GERD, Peptic ulcer disease, Tumors of esophagus and stomach

MUDr. Martin Wasserbauer

Interní klinika FNM a 2.LF UK

GASTROESOPHAGEAL REFLUX DISEASE

Introduction - terminology

- **GER (Gastroesophageal reflux) = reflux of gastric contents into the esophagus**
  - Physiological x patological ???

- **GERD (gastroesophageal reflux disease) = condition that develop when the reflux of stomach contents cause troublesome reflux-associated symptoms**
  1. Erosive ezophagitis – GERD with present visible mucosal breaks in the distal esophageus
     - Based on upper endoscopy result
  2. NERD (Non Erosive Reflux Dissease) = GERD with absent visible mucosal breaks in the distal esophageus
     - Based on upper endoscopy result

Introduction

- **One of the most common gastroenterological problems**
  - 10-30 % of the Western population
  - More often in pregnancy (25%)
- Primary x secundary (DM, operation, sclerodermy,…)
- Disproportion of: extent of pathological reflux, problems, endoscopic findings and histological changes

Pathogenesis

- **Principles**
  - An excessive return of stomach content into the esophagus - resulting to **imbalance between aggressive and protective factors and mechanisms**.
  - **Risc factors**:
    - Smoking, alcohol, coffee, obesity, high fat diet, chocolate, medications (narcotics, calcium channel blockers), pregnancy, age

Pathogenesis

- **<u>Agresive factors</u>**
  - Character of reflux – pH, composition (HCl, pepsin, bile acid, pancreatic fluid)
  - Esophageal dysmotility
  - External influences: diet composition, drugs, smoking, coffeine, lifting
  - Delayed gastric emptying
  - Hiatal hernia – particularly if it is large (over 5cm)
  - Operations
  - Increased intraabdominal pressure (obesity, pregnancy,…)
  - Dysfunction of LES (hypotensive)
    - Basal pressure between 5-6mmHg (fyzio 8-20mmHg)
    - TLERS

Pathogenesis

- **Protective factors**
  - Adequate function of LES
  - Sufficient length of intraabdominal part of the esophagus
  - Anatomical conditions: adequate function of diafragm and frenoesophageal ligament, Hiss angle
  - Esophageal clearence: salivary secretions, primary (swallowing) and secondary (cleaning in sleep) peristalsis
  - Esophageal mucosal defense mechanisms
    - Mucous and bicarbonate layer, cell membranes, intercellular junctional complexes, adequate mucosal blood flow

Clinical presentation

- **Typical x atypical**
- **Esophageal x extraesophageal**

- Worsen: lying position, leaning forward and lifting loads

- No correlation: the extent of pathological reflux - clinical presentation - complications - endoscopic and histological picture

Clinical presentation

1. **Esophageal**
   - Typical: Heartburn, regurgitation
   - Atypical: Dysphagia, chest pain, odynophagia, vomiting, upper abdominal pain, nauzea, globus sensation
2. **Extraesophageal**
   - Proven: Chronic cough, laryngitis, asthma, dental erosion
   - Expected: sinusitis, recurrent otitis, idiopathic pulmonary fibrosis, pharyngitis, hoarseness

- **The warning signs = complications**
  - Dysphagia, odynophagia, anemia, haematemesis, melaena, anorexia

Diagnostic methods

- **Anamnesis**
- **Physical examination**
- **Upper endoscopy – gold standard procedure**
  - Degree of esophageal mucosal injury, complications and tissue sampling
  - Erosive esophagitis (Savary-Millera, OMED, IWGCO clasification)
  - NERD – negative endoscopic findings
  - NBI – narrow-band imaging

Diagnostic methods

- **Ambulatory 24-hour esophageal pH monitoring**
  - Indications: symptoms with negative upper endoscopy (NERD), extraesophageal symptoms before surgery, after surgery with persistent symptomatology, no effect of PPI treatment
  - The gold standard method
  - Ambulatory continuous measurement of the pH in the distal esophagus with a thin tube + correlation with the difficulties of the patient
- **Ambulantory 24-hour multichannel impedance with pH monitoring**
  - Diagnosis of: all types of reflux (acidic, weakly acidic, weakly alkaline), refluxed fluid type (water, air), determine the height of pathological reflux
- **Manometry**
  - Determine the location of LES
  - Other diseases (achalasia), before antireflux surgery
- **Wireless pH capsule**
  - More patient-friendly method of pH monitoring

