The problem of growing resistance of microorganisms to antibiotic therapy and prospects for Helicobacter pylori eradication

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Science knows tens of thousands of bacteria; moreover, there are considerable numbers of unknown ones. A huge number of species of bacteria coexists with a macroorganism according to the principle of mutualism (mutual benefit), or commensalism (compromise: commensal — table companion). Of course, there are several hundred human-pathogenic bacteria found [32].

First antibiotics were used to fight bacterial infection in the mid 20th century. Their creation (obviously) was a boon for mankind, letting preserve the health and lives of many millions of people.

However, antibiotics and other antimicrobials (AM) eliminate endosymbiotic microflora simultaneously with the destruction (eradication) of pathogenic bacteria, necessary for normal functioning of the human body. Normobiocoenosis, created in the process of evolution and natural selection, holding certain niches (habitats) in the macroorganism, was under the threat of destruction [45].

The risk of loss of endosymbiotic bacteria under the influence of ubiquitous, often uncontrolled and unjustified use of AM with a wide spectrum of antibacterial activity consists in the gradual disappearance of biologically appropriate macroorganism symbioses with bacteria. This inevitably leads to a reduction in the synthesis of natural immunostimulants and therefore determines inferiority of the immune system and, ultimately, the development of immunodeficiency states.

The existence of an evolutionary-ecological antagonism between bacteria and viruses should be also taken into account, by which a "buffer unit" forms between humans and viruses consisting of endosymbiotic bacteria, which prevents direct contact of the microorganism with the virus. Bacteria have the ability to inhibit the

activity of viruses due to the formation of nucleolytic enzymes (DNase and RNase), dissolving the viral nucleic acid. Upon the destruction of endosymbiotic bacteria by AM this "buffer link" disappears, resulting in the possibility of direct contact of the human and virus, the spread of viral infections [45].

Yearly growing resistance of the pathogenic bacteria to AM used for the eradication of has become one of the most urgent problems of modern antibiotic therapy. This led to a gradual loss of effective AM and the global spread of antibiotic resistance [35].

A steady increase in the number of bacterial diseases, which have recently been successfully treated, became the consequence of the spread of pathogenic bacteria resistant to AM. For example, mortality in sepsis (to 70%), tuberculosis and pneumonia sharply increased, as their pathogens have acquired resistance to AM for their eradication [45].

The uncontrolled and unjustified use of antibiotics, which, according to the WHO, reached 50% in hospitals and 70% in clinics, has broken the delicate balance between man and endosymbiotic bacteria colonizing the organism, where viruses, mycoplasma, chlamydia, L-form bacteria began to occur [45, 46]. In fact, there was a radical change in the traditional human microflora, while usual microcosm transformed into an alien and hostile world of bacteria-mutants and viruses [46]. It is no coincidence that publication have increasingly began to appear in recent years entitled: "The antibiotics as a threat" [11].

The reasons for the growth of antibiotic resistance

The main causes of the spread of resistance of pathogenic bacteria to AM:

- incorrect selection and application of AM (e.g., to intake the antibiotic with a broad spectrum of action in cases when the AM with a narrow spectrum of activity should be prescribed);
- empirical antibiotic therapy with the use of inadequate doses and/or unjustified reduction or extension of the course of treatment with antibiotics;
- virtual absence of recent developments of fundamentally new groups (classes) of AM [38];

- spread of multidrug-resistant pathogenic bacteria due to the generation of β-lactamases [26].

A number of additional reasons are also marked:

- use of prophylactic AM, which leads to selection of resistant strains microorganisms [1];
- independent purchase of AM and self-treatment in various illnesses without consulting the doctor (in 33.2% of cases);
- lack of expertise of many doctors about the rational use of AM;
- AM application in viral infections (influenza, acute respiratory viral infections and others) at which they are ineffective;
- ease of occurrence of gene mutations in bacteria: the adaptability of unicellular microorganisms is actually infinite [17, 45];
- the prevalence among people of the congenital and especially acquired (secondary) immunodeficiencies, contributing to the development of antibiotic resistance in bacteria [6];
- non-compliance with the treatment protocol of patients [2]: the easier is the treatment protocol, the more is the adherence of patient to its compliance [23];
- AM use in agriculture (e.g., cattle nurture: 50% of cases) [28].

Most researchers acknowledge that antibiotic resistance has reached a critical level and tends to further dissemination, including the new AM — it has become a global problem [28]. Especially dangerous is the multiresistance of bacteria to AM [2].

