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Practical Recommendation of the Scientific Community for Human Microbiome Research (CHMR) and the Russian Gastroenterological Association (RGA) on Small Intestinal Bacterial Overgrowth in Adults

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Aim. To optimize the choice of treatment strategies by physicians and gastroenterologists to improve treatment and prevention of small intestinal bacterial overgrowth (SIBO) in adults.
Key points. SIBO is a condition characterized by an increased amount and/or abnormal composition of the microbiota in the small intestine. Clinically, the syndrome is manifested by nonspecific gastroenterological complaints and the development of malabsorption syndrome. Most often, SIBO is associated with various chronic non- infectious diseases (both diseases of the gastrointestinal tract, and the cardiovascular system and the neuromuscular apparatus) and can affect the severity of their symptoms. Specific methods for diagnosing SIBO are the culture method and breath tests. The main approaches to the treatment of SIBO include the elimination of the underlying cause of its occurrence, the use of antibacterial drugs and adherence to dietary recommendations (elemental diet).
Conclusion. Small intestinal bacterial overgrowth is common in patients with various diseases, but has non-specific manifestations, so proper diagnosis of this condition is required. SIBO therapy involves prescription of antibacterial agents, the most studied of which is the non-absorbable antibiotic rifaximin-α.
Keywords: small intestinal bacterial overgrowth, microbiota, breath testing, rifaximin-α
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Практические рекомендации Научного сообщества по содействию клиническому изучению микробиома человека (НСОИМ) и Российской гастроэнтерологической ассоциации (РГА) по диагностике и лечению синдрома избыточного бактериального роста у взрослых

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Цель публикации. Оптимизировать выбор лечебной тактики врачей первичного звена здравоохранения, терапевтов и гастроэнтерологов для улучшения результатов лечения и профилактики синдрома избыточного бактериального роста (СИБР) у взрослых.

Основные положения. СИБР представляет собой состояние, характеризующееся повышенным количеством и/или нарушением состава микробиоты в тонкой кишке. Клинически синдром проявляется неспецифическими гастроэнтерологическими жалобами и развитием синдрома мальабсорбции. Чаще всего СИБР ассоциирован с различными хроническими неинфекционными заболеваниями (как заболеваниями желудочно-кишечного тракта, так и сердечно-сосудистой системы и нервно-мышечного аппарата) и может оказывать влияние на выраженность их симптомов. Специфическими методами диагностики СИБР являются культуральный метод и дыхательные тесты. Основные подходы к лечению СИБР включают устранение основной причины его возникновения, прием антибактериальных препаратов и соблюдение диетических рекомендаций (элементарной диеты).

Вывод. Синдром избыточного бактериального роста часто встречается у пациентов с различными заболеваниями, однако характеризуется неспецифическими проявлениями, что делает актуальным стандартизацию диагностики данного состояния. Терапия СИБР подразумевает назначение антибактериальных средств, наиболее изученным из которых является невсасывающийся антибиотик рифаксимин-α.

Ключевые слова: синдром избыточного бактериального роста, микробиота, дыхательный тест, рифаксимин-α

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1. Definition

Small intestinal bacterial overgrowth (SIBO) refers to a condition in which there is an excess and/or imbalance of the small intestinal microbiota manifested by digestive disorders and malabsorption [1].

2. ICD-10 code

The ICD-10 does not classify SIBO as an individual disease. According to Order of the Ministry of Health of Russia No. 231, dated 9 June 2003, on approval of the industry standard "Patient management protocol. Intestinal dysbacteriosis", the code **R19.8** *"Other specified symptoms and signs involving the digestive system and abdomen"* was proposed to indicate changes in qualitative and quantitative composition of the gut microbiota [2]. The order outlines the concepts of clinical and laboratory syndrome associated with changes in qualitative and/or quantitative composition of the gut microbiota followed by metabolic and immunological disorders with the possible development of gastrointestinal disorders, defined by outdated term "dysbacteriosis". However, this definition is also true for SIBO, which holds the relevance of the proposed ICD-10 code.

3. Epidemiology

The prevalence of SIBO among the general population is poorly studied. SIBO predominantly occurs in women (66 %), and its incidence increases with age (presumably due to the accumulation of risk factors) [3, 4]. SIBO has been reported to be present in 0–20 % of healthy individuals, however, this condition is more common among patients with chronic non-infectious diseases (Table 1) [5].

4. Pathogenesis

Normal autochthonous microbiota of the gastrointestinal tract is an important component of well-being of a healthy person. Bacteria in small and large intestinal microbiota contribute to host defense against pathogens, support immune response regulation, affect nutrient metabolism, and synthesize a number of essential metabolites and vitamins (e.g., short-chain fatty acids, secondary bile acids, B vitamins and vitamin K) [12].

The small intestinal microbiota comprises mainly bacteria of Bacteroidetes and Firmicutes phyla, and, to a lesser extent, bacteria of *Actinobacteria*, *Fusobacteria, Verrucomicrobia*, *Proteobacteria* and *Cyanobacteria* phyla [1, 13]. The microflora of the small intestine parts (duodenum, jejunum, and ileum) differs in the ratio of microbial species, mainly belonging to Firmicutes phylum. This is due to changes in the microbial cell surviving conditions which occur with progression from the proximal intestine to the distal intestine. Thus, the microbiota of duodenum and proximal jejunum is composed mainly of gram-positive aerobic bacteria. Their excessive proliferation is suppressed by aggressive upper GIT environment, including:

- high partial pressure of oxygen;
- bactericidal activity of primary bile acids;
- activity of digestive enzymes and hydrochloric acid;
- propulsive peristalsis;
- low acid-base balance (pH).

The activity of restraining factors weakens in the distal jejunum and in the ileum, thus creating more favorable conditions for bacterial proliferation: their number is $10–10^3$ CFU/mL in the duodenum, $10^4–10^7$ CFU/mL in the jejunum, and $10^3–10^7$ CFU/mL in the ileum. A gradual decrease in the partial pressure of oxygen shifts the bacterial load in favor of gram-negative obligate and facultative anaerobes [13]. However, the number of Paneth cells providing antibacterial protection increases in the small intestine mucosa as it progresses to the colon. Microbial antigens (lipopolysaccharides, lipid A, peptidoglycans, flagella, bacterial DNA or RNA) sensitize Paneth cells, which in response release broad-spectrum antimicrobial peptides, such as cathelicidin, defensins, phospholipase A2, C-type lectin and others [14]. Sensitization of Paneth cells belonging to innate (congenital) immunity indirectly activates the local adaptive (acquired) immune response. Manifestations of the adaptive immune response include synthesis of immunoglobulins A (IgA) by plasma cells and differentiation of $CD4^+$ lymphocytes into type 17 T-helper lymphocytes (Th17), which synthesize interleukins (IL) 17A, 17F, 21, and 22. Interleukins IL-17A and IL-17F stimulate innate immune cells and epithelial cells to produce IL-1, IL-6, and IL-8, which contribute to proinflammatory immune response by increasing neutrophil proliferation and activity. Interleukin 21 supports the activity of natural killers (NK cells) and cytotoxic T cells, whereas IL-22 provides pre-epithelial protection of the mucosal barrier by increasing the production of antimicrobial peptides in the mucosa: lipocalin-2, C-type lectin and calprotectin precursors (Fig. 1) [15–19].

Thus, under normal conditions, the local innate and adaptive immune responses carry out immune-mediated clearance of bacterial overgrowth in the distal small intestine, but no systemic inflammatory response is induced [13, 14].

