https://doi.org/10.22416/1382-4376-2022-32-6-7-19
UDC 616.33-002.2-022.7:579.835.12

Modern Approaches to *H. pylori* Eradication Therapy in Adults (Literature Review and Resolution of Experts Council)

Vladimir T. Ivashkin[1], Anatoly I. Ulyanin[1,*], Igor V. Mayev[2], Roman S. Kozlov[3], Maria A. Livzan[4], Sayar R. Abdulkhakov[5,6], Olga P. Alekseyeva[7], Sergey A. Alekseyenko[8], Dmitry S. Bordin[2,9,10], Natalya N. Dekhnich[3], Natalia V. Korochyanskaya[11], Tatiana L. Lapina[1], Elena.A. Poluektova[1], Vladimir I. Simanenkov[12], Aleksandr S. Trukhmanov[1], Igor B. Khlynov[13], Vladimir V. Tsukanov[14], Arkadiy A. Sheptulin[1]

[1] *I.M. Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation*
[2] *A.I. Yevdokimov Moscow State University of Medicine and Dentistry, Moscow, Russian Federation*
[3] *Smolensk State Medical University, Smolensk, Russian Federation*
[4] *Omsk State Medical University, Omsk, Russian Federation*
[5] *Kazan (Volga Region) Federal University, Kazan, Russian Federation*
[6] *Kazan State Medical University, Kazan, Russian Federation*
[7] *Nizhny Novgorod Regional Clinical Hospital named after N.A. Semashko, Nizhny Novgorod, Russian Federation*
[8] *Far Eastern State Medical University, Khabarovsk, Russian Federation*
[9] *A.S. Loginov Moscow Clinical Scientific Center, Moscow, Russian Federation*
[10] *Tver State Medical University, Tver, Russian Federation*
[11] *Kuban State Medical University, Krasnodar, Russian Federation*
[12] *I.I. Mechnikov North-Western State Medical University, St. Petersburg, Russian Federation*
[13] *Ural State Medical University, Yekaterinburg, Russian Federation*
[14] *Krasnoyarsk Science Center of the Siberian Branch of the Russian Academy of Sciences, an autonomous branch of the Research Institute of Medical Problems of the North, Krasnoyarsk, Russian Federation*

Aim: to analyze current approaches to *H. pylori* eradication therapy in adults and present the materials of Experts Council held on December 9, 2022 in Moscow.
General statements. *H. pylori* infection is the main etiological factor of gastritis, peptic ulcer, and gastric cancer. Eradication of *H. pylori* is recognized as a necessary measure to reduce the incidence of these diseases. The approaches to selecting an eradication regimen should be optimized to take into account epidemiological trends and achieve better treatment outcomes. The updated Maastricht VI Consensus Report presents the means to overcome the difficulties in selecting an approach to the treatment of *H. pylori* infection. However, eradication therapy remains challenging due to adverse events (primarily antibiotic-associated diarrhea), poor treatment tolerance and patient compliance. Eradication therapy can be optimized by supplementing treatment regimens with strain-specific probiotics that reduce adverse events, improve patient compliance and eradication rates, such as *Saccharomyces boulardii* CNCM I-745 strain with established efficacy.
Conclusion. The inclusion of certain probiotics in eradication regimens improves treatment tolerance, reduces the risk of adverse events, improves patient compliance and eradication rates.
Key words: gastritis, gastric cancer, atrophy, *H. pylori*, eradication, compliance, microbiome, microbiota, antibiotics, probiotics, *Saccharomyces boulardii* CNCM I-745
Conflict of interest: Council of Experts was hosted by pharmaceutical company Biocodex.

For citation: Ivashkin V.T., Ulyanin A.I., Mayev I.V., Kozlov R.S., Livzan M.A., Abdulkhakov S.R., Alekseyeva O.P., Alekseyenko S.A., Bordin D.S., Dekhnich N.N., Korochyanskaya N.V., Lapina T.L., Poluektova Ye.A., Simanenkov V.I., Trukhmanov A.S., Khlynov I.B., Tsukanov V.V., Sheptulin A.A. Modern Approaches to *H. pylori* Eradication Therapy in Adults (Literature Review and Resolution of Experts Council). Russian Journal of Gastroenterology, Hepatology, Coloproctology. 2022;32(6):7–19. https://doi.org/10.22416/1382-4376-2022-32-6-7-19

Современные подходы к проведению эрадикационной терапии *H. pylori* у взрослых (обзор литературы и резолюция Экспертного совета)

В.Т. Ивашкин[1], А.И. Ульянин[1,*], И.В. Маев[2], Р.С. Козлов[3], М.А. Ливзан[4], С.Р. Абдулхаков[5,6], О.П. Алексеева[7], С.А. Алексеенко[8], Д.С. Бордин[2,9,10], Н.Н. Дехнич[3], Н.В. Корочанская[11], Т.Л. Лапина[1], Е.А. Полуэктова[1], В.И. Симаненков[12], А.С. Трухманов[1], И.Б. Хлынов[13], В.В. Цуканов[14], А.А. Шептулин[1]

[1] *ФГАОУ ВО «Первый Московский государственный медицинский университет им. И.М. Сеченова» (Сеченовский Университет) Министерства здравоохранения Российской Федерации», Москва, Российская Федерация*

[2] *ФГБОУ ВО «Московский государственный медико-стоматологический университет им. А.И. Евдокимова» Министерства здравоохранения Российской Федерации, Москва, Российская Федерация*

[3] *ФГБОУ ВО «Смоленский государственный медицинский университет» Министерства здравоохранения Российской Федерации, Смоленск, Российская Федерация*

[4] *ФГБОУ ВО «Омский государственный медицинский университет» Министерства здравоохранения Российской Федерации, Омск, Российская Федерация*

[5] *ФГАОУ ВО «Казанский (Приволжский) федеральный университет», Казань, Российская Федерация*

[6] *ФГБОУ ВО «Казанский государственный медицинский университет» Министерства здравоохранения Российской Федерации, Казань, Российская Федерация*

[7] *ГБУЗ НО «Нижегородская областная клиническая больница им. Н.А. Семашко» Министерства здравоохранения Нижегородской области, Нижний Новгород, Российская Федерация*

[8] *ФГБОУ ВО «Дальневосточный государственный медицинский университет» Министерства здравоохранения Российской Федерации, Хабаровск, Российская Федерация*

[9] *ГБУЗ «Московский клинический научный центр имени А.С. Логинова Департамента здравоохранения г. Москвы», Москва, Российская Федерация*

[10] *ФГБОУ ВО «Тверской государственный медицинский университет» Министерства здравоохранения Российской Федерации, Тверь, Российская Федерация*

[11] *ФГБОУ ВО «Кубанский государственный медицинский университет» Министерства здравоохранения Российской Федерации, Краснодар, Российская Федерация*

[12] *ФГБОУ ВО «Северо-Западный государственный медицинский университет им. И.И. Мечникова» Министерства здравоохранения Российской Федерации, Санкт-Петербург, Российская Федерация*

[13] *ФГБОУ ВО «Уральский государственный медицинский университет» Министерства здравоохранения Российской Федерации, Екатеринбург, Российская Федерация*

[14] *ФБГНУ «Федеральный исследовательский центр "Красноярский научный центр Сибирского отделения Российской академии наук"», обособленное подразделение НИИ медицинских проблем Севера, Красноярск, Российская Федерация*

Цель публикации: рассмотреть современные подходы к проведению эрадикационной терапии *H. pylori* у взрослых и представить материалы Экспертного совета, который состоялся 9 декабря 2022 г. в Москве.

Основные положения. Инфекция *H. pylori* является доминирующим этиологическим фактором развития гастрита, язвенной болезни и рака желудка. Эрадикация *H. pylori* признана необходимой мерой, способствующей снижению частоты возникновения данных заболеваний. Подходы к выбору схем эрадикации требуют своевременной оптимизации, которая бы учитывала эпидемиологические тенденции и возможности улучшения исходов лечения. В обновленных положениях консенсуса «Маастрихт VI» представлены актуальные меры по преодолению трудностей, возникающих при выборе подходов к лечению инфекции, вызванной *H. pylori.* Тем не менее в клинической практике сохраняются актуальные проблемы эрадикации: развитие нежелательных явлений (прежде всего антибиотико-ассоциированной диареи), не всегда хорошая переносимость лечения и низкая приверженность пациентов к терапии. Одним из возможных способов оптимизации эрадикации *H. pylori* является включение в схему лечения штаммоспецифичных пробиотиков, которые способны снизить число нежелательных явлений, улучшить комплаенс пациентов и повысить эффективность эрадикации. Одним из таких пробиотиков с доказанной эффективностью является штамм *Saccharomyces boulardii* CNCM I-745.

