Peptic ulcer disease

Plan of the lecture

- 1. Definition of peptic ulcer disease
- 2. Etiologic factors
- 3. Classification
- 4. Clinical presentation of peptic ulcer disease
- 5. Treatment
- 6. The differential diagnosis of peptic ulcer disease

Peptic ulcer disease (PUD) -

- is polygene inherited chronic recurrent disease, manifested by formation of ulcer in stomach or duodenum that can be progressive or develop complications

Code after World wide disease classification (WDC) -10:

К 25 – stomach ulcer

К 26 – duodenum ulcer

- **PUD morbidity is 1 case for 1000 healthy children. Before puberty PUD morbidity is the same in boys and girls, later it's more frequent in males because of protective influence of female sexual hormones.**
- **In PUD structure in children PUD of duodenum is more frequent and compound 81% of all cases, 13% are due to stomach PUD and 6% are combination of duodenum and**

Etiology of PUD

- **The most significant factor of PUD formation is hereditary predisposition (family load is 60 - 80 %, and as for aggressive features of stomach juice in one of the parents it's defined in all 100% of cases)**

Predisposing factors

- HP contamination
- Early formula feeding (it can induce activation of gastrin produced cells and histamine produced cells formation in mucous membrane of stomach antrum)
- Alimentary inaccuracy
- Prolonged consumption of some drugs (salicylic acid, glucocorticoids, cytostatics etc.))
- Peculiarities of family habits – life style, family type of feeding, family relationship
- Hypodynamia or physical over loadings
- Chronic infection focuses
- Intestine parasites
- Neuro -psychic over loading
- Smoking and drug abuse
- Food allergy

Environment factors

- Can change ratio of some regulatory system compartments, actively influence to peptic acid factor, change protective properties of mucous barrier.
- Prolonged acidity in pyloric and duodenal region induce methaplasia of epithelium in this compartment and predispose to HP invasion. HP can impair epithelium and suppress protective mucous membrane properties , initiate auto-aggressive reactions.

- **HP strains of the first type has the highest cytolytic activity so this strain is 4 times more in virulence as compared to another strains. In 90% of affected patients this strain is defined.**