An excessive bacterial load of the small intestine is formed mainly by gram-negative aerobes and anaerobes, among which members of *Escherichia*, *Enterococcus* spp., *Klebsiella* and *Proteus* phyla

Table 1. Prevalence of SIBO among patients with various diseases and conditions

Disease	Prevalence
Gastroenterology profile diseases	
Chronic pancreatitis	34–92 %
Crohn's disease	25–88 %
Ulcerative colitis	81 %
GIT functional diseases (irritable bowel syndrome, functional dyspepsia, etc.)	4–78 %
Celiac disease	9–67 %
Liver cirrhosis	34.8–47.1 % [6]
Cardiovascular diseases	
Chronic heart failure	45 % [7]
Paroxysmal ventricular tachycardia in CHF	80 % [8]
Respiratory diseases	
Bronchial asthma (allergic)	67 % [9]
Bronchial asthma (non-allergic)	43 % [9]
Endocrine and metabolic diseases	
Hyperlipidemia	78.9 % [10]
Hypothyroidism (decompensated)	54 %
Type 1 and type 2 diabetes mellitus (complicated with autonomic neuropathy)	8–44 %
Obesity	17–41 %
Nervous and muscular diseases	
Fibromyalgia	93 %
Muscular dystrophy	65 %
Parkinson's disease	54 %
Gastric surgery	
Bilateral truncal vagotomy	93 %
Roux-en-Y reconstruction	86 %
Gastrectomy	63–78 %
Intestinal and pelvic surgery	
Resection of ileocecal valve, small and large bowel limited resections	32–82 %
Other iatrogenic conditions	
Long-term use of proton pump inhibitors (PPIs)*	26–75 %
Parenteral nutrition (over the year)	70 %
Radiation enteropathy	6 %
Other diseases and conditions	
Chronic fatigue syndrome	81 %
Systemic sclerosis and other connective tissue diseases	43–55 %
Alcohol abuse	47.4 % [11]
Immunodeficiency (congenital and acquired)	30–50 %
Rosacea	46 %
End-stage renal failure	36 %

Note.* certain drugs, doses and duration of PPIs administration are not established.

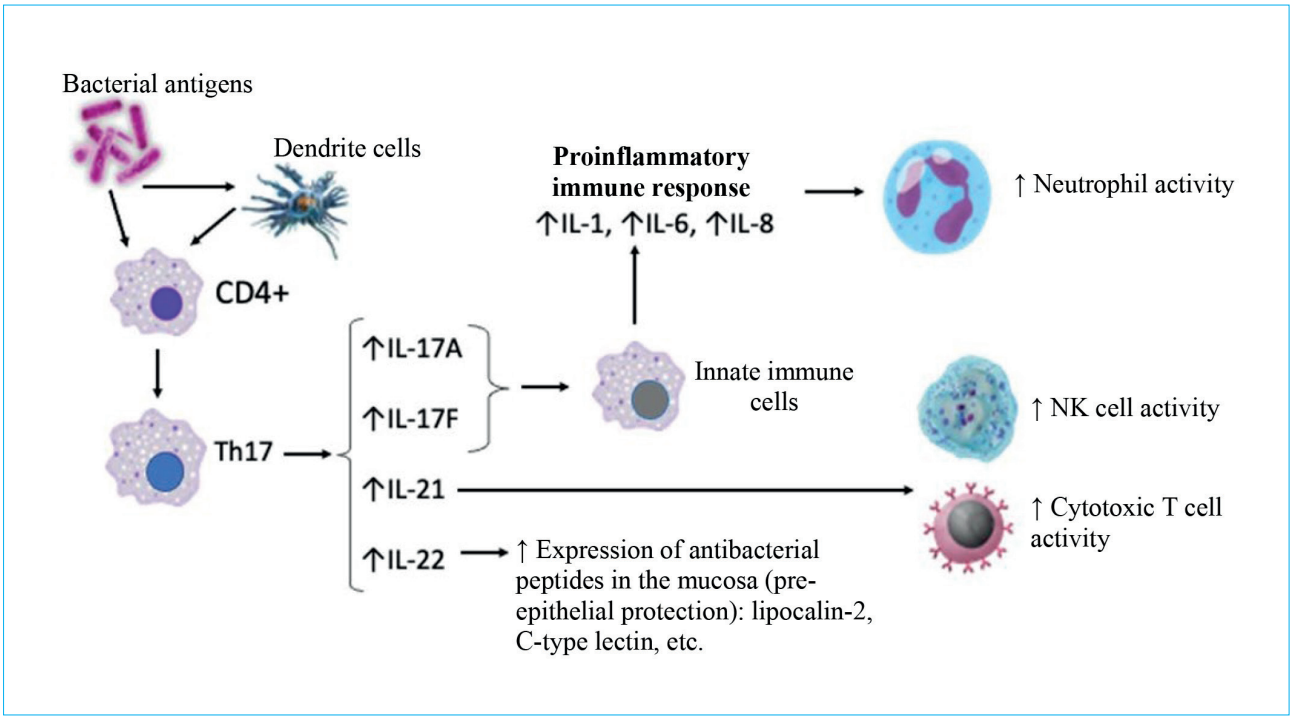

Fig. 1. Mechanisms of bacterial overgrowth clearance in the small intestine by adaptive immune response

are detected more often [20]. Culturing of jejunal aspirate (MacConkey agar) from SIBO patients has identified 141 strains of facultative (*Streptococcus* 60 %, *Escherichia coli* 36 %, *Staphylococcus* 13 %, *Klebsiella* 11 %, etc.) and 117 strains of obligate anaerobes (*Bacteroides* 39 %, *Lactobacillus* 25 %, *Clostridium* 20 %, etc.), but the key bacteria causing SIBO clinical manifestations have not been identified [21]. More specific changes were found in SIBO patients by sequencing of bacterial 16S RNA from jejunal aspirate, in which bacterial overgrowth was detected by culturing on blood agar and MacConkey agar. Compared to healthy volunteers, an increase in the number of *Proteobacteria* species (4.31-fold) and a decrease in the proportion of *Firmicutes* bacteria (1.64-fold) were found in the small intestinal aspirate of SIBO patients, which was also associated with a decrease in microbial α-diversity. In addition, a direct correlation was found between the abundance of the family *Enterobacteriaceae* (class *Gammaproteobacteria*) and the severity of abdominal bloating, as well as between the increased number of the family *Aeromonadaceae* members and the incidence of fecal urgency [22]. Methanogenic archaea, such as *Methanosphaera stadtmaniae* and *Methanobrevibacter smithii*, may be the only microorganisms creating an excessive microbial abundance [23]. Presumably, 15 % to 30 % of SIBO patients are colonized specifically by *Methanobrevibacter* [24, 25].

The pathogenetic mechanisms of SIBO effects on the host are not completely studied. However, it has been found to alter significantly the metabolic and immunological processes in the small intestine:

- active carbohydrate breakdown results in an excess of bacterial metabolic products (e.g., H_2, CH_4, H_2S, CO_2) that cause visceral hypersensitivity, abdominal bloating, and diarrhea [25] (the resulting hydrogen sulfide has an additional direct damaging effect on enterocytes and also stimulates a proinflammatory response by activating the nuclear transcription factor NFkb [26]);
- the amount of produced methane increases (notably with methanogenic archaea overgrowth, which are considered by most authors to be the main producers of methane), which results in slower motility of the large intestine and subsequent increase in the severity of abdominal bloating [27];
- the permeability of the mucosal epithelial barrier of the small intestine increases due to the activation of low-grade inflammation by secondary bile acids (mainly lithocholic acid) and by-products of fatty acid metabolism [28];
- secondary disaccharidase deficiency occurs due to disruption of the brush border of enterocytes, resulting in maldigestion and malabsorption of monosaccharides [28];
- microbial breakdown of amino acids and low-molecular-weight proteins intensifies leading to malabsorption [28];

• fat and fat-soluble vitamins absorption reduces as a result of excessive deconjugation of bile acid salts, which also contributes to malabsorption [29];

• there is an increasing competition between the host and small intestinal microbiota for vitamins B1, B2, B3, B5, and B12 (due to increased number of bacteria utilizing these vitamins) [11, 30, 31];

• there is an increased proportion of toxic metabolites synthesized by bacteria (ammonia, D-lactate, and bacterial peptidoglycans [28]), which results in impaired permeability of the epithelial barrier and increased bacterial translocation [32];

• there is an enhanced intensity of the local and systemic immune response due to the increased amount of proinflammatory cytokines (IL-1a, IL-1b, IL-6 and tumor necrosis factor alpha TNF-α) [33].

