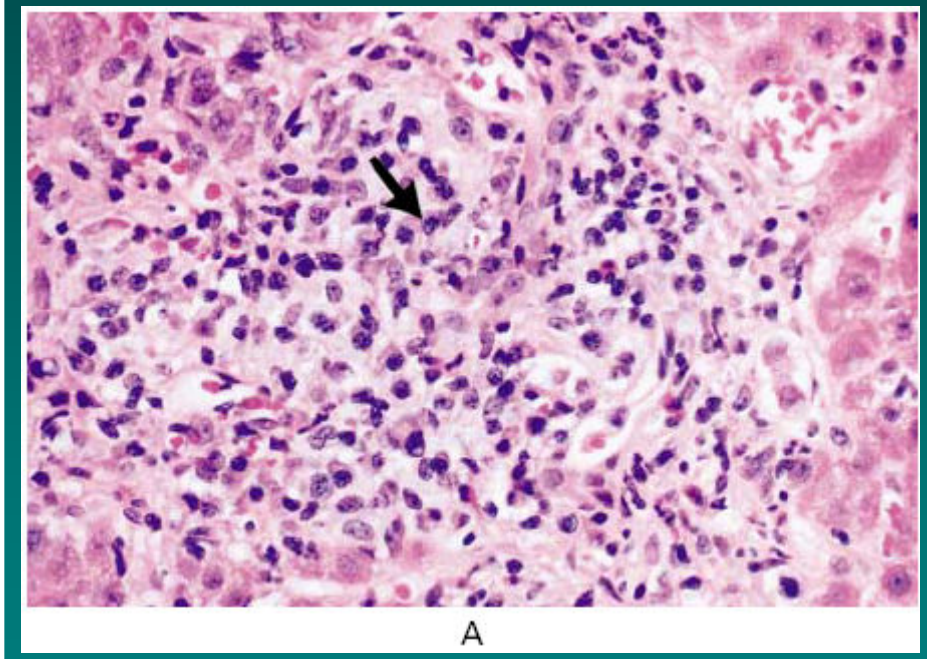


Liver biopsy

- Percutaneous biopsy
- Transjugular biopsy
- Laparoscopic biopsy
- Fineneedle aspiration guided by ultrasonography or computed tomography (CT)

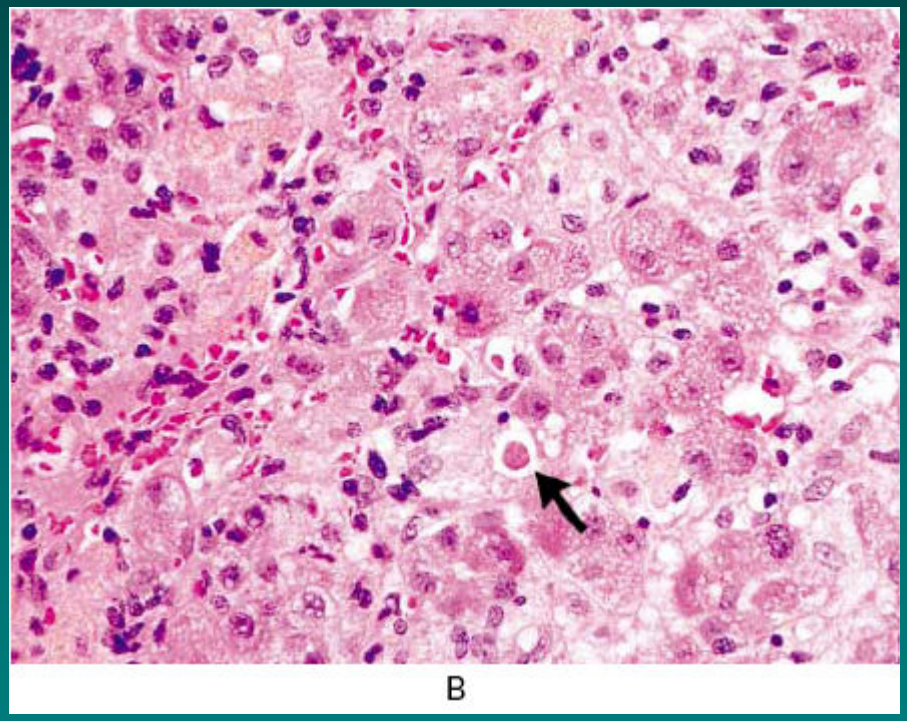
Each of these methods has advantages and disadvantages