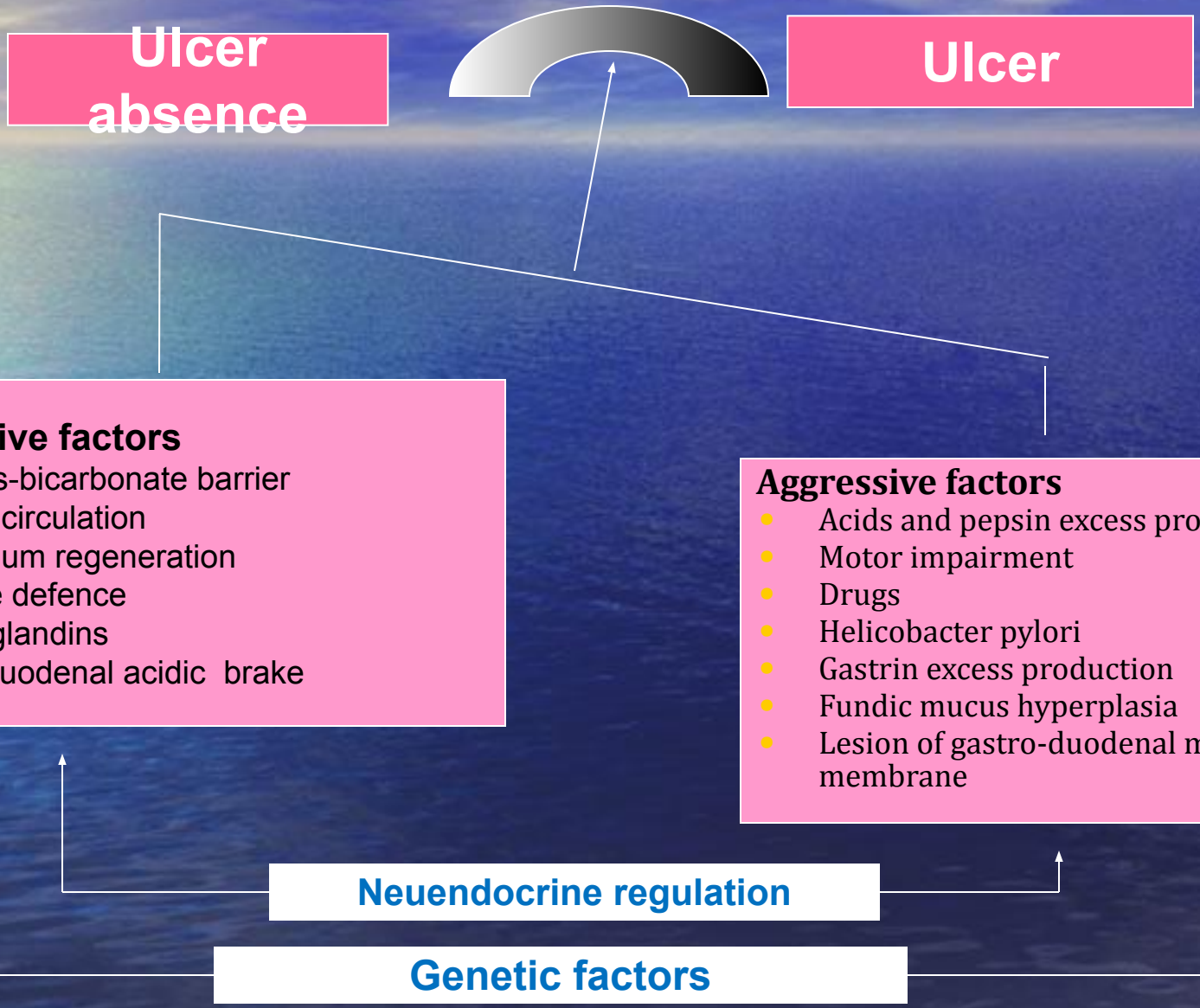
Pathogenesis

Hereditary predisposition in PUD has such features:

- **Hereditary determined peculiarities of mucous membranes structure – elevated quantity of gastrin produced and histamine produced cells, hyperplasia of fundal glands with increased quantity of main and acidic cells.**
- **Increased acidic- peptic aggression due to hereditary increased secretion of pepsinogene A(responsible gene is situated in 11 chromosome) and also quality of these pepsinogene with dominating of A type that induce synthesis of PG3 type.**
- **Decreased resistance of mucous membranes due to suppression of mucin and bicarbonates production.**
- **Peculiarities of motor stomach function- decreased obturative reflex that prevent acidic antrum content to pass into duodenum before its alkalizing in antrum.**

Shiaya balance-

ratio of main protective and aggressive factors that define possibility of ulcer formation



- Classic clinics of typical pain syndrome in PUD was described at the beginning of 20 century by Monigan.

Clinics

Pain syndrome

1. Fasting pain appearance or 1,5-2 hours after feeding (Moinigan rythm)
2. Nocturnal pain predominance
3. Intensity ranges from slight to severe unbearable
4. Localized in epigastrium . If accompanied GERD is present it can irradiate retrosternum space.

DYSPEPTIC SYNDROME

1. Heartburn (usually together with GERD)
2. Acidic regurgitation
3. Vomiting with relieving pain

ABDOMEN PALPATION

Painfulness in epigastrium, sometimes local in pyloric-duodenal region

VAGOTONY SYMPTOMS (in teenagers):

- Cold, moist palms
- Hyperhydrosis
- Acrocyanosis
- Decreasing of BP
- Pulse lability

PUD peculiarities in children

- Classic clinics can be seen less than in 50% patients
- In 15% children complaints are absent (silent ulcer)
- In 3% patient first presentation of disease can be complicated (by bleeding, perforation)
- More younger the child more atypical clinics is seen

Differences among stomach and duodenum ulcer disease

Sign	Duodenum ulcer	Stomach ulcer
Morbidity in children	81 %	13 %
Gender	Boys are affected more frequently	Girls and boys ratio is the same
Family history	Two times more frequent than in stomach ulcer	Isn't present as a rule
Blood group	More frequent 0(I) group	No blood group predisposition
Main cells quantity	Increased	Decreased
Course	Season, periodic (fall-spring time) exacerbations	Seasons and periodic exacerbation isn't constant
Pain intensity	Usually severe acute stinging pain, attack-like	Different intensity of pain, less severe than in duodenum