Diagnostic methods

- **Scintigraphy**
  - postprandial reflux
- **Perfusion test (Berstein test)**
  - Not used today (esophageal perfusion alternatively by HCl and FR)
- **PPI test**
  - Short course of high dose PPI (Omeprazol 40mg/day) → effect ???
  - Sensitivity 66-89%, Specificity 35-73%
- **Barium esophagogram**
  - Hiatal hernia, complications of GERD (stricture, ulceration)

Treatment

- **Lifestyle and diet modification**
- **Medications**
  - Antacids
  - Procinetics drugs
  - PPI, H_2-blocators
- **Antireflux surgery**
  - fundoplication

Lifestyle and diet modification

- **Usually not enough - importance in reducing the dose maintenance therapy and prevention of relapses**

- Eat more often + smaller portions, eating 2-3 hours before going to sleep
- Ex-smoking, ex coffee and chocolate, weight reduction
- elevation of head of the bed at night
- EX Risk drugs (theophylline, progesterone, BKK, nitrates, antidepresives)

Medications

- **PPIs – proton pump inhibitors**
  - Allow an effective control of reflux symptoms, high rate of healinf of erosive esophagitis
  - Omeprazole, pantoprazole, lansoprazole
  - EFFECTS: The faster onset of healing, greater ability to maintain remission, good tolerability, reduction of complications, minimal ADRs
  - Highest healing rate of erosive esophagitis in comparison of other drugs
- **Antacids**
  - Short-term symptomatic relief (effect lasts 1 hour)
  - Does not improve mucosal healing
  - Sodim bicarbonate, calcium carbonate, aluminum hydroxide and magnesium alginate suspension with bicarbonate

Medications

- **H2-blockers**
  - Ranitidine, Famotidine
  - Lesser efficacy than PPI especially in severe GERD
- **Prokinetics**
  - Drugs stimulating the prograde motility
  - Frequently itopride (metoclopramide, domperidone - limited effect for ARs), cisapride withdrawn (arrhythmias, sudden death)
- **TLERs reducers**
  - Baclofen
  - Increase basal LES pressure, reduce TLERS, accelerate gastric emptying
  - Effect in refractery GERD
  - ADRs - somnolence, confusion, dizziness, lightheadedness, drowsiness, weakness, and trembling.

Antireflux surgery

- **Fundoplication according to Nissen-Rossetti**
- Causal therapy
  - Result to augmentation of LES basal pressure

  and decrease in the rate of TLERs
- **indications:**
  - Younger patients with future lifelong pharmacotherapy (anatomical abnormalities)
  - lack of effect of pharmacotherapy - poorly treatable, recurrent esophagitis
  - Aspiration symptoms associated with GERD
  - Complications esophagitis (ulcers, stenosis) – CAVE do not solve Barretts esophagus
- **CAVE - postfundoplication syndrome**

Treatment strategy

- Acute (short-term 6-8 weeks) ± maintenance therapy (continuous treatment x short-term cures on demand in case of complaints of the patient)
- **3 types**
  - Step up: antacids → H2-blockers → PPI (from the least effective modality)
  - **Step down: PPI → H2-blockers → antacids (from the most effective modality)**
    - **TODAY prefer, especially in terms of reduction in PPI, the temporary use or on demand (at least 4 days)**
  - **Step in: initiates and maintains patients on the most potent antireflux modality**

- **Last option: SURGERY**

Therapy in specific situations

- **Extraesophageal symptoms**
  - PPI particularly, insufficient effect = SURGERY
- **Night reflux**
  - PPI full dose + H2-blockers
- **Alkaline / biliary reflux (patients after gastric resection, achlorhydria)**
  - PPI + prokinetics, sucralfate, insufficient effect = SURGERY