A Liver-Biopsy Specimen from a 32-Year Old Man Presumed to Have Acute Hepatitis.



A

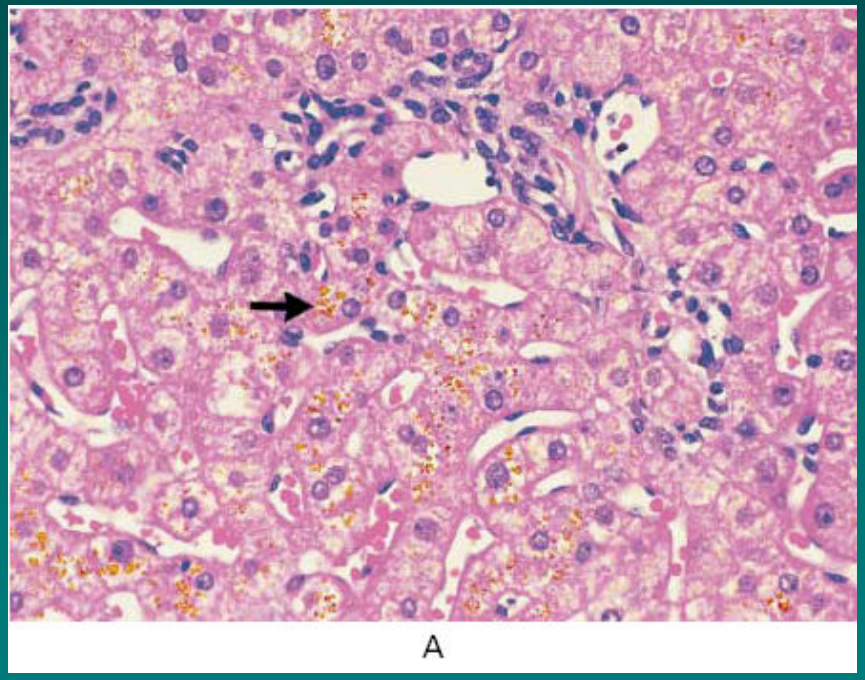
portal mononuclear infiltrate with prominent plasma cells



B

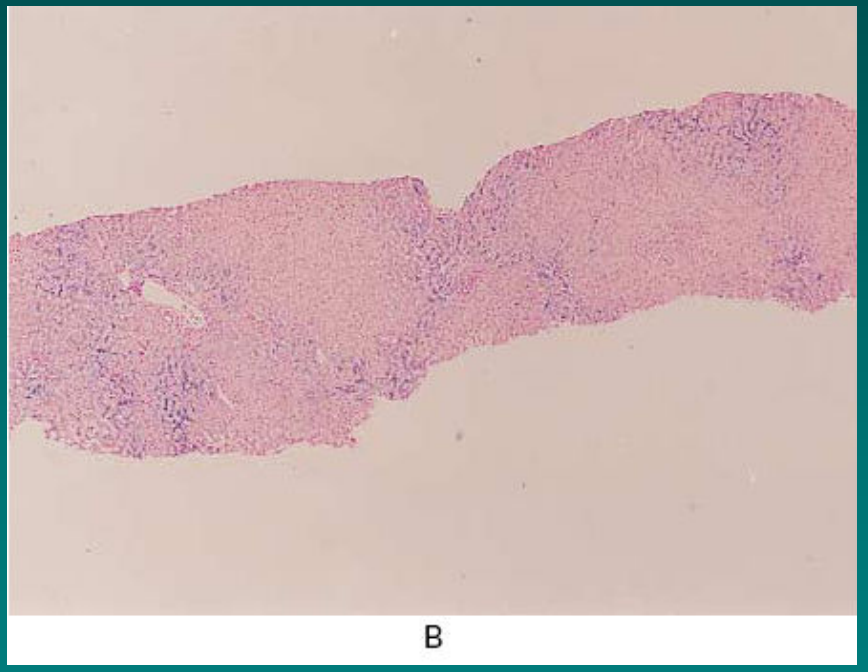
lobular inflammation with apoptotic hepatocytes

