Adherence of patients to medical recommendations (compliance) as an important factor in increasing the effectiveness of treatment (by example of acid-dependent diseases)

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Successful treatment is possible only with full cooperation of the doctor and the patient.
V.H. Vasilenko [3]

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Brief history. *Terms compliance, adherence translated from English mean "consent, matching your wishes"* [16]. They appeared in the English-language medical literature at the end of the 20th century. Use them to indicate adherence to strict patient compliance with medical recommendations, particularly with regard to strict compliance by patients before claim ISAN physician on Pharmacotherapy (medication dose and frequency of administration, duration of treatment rate and so on). In a broader sense of the word, this also applies to the lifestyle of the patient, giving up bad habits (alcohol, smoking, etc.), dietary restrictions, etc.

This problem, of course, is not new. Back in the 10th century AD the well-known Arab doctor and poet Abu-l- Faraj al- Isfahani (897–967 AD), speaking about the patient, exclaimed: *"Look, there are three of us: me, you and the disease. Therefore, if you are on my side, it will be easier for us to defeat it alone. But if you go to its side, I alone will not be able to defeat both of you."* [28].

Outstanding clinician and scientist V.H. Vasilenko drew attention to the fact that *often doctors, especially young ones, forget that* their duties include education of the patient. To convince the patient to change the wrong way of life, to give up bad habits, to convince of the need for consistent treatment, to believe in him, to give up attempts at self-treatment means to make the patient an active assistant, an ally of the doctor in the fight against the disease [3]. *In addition, he argued that* "the situation of the patient will be different depending on whether a person treats his health lightly or attentively" [3].

Another well-known therapist B.S. Shklyar believed: *"In addition to medications, the success of the patients trust in the attending physician and the active participation of the patient himself in restoring his health is also necessary"* [47].

Of course, the attitude of the patient to his health, the strict fulfillment of the doctors prescriptions, largely depends on his general culture, education, upbringing, moral principles, character traits and personal qualities. Psychotherapist K.A. Skvortsov in his monograph *"Essays on the psychotherapy of the somatic patient"* (1958) wrote: *"Patients relate differently to their illness: some hold on above the illness, struggle with it; others do not pay attention to it — dissimulate; still others consider her a shame or completely submit to illness, become her slave and servant; are afraid of the disease, or get used to it, or, on the contrary, are deeply worried"* [22]. This is explained by the fact that the psyche of a sick person changes significantly. As noted by the outstanding domestic neurologist G.I. Rossolimo: *"The disease introduces such changes into the human spiritual world, which, pushing one side, darkens others — sometimes changing the whole harmony of the personality, as well as the nature of the attitude to oneself and everything around so much that the doctor has to reckon in his activities with an ordinary person, and with a suffering person as a special psychological variety"* [18].

Of paramount importance is the ability of the doctor to instill confidence and respect for the patient, to achieve emotional contact with him. Famous Russian writer and doctor V.V. Veresaev (Smidovich) in his famous book *"Notes of the Doctor"* He wrote: *"The doctor can have a huge-inflammatory recognizing talent, ability to note subtle details of their appointments, but it remains fruitless if it does not have the ability to conquer and subdue the soul and the will of the patient"* [4]. It is these qualities that basically determine the willingness of the patient to strictly follow medical prescriptions, which, in essence, is the main content of the term *compliance*.

Compliance value in the treatment of acid- related diseases. *To the group of acid- related diseases rank as* gastroesophageal reflux disease (GERD); peptic ulcer (PU) of the stomach and duodenum (duodenum); antral non-atrophic chronic gastritis (CG), most commonly associated with *Helicobacter* infection *pylori* (HP); disease (syndrome) Zollinger-Ellison syndrome (gastrinoma) — gastrin-producing paraendocrine hydrochloric tumor localized predominantly in pancreas and (with reservations) hCG type C long induced by nonsteroidal anti-inflammatory drugs (NSAIDs), unsuccessfully called NSAID-gastropathy [6, 15, 20, 33, 35, 42]. Some authors additionally include in the number of acid- related diseases the syndrome of functional (gastroduodenal) dyspepsia (SFD) [15], which we consider to be unjustified.

Considering various methods of treating acid-related diseases, most authors limit themselves to discussing the effectiveness of various pharmacological agents, ignoring the importance of *compliance* as an important factor in improving the results of therapeutic interventions.

Meanwhile, patient compliance with the elementary recommendations of the doctor to streamline

lifestyle (*lifestyle modification*), following the advice on dietary restrictions and diet, giving up bad habits, avoiding (if possible) stressful situations and considerable physical exertion, etc. significantly affects the success of treatment.

Of course, decisive importance belongs to the strict fulfillment by patients of medical prescriptions regarding the dose of prescribed drugs, the frequency and time of their admission (morning, evening; before, during or after meals), the duration of the course of treatment, etc.

For all acid- related diseases, a "sparing" diet is prescribed: during the exacerbation of the process — medical table number 1a, and after achieving clinical remission, treatment table No. 1 (main) according to M.I. Pevzner [7]. Their main principle is maximum chemical and mechanical sparing. ***Recommended:*** liquid and semi-liquid food, low-fat varieties of meat and fish, boiled or steamed; split meals (5–6 times/day) in small portions in the form of heat (40-50°C) and at certain times of the day; the last meal is 3 to 4 hours before bedtime. Food and meals that have a sokogonnym effect, including alcoholic beverages (including beer), are excluded from the diet; meat broths and ear; fruit juices, pickles and marinades; fried foods and smoked meats; spicy seasonings (horseradish, radish, vinegar, mustard, pepper, etc.). It is necessary to limit animal fats and carbohydrates; smoking cessation. In GERD, coffee and chocolate are also excluded, which reduce the tone of the lower esophageal sphincter (LES) [7].

GERD is a chronic recurrent disease, which are characteristic clinical symptoms (heartburn, acid regurgitation, dysphagia), which are caused by spontaneous, regularly repeated reflux (reflux) of acid or acid-base (with admixture of bile) stomach contents into the esophagus with a decrease in pH in the lower third (n/3) of the esophagus up to <4.0, damage to its distal (esophagitis, erosion) and the risk of serious complications (ulcer, Barretts esophagus, adenocarcinoma of the esophagus), accompanied by a sharp deterioration in the quality of life (QOL).

In the pathogenesis of GERD claimed important role disorders antireflux mechanism (barrier) of the esophagus caused by the presence of hiatal hernia (hiatal hernia) or decrease spontaneous tone NPS and relaxation; primary disorder of the motor (peristaltic) activity of the esophagus, especially its distal parts. These disorders are believed to be based on disorders of the neuro-humoral control of the NPS tone caused by psycho-vegetative dysfunction (vegetative dystonia) [8, 35, 52].

Among the additional factors contributing to the development of GERD are repeated pregnancies; smoking and alcoholism; long-term use of pharmacological agents that reduce the motor activity of the esophagus and the tone of its sphincters.