Therapy in specific situations

- **Refractory GERD**
  - NO RESPONSE (persistent symptoms) to full dose PPI (10-40% of patients)
  - More often NERD, functional hesrtburn
  - To change the type or dose of PPIs, strict regime, H2-blockers at night, prokinetic drugs, antacids, sucralfate - insufficient effect = SURGERY
- **Pregnancy - often symptoms in pregnancy**
  - Regime, antacids, PPI (pantoprazole, Loseprazol - FDA B x FDA C - omeprazole)

Complications

- **Barretts esophagus, adenocarcinoma**
- **Esophageal stricture**
  - Prolonged reflux with subsequent fibroproductive changes
  - Therapy: bougie dilation, PPIs
- **Ulcerations of the esophagus**
- **Upper GI bleeding**

Barrett´s esophagus

- Occurs as a **complication of chronic GERD** and characterized by **incomplete intestinal metaplasia in the epithelium of the esophagus**
  - Metaplastic changes: replacement of squamous epithelium of the esophagus by columnar epithelium ± metaplastic intestinal type
  - Sequence: intestinal metaplasia → dysplasia → adenocarcinoma
- **Epidemiology**
  - 10-15% of patients with GERD (increases with duration of GERD)
- **Pre-malignant condition:** The risk of developing adenocarcinoma (30-40x) - 0.5% of patients with GERD per year
- **Risc factors:**
  - Main: longstanding GERD
  - Additional: advanced age, male, Caucasian race, hiatal hernia, tobacoo use, obesity

Barrett´s esophagus

- **Clinical presentation**
  - Reflux symptoms or asymptomatic
- **Diagnosis:**
  - GFS + 4-qudrant biopsis every 2cm - REQUIRED FOR DIAGNOSIS
    - Endoscopy: appears as columnar lined epithelium with a pink/salmon color that results in displacement of the squamocolumnar junction proximal to the GEJ
      - The Prague classification system - endoscopic description
    - Multiple biopsies = evaluation of intestinal metaplasia and dysplasia – HISTOLOGICAL DIAGNOSIS
    - Advanced diagnosis: chromoendoscopy, autofluorescence imaging, NBI (typical mucosal and blood vessel patterns), confocal laser endomicroscopy (in vivo miroscopis analysis)
      - Reduce false positives results

Barrett´s esophagus - therapy

- Acid suppresion
  - PPIs – control of symptoms, healing of erosive esophagitis, can decrease markers of proliferation and perhaps development of dysplasia
- Antireflux surgery
  - No firm documented reduction in cancer risk
- Endoscopic eradication therapy
  - Endoscopic mucosal resection
    - Effective in HGD or intramucosal adenocarcinoma
  - Radiofrequency ablation
  - APC
  - Photodynamic therapy
    - Photo sensitization with Photophrin and laser light treatment

ESOPHAGEAL CANCER

Benign tumors of the esophagus

- **Types:**
  - Epithelial: papilloma, adenoma,

    x
  - Mesenchymal: leiomyoma (75%), fibroma, lipoma - intramural
- **Symptomatology:**
  - Mostly asymptomatic (incidental finding) x dysphagia, bleeding
- **Diagnosis:**
  - GFS with biopsy, EUS (mesenchymal), CT + MRI
- **Therapy:**
  - dispensarization

    x
  - endoscopy x surgery - large (symptomatic), can not clearly identify the biological nature

Malignant tumors of the esophagus

- **Classification**
  - Histological:
    - Squamous cell carcinoma
    - Adenocarcinoma - incidence increases (to 50%)
    - Other - leiomyosarcoma

Carcinomas

- **Squamous cell carcinoma or adenomarcinoma – different risc factors**
- **The incidence**
  - SCC declined in Western countries +USA (3-5/100000) x Asian countries (100/100000)
  - ACA – rising incidence in Western countries +USA

Carcinomas

- **Etiopatogenesis**
  - Multifactorial - Genetics + external factors
  - Risc factors
    - SCC: alcohol, tobacco, dietary factors (hot food, spicy food), nitrosamines, mycotoxins, toxic alkaloids, thermal trauma, HPV
    - ACA: Barretts esophagus, obesity, NSAIDs long term
  - Precanceroses: Barrett's esophagus, corrosive stricture, achalasia
- **Symptomatology: LATE**
  - Dysphagia, odynophagia, weight loss, cachexia, regurgitation, gastrointestinal bleeding, retrosternal pain, cough, recurrent pneumonia, aspiration
  - Metastasis early to lymph nodes, hematogenous to lung + liver + kidney