Liver-Biopsy Specimens from a 38-Year-Old Woman with Increased Iron Saturation and Mild Hepatomegaly.



A

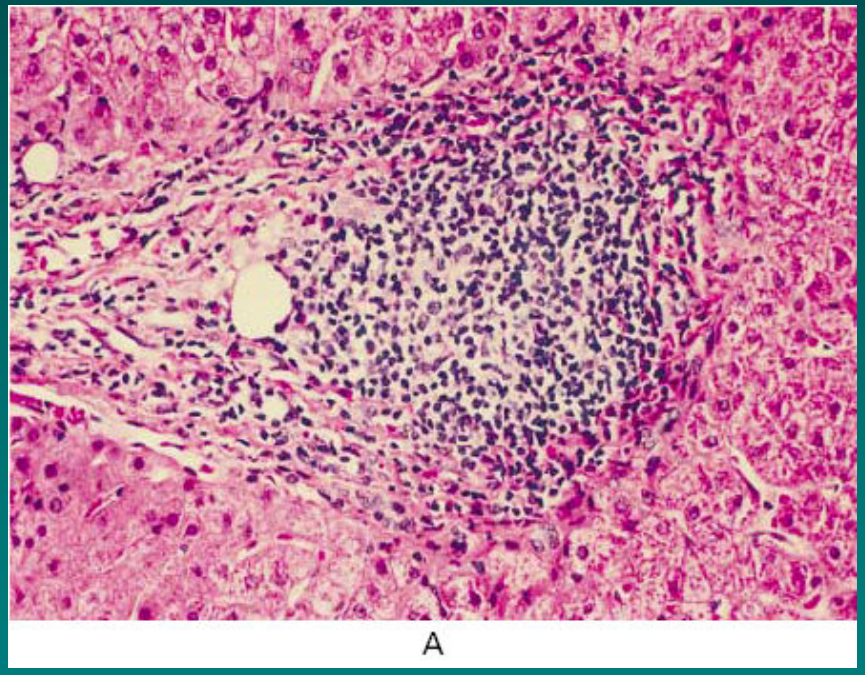
periportal deposition of brown pigment (arrow).