Вывод. Включение определенных пробиотиков в схему эрадикации способствует улучшению переносимости лечения, снижению риска развития нежелательных явлений, повышению приверженности к лечению и эффективности эрадикации.

Ключевые слова: гастрит, рак желудка, атрофия, *H. pylori*, эрадикация, комплаенс, микробиом, микробиота, антибиотики, пробиотики, *Saccharomyces boulardii* CNCM I-745

Конфликт интересов: Экспертный совет состоялся при организационной поддержке фармацевтической компании «Биокодекс».

Для цитирования: Ивашкин В.Т., Ульянин А.И., Маев И.В., Козлов Р.С., Ливзан М.А., Абдулхаков С.Р., Алексеева О.П., Алексеенко С.А., Бордин Д.С., Дехнич Н.Н., Корочанская Н.В., Лапина Т.Л., Полуэктова Е.А., Симаненков В.И., Трухманов А.С., Хлынов И.Б., Цуканов В.В., Шептулин А.А. Современные подходы к проведению эрадикационной терапии *H. pylori* у взрослых (обзор литературы и резолюция Экспертного совета). Российский журнал гастроэнтерологии, гепатологии, колопроктологии. 2022;32(6):7–19. https://doi.org/10.22416/1382-4376-2022-32-6-7-19

Council of Experts meeting focused on optimizing approaches to *H. pylori* eradication therapy in adults and chaired by V.T. Ivashkin, President of the Scientific community for human microbiome research (CHMR), Professor and Academician of the Russian Academy of Sciences, was held in Moscow on December 9, 2022. Council of Experts was face to face, but several experts from the Central, Siberian, Volga, Far Eastern, Southern, Northwestern, and Ural federal districts of the Russian Federation participated remotely.

In his opening remarks, **RAS Academician V.T. Ivashkin** drew attention to the background for optimizing treatment of *H. pylori* infection, including the accumulating experience with eradication, new treatment approaches based on the updated Maastricht VI Consensus Recommendations, understanding the role of microbial factor in clinical practice, and the need to improve treatment outcomes.

Reports on the main issues on the agenda of the meeting outlining potential ways to optimize the treatment of *H. pylori* infection were presented.

A report by **RAS Academician Prof. V.T. Ivashkin** and **Ph.D T.L. Lapina** provided up-to-date data on the epidemiology of *H. pylori* infection and antibiotic resistance in the world and in Russia.

Epidemiological studies have shown that the prevalence of *H. pylori* infection is determined by economic and social conditions and hygiene compliance of children. The effect of age cohorts is an important epidemiological factor. A demographic cohort consists of people who experienced a certain demographic event (a birth, marriage, childbirth, etc.) in a selected time period. Although infection occurs in childhood and *H. pylori* persists in the gastric mucosa for life, the prevalence of infection varies between age cohorts. The cohort effect is also observed in the morbidity and mortality from such socially significant *H. pylori*-associated diseases as gastric cancer and peptic ulcer of the gastric and duodenum [1, 2].

Several epidemiological studies reported a prevalence of *H. pylori* infection of 65–92 % of adults across the regions of the Russian Federation [3]. The proportion of infected individuals in the population has declined in recent years. The prevalence of *H. pylori* detected by the 13Curea breath test in individuals without prior history of eradication therapy (n = 6,480) was 38.8 % (41.8 % in 2017, 36.4 % in 2019, $p < 0.0001$). The lowest (20.2 %) and highest (43.9 %) prevalence rates of *H. pylori* were reported in the < 18 years and 41–50 years age groups, respectively. In 2017, the prevalence of *H. pylori* was significantly higher than in 2019 across all age groups ($p < 0.05$) (except for people <18 and >70 years of age where the rates were similar in both study periods) [4].

The decreasing prevalence of *H. pylori* in our country is accompanied by decreasing incidences of peptic ulcer and gastric cancer. The incidence of gastric and duodenal peptic ulcer was 1,047.0:100,000 in 2010 and 740.8:100,000 in 2020 [5]. The incidence of gastric cancer was 28.3:100,000 in 2010 and 21.89:100,000 in 2020. The decrease in the incidence averaged 1.56 % per year and was 14.37 % over 10 years [6].

Data on the antibiotic susceptibility of *H. pylori* in the Russian Federation were reported in a meta-analysis of the Russian studies performed over 10 years [7]. The rate of *H. pylori* resistance to clarithromycin was 10.39 % (95 % confidence interval [CI] 7.103–14.219), 33.95 % (95 % CI: 15.329–55.639) to metronidazole, 1.35 % (95 % CI: 0.281–3.202) to amoxicillin, 20.0 % (95 % CI: 12.637–28.574) to levofloxacin, and 0.98 % (95 % CI: 0.353–2.163) to tetracycline. The rate of dual resistance to clarithromycin and metronidazole was 2.37 % (95 % CI: 1.136–4.345) [7]. It should be recognized that data on susceptibility of *H. pylori* in the Russian Federation are limited and should be updated, particularly during the COVID-19 pandemic.

The Guideline of the European Helicobacter and Microbiota Study Group (Maastricht VI Consensus) recommend planning eradication therapy based on regional resistance patterns and performing routine antibiotic susceptibility testing (molecular or culture) even in the first-line setting. However, it has been noted that routine antibiotic susceptibility testing has yet to be implemented [8]. In the Clinical Guidelines of the Russian Gastroenterological Association (RGA) for the Diagnosis and Treatment of *Helicobacter pylori* Infection in Adults, an optimal eradication therapy regimen should be selected empirically [3]. When the guidelines were drafted and discussed, V.T. Ivashkin emphasized that the observed in vitro antibiotic resistance patterns should be interpreted with extreme caution when evaluating the response to a multi-drug eradication regimen. In particular, proton pump inhibitors (PPI) induce obvious and significant alterations in gastric pH and viability of bacteria [3].

The RGA Clinical Guidelines for the Diagnosis and Treatment of *Helicobacter pylori* Infection in Adults recognize improving patient compliance an important determinant of successful treatment. A prospective study of 3 eradication regimens showed an eradication rate of only 40.6 % with poor compliance (less than 80 % of the prescribed drugs were taken) and 75 % with adequate compliance [9]. Patient compliance depends on several

factors, but well-tolerated treatment without adverse events is certainly associated with improved compliance. Accumulating evidence suggests that combining probiotics with eradication therapy can improve compliance by preventing adverse events.

In his report, **Professor D.S. Bordin** gave a detailed outline of the updated Maastricht VI Consensus Report [8].

Traditionally, the new guideline includes 5 sections: Indications/Associations, Diagnosis, Treatment, Prevention/Gastric Cancer, *H. pylori* and the Gut Microbiota.

The guideline again recognizes *H. pylori* infection as the main etiological factor of gastritis that predisposes to peptic ulcer disease, gastric cancer, and mucosa-associated lymphoid tissue (MALT) lymphoma. There is still a statement that eradication of *H. pylori* is necessary for the treatment of these diseases to prevent and reverse atrophy and intestinal metaplasia of the gastric mucosa [10]. *H. pylori* infection can be considered to be the main predictor of these diseases due to the secondary role of external factors and the absence of pronounced clinical manifestations in most patients with structural and functional changes in the gastric mucosa.

The updated guideline again recommends a *test-and-treat* (detection of *H. pylori* and further treatment) strategy for new-onset dyspepsia. Gastric functional serology (pepsinogens I and II, gastrin, antibodies against the intrinsic factor Castle and autoantibodies against parietal cells) and can provide clinically valuable information about the risk and etiology of atrophy of the gastric mucosa, and remains relevant. The guideline includes a new statement about the stratification of patients into 2 age cohorts with different priorities for diagnostic measures. In young dyspeptic patients (age below 50) with no specific risk and no "alarm symptoms", non-invasive testing for *H. pylori* infection is recommended, whereas in dyspeptic patients older than 50 years, upper gastrointestinal (GI) endoscopy is required and functional serology may be considered as a complementary diagnostic tool [11].

According to new recommendations, when endoscopy is indicated, it should apply the best available technologies and include biopsy sampling to establish etiological diagnosis and gastritis stage. Any focal lesions should be additionally sampled [12]. Another new statement emphasizes the need for a histological assessment of the severity of gastric atrophy per the OLGA/OLGIM classification for gastritis staging and determining the individual risk of gastric cancer. The histological assessment of atrophy makes intestinal metaplasia subtyping clinically redundant [13–15].