Not so much clinical data, but the minimum inhibitory concentration and AM dosing regimen (dose and duration of treatment) are the main criteria for the growth of bacterial resistance to AM [4, 12]. Eradication of microorganisms becomes effective only when the dose exceeds AM minimum inhibitory concentrations 2-3 times. Under these conditions, the probability of killing (destruction) of the bacteria is very high [4].

Another important factor is the efficiency of AM — the presence of postantibiotic (persistent) action. This figure is determined by the time during which there is no bacterial growth after the abolition of AM [4]**.**

The leading mechanisms of bacterial resistance to AM:

- reduction or loss of the ability of bacteria to bind with specific AM, while maintaining their functional activity;
- AM inactivation;
- active removal of AM from microbial cells (eflux);
- violation of the permeability of the outer structure of microbial cells [31].

Brief description of some of the groups (classes) of antimicrobials

Macrolide antibiotics (clarithromycin, azithromycin, roxithromycin, etc.) have been used since 1952 (erythromycin). Characterized by a high bioavailability (30-65%), long partial ejection, ability to easily penetrate into the tissues (especially azithromycin). Have a direct anti-inflammatory effect, mainly bacteriostatic effect on gram-positive cocci (streptococci, staphylococci) and intracellular bacteria (Legionella, mycoplasma, chlamydia). Clarithromycin is characterized by a high activity against infection *Helicobacter pylori (HP),* acid resistance, high concentration in tissues, long partial ejection ($T_{1/2,}$ about 3-7 hours) and good tolerability. Dose: 500 mg 2 times a day; course of 7-10 days [18, 23, 33, 36]. Azithromycin has a high bioavailability (40%), high content in tissues, long partial ejection ($T_{1/2}$ to 55 hours), allowing to prescribe it to 1 time a day and to use a short-course treatment (1-5 days); provides long postantibiotic effect (5-7 days after discontinuation); well tolerated; active against HP. Dose: 500 mg 1 time a day for 3 days [23, 33, 36, 67, 71].

Fluoroquinolones (levofloxacin, ciprofloxacin, norfloxacin, etc.) are active in streptococcus *(Streptococcus pyogenes, S. viridans)* and staphylococcal *(Staphylococcus aureus*, etc.) infection, Énterobacteriaceae infection *(Escherichia coli*, etc.). Act on negative microflora *(Clostridium perfringens, Peptostreptococcus* and others). Have a bactericidal effect, causing a concentration-dependent destruction of bacteria, give a moderate postantibiotic effect; well tolerated; permanently

circulate in the blood, exceeding the minimum inhibitory concentration for 1 day; easily penetrate tissue. Bioavailability is 100%, $T_{1/2}$ is 6-8 hours. Levofloxacin is active against HP, has a good safety profile [23, 36, 50, 67, 84].

Nitroimidazole derivatives (metronidazole, tinidazole, etc.) are characterized by a high activity against anaerobes and HP (in combination with *clarithromycin), Clostridium difficile, Peptostreptococcus, Bacteroides* and protozoal invasion (Giardia, amoeba, etc.). Bioavailability is 80%, $T_{1/2}$ is 6-8 hours. Dose: 500 mg 2-3 times a day; 7-14 days of treatment [36, 54, 64].

Nitrofuran derivatives (furazolidone, nifuroxazide or nifuratel, etc.) have a wide spectrum of antibacterial and anti-parasitic activity, including strains of bacteria that are resistant to antibiotics; microflora resistance is rarely developed towards them, including HP. However, nitrofuran derivatives have rather high incidence of side effects. Furazolidone acts primarily on gram-negative bacteria, as well as Giardia, etc. Nifuroxazide (ersefuril, nifuratel) is effective against a number of gram-positive bacteria, is not absorbed in the gastrointestinal tract. Effective in the HP-infection (as furazolidone). Doses: furazolidone 100 mg 3-4 times a day, nifuroxazide 200 mg 3-4 times a day; 7-10 days of treatment [19, 24, 37, 72].

Carbapenems (imipenem, meropenem, ertapenem). They are often referred to as the drugs of choice or reserve. This is a group of ß-lactam AM with a broad spectrum of antibacterial activity (gram-negative and gram-positive bacteria, anaerobes et al., in particular *E. coli, Klebsiella, Proteus mirabilis, Pseudomonas aeruginosa*, etc., capable to product ß-lactamases (ESBL: Entended Spectrum Beta-Lactamase)). There are 4 groups of ß-lactamase; their genes are the part of integrons localized at chromosomes or plasmids. The main mechanism of resistance of these bacteria to ß-lactam antibiotics is the production of ß-lactamases, but they don’t show a resistance to the carbapenems.