B

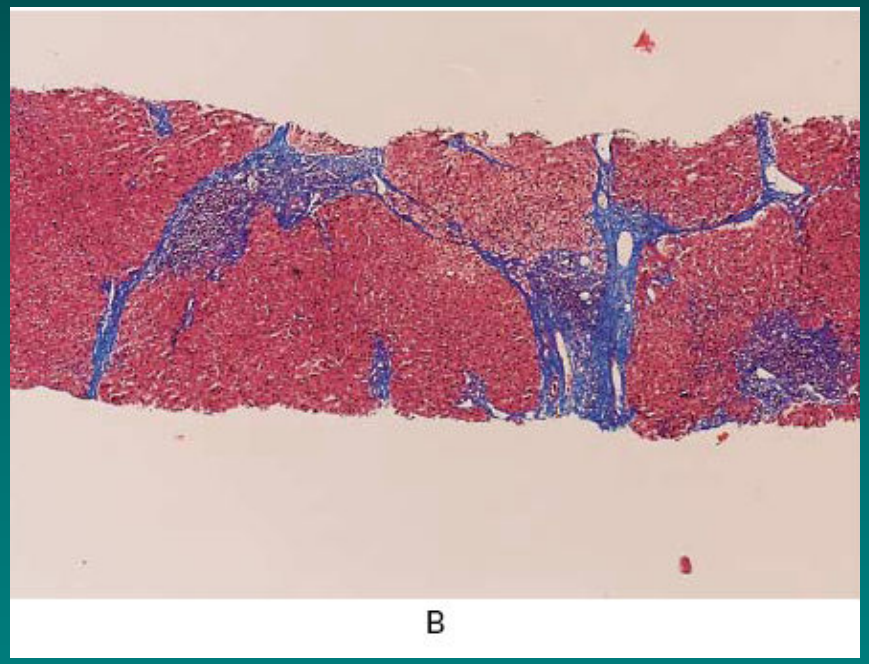
periportal distribution of iron

Liver-Biopsy Specimens from a 45-Year-Old Woman with Chronic Hepatitis C Virus Infection



A

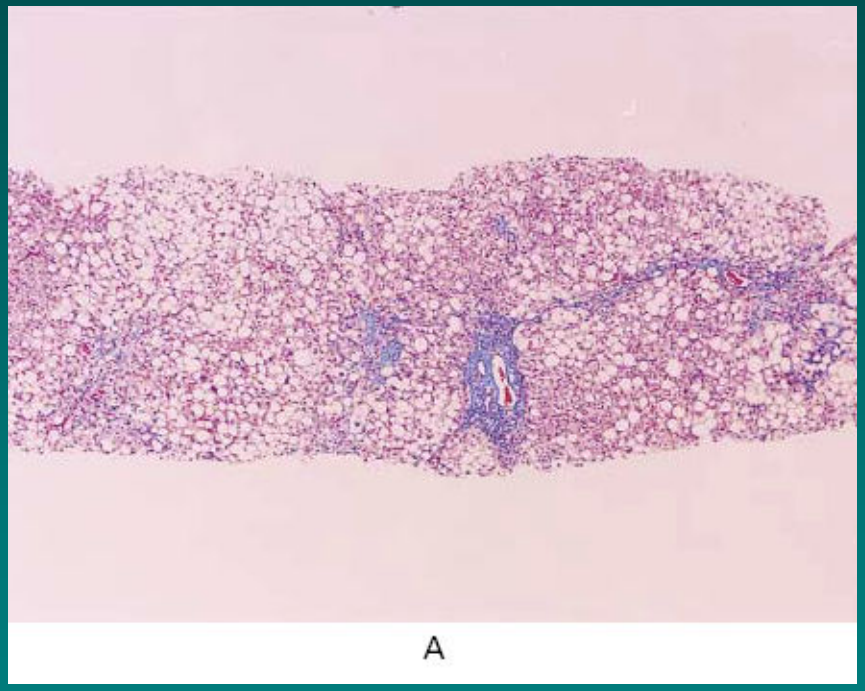
dense portal infiltrate with the formation of lymphoid aggregates