The development of esophagitis and erosions in GERD is due to the effect of reflux and aggressive properties on the mucous membrane of the lower third of the esophagus. The composition and the refluxate are pepsin and hydrochloric acid of the gastric juice, and in the presence of duodenal-gastric reflux a (GHD) and bile containing current bile acids and lysolecithin (detergents) with high damaging potential. Designated values e belongs and increase intra-abdominal pressure (at baa belt, ascites, expressed flatulence). Among predisposition to develop GERD factors must also be called precise hut body mass (obesity), heavy physical work, and others.

In the treatment of GERD, in addition to prescribing pharmacopreparations, it is necessary to provide for the normalization of body weight (for obesity), the cessation of smoking and alcohol, and the avoidance of stressful situations. It is recommended to sleep with a raised headboard (15–20 cm), not to wear tight clothes and tight belts, to refrain from eating for 3-4 hours before sleep, as well as from physical work performed in the slope. It is very important not to take without extreme necessity medicines that reduce the tone of the NPS and the peristaltic activity of the esophagus, stomach and duodenum (M-cholinoblockers, nitrates, antidepressants, tranquilizers, calcium channel blockers, beta-blockers, myotropic antispasmodic "theophylline) [10, 35, 45 52].

In pharmacotherapy GERD used: 1) nonabsorbable antacids containing aluminum and magnesium hydroxide, aluminum phosphate (maalox suspension, phosphalugel, etc.); 2) alginate) (popolcan, Gaviscon); 3) H2-histamine receptor blockers (ranitidine, famotidine); 4) proton pump inhibitors (omeprazole, lansoprazole, pantoprazole, rabeprazole, esomeprazole 5) prokinetics (motilium, ganaton); 6) gastroprotectors (de no; sucralfat and sukrat-gel, etc.).

Antacids are used most often, if necessary, to urgently stop painful heartburn and epigastralgia. They do not control acid production, but only chemically neutralize hydrochloric acid in the cavity of the stomach. The duration of antacids does not exceed 40–60 minutes, and therefore they have to be taken several times during the day. This is symptomatic GERD therapy. Antacids are prescribed in 15 ml 4–5 times/day 1–1.5 hours after a meal and at night [15].

Alginates create an algino-rift barrier, forming an alkaline foam on the surface of the stomach contents, which is thrown into the n / 3 esophagus during each gastroesophageal reflux (GER), neutralizing the hydrochloric acid that has penetrated the esophagus. The dose of poplar and Gaviscon is 10 ml, 1.5 h after a meal and before bedtime [35].

H_2-histamine receptor blockers. Histamine H2 receptors are located on the apical membrane of the

parietal cells of the gastric glands. Acceptance of H_2-HR blockers significantly suppresses acid formation in the stomach for 7–8 hours (ranitidine) and 10–12 hours (famotidine). It is established that famotidine is 8 times more active than ranitidine. However, both drugs have serious drawbacks: 1) after their cancellation, there is a "bounce symptom" — a sharp increase in the production of hydrochloric acid by the gastric glands; 2) with long-term administration of H_2-HR blockers, a "tachyphylaxis phenomenon" is noted — a rapid decrease in efficacy upon repeated administration.

In general, the therapeutic effect of the H_2-HR blockers in GERD is insufficient [20]. The dose of ranitidine in the treatment of GERD usually exceeds the standard 2 times (300–600 mg), as well as the dose of famotidine (40–80 mg), 2 times/day after meals and at night [14, 53, 60, 65].

Proton pump inhibitors (PPIs) block the final link in the production of hydrochloric acid in the stomach — the action of the enzyme $H7K^+$ ATPase (proton pump). These are the most powerful of the currently known inhibitors of acidic gastric secretion, the duration of which reaches 12–14 hours. PPIs are benzimidazole derivatives, which are drugs: they are activated only in the secretory tubules of the parietal cells of the gastric glands. There is no addiction to them.

Currently using five drugs in this group (they were listed earlier). The effectiveness of all five representatives of the PPI group is about the same. Some authors prefer rabeprazole. It has the highest dissociation constant (4.53), while in omeprazole and eso meprazole it is 4.06, and in lansoprazole and pantoprazole it is 3.83. In this regard, rabeprazole quickly becomes active; besides, rabeprazol does not interact with drugs of other pharmacological groups [51, 58, 68]. All PPI are ingested, regardless of the meal.

Standard doses of PPI: omeprazole — 20 mg; lansoprazole — 30 mg; pantoprazole — 40 mg; rabeprazole — 10 mg; esomeprazole — 20 mg.

When treating GERD, standard doses of PPI often have to be doubled, especially in the presence of erosive esophagitis [6, 8, 15, 20, 35, 61, 63, 68].

Prokinetics: Motilium (domperidone) and ganaton (isoprid hydrochloride) strengthen and normalize the motility of the esophagus, stomach, and duodenum. Their use in GERD was even more effective than taking H_2-HR blockers [35]. But the effect of the PPI was still higher. ***In clinically significant cases of GERD, prokinetics are usually prescribed in combination with an PPI.*** The dose of motilium — 10 mg 4 times/day, in ganaton — 50 mg 3 — 4 times/day 30 — 40 minutes after eating, so as not to cause premature emptying of the stomach until the end of the gastric phase of digestion. The course of treatment — 46 weeks or longer [23, 44, 46, 51].

Received recognition in the treatment of GERD and trimebutin (debridat, trimetin) — an antagonist of opiate receptors acting on the enkephalinergic system for the regulation of motility of the digestive tract. It has a normalizing effect on the motility of the esophagus, stomach, and intestines in both hypodyskinesis and hyperdyskinesis. Dose — 100–200 mg 3 times/day after 30–40 minutes after a meal.

Patients with GERD require long-term (prolonged) treatment of PPI, prokinetics, etc. Therefore, after achieving clinical remission, treatment cannot be interrupted. ***Recommended maintenance therapy*** for half-dose PPI or ***periodic treatment: "weekend therapy"*** (on Saturdays and Sundays), "***on-demand therapy***" with the recurrence of clinical symptoms, as well as therapy if necessary ***(pro renata***) [5, 21, 23, 25, 35, 45].

The recommendations "Maastricht consensus 1–4" (MC-1–4) for diagnosis and treatment of diseases associated with HP-yn fektsiey recommended eradication HP in GERD, although it is recognized that ***"HP does not affect the severity, frequency of symptoms, and effectiveness of treatment for GERD, and epidemiological studies show a negative correlation between the spread of HP and the development of GERD and adenocarcinoma"*** [26]. We are opposed to the eradication of HP in GERD, because we consider it completely unfounded.

Numerous evidence-based studies have established the ineffectiveness of HP eradication in GERD. Moreover, HP eradication, especially when identifying its CagA -positive strains in gastric antrum, promotes more frequent cases of GERD and its severe complications: Barretts esophagus (precancer) and esophageal adenocarcinoma [64, 67, 69].