At present, the following carbapenems are used: meropenem or cilastatin, and iminenem and new drug of this group — ertapenem; they provide predictable suppression of vital activity of various bacteria. Efficiency of meropenem and imipenem is comparable. The new drug ertapenem has a higher activity in

polymicrobial infections of the abdomen and a longer partial ejection. In difficult cases, we recommend a combination of carbapenems with aminoglycosyls (tobramycin). Doses: imipenem is prescribed intravenously at 500-1000 mg 3 times a day at 100 ml of 5% glucose or 500-750 mg intramuscularly, 2 times a day, meropenem is prescribed intravenously during 30 minutes at 500-1000 mg 3 times a day, ertapenem is prescribed at 1000 mg 1 time per day in the form of infusion [3, 74, 76, 80].

Due to the growing spread of resistance to antibiotic therapy, carbapenems are considered the "last line (bastion) of defense." Antibiotics capable of replacing carbapenems haven't been known yet [3, 4, 38, 74, 76, 80].

In the treatment of infections caused by a *Enterococcus faecalis* and *E. faecium*, vancomycin or teicoplanin are recommended, and in the presence of resistance to them — linezolid (from the group of oxazolidinone) in a dose of 400-600 mg 2 times a day *per os* or intravenously [30].

Upon methicillin-resistant strains of staphylococci, daptomycin (cyclic monopeptide antibiotic acting only on gram-positive bacteria) or ceftobiprole (cephalosporin antibiotic) are used. They reach the effect in the treatment of infections caused by multiresistant gram-positive bacteria; their disadvantage — the high cost [32].

Ways to enhance the effect of antibiotic therapy

Different ways to improve AM efficiency and safety are offered. The main ones are:

- "life extension" of existing antibiotics that can suppress the vital activity of bacteria, but do not harm the eukaryotic macroorganism cells [38]. It is important to provide strict policies of AM compliance, prescribing them only upon scientifically grounded substantiations;
- optimization of AM dosing regimen (the dose, dosing frequency, duration of treatment);
- use of reasonable combinations of AM with different spectrum of antibacterial activity;

- preliminary determination of the sensitivity of isolated strains of microorganisms for specific AM (in fact, resistance of bacteria to AM is not determined in Russia [35]);
- awareness of the predictors ineffective eradication;
- combined use of AM and immunomodulating agents (immunofan, gepon, galavit, taktivin, levamisole, etc.) [1, 9, 10, 20, 42]. The disease is developing only when protection (adaptation) reactions of macroorganism are suppressed (depleted) [29].
- inclusion of pre- and probiotics (synbiotics) in AM complex [25, 40, 47, 57].
- creation of fundamentally new AM;
- creation of the vaccines that provide active immunity against a disease caused by a specific infectious agent (including those against HP infection) [1, 4, 5, 22, 26, 30, 31].

The above-mentioned offers have received the name "Antibacterial stewardship" [4].

Recommendation of AM planned rotation and/or their combined use proceeds from the fact that the replacement should improve the selective pressure on the microorganisms [5, 57]. Of course, the AM quality matters (for example, poor quality of some generic drugs, their substandards, falsification of medicines, etc.). [26].

Side (undesirable) effects (reactions) of antibiotic therapy

AM is the cause of 30% of all adverse drug reactions [27].

In analyzing the undesirable (adverse) effects of AM, retrospective (case-control) and prospective (cohort) studies using statistical methods of combining the results (meta-analysis) are the most informative [59, 68].

The most frequent side effects of AM:

- dysfunction of the gastrointestinal tract: diarrhea, abdominal discomfort and abdominal pain; dyspeptic symptoms (nausea, rarer — vomiting, perversion of taste sensations — a metallic taste in the mouth, etc.); intestinal dysbiosis et al. (17.5-73.5%);

- skin reactions: allergic reactions (urticaria, angioedema), rash, etc. (12-41%);
- hematologic violations: myelotoxicity, eosinophilia, thrombocytopenia, leukopenia, neutropenia (15.4-42.9%);
- hepatotoxicity: increased transaminases, intrahepatic cholestasis, and others. (9-24%);
- common symptoms: general weakness, fatigue, headache, dizziness, etc. (16.7- 34.2%);
- other effects: anaphylactoid reactions, nephrotoxicity; chondro- and arthropathy; photosensitivity reaction (erythema, burning sensation, etc.) [21, 22, 27, 33].