B

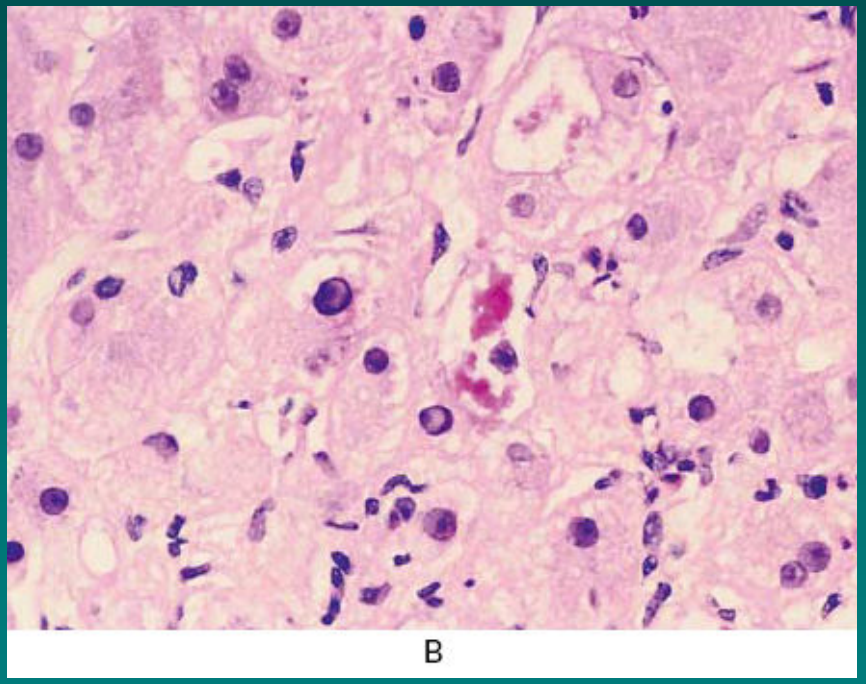
bridging fibrosis with architectural distortion and early cirrhosis (Masson trichrome)

Liver-Biopsy Specimens from a 40-Year-Old Man with Obesity, Diabetes, and Mildly Elevated Liver-Enzyme Levels.



A

moderate-to-marked steatosis with increased fibrosis (trichrome)



B

single cell (center) containing intracytoplasmic Mallory's bodies

PANKREAS EXOCRINE FUNCTION

Direct pancreatic stimulation or indirect stimulation by diet or test diet

- i.v. administration of secretin or secretin+ Cholecystokinin (CCK) or ingestion of test meal
- Measurement of pancreatic secreation in duodenum (45 – 120 minut)
  - Volume (>2mL/kg/h)
  - Bicarbonate (>80 mmol/L and 10 mmol/h)
  - when S+CCK or diet
    - measurement of pancreatic enzyme activity
      - amylase, lipase, chymotrypsin, trypsin

Analysis of stool

- **Nutrient digestion**
  - standard amount of fat in diet for 72 h
  - expected digestion of more than 93% of ingested fat
  - more than 20% of ingested fat in stool = pancreatic insufficiency
- **Fecal pancreatic enzyme measurement**
  - trypsin and chymotrypsin

Pancreas function test: Bentiromide test

- Bentiromide bound on para-aminobenzoic acid (PABA) is administered orally
- Bentiromide is hydrolyzed by chymotrypsin in duodenum and free PABA is absorbed in proximal part of small intestine, conjugated in the liver and PABA metabolites are excreted in the urine
- The amount of PABA in the urine correlate with the activity of chymotrypsin
- The results may be influenced by intestinal mucosal defects, liver diseases, and kidney diseases.

Bentiromid was withdrawn in the US in October 1996

Pancreatic Enzymes In Body Fluids

- **Serum amylase**
  - pancreatic isoamylase (33% of total serum amylases)
  - screening for acute pancreatitis (pts with acute abdominal or back pain)
  - 20-40 % fals positive,
  - sensitivity 70-75%
  - values 3x of normal AP very likely
  - elevated within 24 h, up for 3-5 days
- **Serum lipase**
  - specificity is higher than amylase
  - sensitivity 70-85%