Trying to justify the need for the eradication of HP in GERD, they usually refer to the fact that with prolonged use of PPI, atrophic chronic hepatitis develops and the risk of its transformation into gastric cancer (GC) increases. However, as established by the ***American Committee on Gastroenterology Medicine*** (Food and Drug Administration), there is no risk of developing atrophic CG, intestinal metaplasia and gastric cancer with long-term administration of PPI [10]. At the same time, it was shown that after long-term treatment of PPIs, which sharply inhibit acidic gastric secretion, vitamin B_{12} deficiency develops already in 2 years in 65% of patients with GERD due to suppression of the formation of an internal Castle factor [20].

Gastric ulcer and duodenal ulcer is a common gastroenterological (and not infectious) disease with unclear etiology, complex multifactorial pathogenesis and genetic predisposition, which is characterized by a chronic polycyclic course with a change of exacerbations and remissions and a general pathomorphological feature — the formation of a single (usually) venom of anxiety and remission those parts of the gastroduodenal mucosa that are "washed" by active gastric juice [31, 33].

The etiology of ulcer is still unknown. The assumption about the etiological role of HP infection with ulcer could not be proved. It was established that these bacteria as an etiological factor of BU do not meet two (out of three) requirements for pathogens of ***R. Kochs triad:*** 1) one-time volunteer attempts to reproduce PU by injecting a concentrated suspension of pure HP culture into the stomach (10^9 microbial bodies) were unsuccessful (they developed transient acute gastritis, but not PU); 2) revealed that in addition to HP-associated ulcer cases a large part of BU develops without any participation of these microorganisms, it HP-negative form of the disease, the frequency of which varies from 12–20% 40–50% [9, 32, 50, 57, 59].

We studied the spectrum of mucosal microflora (M-microflora) in the biopsy specimens from the periulterose zone in the ulcer using modern methods of microbiological research. We obtained microflora growth in 90.5% of patients with ulcer disease, including in the form of microbial associations, in 69.4%. 93 bacterial strains were isolated from biopsy specimens of the gastric mucosa and duodenum, with streptococci (57.1%), HP (52.4%), and ***Candida*** fungi (40.5%) predominating. The degree of colonization (the average concentration of microbial cells in the periucerous zone) was 2.7 lg CFU/g. It is important to note that the selected microflora possessed pronounced viruses. adhesive properties (56.4±6.7%), including urease activity and pathogenicity factors (production of lactamase, etc.).

For some reason, these facts are ignored, and HP infection plays an exclusive role in the pathogenesis of ulcer disease [36].

The proposed pathogenesis concept of ulcer is based on the ***theory of functional systems,*** which is a dynamic central-peripheral organization, united by nervous and humoral regulatory mechanisms, the components of which interact with each other in order to provide an adaptive result useful for the organism [24]. One of such functional systems is the gastroduodenal gastric (more precisely, gastroduodenoholangiopancreatic) self-regulation system, built on the hierarchical principle of sequential interaction [19, 33], which begins with gastroduodenal complex, and ends at the level of cortical-subcortical formations of the brain and includes the mechanisms of pathogenesis and sanogenesis [33].

In addition, hereditary aggravation of ulcer is involved in the pathogenesis of ulcer; secondary developing immunodeficiency in the form of its combined form with predominant inhibition of the T-cell immunity; psychosomatic mechanisms and oxidative stress [1, 2, 32, 33, 34, 37, 39, 40, 66].

As for the aggressive properties of acid-peptic factor, as well as HP- infection and other M-microflora of the stomach and duodenum, we give them the role of local factors in the pathogenesis of ulcer. Moreover, if hydrochloric acid is an obligate factor in the pathogenesis of ulcer ("no ulcer without acid"), then HP infection is optional, since ulcer can develop without its participation (HP negative forms of ulcer) [33].

Treatment of PU. Proponents of the leading role of HP in the development of ulcer consider it possible, in its treatment, to limit exposure to only local pathogenetic factors — acidopeptic and HP infection by administering IPP and 2-3 antibacterial agents for HP eradication. ***The use of standard schemes leche Nia I B does not take into account the need for a simultaneous impact on the general mechanisms of the pathogenesis of the disease and the individualization of therapeutic measures.***

Consider the recommendations of MK-1–4 for the treatment of ulcer with the possibility of compliance with patients ***compliance.*** MK offers ***standard treatment regimens for all patients with PU.*** Initially, a "triple" therapy regimen called "***first-line therapy***" is recommended***:*** PPI (omeprazole or its analogues) + clarithromycin (500 mg 2 times/day) + amoxicillin (1000 mg 2 times/day), which can be replaced with metronidazole (500 mg 2 times/day) within 7 days.

In treatment failure (eradication of HP <80%) go to ***"quadruple"*** or ***"second-line therapy":*** STI (double dose) + de-nol (bismuth tripotassium dicitratobismuthate 120 mg of 4 times/day) + tetracycline (750mg 2 times/day) + furazolidone (200 mg four times/day) 10–14 days.

Recently, due to the steadily increasing secondary resistance HP to those used for their eradication of antimicrobial and critical decrease of its efficiency is proposed to use ***a backup antibiotic — levofloxacin*** (500 mg, 2 times/day) and additionally assign ***probiotics*** (bifiform, lineks etc. on. 2 cap pp. 2 times/day after meals for 2 to 4 weeks) [26, 41] for the correction of developing (in 100% of cases) of colonic dysbiosis.

"First-line therapy" with a double dose of pharmacopoeia (in the morning and in the evening) for 7 days is convenient and easy to do. At the same time, ***"second-line therapy"*** creates serious difficulties for the patient, since two of the recommended medicines should be taken 2 times/day, and the other two 4 times/day. In addition, the treatment is extended from 7 to 10–14 days, which increases the effect of HP eradication by only 5% (!). This is less than the statistical error frames, but it is 1.5–2 times the rate increases the cost of treatment [26].

In addition, denol is recommended to be taken 40–60 minutes before a meal, furazolidone — after a meal, tetracycline — before a meal, and PPI — regardless of the meal.

It should be borne in mind that eradication therapy acts not only on HP, but on the entire M-microflora of the stomach and duodenum, therefore its effectiveness cannot serve as evidence of the exceptional role of HP in the pathogenesis of PU [33].

We believe that many ulcer patients need complex and personalized treatment, affecting the general

pathogenetic mechanisms of ulcer development, including (if indicated) in prescribing neurotropic and immunomodulating agents, antioxidants, etc. In particular, we have shown the effectiveness of nootropil (400 mg 3 times/day for 3 weeks), immunopath for (0.005% — 1 ml intravenously every other day) + tactivin (0.01% — 1 ml subcutaneously every other day) alternately for 10 days; sea buckthorn oil (1 des. spoon 3 times/day for 30 — 40 minutes before meals and before bedtime) or dibunol (200 mg 4 times/day for 3–4 weeks), which have anti oxidative action [17, 33, 37, 38, 41, 43].