The updated statement of this section also offers opportunities to decrease the rate of resistant *H. pylori* infection. The role of molecular methods (real time-PCR, whole genome sequencing, and digital PCR) that allow detection of *H. pylori* mutations associated with resistance to clarithromycin, levofloxacin, tetracycline, and rifampicin is emphasized [16]. If available, clarithromycin susceptibility testing through molecular techniques or culture, is recommended before prescribing any clarithromycin containing therapy [17]. Antibiotic susceptibility testing should be performed before first-line eradication therapy, although this approach has been poorly investigated in routine clinical practice. There is a new statement that gastric biopsies recovered from rapid urease tests can be reused for molecular testing by PCR to identify genetic markers associated with antibiotic resistance [18].

The updated recommendations in the Treatment section aim at improving eradication rates, primarily through the rational use of antibiotics. As before, statements about selecting recommended treatment regimens, prolonging the treatment course up to 14 days, using high doses of novel modern PPIs (esomeprazole or rabeprazole), and improving patient compliance have high levels of agreement. Unlike the previous Maastricht V Consensus Report, the new guideline offers the susceptibility-guided and empirical strategies based on monitoring regional eradication rates of different regimens and local clarithromycin resistance patterns, as stated earlier.8 Since both approaches have their advantages and disadvantages, the speaker presented the results of a meta-analysis of 54 RCTs comparing the outcomes of empirical (7,895 patients) and susceptibility-guided (6,705 subjects) eradication strategies. Eradication rates were 76 % and 86 %, respectively (RR 1.12; 95 % CI: 1.08–1.17), with no significant differences in diagnostic significance between culture-guided (RR 1.12; 95 % CI: 1.06–1.18) and PCR-guided (RR 1.14; 95 % CI: 1.05–1.23) antibiotic susceptibility testing. Although susceptibility-guided triple therapy was more efficacious (RR 1.15; 95 % CI: 1.11–1.20; I2 : 79 %), there were no significant differences in the eradication rate between empirical bismuth and non-bismuth quadruple regimens (RR 1.04; 95 % CI: 0.99–1.09) [19].

The updated guidelines suggest triple therapy with rifabutin (PPI + amoxicillin + rifabutin) as rescue therapy when choosing an empirical treatment strategy. This treatment regimen is effective regardless of regional rates of clarithromycin resistance.

The Study Group also noted that potassium-competitive acid blockers – antimicrobial combination

treatments are superior, or not inferior, to conventional PPI-based triple therapies for first- and second-line treatment, and superior in patients with evidence of antimicrobial resistant *H. pylori* infection [20–22].

The Prevention/Gastric Cancer section contains a statement that *H. pylori* eradication offers the chance for gastric cancer prevention at any age in adulthood; however, the magnitude of the benefit decreases with age. The latter may be due to an age-related increase in the severity of atrophy and an increase in the risk of intestinal metaplasia [23]. This statement reiterates the statement of the previous consensus where *H. pylori* eradication was considered to be the most effective for gastric cancer prevention before the development of severe chronic atrophic gastritis [24].

The *H. pylori* and the Gut Microbiota section discusses the negative impact of antibiotics on the gut microbiota [25]. It has been noted that the widespread use of antibacterials, both for eradication and for other indications, contributes to the emergence of antibiotic-resistant strains of the gut microbiota [26].

The new guidelines contain earlier statements regarding the effectiveness of certain probiotics in reducing GI side effects caused by eradication therapy that is closely associated with higher eradication rates [27]. Professor D.S. Bordin noted that various meta-analyses support the efficacy of several *Lactobacillus* and *Bifidobacterium* strains and the *Saccharomyces boulardii* species.8 Strain *Saccharomyces boulardii* CNCM I-745 has demonstrated efficacy in improving the eradication rate and is included in the practical guidelines on probiotic therapy of the CHMR and RGA [28].

At the end of the report, Professor D.S. Bordin noted that the new consensus report addresses many issues related to eradication therapy, but further studies are needed.

In his report, **Professor A.S. Trukhmanov** focused on the use of probiotics as part of *H. pylori* eradication therapy and gave an overview of domestic and foreign guidelines.

The clinical significance of the microbial factor in the development of gastric diseases became relevant after the discovery of the gastric microbiota. Despite accumulating scientific data, the composition of the gastric commensal microbiota and its relationship with *H. pylori* are poorly understood. A Russian analysis of the gastric microbiome using 16s ribosomal RNA sequencing showed that the gastric microbiome consists of *Firmicutes* (27 %), *Bacteroidetes* (24 %), *Proteobacteria* (19.1 %), *Actinobacteria* (9 %), and *Fusobacteria* (7 %). However, the gastric microbiome is altered in patients infected with *H. pylori*, with decreased overall microbial diversity and predominance of the *Proteobacteria* phylum [29]. Eradication of *H. pylori* significantly improves the diversity of the gastric microbiota ($p < 0.00001$) [30].

Since eradication therapy is associated with the risk of side effects which reduce patient compliance, it should be optimized using measures with established effectiveness, such as supplementing an eradication regimen with probiotics.

In the World Gastroenterology Association guidelines, a role for probiotics in improving eradication rates has been claimed; however, the addition of probiotic strains to eradication therapy is seen as a means to reduce the severity of side effects [31]. According to the RGA Clinical Guidelines on the Diagnosis and Treatment of *H. pylori* in Adults, probiotics are advisable both to reduce the incidence of adverse events of eradication therapy, including *C. difficile*-associated disease, and to increase the eradication rate (level of evidence (LoE) 1, strength of recommendation (SoR) B) [3]. Not all probiotics have these properties, and, therefore, the results of well-designed clinical studies should be considered when selecting the optimal probiotic.

In vitro studies have shown that certain probiotics have direct (competition for habitat, synthesis of bacteriocins, and coaggregation with *H. pylori*) and indirect (regulation of the immune response, maintenance of the epithelial barrier integrity, stimulation of mucin production) antagonism to *H. pylori*, and improve patient compliance, affecting eradication rates [32, 33].

The clinical efficacy of probiotics has been confirmed in several well-designed studies. In a meta-analysis of 45 RCTs (6,997 participants), probiotics significantly reduced the incidence of adverse events of conventional eradication therapy (RR 0.59, 95 % CI: 0.48–0.71; $p < 0.001$) and improved eradication rates (RR 1.11, 95 % CI: 1.08–1.15; $p < 0.001$) [34]. A recent meta-analysis of 40 RCTs (8,924 subjects) reported a higher eradication rate in patients receiving probiotics before and during eradication therapy (81.5 % in the probiotic group versus 71.6 % in the control group, RR 1.14, 95 % CI: 1.10–1.18). Side effects (diarrhea, abdominal pain, nausea, vomiting, constipation, and taste disturbance) were reported by 18.9 % of patients in the probiotic group and by 39 % of patients in the control group [35].

Saccharomyces boulardii, as one of well-known probiotics, is capable to improve eradication rates by reducing the severity of side effects. A meta-analysis of 5 RCTs (1,307 patients) showed a significant increase in the eradication

rate (RR 1.13; 95 % CI 1.05–1.21) and reduced risk of common side effects (RR 0.46; 95 % CI 0.3–0.7), including diarrhea (RR 0.47; 95 % CI 0.32–0.69) in patients receiving *S. boulardii* with triple therapy.36 Another controlled study showed the benefits of adding *Saccharomyces boulardii* to quadruple eradication therapy. Probiotic supplementation significantly reduced the incidence of common side effects (27.8 % versus 38.5 %, $p = 0.034$) and diarrhea (11.2 % versus 21.2 %, $p = 0.012$), with significant reductions in the duration of diarrhea (5.0 days versus 7.7 days, $p = 0.032$) and the incidence of severe diarrhea events (4.7 % versus 10.1 %, $p = 0.040$) [37]. A recent meta-analysis of 18 RCTs ($n = 3,592$) demonstrated the clinical benefits of *S. boulardii* in reducing the risk of common adverse events (RR 0.47, 95 % CI 0.36–0.61) and diarrhea (RR 0.37, 95 % CI 0.23–0.57) during eradication therapy, and increasing eradication rate (RR 1.09, 95 % CI 1.05–1.13) [38].

The inclusion of probiotics in the *H. pylori* eradication treatment regimen did not reduce patient compliance (RR 0.98; 95 % CI 0.68–1.39; $p = 0.889$) which is important in real-world practice [34].

