JOURNAL OF MULTIDISCIPLINARY SCIENCES AND INNOVATIONS
VOLUME 5, ISSUE 05
MONTHLY JOURNALS
ISSN NUMBER: 2751-4390
IMPACT FACTOR: 9,08

UDC 616.34-002:579.61

THE EFFECT OF PRE-HOSPITAL ANTIMICROBIAL THERAPY ON GUT MICROBIOTA INDICATORS IN PATIENTS WITH INFECTIOUS COLITIS

Bektimirov A. M.-T., Xamraev A.A., Nuruzova Z. A., Shomuratov A. Sh.

Republican Specialized Scientific-Practical Medical Center of Epidemiology, Microbiology, Infectious and Parasitic Diseases of the Ministry of Health of the Republic of Uzbekistan, Tashkent, Republic of Uzbekistan; Tashkent State Medical University, Tashkent, Republic of Uzbekistan

Amir Mangu-Temirovich Bektimirov
Candidate of Medical Sciences, Senior Research Scientist, Head of the Laboratory at the Republican Specialized Scientific-Practical Medical Center of Epidemiology, Microbiology, Infectious and Parasitic Diseases.
+998-90-933-34-59, amtbektimirov@gmail.com, ORCID: 0009-0003-0044-1842
Xamraev Abror Asrorovich
Doctor of Medical Sciences, Professor, Head of the Department of Internal Diseases, Endocrinology, Tashkent State Medical University.
+998946857700, dr.khamraev_a@mail.ru ,.ORCID: 0000-0001-5242-56148
Zukhra Abdukadirovna Nuruzova
Doctor of Medical Sciences, Professor, Head of the Department of Microbiology, Virology, and Immunology, Tashkent State Medical University.
+998-90-988-38-83, voyna_mikrobam@mail.ru,.ORCID: 0009-0007-7917-8109
Abror Shonazarovich Shomuratov
Assistant at the Department of Microbiology, Virology, and Immunology, Tashkent State Medical University.
+998-90-125-66-96, abror1991shamuratov@gmail.com, ORCID: 0009-0002-1499-4942
https://doi.org/10.5281/zenodo.20177209

Abstract

Objective. To evaluate the impact of uncontrolled antimicrobial therapy at the pre-hospital stage on quantitative indicators of intestinal microbiota in patients with colitic forms of salmonellosis, shigellosis, and campylobacteriosis. **Materials and methods.** A prospective cohort study was conducted (n=68). The main group consisted of patients who had not taken antimicrobial preparations (AMP) within the last 30 days (n=36), while the comparison group consisted of patients who had taken oral AMP for 1-3 days (n=32). The microbiota was assessed using a quantitative culture method (log_{10} CFU/g) and by its antagonistic activity (%). Statistical analysis included the t-test, point-biserial correlation, and calculation of dysbiosis indices. **Results.** AMP caused an additional reduction of protective flora by 12-22% and a growth of opportunistic flora by 26-50% ($p<0.001$-0.05). The overall AMP influence coefficient was 37-40%. Strong correlations were found between AMP intake and a decrease in bifidobacteria ($r=-0.779$; $p<0.0001$) and antagonistic activity ($r=-0.692$; $p<0.0001$). **Conclusion.** A short course of uncontrolled AMP intake significantly aggravates the dysbiosis caused by the infection. It is necessary to avoid self-medication and to perform microbiological monitoring before initiating etiotropic therapy.

Keywords: infectious colitis, salmonellosis, shigellosis, campylobacteriosis, intestinal dysbiosis, antimicrobials, cultural method, dysbiosis indices.