Character of pain	Night, fasting or late (1,5-2 hours after meals)	After meals
Pain localization	Right of middle abdomen line	Left of middle abdomen line
Pain relievers	Food and basics	Basics and vomitting
Dyspeptic disorders	Expressed	Absent or mild
Stomach motor disorders	Enhanced (prompt evacuation, spasms)	Flaccid or normal
pH	Increased	Decreased or normal
Basal secretion	Increased	Normal
Night secretion	Increased	Normal

Most helpful diagnostic examining

- Endoscopy .
- X-ray (not obedient for non-complicated cases).
- Examining of secretory function (increasing of basal and stimulating secretion fractions)- is helpful to define functional disorders but not ulcer itself .
- Helicobacter pyloric contamination.

PUD classification

1. **Severity** (first defined, mild-recurrence once per year and less , **moderate** – relapse 2 times per year, **severe** – recurrence more than 2 times per year and complicatiuons).
2. **Phase – exacerbation, partial remission, remission.**
3. **Clinic-endoscopic stage – fresh ulcer, scarring defect, scar, scar-ulcer deformity.**
4. **Ulcer localization – Stomach (cardiac, subcardial portion, little, big curvature, pyloric region; duodenum (bulbus, post bulbar region)**
5. **Gastritis character** (superficial, atrophic, and localization of it) **gastroduodenitis** (active, erosions, hyperplastic, associated with H.P.)
6. **Functional characteristics** (with decreased acidic production, preserved or increased).
7. **Complications– penetration in pancreas, hepatoduodenal legamentum, gall bladder, liver, colon), acute bleeding** , perforation, stenosis (compensated, subcompensated, decompensated, reflux-esophagitis)

PUD complications

BLEEDING – most frequent (80%) complication.

- **Clinics: emesis, melena, symptoms of acute blood loss .**
- **Coffe-like vomiting (Hb under influence of HCl turn into hematin with dark-brown color)**
- **Melena – is black stool can be seen after the loss of more than 60 ml of blood (ferrum sulfate realizes under the influence of digestive enzymes)**
- **Symptoms of blood loss appear in the case of big blood loss weakness, nausea, paleness, tachycardia, cold, clammy sweat, BP decreasing, dizziness, vertigo, conscience loss sometimes**
- **Bleeding can be hidden . In stool you can find hidden blood (positive Gregersen reaction)**

Diagnostics approach algorithm in the case of PUD bleeding

- Taking history and patient inspection
- Blood group and Rh defining
- Endoscopy and X-ray of stomach and duodenum if necessary
- Ultrasound diagnostics of abdomen

- **Perforation (8 %) – sudden knife-like pain in epigastrium, nausea, defans of anterior abdomen wall , vomiting without condition improvement**
- **Penetration (1,5 %) – spreading of ulcer into surrounding tissues. It can be defined by X-ray examining by changing of the near organs functioning**
- **Pyloro- duodenal stenosis (11 %). Formed steadily . Accompanied by sensation of stomach overfilling, nausea, regurgitation, burning, vomiting with relief of condition. The splash sound in epigastrium. By X-ray stomach dilation with retardation of its emptying.**

Differential diagnosis

Must be performed with acute symptomatic ulcers.

- **STRESS -ulcers They can appear in burnings, trauma, freezing. Clinics is scanty. The first presentation can be bleeding, more rae –perforation.**
- **Due to medicine influences Appear after consuming the medications that can disturb barrier properties of mucus (non-steroid and steroid drugs, cytostatics, etc). They are presented by asymptomatic course. Bleeding can be the first manifestation,**
- **Hepatogenic. Can appear if inactivation of gastrin and histamine is impaired in liver. Clinics is vague and atypical, course is torpid, badly corrected by treatment.**
- **Pancreogenic. Appear in the case of decreased production of bicarbonates and increased production of kinins. Pain syndrome is manifested and induced by food consuming. Course is constant.**

- **Endocrine. Very rare development in diabetes, hypothyroidism. Course of this ulcer disease id similar to severe course of PUD.**
- **Zollinger-Ellison syndrome – gastrin produced neoplasms (gastrinoma) . IT's usually localized in antral part of stomach or in pancreas, in 16% of cases it can be malignant. It's resistant to PUD therapy. Screening test is elevation of gastrin in fasting condition in serum.**
- **Allergic ulceration more frequently can be developed in the case of food allergy.**
- **In chronic renal failure due to impairment of gastrin degradation in kidneys and as a result disturb of protective barrier in stomach**
- **In diffuse connective tissue disorders due to impairment of microcirculation .**