It is extremely difficult for patients to strictly adhere to all these recommendations; therefore, very often they are not implemented, which inevitably leads to a decrease in the effectiveness of treatment.

Antral non-atrophic CG associated with HP infection. CG is a polyetiological and polypathogenetic disease of the stomach with a chronic progressive course, the morphological basis of which is a specific inflammatory process with lymphoplasmacytic infiltration and a neutrophilic (granulocytic) component, accompanied by a structural reorganization of its mucous membrane and the development of disregenerative, dis- and atrophic changes, , disfigurative gastric insufficiency [1, 30].

"Sydney classification system" CG and its Houston variant distinguish the most frequent form (65-80%) of antral non-atrophic CG associated with HP infection (type B). In addition, the existence of a special infectious form of chronic hepatitis is recognized, in the development of which other microorganisms (bacteria, viruses, pathogenic fungi, parasites) are involved [27].

We studied the spectrum of M-microflora in biopsy specimens of the antrum of the stomach in acute and chronic hepatitis using modern microbiological methods and found that the gastric antrum mucosa 80.3% is colonized by a large group of microorganisms (105 bacterial strains), including in the form of microbial associations (55, 7%). Most often, streptococci (52.5%), staphylococci (23%) and fungi of the genus ***Candida*** (19.7%) were detected; HP were detected in 18% of cases. The average concentration of microbial cells was 3.4 lg CFU/g. A significant part of the isolated bacterial strains possessed virulence (56.4±6.7%), including urease activity (27.3±6.0%) [36].

Treatment. As with PU, patients with type B CGB are recommended treatment Table 1 (main); need to streamline lifestyle.

The main method of treatment is HP eradication, which is carried out according to the same principles as with PUD associated with HP infection. In case of erosion, gastroprotectors (denol, sucralfate) are also prescribed. Eradication therapy affects the entire M-microflora of the stomach, not just HP.

CG induced by taking NSAIDs. In accordance with the Houston variant of the "Sydney Classification System" of chronic hepatitis, erosive and ulcerative lesions of the gastroduodenal zone with prolonged intake of NSAIDs should be attributed to the chemical form of chronic hepatitis C (type C). However, most foreign and (after them) domestic authors use the amorphous term ***NSAID- gastropathy,*** which we consider unsuccessful, because it does not reflect the nature of the pathological process in the stomach and duodenum (inflammatory, tumor, etc.) [42].

Etiology and pathogenesis. The main mechanism of the damaging action of NSAIDs (diclofenac, ibuprofen, piroxicam, nimesulide, etc.) on the gastric mucosa and the duodenum is blockade of the cyclooxygenase (COX) enzyme, which exists in two isomers: COX-1 and COX-2. While COX-2 blockade provides therapeutic (anti-inflammatory and analgesic) effects for rheumatic diseases (rheumatoid arthritis, etc.), COX-1 blockade causes depression of prostaglandin synthesis (PG) and prostaglandin deficiency. NSAIDs interrupt the cyclo-oxygenase and lipo-oxygenase metabolic pathways of arachidonic acid, interfering with the synthesis of PG, prostacyclin and thromboxane, which leads to local damage to the gastric mucosa and duodenum, hyperproduction of hydrochloric acid and pepsin, increased retrodiffusion of H+ ions and the formation of erosions and jones. At the same time, the protective mucous-bicarbonate barrier of the stomach weakens due to the inhibition of the formation of bicarbonates and mucus.

In the treatment of NSAIDs-gastritis (gastropathy) and its complications (bleeding), the main pharmaceutical preparations are PPI (omeprazole in a dose of 20 mg, lansoprazole — 30 mg, pantoprazole — 40 mg, rabeprazole — 10 mg or esomeprazole — 20 mg) 2 times/day independently from food intake. The course of treatment — 4–6 weeks, sometimes have to double the dose. The N_2-RH blockers are significantly inferior to the effect of PPI. Instead of an API, ***misoprostol,*** a synthetic analogue of PG, can be administered. He warns ulcerogenic action of NSAIDs by reducing the production of acidic gastric juice and strengthening the mucous- bicarbonate barrier of the same barrel (gastroprotective effect). The dose of misoprostol — 200 mg 4 times a day, the last dose before bedtime (800 mg/day). The disadvantages of misoprostol are frequent (25%) side effects (abdominal pain, diarrhea, nausea and vomiting, flatulence) and short duration of effect, forcing it to take 4 times/day, therefore, treatment with PPI is preferable [12, 13, 42].

In ***MK-1–4,*** it is recommended to conduct a course of HP eradication before starting a course of treatment with NSAIDs, although they recognize that ***"Eradication of HP does not eliminate the risk of ulcer formation in the stomach when taking NSAIDs"*** [26]. We consider HP eradication in NSAID straight unjustified [42]. Studies of foreign authors, carried out in compliance with the principles of evidence-based medicine, demonstrated its inexpediency [55, 56].

The disease (syndrome) of Zollinger-Ellison (gastrinoma) is a gastrin-producing tumor, most often localized (in 85%) in the pancreas, synthesizing gastrin G34. Usually it is a single malignant (in 60–70%) tumor, giving metastases to the liver, bones lymph nodes and having a tendency to invade tumor cells into blood vessels.

The main clinical feature of gastrinoma is continuous (round-the-clock) hypersecretion of acidic gastric juice with high peptic activity, which is complicated by the formation of single (more often) or multiple ulcerations and erosions localized more often in the duodenum than in the stomach (90–95%), including its post-bulbar section. The disease occurs with ulcer-like pain syndrome, diarrhea (65%), repeated vomiting, with abundant acidic contents of the stomach, and heartburn [29, 62].

The treatment is mainly surgical (total gastrectomy). When a tumor is available for operative enucleation, it is surgically removed. In other cases, high doses of PPI administered exceeding standard 4–5 times, and sandostatin (octreotide) — a synthetic analogue of somatostatin (10–20 mg deep intramuscularly in the buttock every 4 weeks for 12 weeks or more). Furthermore, use of antineoplastic drugs: ***5-fluorouracil*** (antimetabolite) — slow intravenous injection of 10–15 mg/kg body weight daily, 8–15 days — up of the phenomenon of side effects (inhibition of hematopoiesis, diarrhea, vomiting, alopecia. etc.) and ***deksorubitsin*** (antineoplastic anti biotic) — intravenously at 30 mg/m^2 of body surface daily for 3 days; repeated courses in 3–4 weeks [11, 29].

Conclusion. The key to successful treatment of any disease is the active involvement of the patient in the therapeutic process. Of course, important is the presence of a patient desire to cooperate with the doctor.