***Helicobacter pylori* infection*:* the validity of methods of its eradication and their evolution**

In 1983, Australian researchers J. Warren and B. Marshall discovered in the antrum of the stomach in patients with chronic gastritis (CG), a previously unknown bacterium called first *Campylobacterpyloridis,* and then renamed *Helicobacter pylori* [85, 86].

HP — is a gram-negative spiral acid-resistant non-invasive bacterium, having 4-5 flagella by which it is able to move in the surface layer of mucus searching for the optimal conditions for its activity (pH, osmolarity, etc.).

According to the molecular-biological research, HP "age" does not exceed 10-11 thousand years [51].

A retrospective study of publications of the microbiologists in different countries revealed that the first mention of the presence of bacteria in the stomach spiral referred to 1906.

As it was stated, HP can colonize only the human stomach: a layer of surface mucus, a single-layer surface epithelium (between the fibers) and extracellular space (due to the destruction of the contacts between the cells). They are not usually detected in the subepithelial space and in the epithelium of the gastric glands,.

Forming enzyme urease, HP cleave urea, which is contained in food, surrounding itself (like clouds) by ammonia (alkali), and thus protecting from the bactericidal action of acid gastric juice. Enzyme protease (mucinases) synthesized by HP destroys the gastric mucus glycoproteins, helping them to penetrate in the epithelium of the stomach. Thus, HP vital activity is limited by the gastric compartment. HP can exist neither on a stratified squamous epithelium of the esophagus, nor on the cylindrical epithelium of the intestine.

Epidemiological studies have found that HP-infection is common in the world: 60% of the population in all continents and in all ethnic groups is infected with HP.

The spectrum of pathological changes in the stomach caused by HP-infection is represented by the destruction of parietal mucus, degeneration and necrosis of epithelial cells, disruption of intercellular contacts and the development of the inflammatory process. A favorite place of HP colonization of the gastric mucosa is antrum, but under certain conditions (atrophic process in the fundal part), HP can spread in the antrocardial direction, thus settling the fundal part.

HP etiologic role has been established in the development of non-atrophic antral CG (type B), in the pathogenesis of HP-associated peptic ulcer (PU) and distal gastric cancer (GC), and gastric low-malignant MALToma (MALT-lymphoma). Frequency of HP-associated CG is 60-75%, PU — 12-15%, GC — 1%, gastric MALToma — 0.5% [13]. However, it is proved that HP-negative forms of PU often occur (20-30% of duodenal and 40-50% of gastric ones) [16, 58, 78]. Proximal (cardial) gastric cancer is not associated with HP-infection [85]. Thus, HP participation in the development of GC and PU is not necessary — they are the multifactorial diseases, in the pathogenesis of which other environmental factors and family history of GC and PU play an important role. Regarding the role of infectious agent (HP) in the development of CG, PU and GC, it can’t be ignored that the gastric mucosa in these diseases is colonized, in addition to HP, by another mucosal microflora (streptococci, staphylococci, micrococci, fungi of the genus *Candida*, etc.) possessing adhesiveness, invasiveness and virulence (unlike HP). Therefore, it is correct to speak about gastric dysbacteriosis instead of helicobacteriosis [14, 15, 47].

Under our proposed concept of the relationship HP-infection and macroorganism, HP was originally commensal and comfortably had been coexisting with human ("host") for thousands of years without doing any harm. Only with the beginning of the era of antibiotics (middle of the 20th century), and (especially) after the discovery of HP (1983) and the proclamation of the strategy for its total destruction (test and treat strategy), part of HP acquired resistance to antibiotics as a result of numerous mutations under the influence of AM, and another part — pathogenecity-associated island (PAI), containing genes of cytotoxicity (cagA, VacA, IceA et al.), and began to threaten human health [41, 44].

However, it was not possible to prove the connection between cytotoxic HP strains and specific gastroduodenal diseases: ulcerogenic, cancer-causing strains of HP do not exist [61].

According to a well-known researcher of this problem M. Blaser [53, 54, 55, 56], HP are the part of human microbiocenosis and depending on the specific conditions (circumstances) may act as both commensal, and pathogen.