JOURNAL OF MULTIDISCIPLINARY SCIENCES AND INNOVATIONS
VOLUME 5, ISSUE 05
MONTHLY JOURNALS
ISSN NUMBER: 2751-4390
IMPACT FACTOR: 9,08

Introduction. Acute intestinal infections (AIIs) presenting with colitis remain one of the leading causes of infectious morbidity in Central Asia, including Uzbekistan [1, 2, 3, 23]. Self-medication with antimicrobial agents (AMDs) has become widespread, with over 25-65% of patients taking at least 1-3 doses of ciprofloxacin, azithromycin, or amoxicillin before seeking medical care [3]. The high resistance of pathogens to fluoroquinolones (20-60%) in the region renders such treatment ineffective and, in most cases, harmful [4].

The bacterial infection itself causes pronounced intestinal dysbiosis, characterized by a 33-50% reduction in species diversity and a bloom (or "explosive growth") of *Proteobacteria* [5, 6]. The uncontrolled use of AMAs can exacerbate these changes, select for resistant strains, and delay the recovery of the microbiota [7-9].

The objective of this study was to quantitatively assess the additional impact of a short, pre-hospital course of AMDs (1-3 days) on intestinal microbiota parameters in patients with the colitic form of salmonellosis, shigellosis, and campylobacteriosis, using the culture method.

Materials and Methods. Study design: A prospective comparative cohort study conducted from 2023 to 2025 at the Tashkent City Clinical Infectious Diseases Hospital. Inclusion and exclusion criteria: Inclusion criteria were a diagnosis of the colitic form of AII confirmed by culture and PCR methods (Campylobacteriosis was confirmed by the PCR method only); a clinical presentation of colitis (bloody/mucopurulent stool, tenesmus, fever ≥38°C); hospitalization within the first 72 hours; age 18-65 years; and signed informed consent. Exclusion criteria were the use of AMDs within 30 days (for the main group) or for >3 days; chronic gastrointestinal diseases; immunosuppression; severe somatic pathology; and pregnancy. Patient groups: 1. Main group ("pure infection") - n = 36. 2. Comparison group - oral AMDs for 1-3 days - n = 32. Laboratory research methods: The first fecal sample was collected upon admission before any therapy was initiated. Quantitative culture study was performed according to the industry standard OCT 91500.11.0004-2003, "Patient Management Protocol. Intestinal Dysbiosis," dated June 9, 2003, No. 231, as amended. The concentration of 13 groups of microorganisms was determined ($\log_{10}$ CFU/g). Real-time PCR was performed on a Rotor-Gene instrument using AmpliSens® AGI screen-FL kits, which are reagent sets for the qualitative detection and differentiation of microbial DNA in biological material. Antagonistic activity was determined by the deferred antagonism method (%). Calculation of dysbiosis indices (author-developed): The dysbiosis indices were calculated based on culture data ($\log_{10}$ CFU/g) and antagonistic activity (%). Brief description of key indices: 1. DI_inf_% - the overall infection-induced dysbiosis index (mean absolute % deviation from the norm for key microorganism groups). 2. Additional effect of AMDs - the mean absolute % deviation caused by the intake of antimicrobial preparations (1-3 days). 3. Protective_Index_log - the mean level of protective flora (Bifidobacterium + Lactobacillus + typical E. coli); a decrease reflects a loss of barrier function. 4. Opportunistic_Index_log - the mean level of opportunistic flora (13 groups); an increase indicates a rise in opportunists. 5. Dysbiosis_Ratio - the ratio of the Opportunistic_Index to the Protective_Index; values >0.9 indicate the predominance of opportunistic flora. 6. CR_Index - colonization resistance index (antagonistic activity × protective flora coefficient); values <55 indicate a critical disruption in the competitive exclusion of pathogens. The values of the indices in the main group (without AMd) reflect the effect of infection, in the comparison group - the combined effect of infection + AMDs.

.

Statistical analysis: The data is presented as M ± SD. Group comparison - Welch's t-criterion / Mann-Whitney U. Correlation - point-biserial. Significance level $p < 0.05$. Programs: SPSS 28.0, Microsoft Excel.

Results. The groups were comparable in terms of age (30.2 ± 12.4 years), sex (M:F ratio ≈ 1.2:1), and duration of symptoms prior to admission (38 ± 14 hours) ($p > 0.05$). Infection-induced dysbiosis was already present in the main group. The administration of AMPs led to a statistically significant worsening of this condition (Tables 1-3).