The above mechanisms lead to the development of symptoms such as bloating or abdominal pain, diarrhea or constipation, and the manifestation of malabsorption. The bacterial content in the small intestine does not always correlate with disease activity. It is supposed that prominent clinical manifestations occur only when invasive bacterial strains are overgrown [34].

5. Risk factors

Risk factors for bacterial overgrowth include conditions or diseases that impair bacterial elimination in the small intestine or create favorable conditions for bacterial proliferation. These include:

- small and large intestine dysmotility (in IBS [35], altered intestinal anatomy after surgery [36], systemic sclerosis [37], hypothyroidism [38], autonomic diabetic neuropathy [39], opiate use [40], ileocecal valve dysfunction [41], etc.);
- small intestinal hypochlorhydria (with long-term use of PPIs, atrophic gastritis, gastric resection [42], gastroparesis [43], etc.);
- inflammation in the small and large intestine (in ulcerative colitis, Crohn's disease, radiation enteritis [35]);
- immunodeficiency (congenital, acquired, selective IgA immunodeficiency [28, 44]);
- decreased amounts of primary bile acids (e.g., in cholestasis [45]);
- maldigestion or malabsorption (in pancreatic exocrine insufficiency [40, 46], celiac disease [47], etc.).

6. Clinical presentation

Most SIBO patients complain of abdominal pain without clear localization, diarrhea and bloating, but the prevalence of these symptoms cannot be assessed [27]. SIBO can also be diagnosed in patients with constipation complaints due to the abundance of methanogenic microorganisms in these patients (e.g., bacterial overgrowth is detected in 22.5–25.2 % of those with IBS with constipation) [23]. The above complaints occur in more than 2/3 of SIBO patients, and the rest of the patients experience symptoms characteristic of the disease complications, or have no complaints [36].

SIBO complications include various manifestations of malabsorption, including steatorrhea, weight loss and weakness, as well as neurological disorders (when absorption of B vitamins is impaired) and various symptoms associated with hypovitaminosis of fat-soluble vitamins A, D3, E (vitamin K deficiency is usually not observed in SIBO) [48].

SIBO may affect the severity of symptoms of other diseases, presumably by enhancing the non-specific proinflammatory immune response. Thus, SIBO treatment in patients with rosacea [49], liver cirrhosis [50], and chronic heart failure [6] significantly improves their well-being and short-term prognosis. It is difficult to suspect SIBO in these patients, particularly when they do not have the mentioned complaints.

When questioning a patient, it is essential to consider the patient's medical history, as a history of GIT surgeries and chronic non-infectious diseases associated with SIBO allow to suspect this condition.

Physical examination of SIBO patients most commonly reveals moderate pain in different parts of the abdomen upon palpation, pronounced tympanic sound upon abdominal percussion, and irregular weakening of intestinal peristalsis upon auscultation. If avitaminosis develops, corresponding changes in the skin, nails, hair and tongue may be found (due to fat-soluble vitamins and B vitamins deficiency).

7. Laboratory and instrumental diagnostics

7.1. Laboratory diagnostic tests

No specific deviations in routine laboratory blood and fecal tests are typical of SIBO. Non-specific parameter changes are identical to those in malabsorption, but they are expressed insignificantly in most cases.

7.2. Instrumental tests

The specific diagnosis of SIBO presents two main methods: culture method **(LE 1, GR B)** and breath tests **(LE 1, GR B)** [51]. The assessment criteria for grades of recommendations and levels of evidence for diagnostic methods are shown in Table 2 and Table 3 [61]. Both methods have their advantages and disadvantages.

Table 2. Grades of Recommendation (GR) Assessment Score for methods of prevention, diagnosis, treatment, medical rehabilitation, including those based on the use of natural healing factors (preventive, diagnostic, therapeutic, rehabilitation interventions)

Level	Interpretation
A	Strong recommendation (all considered efficacy criteria (outcomes) are important, all studies are of high or satisfactory methodological quality, and their conclusions on the outcomes of interest are consistent)
B	Conditional recommendation (not all considered efficacy criteria (outcomes) are important, not all studies are of high or satisfactory methodological quality, and/or their conclusions on the outcomes of interest are not consistent)
C	Weak recommendation (all considered efficacy criteria (outcomes) are unimportant, all studies are of poor methodological quality, and their conclusions on the outcomes of interest are inconsistent).

Table 3. Levels of Evidence (LE) Assessment Score for diagnostic methods (diagnostic interventions)

LE	Interpretation
1	Systematic reviews of reference-controlled studies or a systematic review of randomized clinical studies using meta-analysis
2	Individual reference-controlled studies or individual randomized clinical studies and systematic reviews of studies of any design, except for randomized clinical studies, using meta-analysis
3	Studies without consecutive reference control or studies with a reference method that is not independent of the study method or non-randomized comparative studies, including cohort studies
4	Non-comparative studies, clinical case report
5	There is only a rationale for the mode of action or expert opinion

7.2.1. Culture method

This method implies culturing small intestine aspirate on media with subsequent CFU counting.

It has been conventionally suggested that the microbial composition of the small intestine is considered excessive when ≥ 1×10^5 CFU per milliliter of aspirate is detected. However, this insight was based on early studies involving patients with the blind loop syndrome and did not consider the microflora of patients with preserved intestinal anatomical continuity. Subsequent systematic reviews have demonstrated the low validity of this criterion, so the current threshold value for overgrowth in SIBO is ≥ 1×10^3 CFU per mL of mucosal surface aspirate [51].

Aspiration of small intestinal contents is carried out with an endoscope, which is used to take 3–5 mL of duodenal or at least 2 mL of jejunal fluid. The aspirate is cultured on agar media (blood or chocolate agar, MacConkey agar) or on whole blood in anaerobic conditions at 37 °C for 5 days, after which CFU is calculated. If necessary, the microbial composition can be identified and antibiotic susceptibility can be determined by routine microbiological methods [24, 36]. The culture testing procedure does not require special approaches or preparation, but there are some difficulties:

- sterile aspiration of the small intestinal contents must meet strict standards in order to avoid microbiota contamination in the upper GIT (an endoscope equipped with a catheter can greatly simplify this task) [52];
- it is difficult to determine the optimal site wit in the small intestine for content sampling [53];
- the sampled surface contents are to be immediately transferred to a microbiological laboratory in order to ensure the survival of bacterial cells for subsequent culturing [54];
- SIBO diagnosis with culture of the small intestinal contents is a time-consuming, expensive and invasive procedure that is associated with common endoscopic risks, so the method is difficult to perform in routine clinical practice.

Despite its limitations, the culture method is conventionally considered to be the gold standard for SIBO verification [24, 54].

7.2.2. Breath tests

The concept of breath tests (BTs) is to determine the amount of hydrogen and/or methane in the exhaled air after a carbohydrate load. The human body is not capable of producing these metabolites, so they occur in exhaled air due to microbial fermentation of carbohydrates in the small and large intestine, followed by absorption into the blood and, after passing through the liver, their excretion by the lungs [55].

Table 4. Comparative analysis of substrates for breath testing

Substrate	Characteristics	Substrate amount and test duration	Positive result interpretation (growth threshold from the zero point)	Notes
Glucose	· Monosaccharide · Absorbed in the small intestine	· Glucose 50 g or 75 g and water 250 mL · 90–120 minutes	· ≥20 ppm for H_2* · ≥10 ppm for CH_4 · ≥15 ppm H_2 and CH_4	· Negative test excludes proximal but not distal SIBO · Not applicable for diabetic patients
Lactulose	· Disaccharide · Not absorbed · Reaches the large intestine · Also used to assess the orocecal transit time	· Lactulose 10 g (may be taken with a small amount of water) · 180–240 minutes	· ≥20 ppm for H_2 · ≥10 ppm for CH_4 · interval of 0–90 minutes**	· May accelerate motility yielding a false negative result · May cause abdominal bloating or diarrhea · Interpretation is difficult if a single growth peak is detected
Fructose	· Monosaccharide · Disaccharide · Absorbed in the distal small intestine · Applicable for diabetic patients	· Fructose 25 g and water 250 mL · 180 minutes	· ≥20 ppm for H_2 · ≥10 ppm for CH_4 · ≥15 ppm H_2 and CH_4	· Low evidence for interpretation of the results · Difficult to differentiate SIBO from fructose intolerance · Applicable for diabetic patients

Note: * – for glucose 50 g, an increase in H_2 ≥ 15 ppm indicates a positive result; ** – some authors verify a positive result only when there are two peaks of H_2 increase, which are in the small intestine (within the interval of 90 minutes) and in the large intestine (after 90 minutes).