In conclusion, A.S. Trukhmanov noted that the microbial factor plays not only a negative role in the eradication of *H. pylori*, and the benefits of other microorganisms should be taken into account.

In his report, **Professor V.I. Simanenkov** dwelled in detail on the evidence supporting the effectiveness of combining *Saccharomyces boulardii* CNCM I-745 with *H. pylori* eradication therapy. The speaker emphasized that eradication therapy is a real challenge for physicians due to the global increase in antibiotic resistance and numerous side effects, and, therefore, more effective and less dangerous treatments are needed [39]. Ideal *H. pylori* eradication therapy is simple and cost-effective, neither impairs the gut microbiota nor causes antibiotic resistance [40]. Considering these statements, the prevalence of primary and secondary resistance of *H. pylori* to clarithromycin, metronidazole, and levofloxacin, and low eradication rates of triple therapy, prerequisites are created for the optimization of *H. pylori* therapy, by increasing role of probiotics. Notably, eradication rates of 12–16 % were reported for probiotic monotherapy versus placebo (RR 7.91; 95 % CI 2.97–21.05; $p < 0.001$), with comparable rates of adverse effects (RR 1; 95 % CI 0.06–18.08) [42].

The Maastricht VI Consensus Report draws particular attention to probiotics containing *Saccharomyces boulardii* that are prescribed to reduce antibiotic-related side effects. However, these statements do not specify the strain specificity of probiotics [8]. Because the results of published studies for most probiotic strains and formulations are inconsistent, clinicians need a better understanding of the risks and benefits of probiotics due to strain specificity which is an important criterion for achieving the claimed effects.43 Strain *Saccharomyces boulardii* CNCM I-745 has a high level of evidence and is included in the practical guidelines on probiotic therapy of CHMR and RGA [28, 31].

This strain has well-established benefits, e.g., rapid achievement of high concentrations in the colon, natural resistance to antibiotics, inability to accumulate antibiotic resistance genes, and stable colonization of the colon [44].

From the standpoint of eradication therapy, the strain is also effective due to the direct and indirect antagonistic effects on *H. pylori*. The direct mechanisms include the adhesive property with subsequent elimination of *H. pylori*, inactivation of bacterial virulence factors (bacterial lipopolysaccharides and toxins), as well as maintenance of a targeted immune response. The indirect mechanisms aim at ensuring the integrity of the epithelial barrier and maintaining the anti-inflammatory immune response of the stomach, as well as inhibition of hydrochloric acid secretion by suppressing cAMP-dependent chloride secretion.45 *Saccharomyces boulardii* CNCM I-745 is also able to prevent antibiotic-associated diarrhea by directly inhibiting pathogenic microorganisms and their toxins, suppressing infection-induced signaling cascades of the pro-inflammatory immune response, and maintaining of the integrity of the colonic epithelial barrier [46, 47]. This strain is also able to impede the formation of *C. difficile* biofilms which may determine its benefit of preventing *C. difficile*-associated disease [48].

Despite this, probiotic monotherapy yields an eradication rate of 12 % only (95 % CI 0–29 %) and cannot be used as the primary eradication tool. Nevertheless, in a meta-analysis of 11 RCTs involving 2,200 patients, eradication rate was 80 % (679/853, 95 % CI 0–29 %) in the probiotic group compared with 71 % in the placebo group (608/855; 95 % CI 68–74 %). Probiotic therapy was associated with a reduced risk of antibiotic-related adverse events (RR 0.44; 95 % CI 0.31–0.64), especially diarrhea (RR 0.51; 95 % CI 0.42–0.62) and nausea (RR 0.6; 95 % CI 0.44–0.83) compared with the control group [42].

In his report, Professor V.I. Simanenkov pointed out that *Saccharomyces boulardii* CNCM I-745 prevented antibiotic resistance after eradication therapy in a recent study examining genetic markers of antibiotic resistance in stool samples from

patients who received triple eradication therapy with/without a probiotic. The number of genes of resistance to lincosamides, tetracyclines, macrolides, and beta-lactams was significantly lower in the probiotic group compared with the control group (FDR < 0.05).49 A study in mice showed that coadministration of *S. boulardii* probiotic and amoxicillin did not alter the pharmacokinetics of amoxicillin and thus does not contribute to amoxicillin resistance.50 It was also noted that adding *S. boulardii* CNCM I-745 to eradication therapy not only significantly reduced adverse effects ($p = 0.028$), but also preserved greater diversity of the gut microbiota ($p = 0.0156$) after eradication therapy [51].

In conclusion, V.I. Simanenkov noted that increasing rates of antibiotic resistance and the impact of eradication on the GI microbiome should be considered along with eradication rates and antibiotic-related adverse effects, highlighting the benefits of supplementing eradication therapy with probiotic support. The above data support the inclusion of *S. boulardii* CNCM I-745 strain in the clinical guidelines for the treatment of *H. pylori* infection.

In his closing remarks, **RAS Academician V.T. Ivashkin** emphasized the relevance of the presented data and insightfulness of the discussion. A Resolution was adopted after discussing the presented reports.

Resolution of Council of Experts

1. The decreasing prevalence of *H. pylori* infection in the Russian population is accompanied by a decreasing incidence of peptic ulcer and gastric cancer.

2. The choice of treatment strategy is based on the empirical optimization of eradication therapy. The lack of regional data on antibiotic resistance of *H. pylori* does not justify abandoning *H. pylori* therapy.

3. Improving *H. pylori* eradication rates involves several measures, including doubling the doses of PPIs, prescribing 14-day courses of eradication therapy, and prescribing probiotics.

4. Maximum patient compliance is an important determinant of *H. pylori* eradication success. Greater attention should be paid to encouraging patient compliance during eradication therapy.

5. Supplementing eradication therapy with certain probiotic strains that demonstrated efficacy in clinical trials reduces antibiotic-related adverse events and improves patient compliance.

6. Coadministration of *Saccharomyces boulardii* CNCM I-745 and antibacterial drugs reduces the rates of side effects, improves patient compliance and eradication rate. The obtained results support the incorporation of *S. boulardii* CNCM I-745 strain in the clinical guidelines for the diagnosis and treatment of *H. pylori* infection.