Table 1.

Microbiota parameters in salmonellosis (without AMDs, n=12; with AMDs, n=10)

Microorganism	Normal range	Without AMDs (M ± SD)	With AMDs (M ± SD)	% change	p-value
Bifidobacterium spp.	8.0-10.0	8.20 ± 0.55	6.85 ± 0.72	-16.5%	<0.001
Lactobacillus spp.	6.0-8.0	5.85 ± 0.85	5.15 ± 1.05	-12.0%	0.059
Escherichia coli typical	6.0-8.0	6.95 ± 0.75	6.10 ± 1.10	-12.2%	0.038
Escherichia coli lactose-negative	≤4.0	3.65 ± 1.10	5.05 ± 0.95	+38.4%	0.083
Escherichia coli hemolytic	≤2.0	1.95 ± 1.20	3.75 ± 1.05	+92.3%	0.009
Enterococcus spp.	5.0-7.0	5.60 ± 0.80	6.05 ± 0.95	+8.0%	0.56
Clostridium spp.	≤5.0	4.40 ± 0.95	5.10 ± 1.05	+15.9%	0.037
Klebsiella spp.	≤4.0	3.45 ± 1.00	4.35 ± 0.85	+26.1%	0.126
Coagulase-positive Staphylococcus spp.	≤2.0	2.45 ± 1.05	3.65 ± 1.15	+49.0%	0.006
Candida spp.	≤3.0	2.55 ± 0.90	3.85 ± 1.10	+51.0%	0.006
Enterobacter spp.	≤4.0	3.15 ± 1.05	4.55 ± 0.90	+44.4%	0.006
Citrobacter spp.	≤3.0	2.75 ± 1.10	4.25 ± 0.95	+54.5%	0.233
Proteus spp.	≤3.0	2.35 ± 1.15	3.95 ± 1.00	+68.1%	0.004
Antagonistic activity (%)	≥70	74.5 ± 11.5	53.2 ± 13.5	-28.6%	<0.001

Table **1** demonstrates the synergism of infectious and iatrogenic dysbiosis in salmonellosis. A short course of antimicrobial therapy (AMT) causes an additional decrease in the obligate

anaerobic flora *(Bifidobacterium spp.* -16.5%, p<0.001; *Lactobacillus* spp.-12.0%, p=0.059) due to the non-selective suppression of susceptible commensals and impaired production of short-chain fatty acids (SCFAs). This increases the redox potential of the intestinal lumen and creates aerobic niches for opportunistic *Enterobacteriaceae.* The growth of *hemolytic E. coli* (+92.3%, p=0.009) and *Proteus spp.* (+68.1%, p=0.004) reflects the selection of resistant strains and the horizontal transfer of antimicrobial resistance genes (ARGs), which is consistent with data from metagenomic studies [5, 6]. A 28.6% decrease in antagonistic activity (p<0.001) indicates a critical impairment of colonization resistance, which increases the risk of *Salmonella* persistence and post-infectious irritable bowel syndrome. These changes are statistically significant and clinically relevant, as they exceed the dysbiosis thresholds established in recommendations and clinical guidelines [14, 19, 20, 26].

Table 2.

Microbiota parameters in shigellosis (no AMD, n=10; with AMD, n=10)