It is reasonable to conduct BTs evaluating both hydrogen and methane levels **(LE 5, GR C)** [46]. BTs with methane level evaluation **(LE 1, GR B)** should be performed in patients with constipation symptoms [25, 56, 69].

The hydrogen or methane concentration in the air is determined in parts per million (ppm) using a gas chromatograph or a special gas analyzer equipped with electrochemical and/or infrared sensors. The air sampling is performed sequentially starting from a zero point (on an empty stomach, just before ingestion of carbohydrate substrate) with an interval of 15 minutes. The rise of metabolite concentration in the first 90 minutes reflects the enzymatic activity of the small intestinal microbiota, and over 90 minutes – of the large intestinal microbiota [25, 56].

Glucose, lactulose and fructose are the most commonly used carbohydrate loads for the breath test **(LE 2, GR B)** [51, 55]. Comparative analysis of BTs with these substrates and interpretation methods are presented in Table 4.

An example of metabolite level increase in a breath test is shown in Figure 2.

Compared with the culture method, the sensitivity of the glucose breath test (GBT) varies from 20 % to 93 %, with specificity ranging from 30 % to 86 %. For the lactulose breath test (LBT), these values are 31–68 % and 44–100 %, respectively [51, 55].

Preliminary preparation is required before BTs [56, 57]:

· *2–4 weeks before testing:* avoid antibiotics (including intravenous) and probiotics **(LE 5, GR C)**;

· *2 weeks before testing:* avoid endoscopic or surgical interventions that require large intestine preparation with laxatives **(LE 5, GR C)**;

· *1 week before testing:* eliminate medications that affect motility, such as metoclopramide or loperamide (some researchers recommend avoiding these medications 48 hours before the test) **(LE 5, GR C)**;

· *24 hours before testing:* not to consume alcohol and fibers (vegetables, fruits, cereals, grains) **(LE 5, GR C)**;

· *12 hours before testing:* fast (but drinking plain water is allowed) **(LE 5, GR C)**;

· *in the morning before testing:* avoid strenuous activity provoking hyperventilation (taking regular medications other than those listed above is allowed) **(LE 5, GR C)**, no smoking **(LE 4, GR C)** [70].

To reduce the variability of the recorded data when taking exhaled air, the patient should take a deep breath, hold it for 15 seconds, then slowly exhale approximately 50 % of the inhaled volume and only then exhale into the gas analyzer or into the

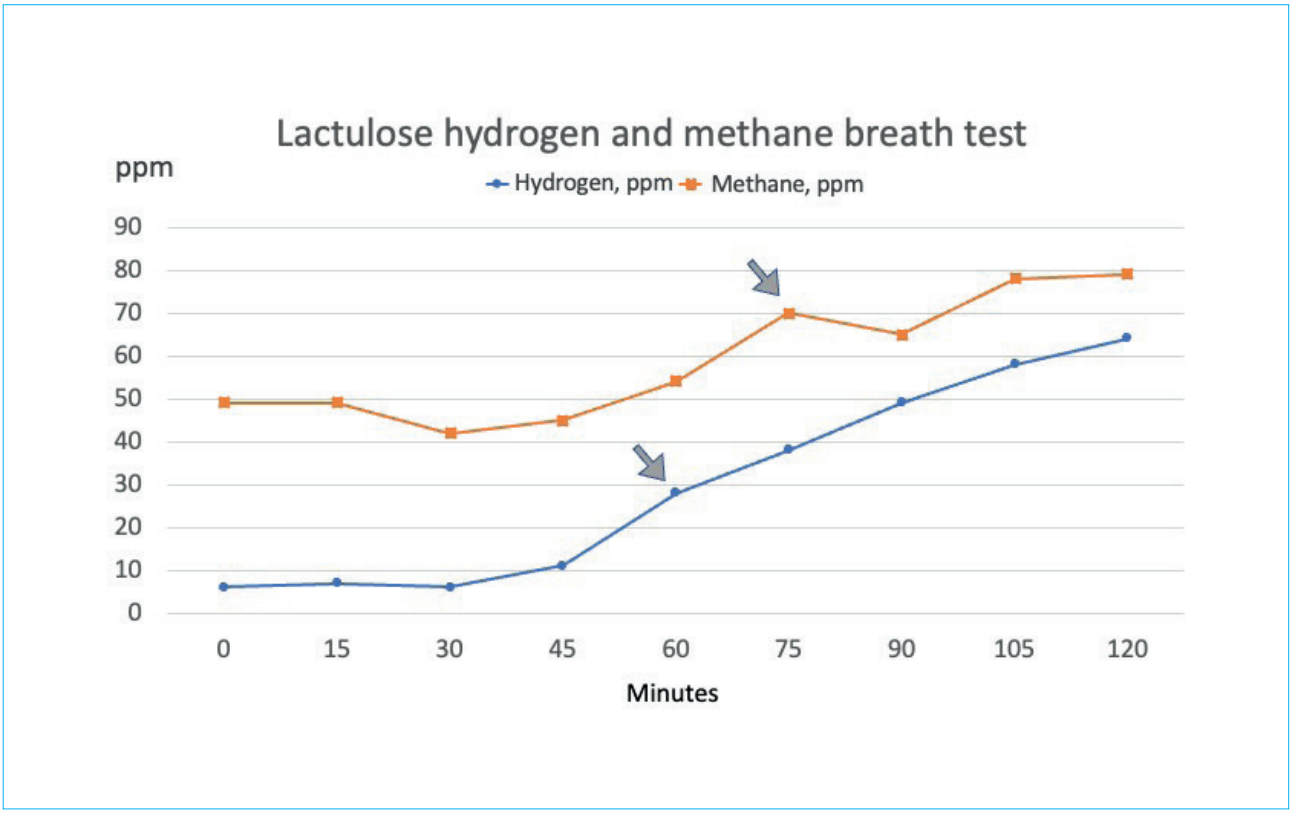

Fig. 2. Elevated hydrogen and methane levels in exhaled air at lactulose hydrogen and methane testing in a SIBO patient. Arrows indicate diagnostically significant peaks of metabolite level increase: hydrogen at the 60th minute (28 ppm, the baseline is 6 ppm) and methane at the 75th minute (70 ppm, the baseline is 49 ppm)

plastic bag for air sample collection. Such procedure allows reducing the impact of "dead" space (about 150–200 mL) and measuring a portion of alveolar air representing the concentration of the studied gas metabolites in the venous blood as much as possible [54, 57, 58].

The breath test is an inexpensive, non-invasive, simple, and widely available method for SIBO diagnosis. However, there are some disadvantages:

- low sensitivity and specificity compared to the culture method;
- the content of hydrogen and/or methane in exhaled air is directly influenced by the composition of the small intestinal microbiota, i.e. methanogenic archaea utilize H_2 to reduce CO_2 to CH_4, and sulfate-reducing bacteria utilize hydrogen to form H_2S [54];
- the composition of the microbiota causing microbial overgrowth is difficult to assess. There is evidence of a positive correlation between the levels of *Gammaproteobacteria* class and *Enterobacteriaceae* family members, the area under the curve for H_2 within the first 90 minutes of LBT, and the severity of abdominal bloating in SIBO [22];
- air analyzers capable of simultaneous assessment of hydrogen and methane concentrations are often more expensive.