It had been considered until now that, due to the bactericidal action of gastric juice, microflora penetrated into the stomach was killed within 30 minutes, but modern methods of microbiological studies have shown that it is wrong. The frequency of detection of various mucosal microflora in the stomach in healthy people is 10^3-10^4/ml (3 CFU/g), including HP detected in 44.4% (5.3 CFU/g), 55.5 % — streptococci (4 CFU/g), 61.1% — staphylococci (3.7 CFU/g), 50% — lactobacilli (3.2 CFU/g), 22.2% — fungi of the genus Candida (3.5 CFU/g). Moreover, bacteroides, corynebacteria, micrococci and other bacteria in the amount of 2.7-3.7 CFU/g have been inoculated. It should be noted that HP was defined only in association with other bacteria. The medium in the stomach was sterile in healthy people is only 10% of cases [7, 63].

Gastric flora conventionally divided by its origin into salivary-nasal (type 1) and fecal (type 2) [7, 63]. In 2005, there was a discovery of strains of lactic acid bacteria in the stomach of healthy people that have adapted (like HP) to exist in

strongly acidic environment of the stomach: *Lactobacillus gastricus, L. antri, kalixensis L., L. ultunensis* [82].

In various diseases (CG, PU, GC), the number and variety of bacteria colonizing the stomach increase significantly. In CG the largest number of mucosal microflora is found in the antrum, in PU — in periulcerous zone (in the inflammatory roller). Streptococci, staphylococci, enterobacteria, micrococci, lactobacilli, fungi of the genus Candida often predominate, but not HP [14, 15].

In 1987, the European Helicobacter Study Group (EHSG) was created in Europe, which, has regularly (since 1996) published updated recommendations for the diagnostics and treatment of HP-associated diseases, called the recommendations of the Maastricht Consensus (MC). To date, it has published 4 MC (the last, MK-4 in 2011). In fact, this group of scientists has monopolized the right to define the strategy and tactics of anti-HP-therapy.

We consider it necessary to note that the consensus meetings of the MC-type don’t correspond to the basic principles of evidence-based medicine, as they don’t presuppose the necessity of clinical thinking and analysis of the scientific and clinical information; the doctor becomes a simple technical executor of recommendations of the consensus meeting [34].

In addition, the recommendations of the MC have made some serious mistakes that contributed to the rapid spread of drug-resistant HP strains and selection of its cytotoxic strains that are dangerous to human health.

- Compilers of the MC recommend a strategy of total HP eradication "test and treat". This erroneous strategy is manifested in the fact that the eradication of HP is preferably carried out not only in HP-associated forms of CG, PU, MALToma and after surgery for gastric cancer, where the value of HP infection to some extent is confirmed by definitive studies, but also in gastroesophageal reflux disease, syndrome of functional (gastroduodenal) dyspepsia and so-called NSAIDs gastropathy. And this happens despite the numerous evidence-based studies that have established the independence of their development and the clinical course on HP-infection [60, 66, 69].

- MC offers to carry out HP eradication in the healthy bacillicarriers with reservation "on the request of the patient", placing solution of question about HP eradication on people not having medical education, that is unacceptable [49]. It is evident that eradication of HP in the healthy people is not justified and unreal, as it is impossible to carry out eradication therapy in 3.5-4 billion of healthy people infected with HP. Moreover, the mass eradication of HP in the healthy people will inevitably cause catastrophic and irreversible spread of HP strains, resistant to AM.
- EHSG has intentionally set deliberately understated line (lower limit) of effective HP eradication (80%). It is obvious that exactly "survived" HP (up to 20%) after the course of eradication therapy are resistant to treatment. They begin rapidly spread instead of bacteria more sensitive to AM on the territory freed from less "fortunate competitors" and give offspring consisting of HP strains resistant to AM.
- Throughout the years of the MC existence (since 1996), its drafters have recommended actually the same AM for eradication therapy (clarithromycin, amoxicillin, metronidazole, tetracycline or doxycycline), ignoring the well-known regularity: the more often we use one or another AM, the faster microbial resistance is developing to it [11, 79]. Approval of certain authors that there is no HP resistance to amoxicillin was disproved by evidence-based studies of the foreign researchers [26, 52].
- In various countries HP resistance to metronidazole has reached 53-77%, clarithromycin — 24-43.8%, amoxycillin — 26%, doxycycline — 33.3% and annually continues to increase [48, 77]. In connection with this fact, the more acute is a call to have more responsible attitude towards the expansion of indications for HP eradication. The world community must realize danger of passive attitude to the rise and the spread of bacteria resistant to AM, as this will inevitably lead to the loss of human in fight with pathogenic bacteria on population level [31]. Thus, in the MC recommendations amount the number of AM included in schemes of HP

eradication, has gradually increased from 2 to 3, the dose of proton pump inhibitors (PPIs), clarithromycin and ampitsilllina — in 2 times, the frequency of reception of various drugs in treatment schemes was varied from 2 to 4 times in day, and the duration of a course of eradication increased from 7 to 10 and 14 days [73].