Carcinomas

- **Diagnosis**
  - Anamnesis – GERD, tobacco and alcohol use
  - Physical examination – lymphadenopathy, cachexia, fecal occult blood, hepatomegaly
  - Laboratory: anemia, hypoalbuminemia,
  - Barium esophagography
  - GFS (chromoendoscopy, NBI, endomiceoscopy) + multisegmental biopsy, EUS of the esophagus, CT, PET / CT
    - SCA: proximally in the esophagus
    - ACA: distally in the esophagus

Carcinomas

- **Therapy**
  - Depedent on staging
  - Modalities:
    - Surgery – esophagectomy ± lymfadenectomy (stage II+III)
    - (Neo)adjuvant RT+CHT
    - Endoscopy:
      - endoscopic mucosal resection (T1m)
      - Endoscopic submucosal dissection
  - Paliative therapy: RT, brachytherapy, PEG, metal stent, laser therapy - (stage IV)

Carcinoma

- **Prognosis**
  - 50% of patient are incurable at diagnosis

- **Prevention:**
  - Lifestyle modification (smoking-…)
    - Reduce risc factors
  - routine screening is not cost-effective, except in the highest risk groups

PEPTIC ULCER DISEASE

Introduction

- **Ulcer** = mucosa defect which penetrates through the lamina muscularis mucosae
  - formation is associated with the presence of hydrochloric acid and pepsin
- **Erosion** = mucosa defect which does not penetrate through the lamina muscularis mucosae

- German internist Schwarz in 1910: „No acid, no ulcer.„
- relatively frequent
- Prevalence: 5-10% (people with Helicobacter pylori positive 10 to 20%)
- Incidence: 0.1% per year
- Trend to decrease: prevalence of peptic ulcer and gastric cancer, number of hospitalizations for peptic ulcer and peptic ulcer lethality (because of complications).

Etiopathogenesis

- **Influence of protective and aggressive factors**
  - VCHGD = imbalance of these factors
- Role of Genetics
  - Polymorphisms of COX-1, IL-1-beta, blood group 0
- The role of the external environment
  - Smoking, stress

Etiophatogenesis

Protective factors:

- The normal composition of gastric mucus
- The alkaline bicarbonates secretion
- Intact microcirculation in the gastric mucosa and regenerative capacity of the epithelium
- Normal secretion of endogenous prostaglandins

Aggresive factors:

- HCl, pepsin
- Helicobacter pylori
- Ulcerogenic effect of drugs - NSAIDs
- duodenogastric relfux
- Smoking, stress
- Fault microcirculation in the mucosa and submucosa
- Slow gastric evacuation

Etiopathogenesis

- **Etiology:**
  - Common causes
    - Helicobacter pylori
    - NSAIDs
  - Uncommon causes
    - Crohns disease
    - Conditions causing acid hypersecretion (Z-E sy, multiple endocrine neoplacia, mastocytosis)
    - Severe physical stress (ICU,..)
    - Mucosal ischemia (vascular disease, radiation)

Helicobacter pylori

- originally named as Campylobacter pylori
- In developed countries - 10-20% of the population x in developing countries - 90% of the population
- oro-oral or oro-fecal transfer
- Role in VCHGD cancer, stomach MALT lymphoma
  - the most common cause of peptic ulcer
- Mucosa colonization by H. pylori leads to the development of diffuse antral gastritis (also known as chronic gastritis type B or hypersecretory gastritis)

Symptomatology

- Depends on the localisation of the ulcer
- Variable intensity of difficulties
- The most frequently:
  - pain, abdominal discomfort, weight loss, nausea and vomiting, loss of appetite
- The character and intensity of pain can be different - often asymptomatic in elderly patient and patients with DM
- seasonal course with exacerbations in spring and autumn
- 10-20% of patients are asymptomatic peptic ulcer - symptomatology of complications