7.2.3. Other diagnostic methods

Abdominal ultrasound (US) and esophagogastroduodenoscopy (EGDS) are not the methods of choice for SIBO diagnosis. Nevertheless, abdominal USI of SIBO patients in more than 84 % reveals increased gas and fluid in the lumen of the small intestine, subtle thickening of the jejunum walls and of the small intestine folds, as well as enhanced small intestinal peristalsis, which does not contradict the SIBO diagnosis [59]. EGDS in SIBO patients may show non-specific endoscopic findings such as mucosal edema, vascular depletion, patchy erythema, and mucosal erosions or ulcerations (in rare cases). Morphological changes in small intestinal biopsy specimens from these patients are also non-specific and may be represented by intraepithelial lymphocytosis, eosinophilia, flattened villi, or cryptitis [60].

Table 5. Levels of Evidence (LE) Assessment Score for methods of prevention, treatment, medical rehabilitation, including those based on the use of natural healing factors (preventive, therapeutic, rehabilitation interventions)

Level	Interpretation
1	A systematic review of randomized clinical studies using meta-analysis
2	Individual randomized clinical studies and systematic reviews of studies of any design, except for randomized clinical studies, using meta-analysis
3	Non-randomized comparative studies, including cohort studies
4	Non-comparative studies, clinical case or case series report, case-control study
5	There is only a rationale for the mode of action of the intervention (non-clinical studies) or an expert opinion

Table 6. Doses, duration of administration, and levels of evidence for efficacy of antibiotics recommended for SIBO eradication

Antibiotic	Doses	Duration of administration	Level of evidence for efficacy
Non-systemic antibiotics			
Rifaximin-α	400 mg thrice daily	7–14 days	1
Systemic antibiotics			
Norfloxacin	400 mg twice daily	7–10 days	2
Amoxicillin (in combination with clavulanic acid)	875 mg twice daily	7 days	3
Metronidazole	250 mg thrice daily	10 days	3
Tetracycline	250 mg 4 times daily	7 days	3
Ciprofloxacin	500 mg twice daily	5–10 days	3

8. Differential diagnosis

The differential diagnosis should be carried out between all diseases manifested by defecation disorders, bloating, symptoms of malabsorption and maldigestion **(LE 5, GR C)** [28].

SIBO symptoms often conceal the symptoms of those diseases that have caused it, which greatly complicates the diagnosis. This is partially due to the same clinical presentation of SIBO and its causes. For example, in a patient with chronic pancreatitis, it is difficult to determine whether diarrhea is caused by exocrine pancreatic insufficiency or SIBO, and which has a greater impact on the severity of the defecation disorder. Similarly, in patients with inflammatory bowel diseases following surgery, the abdominal pain, bloating and diarrhea may be either manifestations of SIBO or active inflammation, malabsorption, or peritoneal adhesions [54].

9. Treatment

The optimal treatment of SIBO includes elimination of the underlying cause, decontamination of bacterial overgrowth, and substitution therapy for malabsorption [55].

The assessment criteria for grades of recommendations and levels of evidence for treatment modalities are shown in Table 2 and Table 5 [61].

9.1. Antimicrobial therapy

Antimicrobial therapy is the preferred strategy for bacterial overgrowth eradication in the small intestine **(LE 1, GR B)** [55].

Studies of the efficacy of antibiotics (systemic drugs in particular) for SIBO vary in terms of subject populations, SIBO diagnostic approaches, dose, and duration of treatment. The lack of data on successful treatment of the underlying disease which has caused SIBO makes it difficult to assess the efficacy of therapy. The low level of methodological quality of the studies determines the **grade B** recommendations for antibiotic prescription (conditional recommendation) [56]. The main antibiotics used to treat SIBO are amoxicillin (along with clavulanic acid), doxycycline, metronidazole, norfloxacin, rifaximin-α, tetracycline, and ciprofloxacin (Table 6).

In a cross-over study, the effect of SIBO treatment with amoxicillin with clavulanic acid or norfloxacin was evaluated in 20 SIBO patients (the diagnosis confirmed by GBT). For 7 days, 10 patients received amoxicillin at a dose of 875 mg twice daily, and the same number of subjects received norfloxacin at a dose of 400 mg twice daily. A repeated breath test after therapy showed a negative result in 5 patients in the first group (50 %) and in 3 patients in the second group (30 %) [58].

There was a randomized, placebo-controlled study that evaluated the efficacy of treatment with norfloxacin at a dose of 400 mg twice daily for 10 days in 15 patients with IBS and SIBO detected by small intestine aspirate culturing. The norfloxacin effect was observed in all subjects who consented to SIBO reassessment (n = 4), and all untreated control group participants (n = 7) were again found to have bacterial overgrowth when reassessed [62].

Tetracycline administration in SIBO has been studied only in a single study involving 24 patients with SIBO evaluated before and after treatment by jejunal aspirate culturing. There was no bacterial overgrowth in 21 subjects (87.5 %) after administration of tetracycline at a total daily dose of 1000 mg for 7 days [56].

The effect of ciprofloxacin in SIBO eradication has been evaluated in 2 clinical studies. In one of them, administration of 500 mg of ciprofloxacin twice daily for 5 days was effective in 6 of 12 (50 %) patients with nonalcoholic steatohepatitis (GBT before and after therapy) [63]. The second study compared the outcomes of 10-day administration of ciprofloxacin (500 mg twice daily) or metronidazole (250 mg thrice daily) in 29 patients with Crohn's disease and SIBO (GBT before and after treatment). All 14 patients who received ciprofloxacin responded to therapy (100 %), whereas metronidazole administration was effective in 13 of 15 subjects (86 %) [64].

The non-absorbable antibiotic rifaximin-α is the most studied drug used for SIBO treatment. Its advantages over systemic antibiotics include low gastrointestinal absorption (less than 0.4 %), low incidence of systemic side effects, and low risk of antibiotic-resistant bacterial strains [65].

A systematic review and meta-analysis of 32 studies of rifaximin-α treatment for SIBO has shown its efficacy in 72.9 % of patients (95 % CI, 65.5–79.8). However, the studies included in the meta-analysis were notable for their wide range of doses (600–1600 mg per day) and duration of treatment (5–28 days). Nevertheless, the meta-analysis showed a dose-dependent effect of rifaximin-α on the success of SIBO eradication, with most studies dosing 400 mg thrice daily for 7–14 days. The drug is well tolerated, and the adverse events (AEs) such as weakness, headache, constipation, increased diarrhea, dizziness, sleep disorders, nausea, skin rash, dry skin (described by subjects as mild), anaphylaxis (1 case) and development of Clostridium difficile-associated disease (1 case) occurred in 4.6 % of 815 subjects in 17 studies reporting such events. Drug cessation due to AEs (nausea without vomiting, headache, dry skin) was reported in only one study, in which 5 out of 120 patients (6 % of subjects) discontinued the drug [65].

It should be noted that empiric antibiotic administration to patients without a confirmed SIBO diagnosis is not justified as it exposes them to an unreasonable risk of antibiotic resistance, antibiotic-associated diarrhea, and C. difficile-associated disease [1].

9.2. Elementary diet

An alternative approach to eliminating SIBO is an elementary diet based on the consumption of highly-digestible nutrients in liquid or powder form **(LE 4, GR C)** [66].

The elementary diet is liquid mixtures or powders to be diluted in liquids, consisting of highly-digestible proteins, amino acids, fats and carbohydrates, enriched with vitamins. These nutrients are mainly absorbed in the proximal small intestine limiting their delivery to bacteria in the distal part. In a retrospective review, an elementary diet for 14 days in 74 of 93 patients (80 %) with SIBO resulted in normalization of their lactulose breath test score, which was accompanied with stool frequency normalization in 12 of 14 patients with diarrhea and in 9 of 12 patients with symptoms of constipation. However, this diet is difficult to follow due to its unpleasant taste and necessity of substantial patient motivation [66].

A diet containing low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (Low-FODMAP) reduces exposure of substrates undergoing bacterial metabolism in the small intestine, which is effective in reducing the severity of similar symptoms in patients with diarrhea-predominant IBS [67]. This type of diet is also supposed to suppress microbial overgrowth in the small intestine, however, no convincing data are available.