GIT – Case 1

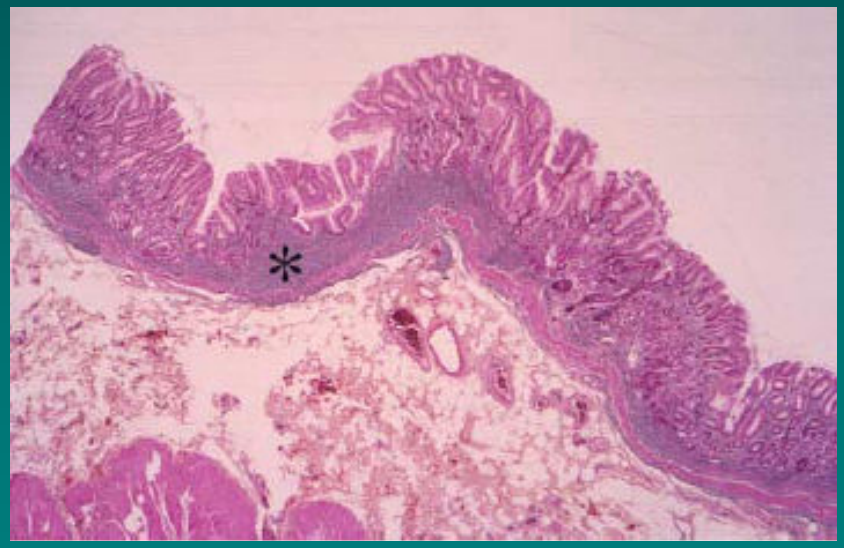
- History
  - A 65-year-old woman diagnosed with H. pylori-associated GML in July 1998.
  - Past history of gastric ulcer since 1960.
  - Gastric biopsies:
    - mucosa did not show any intestinal metaplasia nor glandular atrophy
  - Molecular studies:
    - clonal rearrangement of the immunoglobulin gene
    - t(11;18) fusion transcript was detected retrospectively in a frozen tumour sample taken in 1999

GIT – Case 1

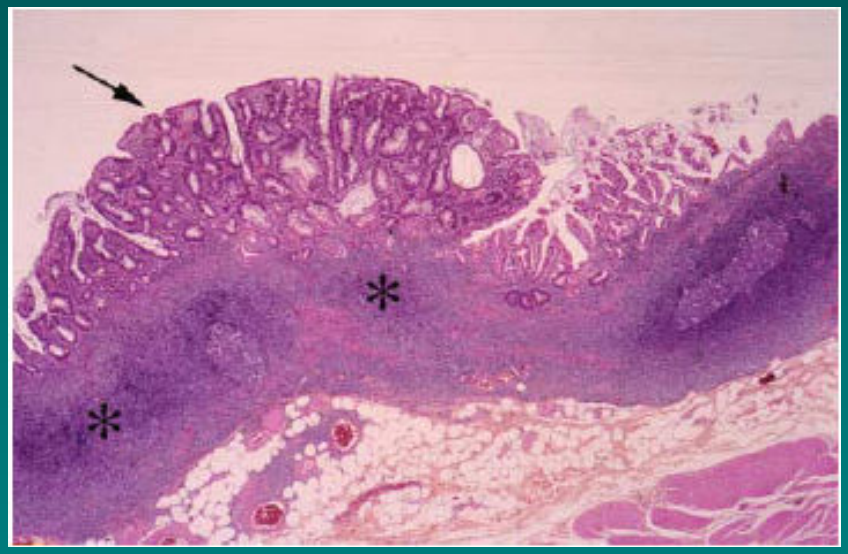
- She did not respond to H. pylori eradication therapy and was treated with an alkylating agent for a period of 1 year
- Follow-up gastric biopsies disclosed minimal residual disease for 2 years but she relapsed in January 2002, when intestinal metaplasia and low-grade dysplasia of the corpus were observed
- Because of massive gastric bleeding she underwent a total gastrectomy and splenectomy in December 2002

GIT – Case 1

GML was observed in the deep part of the corpus and extended throughout the gastric wall.



An early gastric cancer (EGC) of intestinal type limited to the mucosa was diagnosed, overlying the lymphoma.



Patients with gastric MALT lymphoma (GML) and early gastric cancer (EGC) carcinoma in situ.