References / Литература

1. *Sonnenberg A.* Epidemiology of Helicobacter pylori. *Aliment Pharmacol Ther.* 2022;55 (Suppl 1):S–S13. DOI: 10.1111/apt.16592
2. *Graham D.Y.* History of Helicobacter pylori, duodenal ulcer, gastric ulcer and gastric cancer. *World J Gastroenterol.* 2014;20(18):5191–204. DOI: 10.3748/wjg.v20.i18.5191
3. *Ивашкин В.Т., Маев И.В., Лапина Т.Л., Шептулин А.А., Трухманов А.С., Баранская Е.К.* и др. Клинические рекомендации Российской гастроэнтерологической ассоциации по диагностике и лечению инфекции Helicobacter pylori у взрослых. Рос журн гастроэнтерол гепатол колопроктол. 2018;28(1):55–70. [Ivashkin V.T., Mayev I.V., Lapina T.L., Sheptulin A.A., Trukhmanov A.S., Baranskaya E.K., et al. Diagnostics and treatment of Helicobacter pylori infection in adults: Clinical guidelines of the Russian gastroenterological association. *Rus J Gastroenterol Hepatol Coloproctology*. 2018;28(1):55–70 (In Russ.)]. DOI: 10.22416/1382-4376-2018-28-1-55-70
4. *Bordin D., Morozov S., Plavnik R., Bakulina N., Voynovan I., Skibo I., et al.* Helicobacter pylori infection prevalence in ambulatory settings in 2017-2019 in Russia: The data of real-world national multicenter trial. *Helicobacter.* 2022;27(5):e12924. DOI: 10.1111/hel.12924
5. *Здравоохранение в России.* 2021: Статистический сборник. М.: Росстат, 2021. [Health care in Russia. 2021: Statistical compendium. Moscow: Rosstat, 2021 (In Russ.)]. https://rosstat.gov.ru/storage/mediabank/Zdravoohran-2021.pdf
6. *Каприн А.Д., Старинский В.В., Шахзадова А.О.* (ред.) Злокачественные новообразования в России в 2020 году (заболеваемость и смертность). М.: МНИОИ им. П.А. Герцена — филиал ФГБУ «НМИЦ радиологии» Минздрава России, 2021. [Kaprin A.D., Starinsky V.V., Shakhzadova A.O. (ed.) Malignant neoplasms in Russia in 2020 (morbidity and mortality). Moscow: MNIOI im. P.A. Herzen — a branch of the Federal State Budgetary Institution "NMITs Radiology" of the Ministry of Health of Russia, 2021 (In Russ.)].
7. *Андреев Д.Н., Маев И.В., Кучерявый Ю.А.* Резистентность *Helicobacter pylori* в Российской Федерации: метаанализ исследований за последние 10 лет. *Терапевтический архив.* 2020;92(11):24–30. [Andreev D.N., Maev I.V., Kucheryavyy Yu.A. Helicobacter pylori resistance in the Russian Federation: a meta-analysis of studies over the past 10 years. *Therapeutic Archive.* 2020;92(11):24–30 (In Russ.)]. DOI: 10.26442/00403660.2020.11.000795
8. *Malfertheiner P., Megraud F., Rokkas T., Gisbert J.P., Liou J.M., Schulz C., et al.* Management of Helicobacter pylori infection: the Maastricht VI/Florence consensus report. *Gut.* 2022:gutjnl-2022-327745. DOI: 10.1136/gutjnl-2022-327745
9. *Kim B.J., Lee H., Lee Y.C. Jeon S.W., Kim G.H., Kim H.S., et al.* Ten-Day Concomitant, 10-Day Sequential, and 7-Day Triple Therapy as First-Line Treatment for Helicobacter pylori Infection: A Nationwide Randomized Trial in Korea. *Gut Liver.* 2019;13(5):531–540. DOI: 10.5009/gnl19136
10. *Venneman K., Huybrechts I., Gunter M.J., Vandendaele L., Herrero R., Van Herck K.* The epidemiology of Helicobacter pylori infection in Europe and the impact of lifestyle on its natural evolution toward stomach cancer after infection: A systematic review. *Helicobacter.* 2018;23(3):e12483. DOI: 10.1111/hel.12483
11. *Derakhshan M.H., El-Omar E., Oien K., Gillen D., Fyfe V., Crabtree J.E., McColl K.E.* Gastric histology, serological markers and age as predictors of gastric acid secretion in patients infected with Helicobacter pylori. *J Clin Pathol.* 2006;59(12):1293–9. DOI: 10.1136/jcp.2005.036111
12. *Bisschops R., Areia M., Coron E., Dobru D., Kaskas B., Kuvaev R., et al.* Performance measures for upper gastrointestinal endoscopy: a European Society of Gastrointestinal Endoscopy (ESGE) Quality Improvement Initiative. *Endoscopy.* 2016;48(9):843–64. DOI: 10.1055/s-0042-113128
13. *Pimentel-Nunes P., Libânio D., Lage J., Abrantes D., Coimbra M., Esposito G., et al.* A multicenter prospective study of the real-time use of narrow-band imaging in the diagnosis of premalignant gastric conditions and lesions. *Endoscopy.* 2016;48(8):723–30. DOI: 10.1055/s-0042-108435
14. *Marcos P., Brito-Gonçalves G., Libânio D., Pita I., Castro R., Sá I., et al.* Endoscopic grading of gastric intestinal metaplasia on risk assessment for early gastric neoplasia: can we replace histology assessment also in the West? *Gut.* 2020;69(10):1762–8. DOI: 10.1136/gutjnl-2019-320091
15. *Libânio D., Braga V., Ferraz S., Castro R., Lage J., Pita I., et al.* Prospective comparative study of endoscopic submucosal dissection and gastrectomy for early neoplastic lesions including patients' perspectives. *Endoscopy.* 2019;51(1):30–9. DOI: 10.1055/a-0628-6601
16. *Wang Y.H., Li Z., Wang L., Zhu-Ge L.Y., Zhao R.L., et al.* A systematic review and meta-analysis of genotypic methods for detecting antibiotic resistance in *Helicobacter pylori*. *Helicobacter.* 2018;23(2):e12467. DOI: 10.1111/hel.12467
17. *Bénéjat L., Ducournau A., Lehours P., Mégraud F.* Real-time PCR for Helicobacter pylori diagnosis. The best tools available. *Helicobacter.* 2018;23(5):e12512. DOI: 10.1111/hel.12512
18. *Chung W.C., Jeon E.J., Oh J.H., Park J.M., Kim T.H., Cheung D.Y., et al.* Dual-priming oligonucleotide-based multiplex PCR using tissue samples from the rapid urease test kit for the detection of Helicobacter pylori in bleeding peptic ulcers. *Dig Liver Dis.* 2016;48(8):899–903. DOI: 10.1016/j.dld.2016.04.012
19. *Nyssen O.P., Espada M., Gisbert J.P.* Empirical vs. Susceptibility-Guided Treatment of Helicobacter pylori Infection: A Systematic Review and Meta-Analysis. *Front Microbiol.* 2022;13:913436. DOI: 10.3389/fmicb.2022.913436
20. *Scarpignato C., Hunt R.H.* Acid Suppressant Therapy: a Step Forward with Potassium-Competitive Acid Blockers. *Curr Treat Options Gastro.* 2021;19:94–132. DOI: 10.1007/s11938-020-00330-x
21. *Graham D.Y., Lu H., Shiotani A.* Vonoprazan-containing Helicobacter pylori triple therapies contribution to global antimicrobial resistance. *J Gastroenterol Hepatol.* 2021;36(5):1159–63. DOI: 10.1111/jgh.15252
22. *Jung Y.S., Kim E.H., Park C.H.* Systematic review with meta-analysis: the efficacy of vonoprazan-based triple therapy on Helicobacter pylori eradication. *Aliment Pharmacol Ther.* 2017;46(2):106–114. DOI: 10.1111/apt.14130
23. *Chen Q., Liang X., Long X., Yu L., Liu W., Lu H.* Cost-effectiveness analysis of screen-and-treat strategy in asymptomatic Chinese for preventing Helicobacter pylori-associated diseases. *Helicobacter.* 2019;24(2):e12563. DOI: 10.1111/hel.12563
24. *Ferreira C.N., Serrazina J., Marinho R.T.* Detection and Characterization of Early Gastric Cancer. *Front Oncol.* 2022;12:855216. DOI: 10.3389/fonc.2022.855216
25. *Palleja A., Mikkelsen K.H., Forslund S.K., Kashani A., Allin K.H., Nielsen T., et al.* Recovery of gut microbiota of healthy adults following antibiotic exposure. *Nat Microbiol.* 2018;3(11):1255–65. DOI: 10.1038/s41564-018-0257-9
26. *Megraud F., Bruyndonckx R., Coenen S., Wittkop L., Huang T.D., Hoebeke M., et al.* Helicobacter pylori resistance to antibiotics in Europe in 2018 and its relationship to antibiotic consumption in the community. *Gut.* 2021;70(10):1815–22. DOI: 10.1136/gutjnl-2021-324032
27. *Lv Z., Wang B., Zhou X., Wang F., Xie Y., Zheng H., Lv N.* Efficacy and safety of probiotics as adjuvant agents for Helicobacter pylori infection: A meta-analysis. *Exp Ther Med.* 2015;9(3):707–16. DOI: 10.3892/etm.2015.2174
28. *Ивашкин В.Т., Маев И.В., Абдулганиева Д.И., Алексеенко С.А., Горелов А.В., Захарова И.Н.* и др. Прак-

тические рекомендации Научного сообщества по содействию клиническому изучению микробиома человека (НСОИМ) и Российской гастроэнтерологической ассоциации (РГА) по применению пробиотиков, пребиотиков, синбиотиков и обогащенных ими функциональных пищевых продуктов для лечения и профилактики заболеваний гастроэнтерологического профиля у детей и взрослых. *Российский журнал гастроэнтерологии, гепатологии, колопроктологии.* 2021;31(2):65–91. [Ivashkin V.T., Mayev I.V., Abdulganieva D.I., Alekseenko S.A., Gorelov A.V., Zakharova I.N., et al. Practical Recommendations of Scientific Society for the Study of Human Microbiome and the Russian Gastroenterological Association on Use of Probiotics, Prebiotics, Synbiotics and Functional Foods in Treatment and Prevention of Gastroenterological Diseases in Children and Adults. *Russian Journal of Gastroenterology, Hepatology, Coloproctology.* 2021;31(2):65–91 (In Russ.)]. DOI: 10.22416/1382-4376-2021-31-2-65-91