Symptomatology

Duodenal ulcer

- more frequently in men, usually between 20-40 years of age, episodic
- 90% is established by Helicobacter pylori infection
- pain is usually localized in the epigastrium and right of the midline, appearing for more than 2 hours after a meal (after the resolution of the neutralizing effect of diet), more before meal and overnight (in the context of the diurnal secretion of HCl), relieved by antacids and food (milk)
- Described as a gnawing or hunger pain

Gastric ulcer

- in both sexes more equally, more middle-aged and elderly
- Helicobacter pylori is positive in about 70%
- pain is usually localized in the epigastrium, link to food is less typical, pain occur soon after meals and less likely to be relieved by food
- Atypical symptomatology are more common

Diagnostic methods

- **Laboratory:**
  - Gastrin (Z-E sy), complications
- **Endoscopy:**
  - Method of choice
  - Biopsy
    - mucosal colonization by Helicobacter pylori (biopsies from antrum and corpus ALWAYS)
    - exclusion of malignant etiology – important role (often imitates)
  - patients with gastric ulcer should be endoscopically observed until the ulcer will be completely healed, duodenal ulcer is no need to monitor the healing
  - Forrest classification

Diagnostic methods

- **X-ray examination**
  - role in the diagnosis of complications of peptic ulcer disease
    - obstruction (using X-ray contrast agent)
    - ulcer perforation (presence of pneumoperitoneum on the native image of the abdomen, leakage of contrast medium outside the lumen).

Diagnostic methods

- **Helicobacter pylori diagnostics**
  - Invasive methods: during gastroscopic examination and biopsy
    - Urease test and cultivation, histology
  - non-invasive methods: particularly suitable to evaluate the effectiveness of treatment of infection (eradication of Helicobacter pylori)
    - Breath test
    - Determination of the Helicobacter pylori antigen in feces
    - Serological detection of antibodies against Helicobacter pylori
    - Stimulation of pentagastrin
    - Serum gastrin

Complications

- **Bleeding from ulcers:**
  - Bleeding in the upper GI – the commonest cause (60%)
  - Indicated to urgent endoscopy or angiography or surgery
  - Hematemesis, melena, shock
  - Therapy:
    - Endoscopy (adrenaline injection, clipping, heat-based or light-based coagulation)
    - PPI intravenous
    - Ex NSAIDs and aspirin, H.pylori eradication
  - 8% mortality

Complications

- **Penetration ulcer:**
  - gradual deepening of the ulcer - penetrates the wall of stomach into nearby organs
  - the most common is the penetration of duodenal ulcer into the pancreas

Complications

- **Ulcer perforation:**
  - More common in duodenal ulcer, smokers and aspirin or NSAIDs users
  - Symptoms: sudden severe pain, signs of peritoneal irritation (CAVE the perforation into the limited space defined by adhesions may be less pronounced clinical picture), hypotension, shock
  - Diagnosis: plain radiography
  - Treatment: strictly surgical
  - 10% mortality

Complications

- **Stenosis of the pylorus or the duodenum:**
  - Relatively uncommon (2% of patients with ulceration))
  - arise a failure of GI passage, content stagnation
  - Symptomatology:
    - Mainly vomiting and epigastric pain + distension
  - Diagnosis:
    - Radiographic findings, endoscopy + biopsies
  - Treatment:
    - NGT (to derivate fluids), rehydration, PPI,
    - Surgery
    - Endoscopic baloon dilatation

Therapy

- **Dietary restrictions**
  - Smaller amounts of food
  - Ex milk products
  - Ex smoking and coffee

- **Ex NSAIDs**
  - stopping the drug or switching to one that does not damage the stomach or duodenum
  - An alternative is to continue the NSAID where needed, at the lowest possible dose, and to give concurrent antiulcer prophylaxis, usually with a PPI.