Clinics of symptomatic ulcers

- Diagnostic difficulties
- Absence of typical pain syndrome and dyspeptic symptoms
- Absence of seasonal periodic exacerbation
- High risk of life threatening conditions (bleeding, perforation)

Endoscopic data

- Ulcers can be singular or multiple
- Ulcer diameter usually is not more than 1 cm .
- Shape of ulcer defect is oval or round, so called “punched ulcers”
- Bottom of ulcer defect is plant crater-like.
- Around the defect there is bright red crown, but inflammatory ring is absent.
- Main localization is stomach
- Prompt epithelization.

Treatment goals

- To reduce PUD symptoms and provide reparation of ulcer defect
- Eradicate contamination of H.P. of mucus.
- Not only get the healing of defect but restitute functional capacity of mucous membrane.
- Prevent development of exacerbations and complications.

PUD treatment

PUD treatment is directed to suppress aggression factors like acidic –peptic factor and contamination of mucous membrane by **HELICOBACTER PYLORI .**

Main principles :

1. Reject of smoking, alcohol taking.
2. Stop to get non-steroid and steroid medications, if it can't be stopped to decrease dosages.
3. Rational feeding. It means frequent intake 5-6 times per day with excluding of spicy products. Diet N 1-b in the case of exacerbation signs.

Medication treatment.

1. **HELICOBACTER PYLORI** eradication
2. Suppressing of acidity and peptic factors production
3. Correct motor evacuative function .
4. Stimulation of reparative processes.

Medication treatment of PUD

- PUD is obligatory indication for H.P. eradicative therapy in any stage of disease
- Treatment include first and second line of eradicative therapy.
- First line is performed after diagnosis of PUD in any period (exacerbation or remission) and complications.
- Control of its efficiency is performed a month later the treatment not earlier predominantly by noninvasive methods: breathing test (carbonic C13 or Helic-test) or test of H.P defining in stool.
- If test is positive for H.P. second line therapy is proposed. If test is negative therapy is stopped.

HELICOBACTER PYLORI eradication provides regression of inflammatory and dystrophic changes and restitutes protective properties of stomach mucous membranes.

Antihelicobacter pylori medications – methronidazole, Clarythromycine, Amoxycylline, colloid Bismuthi subcytrate.

Approximal eradicative schemes:

1. Omeprazol + Clarythromycine + Methronidazole
2. Omeprazol + Amoxycilline + Clarythromycine
3. Omeprazole + colloid Bismuthi subcytrate +Methronidazole + Amoxycilline

COMBINED ANTIBACTERIAL MEDICATIONS.