The dangerous trend towards the escalation of the number and doses of AM, the multiplicity of intake and duration of eradication therapy not only significantly increases the cost of treatment, that becomes unavailable for the majority of low-income people, but also greatly complicates the observance of the treatment protocol, increases the incidence of side (undesirable effects of anti-HP-therapy (2 times or more) and exacerbates their severity, contributing to the further growth of HP resistance to AM and selection of cytotoxic HP strains.

Triple HP eradication therapy (standard dose of PPIs + 500 mg of clarithromycin + 1000 mg of amoxicillin or 500 mg of metronidazole 2 times daily for 7 days) is called first-line therapy.

Quadruple HP eradication scheme (standard dose of PPIs + 120 mg of bismuth tripotassium dicitrate or de-nol 4 times daily + 500 mg of tetracycline 4 times daily or 200 mg of doxycycline 2 times a day + 100 mg of furazolidone 4 times daily for 7 days) was named second-line therapy. At the same time, various schemes of HP eradication proposed by the MC could not solve the problem of HP resistance to AM. The effectiveness of treatment had dropped to a critical level by 2002: for the triple eradication schemes — to 43-50%, and 68-69% for quadruple [64].

In this regard, searching and testing of alternative schemes of HP eradication began all over the world with the help of backup AM not previously used for this purpose: macrolides (azithromycin, roxithromycin), fluoroquinolones (levofloxacin, sparfloxacin), nitrofuran derivatives (nifuroxazide or ersefuril), nitrotiazolamides (nitazoksamid), rifabutin, etc. This alternative anti-HP therapy became known as ‘rescue therapy’, although it would be better to call it a ‘despair therapy’.

In addition, the effect of auxiliary medical means was experienced: probiotics and prebiotics (synbiotics) that can prevent the development of colonic dysbiosis and

its symptomatic forms (antibiotic-associated diarrhea and pseudomembranous colitis) and to increase the effect of eradication (10-12%) due to the phenomenon of microbial antagonism [25, 40], as well as gastroprotectives (capsaicin, silver nitrate, sucralfate or sucrat — gel per os, etc.). [39, 41]. However, all these innovations have not been able to radically solve the problem of growing HP resistance to AM included in the schemes of eradication.

The MK-4 (2011) recommends only probiotics and levofloxacin from all the tested backup AM and auxiliary therapeutic agents, but as the drafters admit, HP resistance to it also increases quickly, which could have been foreseen, as immediately after the start of using a new AM in the schemes of eradication, the next "round" of selection of resistant HP strains begins. We can’t ignore the fact that reinfection of gastric mucosa occurs in the next few years after the successful HP eradication, which, according to the cumulative Kaplan-Meier index, is 32±11% in 3 years, 82-87% in 5 years, and 90.9% in 7 years [8, 70, 75].

Thus, the prospects for overcoming the growing HP resistance for AM seem very vague.

We consider it necessary to make a particular note on terminology. In Russia, according to the initiative of the Russian HP study group I. A. Morozov, HP presence in the stomach is called "хеликобактериоз", which is incorrect. In the journal article (1996) devoted to the terminological problems in gastroenterology, we indicated that all the medical terms in the Russian transcription that begin with a Latin letter "H" should be denoted by the letter "Г": hepatitis (гепатит) hormonum (гормон), histologia (гистология), Hippocrates (Гиппократ), etc. Terms that refer to the Latin letters «Ch» begin with the Russian letter «Х»: cholecystitis (холецистит), Chlamidia (хламидия), chromosoma (хромосома), etc. [43]. Thus, we should use the term "геликобактериоз" rather than "хеликобактериоз".

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The problem of growing resistance of microorganisms to antibiotic therapy and prospects for Helicobacter pylori eradication

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Key words: Helicobacter pylori, antibiotic therapy, antibiotic resistance, treatment, side effects

The problem of growing resistance of microorganisms to antibiotic therapy acquires increasingly greater significance as threatening the loss of endosymbiotic bacteria. The causes, mechanisms, and consequences of this phenomenon are considered in the present paper. Several groups of modern antibiotic drugs are characterized along with the methods for improving their efficacy and preventing side effects. The schemes for Helicobacter pylori eradication as recommended by the Maastricht consensus are discussed in conjunction with major mistakes accounting for marked reduction of their effectiveness. Terminological issues are briefly considered.