10. Prophylaxis

There is no specific prophylaxis for SIBO. Forty-four percent of SIBO patients experience symptom recurrence within 9 months after antibacterial treatment, which is probably due to ineffective treatment of the underlying disease [68]. To achieve effective eradication in SIBO patients with a recurrent course of the disease, a targeted antimicrobial therapy based on identification of provocative microorganisms and their

antibiotic susceptibility determination by culturing the small intestinal surface content is feasible [56, 68].

11. Conclusions

SIBO results from impaired bacterial clearance in the small intestine and is closely associated with different diseases. The clinical presentation of SIBO is non-specific, so a proper diagnosis based on the culture method or breath tests is required to confirm the diagnosis. SIBO therapy involves prescription of antibacterial agents, the most studied of which is the non-absorbable antibiotic rifaximin-α. These Recommendations are prepared to optimize the choice of diagnostic and treatment strategies for adult SIBO patients. Key points of the CHMR and RGA best practices on small intestinal bacterial overgrowth in adults are shown in Table 7.

Table 7. Key points of the CHMR and RGA best practices on small intestinal bacterial overgrowth in adults

Statement	LE	GR
Diagnosis		
Specific methods for SIBO diagnosis are the culture method and breath tests	1	B
It is reasonable to perform a breath test with simultaneous evaluation of hydrogen and methane levels for SIBO diagnosis	5	C
A breath test with methane level evaluation is diagnostically significant in patients with symptoms of constipation	1	B
Glucose, lactulose or fructose are used as a carbohydrate load for the breath test	2	B
The differential diagnosis should be carried out between all diseases manifested by defecation disorders, bloating, symptoms of malabsorption and maldigestion	5	C
Preparation before breath testing		
One should avoid use of antibiotics (including intravenous) and probiotics for 4 weeks	5	C
One should refrain from endoscopic or surgical interventions that require large intestine preparation with laxatives for 2 weeks	5	C
It is recommended to exclude drugs affecting the intestinal motility for 7 days	5	C
One should refrain from consuming alcohol and fiber-rich foods for 24 hours	5	C
It is necessary to fast for 12 hours before the test (but drinking plain water is allowed)	5	C
One should avoid strenuous activity provoking hyperventilation on the test day	5	C
One should refrain from smoking immediately before the test	4	C
Treatment		
Administration of antibacterial drugs is the preferential strategy for bacterial overgrowth eradication	1	B
The non-absorbable antibiotic rifaximin-α is the most effective antibacterial drug for SIBO treatment	1	B
An elementary diet for at least 14 days may be recommended to eradicate bacterial overgrowth	4	C

References / Литература

1. *Achufusi T.G.O., Sharma A., Zamora E.A., Manocha D.* Small Intestinal Bacterial Overgrowth: Comprehensive Review of Diagnosis, Prevention, and Treatment Methods. *Cureus.* 2020;12(6):e8860. DOI: 10.7759/cureus.8860
2. Министерство Здравоохранения Российской Федерации. Приказ 9 июня 2003 г. № 231 «Об утверждении отраслевого стандарта "Протокол ведения больных. Дисбактериоз кишечника"». https://docs.cntd.ru/document/901869098
3. *Choung R.S., Ruff K.C., Malhotra A., Herrick L., Locke G.R. 3rd, Harmsen W.S., Zinsmeister A.R., Talley N.J., Saito Y.A.* Clinical predictors of small intestinal bacterial overgrowth by duodenal aspirate culture. *Aliment Pharmacol Ther.* 2011;33(9):1059–67. DOI: 10.1111/j.1365-2036.2011.04625.x
4. *Erdogan A., Rao S.S., Gulley D., Jacobs C., Lee Y.Y., Badger C.* Small intestinal bacterial overgrowth: duodenal aspiration vs glucose breath test. *Neurogastroenterol Motil.* 2015;27(4):481–9. DOI: 10.1111/nmo.12516
5. *Grace E., Shaw C., Whelan K., Andreyev H.J.* Review article: small intestinal bacterial overgrowth-prevalence, clinical features, current and developing diagnostic tests, and treatment. *Aliment Pharmacol Ther.* 2013;38(7):674–88. DOI: 10.1111/apt.12456
6. *Maslennikov R., Pavlov C., Ivashkin V.* Small intestinal bacterial overgrowth in cirrhosis: systematic review and meta-analysis. *Hepatol Int.* 2018;12(6):567–76. DOI: 10.1007/s12072-018-9898-2
7. *Song Y., Liu Y., Qi B., Cui X., Dong X., Wang Y., et al.* Association of Small Intestinal Bacterial Overgrowth With Heart Failure and Its Prediction for Short-Term Outcomes. *J Am Heart Assoc.* 2021;10(7):e015292. DOI: 10.1161/JAHA.119.015292
8. *Fadeeva M.V., Skhirtladze M.R., Ivashkin V.T.* Small Intestinal Bacterial Overgrowth Syndrome as a Risk Factor for Ventricular Tachycardia in Chronic Heart Failure with Left Ventricular Systolic Dysfunction. *Russian Journal of Gastroenterology, Hepatology, Coloproctology.* 2019;29(3):38–48 (In Russ.) DOI: 10.22416/1382-4376-2019-29-3-38-48
9. *Potskhverashvili N.D., Zolnikova O.Yu., Kokina N.I., Dzhakhaya N.L., Sedova A.V., Bueverova E.L., Trukhmanov A.S.* Small Bowel Bacterial Overgrowth Syndrome in Patients with Bronchial Asthma. *Russian Journal of Gastroenterology, Hepatology, Coloproctology.* 2018;28(4):47–54.(In Russ.) DOI: 10.22416/1382-4376-2018-28-4-47-54
10. *Villette R., Kc P., Beliard S., Salas Tapia M.F., Rainteau D., Guerin M., Lesnik P.* Unraveling Host-Gut Microbiota Dialogue and Its Impact on Cholesterol Levels. *Front Pharmacol.* 2020;11:278. DOI: 10.3389/fphar.2020.00278
11. *Gabbard S.L., Lacy B.E., Levine G.M., Crowell M.D.* The impact of alcohol consumption and cholecystectomy on small intestinal bacterial overgrowth. *Dig Dis Sci.* 2014;59(3):638–44. DOI: 10.1007/s10620-013-2960-y
12. *Yoshii K., Hosomi K., Sawane K., Kunisawa J.* Metabolism of Dietary and Microbial Vitamin B Family in the Regulation of Host Immunity. *Front Nutr.* 2019;6:48. DOI: 10.3389/fnut.2019.00048
13. *Martinez-Guryn K., Leone V., Chang E.B.* Regional Diversity of the Gastrointestinal Microbiome. Cell *Host Microbe.* 2019;26(3):314–24. DOI: 10.1016/j.chom.2019.08.011
14. *Wu W., Chen F., Liu Z., Cong Y.* Microbiota-specific Th17 Cells: Yin and Yang in Regulation of Inflammatory Bowel Disease. *Inflamm Bowel Dis.* 2016;22(6):1473–82. DOI: 10.1097/MIB.0000000000000775
15. *Behnsen J., Jellbauer S., Wong C.P., Edwards R.A., George M.D., Ouyang W., Raffatellu M.* The cytokine IL-22 promotes pathogen colonization by suppressing related commensal bacteria. *Immunity.* 2014;40(2):262–73. DOI: 10.1016/j.immuni.2014.01.003
16. *Hooper L.V., Macpherson A.J.* Immune adaptations that maintain homeostasis with the intestinal microbiota. *Nat Rev Immunol.* 2010;10(3):159–69. DOI: 10.1038/nri2710
17. *Cash H.L., Whitham C.V., Behrendt C.L., Hooper L.V.* Symbiotic bacteria direct expression of an intestinal bactericidal lectin. *Science.* 2006;313(5790):1126–30. DOI: 10.1126/science.1127119
18. *Everard A., Lazarevic V., Gaïa N., Johansson M., Ståhlman M., Backhed F., et al.* Microbiome of prebiotic-treated mice reveals novel targets involved in host response during obesity. *ISME J.* 2014;8(10):2116–30. DOI: 10.1038/ismej.2014.45
19. *Denning T.L., Sitaraman S.V.* Segmented filamentous bacteria shape intestinal immunity. *Gastroenterology.* 2010;139(1):351–3. DOI: 10.1053/j.gastro.2010.05.032
20. *Sachdev A.H., Pimentel M.* Gastrointestinal bacterial overgrowth: pathogenesis and clinical significance. *Ther Adv Chronic Dis.* 2013;4(5):223–31. DOI: 10.1177/2040622313496126
21. *Pyleris E., Tzivras D., Barbatzas C., Giamarellos-Bourboulis E.J., Koussoulas V., Pimentel M.* The prevalence of overgrowth by aerobic bacteria in the small intestine by small bowel culture: Relationship with irritable bowel syndrome. *Dig Dis Sci.* 2012:57(5):1321–9. DOI: 10.1007/s10620-012-2033-7
22. *Leite G., Morales W., Weitsman S., Celly S., Parodi G., Mathur R., et al.* The duodenal microbiome is altered in small intestinal bacterial overgrowth. *PLoS One.* 15(7):e0234906. DOI: 10.1371/journal.pone.0234906
23. *Takakura W., Pimentel M.* Small Intestinal Bacterial Overgrowth and Irritable Bowel Syndrome – An Update. *Front Psychiatry.* 2020;11:664. DOI: 10.3389/fpsyt.2020.00664
24. *Ghoshal U.C.* How to interpret hydrogen breath tests. *J Neurogastroenterol Motil.* 2011;17(3):312–7. DOI: 10.5056/jnm.2011.17.3.312
25. *Gandhi A., Shah A., Jones M.P., Koloski N., Talley N.J., Morrison M., Holtmann G.* Methane positive small intestinal bacterial overgrowth in inflammatory bowel disease and irritable bowel syndrome: A systematic review and meta-analysis. *Gut Microbes.* 2021;13(1):1933313. DOI:10.1080/19490976.2021.1933313
26. *Ghashghaeinia M., Mrowietz U.* Human erythrocytes, nuclear factor kappaB (NFκB) and hydrogen sulfide (H_2S) – from non-genomic to genomic research. *Cell Cycle.* 2021;20(20):2091–101. DOI: 10.1080/15384101.2021.1972557
27. *Suri J., Kataria R., Malik Z., Parkman H.P., Schey R.* Elevated methane levels in small intestinal bacterial overgrowth suggests delayed small bowel and colonic transit. *Medicine (Baltimore).* 2018 May;97(21):e10554. DOI: 10.1097/MD.0000000000010554
28. *Bures J., Cyrany J., Kohoutova D., Förstl M., Rejchrt S., Kvetina J., et al.* Small intestinal bacterial overgrowth syndrome. *World J Gastroenterol.* 2010;16(24):2978–90. DOI: 10.3748/wjg.v16.i24.2978
29. *Montoro-Huguet M.A., Belloc B., Domínguez-Cajal M.* Small and Large Intestine (I): Malabsorption of Nutrients. *Nutrients.* 2021;13(4):1254. DOI: 10.3390/nu13041254
30. *Lakhani S.V., Shah H.N., Alexander K., Finelli F.C., Kirkpatrick J.R., Koch T.R.* Small intestinal bacterial overgrowth and thiamine deficiency after Roux-en-Y gastric bypass surgery in obese patients. *Nutr Res.* 2008;28(5):293–8. DOI: 10.1016/j.nutres.2008.03.002
31. *Parlesak A., Klein B., Schecher K., Bode J.C., Bode C.* Prevalence of small bowel bacterial overgrowth and its association with nutrition intake in nonhospitalized older adults. *J Am Geriatr Soc.* 2003;51(6):768–73. DOI: 10.1046/j.1365-2389.2003.51259.x
32. *Maslennikov R., Pavlov C., Ivashkin V.* Is small intestinal bacterial overgrowth a cause of hyperdynamic circulation in cirrhosis? *Turk J Gastroenterol.* 2019;30(11):964–75. DOI: 10.5152/tjg.2019.18551