29. *Румянцева Д.Е., Трухманов А.С., Кудрявцева А.В., Краснов Г.С., Параскевова А.В., Сторонова О.А., Пономарев А.Б.* Микробиота пищевода и желудка у больных гастроэзофагеальной рефлюксной болезнью и здоровых добровольцев. *Российский журнал гастроэнтерологии, гепатологии, колопроктологии.* 2018;28(4):36–46. [Rumyantseva D.E., Trukhmanov A.S., Kudryavtseva A.V., Krasnov G.S., Paraskevova A.V., Storonova O.A., Ponomarev A.B. Microbiota of the Esophagus and Stomach in Patients with Gastroesophageal Reflux Disease and Healthy Volunteers. *Russian Journal of Gastroenterology, Hepatology, Coloproctology.* 2018;28(4):36–46 (In Russ.)]. DOI: 10.22416/1382-4376-2018-28-4-36-46
30. *Sung J.J.Y., Coker O.O., Chu E., Szeto C.H., Luk S.T.Y., Lau H.C.H., Yu J.* Gastric microbes associated with gastric inflammation, atrophy and intestinal metaplasia 1 year after Helicobacter pylori eradication. *Gut.* 2020;69(9):1572–80. DOI: 10.1136/gutjnl-2019-319826
31. *World Gastroenterology Organization.* Probiotics and prebiotics. 2017. https://www.worldgastroenterology.org/guidelines
32. *Keikha M., Karbalaei M.* Probiotics as the live microscopic fighters against Helicobacter pylori gastric infections. *BMC Gastroenterol.* 2021;21(1):388. DOI: 10.1186/s12876-021-01977-1
33. *Xu W., Xu L., Xu C.* Relationship between Helicobacter pylori infection and gastrointestinal microecology. *Front Cell Infect Microbiol.* 2022;12:938608. DOI: 10.3389/fcimb.2022.938608
34. *Zhang M.M., Qian W., Qin Y.Y., He J., Zhou Y.H.* Probiotics in Helicobacter pylori eradication therapy: a systematic review and meta-analysis. World J Gastroenterol. 2015;21(14):4345–57. DOI: 10.3748/wjg.v21.i14.4345
35. *Shi X., Zhang J., Mo L., Shi J., Qin M., Huang X.* Efficacy and safety of probiotics in eradicating Helicobacter pylori: A network meta-analysis. Medicine (Baltimore). 2019;98(15):e15180. DOI: 10.1097/MD.0000000000015180
36. *Szajewska H., Horvath A., Piwowarczyk A.* Meta-analysis: the effects of Saccharomyces boulardii supplementation on Helicobacter pylori eradication rates and side effects during treatment. *Aliment Pharmacol Ther.* 2010;32(9):1069–79. DOI: 10.1111/j.1365-2036.2010.04457.x
37. *Zhao Y., Yang Y., Aruna, Xiao J., Song J., Huang T., et al.* Saccharomyces boulardii Combined With Quadruple Therapy for Helicobacter pylori Eradication Decreased the Duration and Severity of Diarrhea: A Multi-Center Prospective Randomized Controlled Trial. *Front Med (Lausanne).* 2021;8:776955. DOI: 10.3389/fmed.2021.776955
38. *Zhou B.G., Chen L.X., Li B., Wan L.Y., Ai Y.W.* Saccharomyces boulardii as an adjuvant therapy for Helicobacter pylori eradication: A systematic review and meta-analysis with trial sequential analysis. *Helicobacter.* 2019;24(5):e12651. DOI: 10.1111/hel.12651
39. *Meliț L.E., Mărginean C.O., Săsăran M.O.* The Challenges of Eradicating Pediatric Helicobacter pylori Infection in the Era of Probiotics. *Children (Basel).* 2022;9(6):795. DOI: 10.3390/children9060795
40. *Suzuki S., Kusano C., Horii T., Ichijima R., Ikehara H.* The Ideal Helicobacter pylori Treatment for the Present and the Future. Digestion. 2022;103(1):62–8. DOI: 10.1159/000519413
41. *Bai X., Zhu M., He Y., Wang T., Tian D., Shu J.* The impacts of probiotics in eradication therapy of Helicobacter pylori. *Arch Microbiol.* 2022;204(12):692. DOI: 10.1007/s00203-022-03314-w
42. *Losurdo G., Cubisino R., Barone M., Principi M., Leandro G., Ierardi E., Di Leo A.* Probiotic monotherapy and Helicobacter pylori eradication: A systematic review with pooled-data analysis. *World J Gastroenterol.* 2018;24(1):139–49. DOI: 10.3748/wjg.v24.i1.139
43. *Compare D., Sgamato C., Nardone O.M., Rocco A., Coccoli P., Laurenza C., Nardone G.* Probiotics in Gastrointestinal Diseases: All that Glitters Is Not Gold. *Dig Dis.* 2022;40(1):123–32. DOI: 10.1159/000516023
44. *Dinleyici E.C., Kara A., Ozen M., Vandenplas Y.* Saccharomyces boulardii CNCM I-745 in different clinical conditions. *Expert Opin Biol Ther.* 2014;14(11):1593–609. DOI: 10.1517/14712598.2014.937419
45. *Czerucka D., Rampal P.* Diversity of Saccharomyces boulardii CNCM I-745 mechanisms of action against intestinal infections. *World J Gastroenterol.* 2019;25(18):2188–203. DOI: 10.3748/wjg.v25.i18.2188
46. *Terciolo C., Dapoigny M., Andre F.* Beneficial effects of Saccharomyces boulardii CNCM I-745 on clinical disorders associated with intestinal barrier disruption. *Clin Exp Gastroenterol.* 2019;12:67–82. DOI: 10.2147/CEG.S181590
47. *Stier H., Bischoff S.C.* Influence of Saccharomyces boulardii CNCM I-745on the gut-associated immune system. *Clin Exp Gastroenterol.* 2016;9:269–79. DOI: 10.2147/CEG.S111003
48. *Lacotte P.A., Simons A., Bouttier S., Malet-Villemagne J., Nicolas V., Janoir C.* Inhibition of In Vitro Clostridioides difficile Biofilm Formation by the Probiotic Yeast *Saccharomyces boulardii* CNCM I-745 through Modification of the Extracellular Matrix Composition. Microorganisms. 2022;10(6):1082. DOI: 10.3390/microorganisms10061082
49. *Cifuentes S.G., Prado M.B., Fornasini M., Cohen H., Baldeón M.E., Cárdenas P.A. Saccharomyces boulardii* CNCM I-745 supplementation modifies the fecal resistome during Helicobacter pylori eradication therapy. *Helicobacter.* 2022;27(2):e12870. DOI: 10.1111/hel.12870
50. *Selig D.J., DeLuca J.P., Li Q., Lin H., Nguyen K., Scott S.M., et al. Saccharomyces boulardii* CNCM I-745 probiotic does not alter the pharmacokinetics of amoxicillin. *Drug Metab Pers Ther.* 2020;35(1):/j/dmdi.2020.35.issue-1/dmpt-2019-0032/dmpt-2019-0032.xml. DOI: 10.1515/dmpt-2019-0032
51. *Cárdenas P.A., Garcés D., Prado-Vivar B., Flores N., Fornasini M., Cohen H., et al.* Effect of *Saccharomyces boulardii* CNCM I-745 as complementary treatment of Helicobacter pylori infection on gut microbiome. *Eur J Clin Microbiol Infect Dis.* 2020;39(7):1365–72. DOI: 10.1007/s10096-020-03854-3

Information about the authors

Vladimir T. Ivashkin — Dr. Sci. (Med.), RAS Academician, Prof., Departmental Head, Department of Propaedeutics of Internal Diseases, N.V. Chief of Vasilenko Clinic of Internal Disease Propaedeutics, Gastroenterology and Hepatology, Sechenov First Moscow State Medical University (Sechenov University).
Contact information: ivashkin_v_t@staff.sechenov.ru;
119435, Moscow, Pogodinskaya str., 1, bld. 1.
ORCID: https://orcid.org/0000-0002-6815-6015

Anatoly I. Ulyanin* — Gastroenterologist, Department of Chronic Intestinal and Pancreatic Diseases, Vasilenko Clinic of Internal Disease Propaedeutics, Gastroenterology and Hepa- tology, Sechenov First Moscow State Medical University (Sechenov University).
Contact information: ulyanin_a_i@staff.sechenov.ru;
119991, Moscow, Pogodinskaya str., 1, bld. 1.
ORCID: https://orcid.org/0000-0001-5506-5555