Pharmacotherapy

- **PPI**
  - omeprazole, lansoprazole, pantoprazole, rabeprazole, esomeprazole
  - After: twice daily (omeprazole 2x20mg, lansoprazole 2x30mg, pantoprazole 2x40mg)
  - i.v .: omeprazole 80mg IV bolus followed by a continuous infusion 8 mg omeprazol per hour, then twice daily bolus of 40mg of Omeprazol
  - prophylactic therapy for patients at risk for long-term NSAID therapy
- **H2-blockers**
  - today rather reserved for the treatment of functional dyspepsia and in the maintenance treatment of mild forms of esophageal reflux disease
- **Misoprostol**
  - Synthetic analogues of PGE1
- **Pentoxifylline**

Pharmacotherapy

- **Eradication of H. pylori, if positive**
  - heals ulcers and prevents recurrence
  - Indications: VCHGD, MALTom, Menetrierova disease,
  - attempt to achieve the disappearance of bacteria from gastric mucosa
  - after successful eradication of the ulcer, the risk of disease recurrence ranges between 0-10%
  - CAVE resistence to ATB
  - combination therapy
    - Amoxicillin - 2x1000mg / day for 7 days
    - Clarithromycin (azithromycin) - 2x500mg / day for 7 days
    - PPI - e.g. omeprazole 2x20mg / day

Therapy

- **Endoscopy**
  - At gastrointestinal bleeding
- **Surgical treatment**
  - Rarely use
  - Indications: complications, resistance to pharmacotherapy, multiple ulcers
  - Resections - operation according to Billroth I and II. resection of endocrine-active tumor (ZE syndrome)
  - Nonresections performances - vagotomy, supereselective vagotomy (broken n.vagus)
  - Disadvantages:
    - postgastrectomy malnutrition, stomal ulceration, postgastrectomy neoplasia

TUMORS OF THE STOMACH

Benign tumors of the stomach

- **Epithelial**
  - adenomas
    - 5% of polyps in FAP more
    - The risk of cancer
    - Clinic: often asymptomatic, dyspepsia
- **Mesenchymal**
  - Hemangiomas, lipomas, fibromas
  - Submucosal tumors bulge the mucosa
  - Clinic: often bleeding
- **Diagnosis**: GFS with biopsy, EUS
- **Therapy**: polypectomy, CHIR

Malignant tumors of the stomach

- **Epithelial**
  - Adenocarcinoma
- **Non-epithelial**
  - Lymfoma, GISTom

Adenocarcinoma

- **Most frequently observed malignant gastric disease (up to 95% of gastric neoplasms)**
- **Epidemiology**
  - 2x more in men, increase with age
  - Worldwide decrease in prevalence and death rate
  - high incidence: Japan, Korea, China, South America, Eastern Europe

Adenocarcinoma

- **Etiology**
  - Multifactorial – genetic factors + external factors
  - RF: chronic atrophic gastritis (H. pylori), excess salt, nitrates/nitrites, smoking, EBV, st.p. gastric surgery, blood group A
- **Histological types (Lauren classification)**
  - Intestinal type - older people, more men
  - Diffuse type - as well as younger people, worse prognosis

Adenocarcinoma

- **Pathogenesis:**
  - Intestinal type:
    - Sequence: chronic atrophic gastritis - intestinal metaplasia - dysplasia - carcinoma
    - RF: achlorhydria, secondary hypergastrinemia, duodenogastric reflux, nitrosamines
  - Diffuse type:
    - mutations in adherin E, gene polymorphisms (IL1, ...)
  - Based on FAP, Lynch syndrome, Peutz-Jeghers syndrome, Cowden's syndrome

Adenocarcinoma - symptomatology

- **Early gastric cancer**
  - Often asymptomatic or nonspecific symptoms

- **Advanced gastric adenocarcinoma - variable**
  - often asymptomatic for a long time

    x
  - epigastric pain, dyspepsia (fullness, discomfort, ..) without relation to food (also responds to PPI), loss of appetite, nauzea and vomiting, weakness, weight loss, aversion to meat

    x
  - Advanced disease: vomiting, bleeding, anaemization

Adenocarcinoma - complications

- **Bleeding**
  - Symptomatology
    - Chronic occult bleeding – result in anemia

      x
    - Acute profuse bleeding
  - Therapy:
    - Endoscopic therapy, angiographic therapy, pharmacotherapy, surgery

- **Perforation**
  - Unusual
  - Symptomatology:
    - Severe acute abdominal pain, manifestations of peritoneal irritation, shock
  - Diagnosis:
    - Plain radiology
  - Therapy:
    - Correcting hemodynamic and electrolyte imbalances, surgery