33. *Ivashkin K.V., Grechishnikova V.R., Reshetova M.S., Ivashkin V.T.* Irritable Bowel and Bacterial Overgrowth Syndromes: a Bacterial Link Hypothesis of Functional Disease. *Russian Journal of Gastroenterology, Hepatology, Coloproctology.* 2021;31(1):54–63 (In Russ.). DOI: 10.22416/1382-4376-2021-31-1-54-63
34. *Jones R.M., Neish A.S.* Recognition of bacterial pathogens and mucosal immunity. *Cell Microbiol.* 2011;13(5):670–6. DOI: 10.1111/j.1462-5822.2011.01579.x
35. *Shah A., Morrison M., Burger D., Martin N., Rich J., Jones M., et al.* Systematic review with meta-analysis: the prevalence of small intestinal bacterial overgrowth in inflammatory bowel disease. *Aliment Pharmacol Ther.* 2019;49(6):624–35. DOI: 10.1111/apt.15133
36. *Rao S.S.C., Tan G., Abdulla H., Yu S., Larion S., Leelasinjaroen P.* Does colectomy predispose to small intestinal bacterial (SIBO) and fungal overgrowth (SIFO)? *Clin Transl Gastroenterol.* 2018;9(4):146. DOI: 10.1038/s41424-018-0011-x
37. *Polkowska-Pruszyńska B., Gerkowicz A., Szczepanik-Kułak P., Krasowska D.* Small intestinal bacterial overgrowth in systemic sclerosis: a review of the literature. *Arch Dermatol Res.* 2019;311(1):1–8. DOI: 10.1007/s00403-018-1874-0
38. *Patil A.D.* Link between hypothyroidism and small intestinal bacterial overgrowth. *Indian J Endocrinol Metab.* 2014;18(3):307–9. DOI: 10.4103/2230-8210.131155
39. *Feng X., Li X.Q.* The prevalence of small intestinal bacterial overgrowth in diabetes mellitus: a systematic review and meta-analysis. *Aging (Albany NY).* 2022;14(2):975–88. DOI: 10.18632/aging.203854
40. *Lee A.A., Baker J.R., Wamsteker E.J., Saad R., DiMagno M.J.* Small Intestinal Bacterial Overgrowth Is Common in Chronic Pancreatitis and Associates With Diabetes, Chronic Pancreatitis Severity, Low Zinc Levels, and Opiate Use. *Am J Gastroenterol.* 2019;114(7):1163–71. DOI: 10.14309/ajg.0000000000000200
41. *Chander Roland B., Mullin G.E., Passi M., Zheng X., Salem A., Yolken R., Pasricha P.J.* A Prospective Evaluation of Ileocecal Valve Dysfunction and Intestinal Motility Derangements in Small Intestinal Bacterial Overgrowth. *Dig Dis Sci.* 2017;62(12):3525–35. DOI: 10.1007/s10620-017-4726-4
42. *Su T., Lai S., Lee A., He X., Chen S.* Meta-analysis: proton pump inhibitors moderately increase the risk of small intestinal bacterial overgrowth. *J Gastroenterol.* 2018;53(1):27–36. DOI: 10.1007/s00535-017-1371-9
43. *Reddymasu S.C., McCallum R.W.* Small intestinal bacterial overgrowth in gastroparesis: are there any predictors? *J Clin Gastroenterol.* 2010;44(1):e8–13. DOI: 10.1097/MCG.0b013e3181aec746
44. *Esposito S., Biscarini A., Federici B., Cofini M., Argentiero A., Neglia C., et al.* Role of Small Intestinal Bacterial Overgrowth (SIBO) and Inflammation in Obese Children. *Front Pediatr.* 2020; 8:369. DOI: 10.3389/fped.2020.00369
45. *Hegade V.S., Speight .R.A, Etherington R.E., Jones D.E.* Novel bile acid therapeutics for the treatment of chronic liver diseases. *Therap Adv Gastroenterol.* 2016;9(3):376–91. DOI: 10.1177/1756283X16630712
46. *Losurdo G., Marra A., Shahini E., Girardi B., Giorgio F., Amoruso A., et al.* Small intestinal bacterial overgrowth and celiac disease: A systematic review with pooled-data analysis. *Neurogastroenterol Motil.* 2017;29(6). DOI: 10.1111/nmo.13028
47. *El Kurdi B., Babar S., El Iskandarani M., Bataineh A., Lerch M.M., Young M., Singh V.P.* Factors That Affect Prevalence of Small Intestinal Bacterial Overgrowth in Chronic Pancreatitis: A Systematic Review, Meta-Analysis, and Meta-Regression. *Clin Transl Gastroenterol.* 2019;10(9):e00072. DOI: 10.14309/ctg.0000000000000072
48. *Miazga A., Osiński M., Cichy W., Żaba R.* Current views on the etiopathogenesis, clinical manifestation, diagnostics, treatment and correlation with other nosological entities of SIBO. *Adv Med Sci.* 2015;60(1):118–24. DOI: 10.1016/j.advms.2014.09.001
49. *Wang F.Y., Chi C.C.* Rosacea, Germs, and Bowels: A Review on Gastrointestinal Comorbidities and Gut-Skin Axis of Rosacea. Adv Ther. 2021;38(3):1415–24. DOI: 10.1007/s12325-021-01624-x
50. *Ghosh G., Jesudian A.B.* Small Intestinal Bacterial Overgrowth in Patients With Cirrhosis. *J Clin Exp Hepatol.* 2019;9(2):257–67. DOI: 10.1016/j.jceh.2018.08.006
51. *Khoshini R., Dai S.C., Lezcano S., Pimentel M.* A systematic review of diagnostic tests for small intestinal bacterial overgrowth. *Dig Dis Sci.* 2008;53(6):1443–54. DOI: 10.1007/s10620-007-0065-1
52. *Tang Q., Jin G., Wang G., Liu T., Liu X., Wang B., Cao H.* Current Sampling Methods for Gut Microbiota: A Call for More Precise Devices. *Front Cell Infect Microbiol.* 2020;10(151). DOI: 10.3389/fcimb.2020.00151
53. *Kastl A.J. Jr, Terry N.A., Wu G.D., Albenberg L.G.* The Structure and Function of the Human Small Intestinal Microbiota: Current Understanding and Future Directions. *Cell Mol Gastroenterol Hepatol.* 2020;9(1):33–45. DOI: 10.1016/j.jcmgh.2019.07.006
54. *Pimentel M., Saad R.J., Long M.D., Rao S.S.C.* ACG Clinical Guideline: Small Intestinal Bacterial Overgrowth. *Am J Gastroenterol.* 2020;115(2):165–78. DOI: 10.14309/ajg.0000000000000501
55. *Rao S.S.C., Bhagatwala J.* Small Intestinal Bacterial Overgrowth: Clinical Features and Therapeutic Management. *Clin Transl Gastroenterol.* 2019;10(10):e00078. DOI: 10.14309/ctg.0000000000000078
56. *Rezaie A., Buresi M., Lembo A., Lin H., McCallum R., Rao S., et al.* Hydrogen and Methane-Based Breath Testing in Gastrointestinal Disorders: The North American Consensus. *Am J Gastroenterol.* 2017;112(5):775–84. DOI: 10.1038/ajg.2017.46
57. *Hammer H.F., Fox M.R., Keller J., Salvatore S., Basilisco G., Hammer J., et al;* European H_2-CH_4-breath test group. European guideline on indications, performance, and clinical impact of hydrogen and methane breath tests in adult and pediatric patients: European Association for Gastroenterology, Endoscopy and Nutrition, European Society of Neurogastroenterology and Motility, and European Society for Paediatric Gastroenterology Hepatology and Nutrition consensus. *United European Gastroenterol J.* 2022;10(1):15–40. DOI: 10.1002/ueg2.12133
58. *Attar A., Flourié B., Rambaud J.C., Franchisseur C., Ruszniewski P., Bouhnik Y.* Antibiotic efficacy in small intestinal bacterial overgrowth-related chronic diarrhea: a crossover, randomized trial. *Gastroenterology.* 1999;117(4):794–7. DOI: 10.1016/s0016-5085(99)70336-7
59. *Maconi G., Hausken T., Dietrich C.F., Pallotta N., Sporea I., Nurnberg D., et al.* Gastrointestinal Ultrasound in Functional Disorders of the Gastrointestinal Tract — EFSUMB Consensus Statement. *Ultrasound Int Open.* 2021;7(1):E14–24. DOI: 10.1055/a-1474-8013
60. *Greenson J.K.* The biopsy pathology of non-coeliac enteropathy. *Histopathology.* 2015;66(1):29–36. DOI: 10.1111/his.12522
61. Приказ Министерства здравоохранения РФ от 28 февраля 2019 г. № 103н «Об утверждении порядка и сроков разработки клинических рекомендаций, их пересмотра, типовой формы клинических рекомендаций и требований к их структуре, составу и научной обоснованности включаемой в клинические рекомендации информации» (с изменениями и дополнениями).
62. *Ghoshal U.C., Srivastava D., Misra A., Ghoshal U.* A proof-of-concept study showing antibiotics to be more effective in irritable bowel syndrome with than without small-intestinal bacterial overgrowth: a randomized, double-blind, placebo-controlled trial. *Eur J Gastroenterol Hepatol.* 2016;28(3):281–9. DOI: 10.1097/MEG.0000000000000557
63. *Sajjad A., Mottershead M., Syn W.K., Jones R., Smith S., Nwokolo C.U.* Ciprofloxacin suppresses bacterial overgrowth, increases fasting insulin but does not