The reasons for the low commitment of patients to the strict implementation of medical recommendations most often are: 1) the depressed state of the patient; 2) cognitive disorders; 3) disbelief of patients in the effect of treatment; 4) underestimation by the patient of the seriousness of the pathological process; 5) the difficulty of fulfilling the prescription of the doctor for taking the medicine (different frequency of use, at different times, etc.); 6) the presence of side effects of drugs; 7) the high cost of drugs (in the presence of financial difficulties) [11, 49, 54, 70].

To optimize compliance (***adherence) various methods are used:*** 1) conducting educational activities with the patient; 2) involvement of family members in monitoring the implementation of medical recommendations by the patient; 3) creation of conveniences for regular visits (visits) of the patient to the doctor; 4) of informing n s disease patient about the nature and possible consequences of non-compliance with medical prescriptions; 5) an explanation to the patient of the purpose and objectives of treatment; 6) timely correction of the patients lifestyle; 7) a warning about the possible side effects of the prescribed pharmaceutical preparations and measures for their prevention and elimination; 8) taking into account the financial capacity of the patient when writing prescriptions for those or other medicines [49].

Monitoring the implementation of the patients doctors recommendations is carried out with the help of : 1) a questionnaire or a patients self-report on the fulfillment of the doctors prescriptions; 2) keeping a diary of patients with a mark about taking medications; 3) periodic evaluation of the effectiveness of the treatment and its timely correction; 4) questioning the patient using a special questionnaire or developed to this end tests, for example Morisky–Green test [49, 54, 70], which consists of four questions. The patient is offered two questions, and he must choose one of them. ***Compliance*** (***adherence)*** is confirmed if he scored more than four points. ***Another method involves counting the number of tablets*** (capsules), taken for a certain period of time, according to the formula:

Compliance (%) = (real number of tablets taken/expected number of tablets taken) × 100.

In the case where the result of <80%, it is considered that the ***compliance*** of the absent. There is also electronic monitoring that determines patients adherence to treatment with the use of electronic devices and containers for drugs. They are able to generate electronic reports on the timely intake of drugs by patients, automatically informing the doctor, but for the time being they are not available to us [49].

Unfortunately, today the commitment of patients to comply with the doctors prescriptions does not exceed 50%.

References:

1. Аруин Л. И., Копуллер Л. Л., Исаков В. А. Морфологическая диагностика болезней желудка и кишечника. Москва, 1998.
   [Aruin L. I., Kopuller L. L., Isakov V. A. Morfologicheskaya diagnostika bolezney zheludka i kishechnika. Moskva, 1998.]
2. Бутов М. А. Об этиологии и патогенезе язвенной болезни. *Экспер. и клин. гастроэнтерол*. 2003. № 5. С. 5–9.
   [Butov M. A. Ob etiologii i patogeneze yazvennoy bolezni. *Eksper. i klin. gastroenterol*. 2003. № 5. S. 5–9.]
3. Василенко В. Х. Введение в клинику внутренних болезней. Москва, 1985.
   [Vasilenko V. H. Vvedeniye v kliniku vnutrennikh bolezney. Moskva, 1985.]

4. Вересаев В. В. Записки врача. *Собр. соч. Т. 1*. Москва, 1948. С. 583–584.
[Veresayev V. V. Zapiski vracha. *Sobr. soch*. T. 1. Moskva, 1948. S. 583–584.]
5. Гастроэзофагеальная рефлюксная болезнь: нужны ли более мощные ингибиторы желудочной секреции? *Клин. фармакол. и тер*. 2006. № 15 (1). С. 13–16.
[Gastroezofagealnaya reflyuksnaya bolezn: nuzhny li boleye moshchnyye ingibitory zheludochnoy sekretsii? *Klin. farmakol. i ter*. 2006. № 15 (1). S. 13–16.]
6. Гриневич В. Б., Успенский Ю. П. Секретолитическая терапия кислотозависимых заболеваний органов пищеварения с позиций клинициста. *Экспер. и клин. гастроэнтерол*. 2003. № 6. С. 15–18.
[Grinevich V. B., Uspenskiy YU. P. Sekretoliticheskaya terapiya kislotozavisimykh zabolevaniy organov pishchevareniya s pozitsiy klinitsista. *Eksper. i klin. gastroenterol*. 2003. № 6. S. 15–18.]
7. Губергриц А. Я., Линевский Ю. В. Лечебное питание. Киев, 1989.
[Gubergrits A. Y., Linevskiy Y. U. V. Lechebnoye pitaniye. Kyiv, 1989.]
8. Ивашкин В. Т., Трухманов А. С. Программное лечение гастроэзофагеальной рефлюксной болезни в повседневной практике врача. *Российск. журн. гастроэнтерол., гепатол. и колопроктол*. 2003. № 6. С. 18–26.
[Ivashkin V. T., Trukhmanov A. S. Programmnoye lecheniye gastroezofagealnoy reflyuksnoy bolezni v povsednevnoy praktike vracha. *Rossiysk. zhurn. gastroenterol., gepatol. i koloproktol*. 2003. № 6. S. 18–26.]
9. Исаков В. А., Домарадский И. В. Хеликобактериоз. Москва, 2003.
[Isakov V. A., Domaradskiy I. V. Khelikobakterioz. Moskva, 2003.]
10. Калинин А. В. Гастроэзофагеальная рефлюксная болезнь. *Российск. журн. гастроэнтерол., гепатол. и колопроктол*. 1996. № 2. С. 6–11.
[Kalinin A. V. Gastroezofagealnaya reflyuksnaya bolezn. *Rossiysk. zhurn. gastroenterol., gepatol. i koloproktol*. 1996. № 2. S. 6–11.]
11. Калинин А. В. Нейроэндокринные опухоли поджелудочной железы и желудочно-кишечного тракта. *Вестник клуба панкреатологов*. 2009. № 1 (2). С. 64–71.
[Kalinin A. V. Neyroendokrinnyye opukholi podzheludochnoy zhelezy i zheludochno-kishechnogo trakta. *Vestnik kluba pankreatologov*. 2009. № 1 (2). S. 64–71.]
12. Каратеев А. Е. Профилактика опасных осложнений со стороны желудочно-кишечного тракта при лечении НПВС в клинической практике: проблемы и их решения. *Клин. фармакол. и тер*. 2007. № 16 (1). С. 81–84.
[Karateyev A. Y. Profilaktika opasnykh oslozhneniy so storony zheludochno-kishechnogo trakta pri lechenii NPVS v klinicheskoy praktike: problemy i ikh resheniya. *Klin. farmakol. i ter*. 2007. № 16 (1). S. 81–84.]
13. Каратеев А. Е., Муравьев Ю. В. Омепразол и мизопростол при НПВС-индуцированных гастропатиях: сравнительная эффективность курса лечения. *Клин. мед*. 2001. № 5. С. 48–50.
[Karateyev A. Y., Muravyev Y. V. Omeprazol i mizoprostol pri NPVS-indutsirovannykh gastropatiyakh: sravnitelnaya effektivnost kursa lecheniya. *Klin. med*. 2001. № 5. S. 48–50.]
14. Маев И. В., Балашова Н. Н. Современные аспекты терапии гастроэзофагеальной рефлюксной болезни. *Экспер. и клин. гастроэнтерол*. 2003. № 1. С. 5–11.
[Mayev I. V., Balashova N. N. Sovremennyye aspekty terapii gastroezofagealnoy reflyuksnoy bolezni. *Eksper. i klin. gastroenterol*. 2003. № 1. S. 5–11.]
15. Маев И. В., Вьючнова Е. В., Грищенко Е. Б. Современные принципы лечения кислотозависимых заболеваний. *Клин. мед*. 2003. С. 56–63.
[Mayev I. V., Vyuchnova Y. V., Grishchenko Y. B. Sovremennyye printsipy lecheniya kislotozavisimykh zabolevaniy. *Klin. med*. 2003. S. 56–63.]
16. Мюллер В. К. Англо-русский словарь (53 тыс. слов). Москва, 1977.
[Myuller V. K. Anglo-russkiy slovar (53 tys. slov). Moskva, 1977.]
17. Подопригорова В. Т., Молчанов В. В., Хибин Л. С. Эффективность антиоксиданта дибунола и его влияние на слизистую оболочку желудка у больных язвенной болезнью. *Российск. журн. гастроэнтерол., гепатол. и колопроктол*. 1997. № 6. С. 45–50.
[Podoprigorova V. T., Molchanov V. V., Khibin L. S. Effektivnost antioksidanta dibunola i yego vliyaniye na slizistuyu obolochku zheludka u bolnykh yazvennoy boleznyu. *Rossiysk. zhurn. gastroenterol., gepatol. i koloproktol*. 1997. № 6. S. 45–50.]
18. Россолимо Г. И. Врач и больной. Москва, 1906.
[Rossolimo G. I. Vrach i bolnoy. Moskva, 1906.]
19. Салтыков А. Б. Теория функциональных систем и клиническая медицина. *Клин. мед*. 2008. № 1. С. 4–9.
[Saltykov A. B. Teoriya funktsionalnykh sistem i klinicheskaya meditsina. *Klin. med*. 2008. № 1. S. 4–9.]
20. Сереброва С. Ю., Журавлева М. В., Липатова И. С. Современные тенденции в лечении