Adenocarcinoma - complications

- **Obstruction**
  - Uncommon
  - Symptomatology
    - Nausea, vomiting, dysphagia, weight loss
  - Diagnosis
    - Plain radiology, endoscopy
  - Therapy
    - Nasogastric suction, endoscopic stenting and palliative surgical resection

Adenocarcinoma - diagnosis

- **Anamnesis**
  - **Physical examination** - resistance of the epigastrium, lymphadenopathy (Virchow's node, node Sister Mary Joseph, Irish node), ascites, symptoms of metastatic disease, paraneoplastic processes (dermatomyositis, acanthosis nigricans, GN, hemolytic anemia, hypercoagulation), thrombophlebitis (Trousseau sign) ovarian metastases (tumor of Kruckenberger), signs of metastasis (liver – jaundice +pain, lungs – cough + hemoptysis)
- **Gastroscopy** - macroscopic finding (variable appearance) and localization, biopsy (6-8x - edge and base of the ulcer), chromoendoscopy
- **EUS** – assess the extent and stage of tumour, help guide aspiration biopsies of lymph node
- **CT, MR** – detecting distant metastasis
- **Oncomarkers** - CEA, CA 125, CA 72-4
- **LAB** - CRP, ALB, CB, iron deficiency anemia

Adenocarcinoma - classification

- Borrmannova macroscopic classification (polypoid, exulcerated, exulcerated and spreading, infiltrating, advanced unclassified)
- The Paris endoscopic classification (polypoid and nonpolypoid group)
- Vienna histological classification (neoplasia of low and high grade carcinoma invading the submucosa)
- **TNM classification**
- WHO
  - Tubular, papillary, mucinous, from ring-like cells
- According to the depth of invasion
  - Early (just to the lamina muscularis) X Advanced (under the lamina muscularis)
- By location:
  - The pylorus and antrum, body, fornix, cardia

Adenocarcinoma - Therapy

- **DEPENDS ON STAGING**
- **Surgery**
  - Only chance for cure gastric adenocarcinoma
    - Subtotal or total gastrectomy
  - Palliative care – relieve symptoms
- **Endoscopy**
  - EMR or ESD
  - early cancer (to LPM), non-invasive (only epithelium), palliative (metallic stent)
- **Chemotherapy**
  - in patients with advanced gastric cancer
  - Neoadjuvant, adjuvant, palliative
- **Radiotherapy**
  - Resistance – no survival benefit

Adenocarcinoma

- **Screening**
  - In Japan, since 1960
  - early detection

- **Prognosis**
  - The staging and TNM classification is the best prognostic indicator
  - 5 years, only 10% (after CHIR 30%)

Gastric lymphoma

- **Primary gastric lymphoma is defined as a lymphoma that is predominantly located in the stomach.**
- **Generally**
  - 1-5% of all gastrointestinal malignancies
  - 10% of all lymphomas
- **The most commonly primary extranodal NHL (according to the REAL classification, WHO classification)**
  - MALT lymphoma, diffuse large B-cell lymphoma
- **Pathogenesis**
  - The role of H. pylori infection, HIV, autoimmune diseases
  - Recurrent chromosomal translocations, most commonly t(11;18), leads to Helicobacter-independent proliferation

Gastric lymphoma

- **Symptomatology:**
  - NONSPECIFIC: Epigastric pain, dyspepsia, anorexia, nausea, vomiting, weight loss, ... Up to anemia or gastrointestinal bleeding, obstruction or perforation

- **Diagnosis**
  - Gastroscopy(NONSPECIFIC) with biopsies (histology, immunohistochemistry)
  - EUS – depth of invasion and locoregional lymph node involvement
  - CT or MR – extent of disease evaluation = staging

Gastric lymphoma - therapy

- **According to histological and imunohistochemical type and staging**
  - LG-MALTom + positive for H. pylori → H. pylori eradication
    - FOLLOW-UP
  - LG-MALTom resistant to H.pylori eradication → locoregional radiotherapy or single agent chemotherapy (CHOP mode)
  - Relapse, treatment failure, an aggressive form of lymphoma: Rituximab + chemotherapy
  - DLCBL → chemo-immunotherapy (rituximab, CF, doxorubicine, vincristine,…) + radiotherapy
  - Surgery: treatment of complications
- **Complications of therapy**: nauzea, ulceration, pancreatitis, second malignancies, leukopenia,