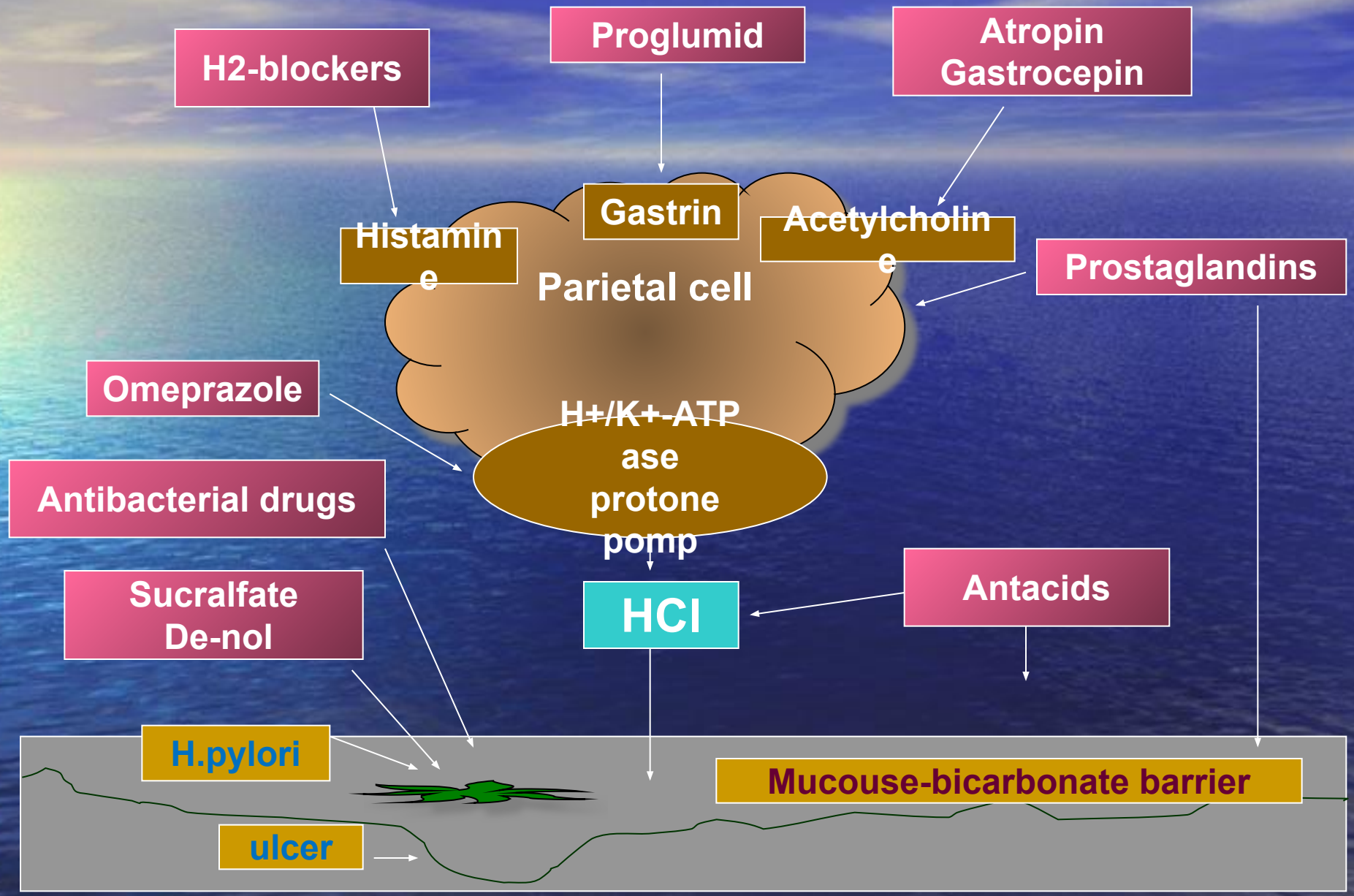
1. Gastrostat (colloid Bismuthi subcytratis + Tetracycline + Methronidazole)
2. Gastropak – (colloid Bismuthi subcytratis + Amoxicilline + Methronidazole)
3. Pylorid (ranitidin + colloid Bismuthi subcytratis)
4. Helicocide (Amoxicilline+ Methronidazole)

Therapy according to schemes is continued for 7 days, later they live only antisecretory therapy

Regulations for antihelicobacter therapy

- If usage of the eradication scheme doesn't provide complete H.pylori eradication you needn't to repeat it once more. It means that H.P . get resistance to one of the components in this scheme.
- If usage of one scheme later another scheme don't provide complete H.P. eradication you need to check susceptibility of Helicobacter pylori to all the spectrum of prescribed antibiotics.
- Appearance of H.pylori in patient earlier than one year after eradication means recurrence of infection but not reinfection. You need to choose more effective treatment scheme.
- Decreasing of antibiotic quantity in scheme leads to H. pylori resistance formation. After finishing of 7 day combined eradicative treatment you can prolong it for 4-5 days in the case o duodenal ulcer and 7-8 weeks in stomach one with usage of one antisecretory drug.

Main medications activity locuse



Antisecretory medications

- Selective M-cholinolytics (pirenzepim, gastrocepin)
- H2-histamine receptor blockers (ranitidin, famotidin)
- Protone pomp inhibitors – blockers of H+/K+ATP –ase in parietal cells (omeprazole)

Antisecretory therapy

1. H2-histamine receptor blockers

- **Selectively block secretion of HCl**
- **Decrease volume of gastric juice**
- **Decrease the level of pepsin**