кислотозависимых заболеваний. *Фарматека*. 2014. № 2. С. 7–11.
[Serebrova S. Y., Zhuravleva M. V., Lipatova I. S. Sovremennyye tendentsii v lechenii kislotozavisimykh zabolevaniy. Farmateka. 2014. № 2. S. 7–11.]
21. Симаненков В. И., Тихонов С. В. Поддерживающее лечение у пациентов с гастроэзофагеальной рефлюксной болезнью. *Фарматека*. 2014. № 2. С. 54–60.
[Simanenkov V. I., Tikhonov S. V. Podderzhivayushcheye lecheniye u patsiyentov s gastroezofagealnoy reflyuksnoy boleznyu. *Farmateka*. 2014. № 2. S. 54–60.]
22. Скворцов К. А. Очерки по психотерапии соматического больного. Москва, 1958.
[Skvortsov K. A. Ocherki po psikhoterapii somaticheskogo bolnogo. Moskva, 1958.]
23. Старостин Б. Д. Эффективность комбинированной терапии гастроэзофагеальной рефлюксной болезни париетом и мотилиумом. *Российск. журн. гастроэнтерол., гепатол. и колопроктол*. 2001. № 6. С. 44–47.
[Starostin B. D. Effektivnost kombinirovannoy terapii gastroezofagealnoy reflyuksnoy bolezni pariyetom i motiliumom. *Rossiysk. zhurn. gastroenterol., gepatol. i koloproktol*. 2001. № 6. S. 44–47.]
24. Судаков К. В. Функциональные системы организма в динамике патологических состояний. *Клин. мед*. 1997. № 10. С. 4–11.
[Sudakov K. V. Funktsionalnyye sistemy organizma v dinamike patologicheskikh sostoyaniy. *Klin. med*. 1997. № 10. S. 4–11.]
25. Тютюнов Н. Н. Рабепразол (париет) и эзомепразол (нексиум): сравнительная оценка клинической эффективности. *Российск. журн. гастроэнтерол, гепатол. и колопроктол*. 2002. № 2. С. 45–50.
[Tyutyunov N. N. Rabeprazol (pariyet) i ezomeprazol (neksium): sravnitelnaya otsenka klinicheskoy effektivnosti. *Rossiysk. zhurn. gastroenterol, gepatol. i koloproktol*. 2002. № 2. S. 45–50.]
26. Циммерман Я. С. «Маастрихтский консенсус-4» (2011): основные положения и комментарии к ним. *Клин. мед*. 2012. № 9. С. 28–34.
[Tsimmerman Y. S. «Maastrikhtskiy konsensus-4» (2011): osnovnyye polozheniya i kommentarii k nim. *Klin. med*. 2012. № 9. S. 28–34.]
27. Циммерман Я. С. Классификация хронических гастритов, разработанная в Хьюстоне, и ее соотношение с «Сиднейской системой». *Клин. мед*. 1998. № 5. С. 64–67.
[Tsimmerman Y. S. Klassifikatsiya khronicheskikh gastritov, razrabotannaya v Khyustone, i yeye sootnosheniye s «Sidneyskoy sistemoy». *Klin. med*. 1998. № 5. S. 64–67.]
28. Циммерман Я. С. Мудрые мысли о медицине и врачевании: изречения, афоризмы, цитаты. Москва, 2009.
[Tsimmerman Y. S. Mudryye mysli o meditsine i vrachevanii: izrecheniya, aforizmy, tsitaty. Moskva, 2009.]
29. Циммерман Я. С. Нейроэндокринные опухоли поджелудочной железы и желудочно-кишечного тракта. *Клин. мед*. 2009. № 12. С. 7–13.
[Tsimmerman Y. S. Neyroendokrinnyye opukholi podzheludochnoy zhelezy i zheludochno-kishechnogo trakta. *Klin. med*. 2009. № 12. S. 7–13.]
30. Циммерман Я. С. Проблема хронического гастрита. *Клин. мед*. 2008. № 5. С. 13–21.
[Tsimmerman Y. S. Problema khronicheskogo gastrita. *Klin. med*. 2008. № 5. S. 13–21.]
31. Циммерман Я. С. Проблема этиологии и патогенеза язвенной болезни: перечитывая В. Х. Василенко. *Клин. мед*. 2011. № 1. С. 14–19.
[Tsimmerman Y. S. Problema etiologii i patogeneza yazvennoy bolezni: perechityvaya V. H. Vasilenko. *Klin. med*. 2011. № 1. S. 14–19.]
32. Циммерман Я. С. Этиология, патогенез и лечение язвенной болезни, ассоциированной с Helicobacter pylori-инфекцией: состояние проблемы и перспективы. *Клин. мед*. 2006. № 3. С. 9–19.
[Tsimmerman Y. S. Etiologiya, patogenez i lecheniye yazvennoy bolezni, assotsiirovannoy s Helicobacter pylori-infektsiyey: sostoyaniye problemy i perspektivy. *Klin. med*. 2006. № 3. S. 9–19.]
33. Циммерман Я. С. Язвенная болезнь: актуальные проблемы этиологии, патогенеза, дифференцированного лечения. *Клин. мед*. 2012. № 8. С. 11–18.
[Tsimmerman Y. S. Yazvennaya bolezn: aktualnyye problemy etiologii, patogeneza, differentsirovannogo lecheniya. *Klin. med*. 2012. № 8. S. 11–18.]
34. Циммерман Я. С., Белоусов Ф. В. Психосоматическая медицина и проблема язвенной болезни. *Клин. мед*. 1999. № 8. С. 9–15.
[Tsimmerman Y. S., Belousov F. V. Psikhosomaticheskaya meditsina i problema yazvennoy bolezni. *Klin. med*. 1999. № 8. S. 9–15.]
35. Циммерман Я. С., Вологжанина Л. Г. Гастроэзофагеальная рефлюксная болезнь: современные представления о патогенезе, клинике, диагностике и лечении. *Клин. мед*. — 2005. № 9. С. 16–24.
[Tsimmerman Y. S., Vologzhanina L. G. Gastroezofagealnaya reflyuksnaya bolezn: sovremennyye predstavleniya o patogeneze, klinike, diagnostike i lechenii. *Klin. med*. — 2005. № 9. S. 16–24.]