Gastric lymphoma

- **Prognosis**
  - MALT lymphoma is an indolent disease with a very good prognosis
    - Depends on disease stage
  - DLCBL has a worse prognosis than MALTom
  - 5-year survival of:
    - Early stage MALTom – 85%
    - DLCBL – 60%

Neuroendocrine tumors

- **Generally**
  - relatively rare
  - The low proliferative capacity of tumors frequently
  - Based on neuroendocrine cells
  - Production of biologically active peptides (neuropeptides, neurotransmitters, hormones specific)
  - slow growth
  - Sometimes familial occurrence
- **Symptomatology:**
  - Asymptomatic x clinical signs of producing biologically active peptides
- **Diagnosis**
  - Anamnesis, gastroscopy, LAB, scintigraphy (TcMIBI), CT or MR

Carcinoid

- **From enterochromatogenic cells - dispersion in the submucosa of the intestine or bronchial tree**
- **Can be in the whole GI tract**
- The incidence of 2.1 / 100,000 per year, more men in the fifth to sixth decade
- **Symptomatology**
  - According to production of biogenic amines
  - Serotonin: intestinal hypermotility and diarrhea
  - Kallikrein-kinin system and catecholamines: flush
  - Bradykinin: bronchospasm

Carcinoid

- **Diagnosis:**
  - Laboratory: according to endocrine overactivity (5-hydroxyindole acetic acid in urine, ..)
  - Endoscopy, ultrasound, CT, MRI, scintigraphy (oktreosken)
- **Therapy**
  - Surgery - a radical resection, metasectomy (with chemoembolization, RFA)
  - Pharmacotherapy - somatostatin analogues, IFN
  - chemotherapy
- **Prognosis**
  - According to localization and metastases (5 years 20%)

Gastrinoma (ZES)

- **From G-cells in the pancreas or duodenum - the production of gastrin - increased gastric acid secretion - hyperplasia of the gastric mucosa - ulceration**
- From 0.1 to 3.1 / 100,000 per year
- 70% of malignant, slow growth, most in the wall of the duodenum
- **Symptomatology:**
  - Ulceration: small and multiple, poorly healing
- **Diagnosis**
  - Gastrin fasting serum (above 500 mIU / L), the low pH of the stomach
  - Calcium or secretin test (gastrin 200-500 NIU / l)
  - Gastroscopy, EUS, scintigraphy, CT and MR
- **Therapy:**
  - SURGERY - foundation
  - Pharmacotherapy - PPI, somatostatin analogs, interferon

Insulinoma

- **From beta cells in the pancreas**
- 1/1 mil. per year
- **Symptomatology:**
  - Whipple's triad: hypoglycemia fasting, retreat after administration of glucose, glucose levels below 2.8 mmol / l
  - Hypoglycemia: diplopia, visual disturbances, confusion, disorientation, sweating, anxiety, hunger, nausea, fatigue, behavioral disorders, headache, amnesia, tremor, convulsions and disorders of consciousness
- **Diagnosis:**
  - Anamnesis, FV, LAB (INS ↑, ↓ GLU, ↑ C-peptide), fasting test, CT or EUS
- **Therapy:**
  - CHIR - aiming at enucleation of the deposits

Gastrointestinal stromal tumor

- **Mesenchymal tumors - from Cajal cells**
- **Uncertain biological nature**
- **Heterogeneous group:**
  - Leiomyoma, schwannomas, GANT, neurofibromas, gangliomas, paragangliomas
- **Symptomatology:**
  - Gastrointestinal bleeding most often, epigastrium pain, vomiting, dyspepsia
- **Diagnosis**
  - Gastroscopy with biopsies, EUS, PET/CT or CT
- **Therapy**
  - CHIR - basic part of therapy
  - Imatinib, sunitinib, VEGF - generalization
- **Prognosis**
  - Better with localization in the stomach, crucial is localization and generalization (only in the stomach = 5 years survival 100%)