- **Cimetedine** group – 1 generation (Cimetedin, Tagamet, Histodyl, Cimehexal, Neutronorm, rimamet)
- **Ranitidin** group – 2 and 3 generation (Ranitidin, Ranisan, Zantak, Ulkodin, Zoran, Histak, Ranigast, Ranitab, Ranitard, Ranitin)
- **Famotidin** group – 2 and 3 generation (Lecidyl, Gastrocydin, Quamatel, Famocyd, Ulfamid, Famodin)
- **Nizatidin** group (Axid)
- **Roxatidin** group (Roxan)

2. **Peripheral M- choline receptors blockers (gastrocepin, pyrenzepin, gastrozem, gastril, pyren)**

- **Suppress HCL and pepsin production**
- **Increase protective properties of ventricular mucus**

3. **H+/K+-ATP ase blockers (protone pomp inhibitors)**

(omeprazol, omez, omeprol, omezak, ornatol, losek)

- **Inhibit HCl production**

Cytoprotectors

1. **Film-forming medications(decrease backward diffusion of Hydrogen ion):**

- **Colloid Bismuthi subcytrate, De-nol** (Tribimol, Ventrixol). Increase prostaglandin production, adsorb pepsin, has antihelicobacter activity.
- **Sukralfat (Venter, antepsyn).** Connect Aluminium with sulfate polysaccharide, in acidic surroundings get adhesive properties. On the surface of erosions and ulcers perform complex compound with protein –helate and create mechanic protective barrier.

Film-forming medications are basic remedies in peptic ulcers with normal secretory function.

2. **PROSTOGLANDINS** – **increase bicarbonates and mucus production, increase protective layer thickness, improve microcirculation. It's mesoprostol (Arboprostyl, Enprostyl)**

It must be taken before meals and before sleeping. Course is 4 weeks.

- If accompanied dysmotility is present (duodeno-gastral reflux, gastro-esophageal reflux) DOPA-receptor blockers (cerucal, motilium) 1mg/kg TID or cizaprid (Coordinax, Propulsid) 0,4-0,5 mg/kg /day can be used.
- Spasmolytics (no-spa, Papaverin, Platiohyllin, Buskopan)

Bleeding treatment

- Urgent hospitalization to provide endoscopic treatment (diathermo coagulation, laser coagulation).
- Intravenous infusion of haemostatic medications (Vicasol, Calcium, Androxol)
- Oral intake of 5 % Sol. Of Aminocapronic acid with Thrombin and Androxol
- Prescribing of H2 –histamine blockers IM (Quamatel, 2mg/kg/day IV)
- If bleeding is significant transfusion of plasma or blood (only of the same group)

- **Duration of hospitalization in the case of Duodenum PUD is 28 days, in Stomach PUD – 30-35 days, in the case of severe course it can be 6-8 weeks.**
- **After ulcer healing (phase of incomplete remission) treatment can be prolonged at ambulatory regimen. In the phase of remission sanatorium treatment is desirable.**

- Efficacy criteria of therapy is clinic and endoscopic remission, exacerbation symptoms absence, healing of ulcer defect and absence of inflammatory signs while endoscopic examining. Observation must be provided for 5 years. It can be finished if remission is stable for 5 years.

Dispensary

- Doctor's examination must be performed 2-4 times per year depending on severity of disease.
- If exacerbations are absent FGDS must be performed once per year. It will be done in the case of therapy inefficiency "on demand" during exacerbation period.
- Stomach secretion must be examined by pH-metry once per year.
- Stool analysis for hidden blood must be performed twice per year.

- During complete remission period diet № 1 is taken for 4-6 mo.
- Child is freed from physical training in the main group.
- During dispensary period two times per year (usually on fall and spring period) prophylactic treatment courses for 3-4 weeks are performed.
- Sanatorium treatment can be recommended only in period of complete remission or period of recovery if signs of gastro-duodenitis are absent. If bleeding has been present sanatorium is permitted not earlier than 6 mo after gaining full remission (such sanatorium will be preferable like Truskavets, Morshin, Berezovsky mineral waters, Ray-Yelenovka etc.)
- If child has no exacerbations for 5 years and he is in complete remission he is stopped to undergo dispensary examination.

Questions

- Prevention of peptic ulcer disease
- Frequency and prognosis
- Clinical symptoms of peptic ulcer disease
- Additional (instrumental) methods of invastigations
- Prevention of complications of peptic ulcer disease
- Principles of treatment of peptic ulcer disease