36. Циммерман Я. С., Захарова Ю. Л, Ведерников В. Е. Сравнительная оценка диагностических тестов определения Helicobacter pylori и спектр мукозной микрофлоры желудка при гастрите и язвенной болезни. *Клин. мед*. 2013. № 4. С. 42–48.
[Tsimmerman Y. S., Zakharova Y. L, Vedernikov V. Y. Sravnitelnaya otsenka diagnosticheskikh testov opredeleniya Helicobacter pylori i spektr mukoznoy mikroflory zheludka pri gastrite i yazvennoy bolezni. *Klin. med*. 2013. № 4. S. 42–48.]
37. Циммерман Я. С., Михайловская Л. В. Нарушения регионарного кровотока и активность процессов перекисного окисления липидов при рецидиве язвенной болезни и возможности их медикаментозной коррекции. *Клин. мед*. 1996. № 4. С. 31–34.
[Tsimmerman Y. S., Mikhaylovskaya L. B. Narusheniya regionarnogo krovotoka i aktivnost protsessov perekisnogo okisleniya lipidov pri retsidive yazvennoy bolezni i vozmozhnosti ikh medikamentoznoy korrektsii. *Klin. med*. 1996. № 4. S. 31–34.]
38. Циммерман Я. С., Михалева Е. Н. Состояние иммунной системы у больных язвенной болезнью двенадцатиперстной кишки и влияние на нее современной терапии и иммуномодулирующих средств. *Клин. мед*. 2003. № 1. С. 41–44.
[Tsimmerman Y. S., Mikhaleva Y. N. Sostoyaniye immunnoy sistemy u bolnykh yazvennoy boleznyu dvenadtsatiperstnoy kishki i vliyaniye na neye sovremennoy terapii i immunomoduliruyushchikh sredstv. Klin. med. 2003. № 1. S. 41–44.]
39. Циммерман Я. С., Михалева Е. Н. Язвенная болезнь и иммунная система организма. *Клин. мед*. 2000. № 7. С. 15–21.
[Tsimmerman Y. S., Mikhaleva Y. N. Yazvennaya bolezn i immunnaya sistema organizma. *Klin. med*. 2000. № 7. S. 15–21.]
40. Циммерман Я. С., Оносова Е. А., Циммерман И. Я. Изучение генетических маркеров язвенной болезни двенадцатиперстной кишки. *Клин. мед*. 1989. № 5. С. 73–77.
[Tsimmerman Y. S., Onosova Y. A., Tsimmerman I. Y. Izucheniye geneticheskikh markerov yazvennoy bolezni dvenadtsatiperstnoy kishki. *Klin. med*. 1989. № 5. S. 73–77.]
41. Циммерман Я. С., Субботина Л. В., Неснисляев В. А. Микробный антагонизм и обоснование включения пробиотиков в комплексное лечение Helicobacter pylori-зависимых заболеваний. *Клин. мед*. 2010. № 4. С. 35–42.
[Tsimmerman Y. S., Subbotina L. V., Nesnislyayev V. A. Mikrobnyy antagonizm i obosnovaniye vklyucheniya probiotikov v kompleksnoye lecheniye Helicobacter pylori-zavisimykh zabolevaniy. *Klin. med*. 2010. № 4. S. 35–42.]
42. Циммерман Я. С., Циммерман И. Я. Гастродуоденальные эрозивно-язвенные повреждения, индуцированные приемом нестероидных противовоспалительных препаратов. *Клин. мед*. 2008. С. 14–19.
[Tsimmerman Y. S., Tsimmerman I. Y. Gastroduodenalnyye erozivno-yazvennyye povrezhdeniya, indutsirovannyye priyemom nesteroidnykh protivovospalitelnykh preparatov. *Klin. med*. 2008. S. 14–19.]
43. Циммерман Я. С., Щеткин Д. И. Пирацетам в комплексной патогенетической терапии рецидива язвенной болезни двенадцатиперстной кишки. *Клин. мед*. 2002. № 1. С. 48–53.
[Tsimmerman Y. S., Shchetkin D. I. Piratsetam v kompleksnoy patogeneticheskoy terapii retsidiva yazvennoy bolezni dvenadtsatiperstnoy kishki. *Klin. med*. 2002. № 1. S. 48–53.]
44. Шептулин А. А. Прокинетический препарат мотилиум: фармакологические свойства и возможности клинического применения. *Клин. мед*. 1997. № 11. С. 48–50.
[Sheptulin A. A. Prokineticheskiy preparat motilium: farmakologicheskiye svoystva i vozmozhnosti klinicheskogo primeneniya. *Klin. med*. 1997. № 11. S. 48–50.]
45. Шептулин А. А. Гастроэзофагеальная рефлюксная болезнь. *Россійск. журн. гастроэнтерол., гепатол. и колопроктол*. 1998. № 6 (1). С. 16–21.
[Sheptulin A. A. Gastroezofagealnaya reflyuksnaya bolezn. *Rossiysk. zhurn. gastroenterol., gepatol. i koloproktol*. 1998. № 6 (1). S. 16–21.]
46. Шептулин А. А. Нарушения двигательной функции желудка и возможности применения нового прокинетика итоприда в их лечении. *Consilium medicum. Гастроэнтерология*. 2006. № 1. С. 13–17.
[Sheptulin A. A. Narusheniya dvigatelnoy funktsii zheludka i vozmozhnosti primeneniya novogo prokinetika itoprida v ikh lechenii. *Consilium medicum. Gastroenterologiya*. 2006. № 1. S. 13–17.]
47. Шкляр Б. С. Врач и больной. *Клин. мед*. 1952. № 2. С. 141–145.
[Shklyar B. S. Vrach i bolnoy. *Klin. med*. 1952. № 2. S. 141–145.]
48. Adami H.-O., Bergstrom R., Nyren O. Is duodenal ulcer really a psychosomatic disease? *Scand. J. Gastroenterol*. 1987. Vol. 22, No 7. P. 889–896.
49. Blaschke T. Compliance on pharmacotherapy. *New Engl. J. Med*. 005. Vol. 353. P. 487–497.
50. Bytzer P, Taglbjaerd P. S. Helicobacter pylori-negative duodenal ulcer: prevalence, clinical characteristics and prognosis: results from a randomized trial with 2-year fallow-up. *Amer. J. Gastroenterol*. Vol. 96. —