Igor V. Maev — Dr. Sci. (Med.), Academician of the Russian Academy of Sciences, Professor, Head of the Department of Propaedeutics of Internal Diseases and Gastroenterology, A.I. Yevdokimov Moscow State University of Medicine and Dentistry.
Contact information: igormaev@rambler.ru;
127473, Moscow, Delegatskaya str., 20, bld. 1.
ORCID: https://orcid.org/0000-0001-6114-564X

Roman S. Kozlov — Dr. Sci. (Med.), Prof., Corresponding Member of Russian Academy of Sciences (RAS), rector, Smolensk State Medical University, director, Research Institute of Antimicrobial Chemotherapy, President of the Interregional Association for Clinical Microbiology and Antimicrobial Chemotherapy (IACMAC).
Contact information: Roman.Kozlov@antibiotic.ru;
214019, Smolensk, Krupskoy str., 28.
ORCID: https://orcid.org/0000-0001-8728-1113

Maria A. Livzan — Dr. Sci. (Med.), Prof., Corresponding Member of Russian Academy of Sciences (RAS); Head of the Chair of Faculty Therapy and Professional Diseases, Rector of Omsk State Medical University. Omsk State Medical University.
Contact information: mlivzan@yandex.ru;
644099, Omsk, Lenina str., 12.
ORCID: https://orcid.org/0000-0002-6581-7017
SCOPUS Author ID: 24341682600

* Corresponding author / Автор, ответственный за переписку

Сведения об авторах

Ивашкин Владимир Трофимович — доктор медицинских наук, академик РАН, профессор, заведующий кафедрой пропедевтики внутренних болезней, гастроэнтерологии и гепатологии, директор клиники пропедевтики внутренних болезней, гастроэнтерологии и гепатологии им. В.Х. Василенко ФГАОУ ВО «Первый Московский государственный медицинский университет им. И.М. Сеченова» (Сеченовский Университет) Министерства здравоохранения Российской Федерации.
Контактная информация: ivashkin_v_t@staff.sechenov.ru;
119991, г. Москва, ул. Погодинская, д. 1, стр. 1.
ORCID: https://orcid.org/0000-0002-6815-6015

Ульянин Анатолий Игоревич* — врач отделения хронических заболеваний кишечника и поджелудочной железы клиники пропедевтики внутренних болезней, гастроэнтерологии и гепатологии им. В.Х. Василенко ФГАОУ ВО «Первый Московский государственный медицинский университет им. И.М. Сеченова» (Сеченовский Университет) Министерства здравоохранения Российской Федерации.
Контактная информация: ulyanin_a_i@staff.sechenov.ru;
119991, г. Москва, ул. Погодинская, д. 1, стр. 1.
ORCID: https://orcid.org/0000-0001-5506-5555

Маев Игорь Вениаминович — доктор медицинских наук, академик РАН, профессор, заведующий кафедрой пропедевтики внутренних болезней и гастроэнтерологии ФГБОУ ВО «Московский государственный медико-стоматологический университет им. А.И. Евдокимова» Министерства здравоохранения Российской Федерации.
Контактная информация: igormaev@rambler.ru;
127473, г. Москва, ул. Делегатская, д. 20, стр. 1.
ORCID: https://orcid.org/0000-0001-6114-564X

Козлов Роман Сергеевич — доктор медицинских наук, профессор, член-корреспондент РАН, ректор ФГБОУ ВО «Смоленский государственный медицинский университет», директор Научно-исследовательского института антимикробной химиотерапии «Смоленского государственного медицинского университета», президент Межрегиональной ассоциации по клинической микробиологии и антимикробной химиотерапии (МАКМАХ).
Контактная информация: Roman.Kozlov@antibiotic.ru;
214019, г. Смоленск, ул. Крупской, д. 28.
ORCID: https://orcid.org/0000-0001-8728-1113

Ливзан Мария Анатольевна — д.м.н., профессор, член-корр. РАН, заведующая кафедрой факультетской терапии и гастроэнтерологии, ректор ФГБОУ ВО «Омский государственный медицинский университет» Министерства здравоохранения Российской Федерации, главный внештатный специалист-терапевт СФО Министерства здравоохранения Российской Федерации.
Контактная информация: mlivzan@yandex.ru;
644099, г. Омск, ул. Ленина, д. 12.
ORCID: https://orcid.org/0000-0002-6581-7017
SCOPUS Author ID: 24341682600

Sayar R. Abdulkhakov — Cand. Sci. (Med.), Head of the Chair of Internal Diseases, Institute of Fundamental Medicine and Biology, Kazan Federal University; Assoc. Prof., Department (Chair) of Outpatient Therapy and General Medical Practice, Kazan State Medical University.
Contact information: sayarabdul@yandex.ru;
420012, Kazan, Kremlyovskaya str., 18.
ORCID: https://orcid.org/0000-0001-9542-3580

Абдулхаков Сайяр Рустамович — кандидат медицинских наук, заведующий кафедрой внутренних болезней Института фундаментальной медицины и биологии ФГАОУ ВО «Казанский (Приволжский) федеральный университет» Министерства здравоохранения Российской Федерации; доцент кафедры поликлинической терапии и общей врачебной практики ФГБОУ ВО «Казанский государственный медицинский университет» Министерства здравоохранения Российской Федерации.
Контактная информация: sayarabdul@yandex.ru;
420012, Казань, ул. Кремлевская, д. 18.
ORCID: https://orcid.org/0000-0001-9542-3580

Olga P. Alekseeva — Dr. Sci. (Med.), Prof., Chair of Hospital Therapy and General Practice named after V.G. Vogralik, Privolzhsky Research Medical University.
Contact information: al_op@mail.ru;
603005, Nizhny Novgorod, Minina i Pozharskogo sq., 10/1.
ORCID: https://orcid.org/0000-0002-1475-6584

Алексеева Ольга Поликарповна — доктор медицинских наук, профессор кафедры госпитальной терапии и общеврачебной практики им. В.Г. Вогралика ФГБОУ ВО «Приволжский исследовательский медицинский университет» Министерства здравоохранения Российской Федерации.
Контактная информация: al_op@mail.ru;
603005, г. Нижний Новгород, пл. Минина и Пожарского, д. 10/1.
ORCID: https://orcid.org/0000-0002-1475-6584

Sergey A. Alekseenko — Dr. Sci. (Med.), Head of the Department of Hospital Therapy, Far-Eastern State Medical University, Ministry of Health of the Russian Federation.
Contact information: sa.alexeenko@gmail.com;
680000, Khabarovsk, Muravyova-Amurskogo str., 35.
ORCID: https://orcid.org/0000-0003-1724-9980

Алексеенко Сергей Алексеевич — доктор медицинских наук, профессор, заведующий кафедрой госпитальной терапии ФГБОУ ВО «Дальневосточный государственный медицинский университет» Министерства здравоохранения Российской Федерации.
Контактная информация: sa.alexeenko@gmail.com;
680000, г. Хабаровск, ул. Муравьева-Амурского, д. 35.
ORCID: https://orcid.org/0000-0003-1724-9980

Dmitry S. Bordin — Dr. Sci. (Med.), Head of the Department of Pancreatic, Bile and Upper Gastrointestinal Pathology, Loginov Moscow Clinical Scientific Center; Prof., Department of Internal Medicine Propaedeutics and Gastroenterology, Moscow State University of Medicine and Dentistry; Prof., Department of general medical practice and family medicine, Tver State Medical University.
Contact information: d.bordin@mknc.ru;
111123, Moscow, Entuziastov highway, 86, bld. 6.
ORCID: https://orcid.org/0000-0003-2815-3992

Бордин Дмитрий Станиславович — доктор медицинских наук, заведующий отделом патологии поджелудочной железы, желчных путей и верхних отделов пищеварительного тракта ГБУЗ «Московский клинический научно-практический центр имени А.С. Логинова», профессор кафедры пропедевтики внутренних болезней и гастроэнтерологии ФГБОУ ВО «Московский государственный медико-стоматологический университет им. А.И. Евдокимова» Министерства здравоохранения Российской Федерации; профессор кафедры общей врачебной практики и семейной медицины ФПДО, ФГБОУ ВО «Тверской государственный медицинский университет» Министерства здравоохранения Российской Федерации.
Контактная информация: d.bordin@mknc.ru;
111123, г. Москва, шоссе Энтузиастов, д. 86, стр. 6.
ORCID: https://orcid.org/0000-0003-2815-3992

Natalya N. Dekhnich — Dr. Sci. (Med.), Prof., Department of Faculty Therapy; Smolensk State Medical University.
Contact information: n.dekhnich@mail.ru;
214019, Smolensk, Krupskoy str., 28.
ORCID: https://orcid.org/0000-0002-6144-3919