correct low acylated ghrelin concentration in non-alcoholic steatohepatitis. *Aliment Pharmacol Ther.* 2005;22(4):291–9. DOI: 10.1111/j.1365-2036.2005.02562.x
64. *Castiglione F., Rispo A., Di Girolamo E., Cozzolino A., Manguso F., Grassia R., Mazzacca G.* Antibiotic treatment of small bowel bacterial overgrowth in patients with Crohn's disease. *Aliment Pharmacol Ther.* 2003;18(11–12):1107–12. DOI: 10.1046/j.1365-2036.2003.01800.x
65. *Gatta L., Scarpignato C.* Systematic review with meta-analysis: rifaximin is effective and safe for the treatment of small intestine bacterial overgrowth. *Aliment Pharmacol Ther.* 2017;45(5):604–16. DOI: 10.1111/apt.13928
66. *Pimentel M., Constantino T., Kong Y., Bajwa M., Rezaei A., Park S.* A 14-day elemental diet is highly effective in normalizing the lactulose breath test. *Dig Dis Sci.* 2004;49(1):73–7. DOI: 10.1023/b:ddas.0000011605.43979.e1
67. *Bellini M., Tonarelli S., Nagy A.G., Pancetti A., Costa F., Ricchiuti A., et al.* Low FODMAP Diet: Evidence, Doubts, and Hopes. *Nutrients.* 2020;12(1):148. DOI: 10.3390/nu12010148
68. *Lauritano E.C., Gabrielli M., Scarpellini E., Lupascu A., Novi M., Sottili S., et al.* Small intestinal bacterial overgrowth recurrence after antibiotic therapy. *Am J Gastroenterol.* 2008;103(8):2031–5. DOI: 10.1111/j.1572-0241.2008.02030.x
69. *Kunkel D., Basseri R.J., Makhani M.D., Chong K., Chang C., Pimentel M.* Methane on breath testing is associated with constipation: a systematic review and meta-analysis. *Dig Dis Sci.* 2011;56(6):1612–8. DOI: 10.1007/s10620-011-1590-5
70. *Rosenthal A., Solomons N.W.* Time-course of cigarette smoke contamination of clinical hydrogen breath-analysis tests. *Clin Chem.* 1983;29(11):1980–1. PMID: 6627640

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