P. 1409–1415.
51. Classen J. R. Gastroesophageal reflux disease: rational approach to management. *Clin. Rev*. 1999. Vol. 9, No 6. — P. 69–72.
52. Dent J., Fendrick A. On behalf of the Genval Workshop Group. An evidence-based appraisal of reflux disease management — the Genval Workshop Report. *Gut*. 1999. Vol. 44, Suppl. 2. P. S1–S16.
53. Diaz-Rubio M. Historical perspective of gastric acid inhibition. *Drugs*. 2005. Vol. 65, Suppl. 1. — P. 1–6.
54. Hill M. N., Miller N. H. Compliance enhancement. A call for Mullidisciplinary team approaches de treatment. *Dialogue*. 1999. Vol. 5. P. 13–15.
55. Lai K., Lau C., Up W. Effect of treatment of Helicobacter pylori on the prevention of gastroduodenal ulcers in patients receiving long term NSAIDs: a double-blind, placebo-controlled trial. *Aliment. Pharmacol. Ther*. 2003. Vol. 42. P. 947–950.
56. Leest de H., Steen K., Lems W. Eradication of Helicobacter pylori has no beneficial effect for prevention of peptic ulcer in patients with long-term NSAID treatment: a randomized, double-blind, placebo-controlled trial. *Gastroenterology*. 2004. Vol. 126. P. 611–616.
57. Leine L., Hopkins R., Gerardi L. Has the impact of Helicobacter pylori therapy on ulcer recurrence in the United State been overstated? A meta-analysis of rigorously disignet trials. *Am. J. Gastroenterol*. 1998. Vol. 93, No 9. P. 1409–1415.
58. Li X., Andersson T., Alstrom M. Comparison of the inhibitory effects of the proton pump inhibiting drugs omeprazole, esomeprazole, lansoprazole, pantoprazole and rabeprazole on human cytochrome p450 activities. *Drug Metab. Dispos*. 2004. Vol. 32. P. 821–827.
59. Meucci G., di Battista R., Abbiati C. Prevalence and risk factor of Helicobacter-negative peptic ulcer: a multicenter study. *J. Clin. Gastroenterol*. 2000. Vol. 31. P. 42–47.
60. Mossner L., Caca K. Developments and the inhibition of gastric acid secretion. *Eur. J. Clin. Invest*. 2005. Vol. 35. P. 469–475.
61. Nguyen L., Birk J. Current and prospective pharmacotherapies in gastroesophageal reflux disease. *Clin. Med. Ther*. 2009. Vol. 1. P. 987–997.
62. Ray O. K., Wenson D. M., Shoyamensh H. Zollinger-Ellison syndrome: clinical presentation in 126 patients. *Medicine (Baltimore)*. 2000. Vol. 79, No 6. P. 379–411.
63. Sachs G. Phisiology of the parietal cell and therapeutic implications. *Pharmacotherapy*. 2003. Vol. 23. P. 68–73.
64. Siman J. H., Forsagen A., Berglund G., Floren C. H. Helicobacter pylori infection is associated with a discreased risk of developing esophageal neoplasms. *Helicobacter*. 2001. Vol. 6. P. 310–316.
65. Stark H. Histamine Receptors. *Biotrend. Rev*. 2007. Vol. 1. P. 1–8.
66. Suadocani P, Hein H. O., Gyntelber F. Genetic and lifestyle determinants of peptic ulcer: a study of 3387 men aged 54 to 74 years. *Scand. J. Gastroenterol*. 1999. Vol. 34. P. 12–17.
67. Vaezi M. F., Falk G. W., Peek R. M. CagA-positive strains of Heli cobacter pylori against Barretts esophagus. *Amer. J. Gastroenterol*. Vol. 95. P. 2206–2214.
68. Wang Y. K., Hsu W. H., Wang A. A. Current pharmacological management of gastroesophageal reflux disease. *Gastroenterol. Res. Pract*. 2013.
69. Weston A. P., Badr A. S., Topolovski M. Prospective evaluation of the prevalence of gastric Helicobacter pylori of the patients with GERD, Barretts dysplasia and Barretts adenocarcinoma. *Amer. J. Gastroenterol*. 2000. Vol. 95. P. 387–394.
70. Zaghloul S. S., Jeremy M., Goodfield D. Objective assessment of compliance with psoriasis treatment. *Arch. Dermatol*. 2004. Vol. 140. P. 408–414.

Adherence of patients to medical recommendations (compliance) as an important factor in increasing the effectiveness of treatment (by example of acid-dependent diseases)

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List of medical terms has been recently supplemented with relatively new notions of *compliance (adherence)*, which means "consent, compliance with your wishes" in English. They are used to denote the patients strict adherence to medical recommendations, especially with regard to pharmacotherapy (use of the drug at the recommended dose with the necessary frequency and duration), correction of lifestyle, rationalization of dietary habits, getting rid of bad habits. High compliance is very important in the treatment of acid-related diseases: organizing a lifestyle, following advice on dietary restrictions and habits, avoiding stressful situations and physical exertion significantly affect the effectiveness of therapeutic measures in gastroesophageal reflux disease, gastric ulcer and duodenal ulcer, non-atrophic gastritis, Zollinger-Ellison syndrome, chronic gastritis induced by nonsteroidal anti-inflammatory drugs. Optimization of *compliance (adherence)*, control over the implementation of prescriptions, elimination of factors that impede the realization of medical recommendations will improve the effectiveness of treatment of acid-related diseases. The key to successful treatment of any pathology is an active involvement of a patient in the treatment process.