Дехнич Наталья Николаевна — доктор медицинских наук, профессор кафедры факультетской терапии; проректор по дополнительному профессиональному образованию и развитию регионального здравоохранения ФГБОУ ВО «Смоленский государственный медицинский университет» Министерства здравоохранения Российской Федерации.
Контактная информация: n.dekhnich@mail.ru;
214019, г. Смоленск, ул. Крупской, д. 28.
ORCID: https://orcid.org/0000-0002-6144-3919

Natalia V. Korochanskaya — Dr. Sci. (Med.), Head of the Gastroenterology Centre, Prof., Chair of Surgery No. 3, Kuban State Medical University; Chief Gastroenterologist of the Ministry of Health of the Krasnodar Territory.
Contact information: nvk-gastro@mail.ru;
350063, Krasnodar, Mitrofana Sedina str., 4.
ORCID: https://orcid.org/0000-0002-5538-9419

Tatiana L. Lapina — Cand. Sci. (Med), Assoc. Prof., Chair of Internal Diseases Propedeutics, Gastroenterology and Hepatology, I.M. Sechenov First Moscow State Medical University (Sechenov University).
Contact information: lapina_t_l@staff.sechenov.ru;
119435, Moscow, Pogodinskaya str., 1, bld. 1.
ORCID: https://orcid.org/ 0000-0003-4456-8725

Elena A. Poluektova — Dr. Sci. (Med.), Prof., Chair of Internal Disease Propaedeutics, Gastroenterology and Hepatology; Gastroenterologist, Department of Chronic Intestinal and Pancreatic Diseases, Vasilenko Clinic of Internal Disease Propaedeutics, Gastroenterology and Hepatology Sechenov First Moscow State Medical University (Sechenov University).
Contact information: poluektova_e_a@staff.sechenov.ru;
119991, Moscow, Pogodinskaya str., 1, bld. 1.
ORCID: https://orcid.org/0000-0003-1312-120X

Vladimir I. Simanenkov — Dr. Sci. (Med.), Prof., Chair of Internal Diseases, Clinical Pharmacology and Nephrology, I.I. Mechnikov North-West State Medical University.
Contact information: visimanenkov@mail.ru;
191015, St.-Petersburg, Kirochnaya str., 41.
ORCID: https://orcid.org/0000-0002-1956-0070

Aleksandr S. Trukhmanov — Dr. Sci. (Med.), Prof., Department of Internal Disease Propaedeutics, Sechenov First Moscow State Medical University (Sechenov University).
Contact information: trukhmanov_a_s@staff.sechenov.ru;
119435, Moscow, Pogodinskaya str., 1, bld. 1.
ORCID: https://orcid.org/0000-0003-3362-2968

Корочанская Наталья Всеволодовна — доктор медицинских наук, профессор кафедры хирургии № 3 ФПК и ППС ФГБОУ ВО «Кубанский государственный медицинский университет» Министерства здравоохранения Российской Федерации; главный гастроэнтеролог Министерства здравоохранения Краснодарского края.
Контактная информация: nvk-gastro@mail.ru;
350063, г. Краснодар, ул. Митрофана Седина, д. 4.
ORCID: https://orcid.org/0000-0002-5538-9418

Лапина Татьяна Львовна — кандидат медицинских наук, доцент кафедры пропедевтики внутренних болезней, гастроэнтерологии и гепатологии Института клинической медицины им. Н.В. Склифосовского ФГАОУ ВО «Первый Московский государственный медицинский университет им. И.М. Сеченова» (Сеченовский Университет) Министерства здравоохранения Российской Федерации.
Контактная информация: lapina_t_l@staff.sechenov.ru;
119991, г. Москва, ул. Погодинская, д. 1, стр. 1.
ORCID: https://orcid.org/0000-0003-4456-8725

Полуэктова Елена Александровна — доктор медицинских наук, профессор кафедры пропедевтики внутренних болезней, гастроэнтерологии и гепатологии Института клинической медицины им. Н.В. Склифосовского; врач-гастроэнтеролог отделения хронических заболеваний кишечника и поджелудочной железы клиники пропедевтики внутренних болезней, гастроэнтерологии и гепатологии им. В.Х. Василенко ФГАОУ ВО «Первый Московский государственный медицинский университет им. И.М. Сеченова» (Сеченовский Университет) Министерства здравоохранения Российской Федерации.
Контактная информация: poluektova_e_a@staff.sechenov.ru;
119991, г. Москва, ул. Погодинская, д. 1, стр. 1.
ORCID: https://orcid.org/0000-0003-1312-120X

Симаненков Владимир Ильич — доктор медицинских наук, профессор кафедры внутренних болезней, клинической фармакологии и нефрологии ФБГОУ ВО «Северо-Западный государственный медицинский университет им. И.И. Мечникова» Министерства здравоохранения Российской Федерации.
Контактная информация: visimanenkov@mail.ru;
191015, г. Санкт-Петербург, ул. Кирочная, д. 41.
ORCID: https://orcid.org/0000-0002-1956-0070

Трухманов Александр Сергеевич — доктор медицинских наук, профессор кафедры пропедевтики внутренних болезней, гастроэнтерологии и гепатологии ФГАОУ ВО «Первый Московский государственный медицинский университет им. И.М. Сеченова» (Сеченовский Университет) Министерства здравоохранения Российской Федерации.
Контактная информация: trukhmanov_a_s@staff.sechenov.ru;
119435, г. Москва, ул. Погодинская, д. 1, стр. 1.
ORCID: https://orcid.org/0000-0003-3362-2968

Igor B. Khlynov — Dr. Sci. (Med.), Assoc. Prof., Chair of Intermediate Therapy and Geriatrics, Ural State Medical University.
Contact information: hlinov.doc@yandex.ru;
620028, Ekaterinburg, Repina str., 3.
ORCID: https://orcid.org/0000-0002-0944-9811

Хлынов Игорь Борисович — доктор медицинских наук, доцент кафедры факультетской терапии и гериатрии ФГБОУ ВО «Уральский государственный медицинский университет» Министерства здравоохранения Российской Федерации.
Контактная информация: hlinov.doc@yandex.ru;
620028, г. Екатеринбург, ул. Репина, д. 3.
ORCID: https://orcid.org/0000-0002-0944-9811

Vladislav V. Tsukanov — Dr. Sci. (Med.), Prof., Head of the Clinical Department of Adult and Infant Digestive Pathology, Research Institute for Medical Problems in the North — Division of Krasnoyarsk Scientific Centre of the Siberian Branch of the RAS.
Contact information: gastro@impn.ru;
660022, Krasnoyarsk, Partizana Zheleznyaka str., 3G.
ORCID: https://orcid.org/0000-0002-9980-2294

Цуканов Владислав Владимирович — профессор, доктор медицинских наук, заведующий Клиническим отделением патологии пищеварительной системы у взрослых и детей ФБГНУ «Федеральный исследовательский центр "Красноярский научный центр Сибирского отделения Российской академии наук"», обособленное подразделение НИИ медицинских проблем Севера.
Контактная информация: gastro@impn.ru;
660022, г. Красноярск, ул. Партизана Железняка, д. 3г.
ORCID: https://orcid.org/0000-0002-9980-2294

Arkadiy A. Sheptulin — Dr. Sci. (Med.), Prof., Chair of Internal Diseases Propedeutics, Gastroenterology and Hepatology, Sklifosovsky Institute of Clinical Medicine, I.M. Sechenov First Moscow State Medical University (Sechenov University).
Contact information: sheptulin_a_a@staff.sechenov.ru;
119435, Moscow, Pogodinskaya str., 1, bld. 1.
ORCID: https://orcid.org/0000-0002-1395-9566

Шептулин Аркадий Александрович — доктор медицинских наук, профессор кафедры пропедевтики внутренних болезней, гастроэнтерологии и гепатологии Института клинической медицины им. Н.В. Склифосовского ФГАОУ ВО «Первый Московский государственный университет им. И.М. Сеченова» (Сеченовский Университет) Министерства здравоохранения Российской Федерации.
Контактная информации: sheptulin_a_a@staff.sechenov.ru;
119435, г. Москва, ул. Погодинская ул., д. 1, стр. 1.
ORCID: https://orcid.org/0000-0002-1395-9566

Submitted: 12.12.2022 Accepted: 26.12.2022 Published: 30.12.2022
Поступила: 12.12.2022 Принята: 26.12.2022 Опубликована: 30.12.2022