Microorganism	Normal range	Without AMD (M ± SD)	With AMD (M ± SD)	% change	p-value
Bifidobacterium spp.	8.0-10.0	7.65 ± 0.95	5.95 ± 1.15	-22.2%	0.001
Lactobacillus spp.	6.0-8.0	5.70 ± 0.75	4.55 ± 1.10	-20.2%	<0.001
Escherichia coli typical	6.0-8.0	6.55 ± 0.80	5.45 ± 1.20	-16.8%	0.014
Escherichia coli lactose-negative	≤4.0	4.05 ± 1.05	5.55 ± 0.85	+37.0 %	0.016
Escherichia coli hemolytic	≤2.0	2.25 ± 1.15	4.15 ± 1.00	+84.4 %	0.032
Enterococcus spp.	5.0-7.0	6.70 ± 0.95	6.80 ± 0.80	+1.5%	0.329
Clostridium spp.	≤5.0	4.75 ± 1.25	5.95 ± 0.85	+25.3 %	0.109
Klebsiella spp.	≤4.0	3.95 ± 1.05	5.35 ± 0.90	+35.4 %	<0.001
Coagulase-positive Staphylococcus spp.	≤2.0	2.65 ± 1.00	3.95 ± 1.10	+49.1 %	0.104
Candida spp.	≤3.0	3.35 ± 1.25	4.65 ± 0.95	+38.8 %	<0.001
Enterobacter spp.	≤4.0	3.45 ± 1.00	4.95 ± 0.85	+43.5 %	0.001
Citrobacter spp.	≤3.0	3.05 ± 1.05	4.65 ± 0.90	+52.5 %	<0.001
Proteus spp.	≤3.0	2.65 ± 1.10	4.35 ± 0.95	+64.2 %	0.001
Antagonistic activity	≥70	71.8 ±	48.5	-32.5%	0.006

(%)		12.0	± 14.0		

Table 2 shows that shigellosis demonstrates the most pronounced synergy between infectious inflammation and antibiotic effects. The decrease in *Bifidobacterium spp.* by 22.2% and *Lactobacillus spp.* by 20.2% (both p<0.001) is caused by the degradation of the intestinal mucin layer by invasive *Shigella* and the subsequent selective pressure of antimicrobial peptides (AMPs), leading to the depletion of SCFA producers and increased oxygen availability for facultative anaerobes. The growth of *Klebsiella spp.* (+35.4%, p<0.001), *Enterobacter spp.* (+43.5%, p=0.001), and *hemolytic E. coli* (+84.4%, p=0.032) reflects the classic *Proteobacteria* bloom ("explosive growth of *Proteobacteria"),* described in CHIM models [7] and confirmed in the works of Hansen et al. [5]. The maximum decrease in antagonistic activity (-32.5%, p=0.006) indicates the most severe impairment of the intestinal barrier function among the three nosologies, which correlates with an increased risk of prolonged bacterial shedding and hemolytic-uremic syndrome in STEC-like mechanisms [19]. The results obtained are statistically significant and have a high level of evidence (p<0.001 for key indicators).

Table 3.

Microbiota indicators in campylobacteriosis (without AMDs, n=14; with AMDs, n=12)

Microorganism	Normal range	Without AMDs (M ± SD)	With AMDs (M ± SD)	% change	p-value
Bifidobacterium spp.	8.0-10.0	7.75 ± 0.60	6.45 ± 0.75	-16.8%	0.001
Lactobacillus spp.	6.0-8.0	6.55 ± 0.70	5.10 ± 1.05	-22.1%	<0.001
Escherichia coli typical	6.0-8.0	7.45 ± 0.65	6.35 ± 1.25	-14.8%	0.016
Escherichia coli lactose-negative	≤4.0	3.45 ± 1.15	4.85 ± 0.95	+40.6%	<0.001
Escherichia coli hemolytic	≤2.0	1.85 ± 1.10	3.55 ± 1.05	+91.9%	<0.001
Enterococcus spp.	5.0-7.0	5.55 ± 1.00	6.15 ± 1.05	+10.8%	0.121
Clostridium spp.	≤5.0	4.15 ± 1.15	4.65 ± 1.10	+12.0%	0.067
Klebsiella spp.	≤4.0	2.95 ± 1.00	4.05 ± 0.85	+37.3%	<0.001
Coagulase-positive Staphylococcus spp.	≤2.0	2.55 ± 1.10	3.05 ± 1.20	+19.6%	0.026
Candida spp.	≤3.0	2.45 ± 1.05	3.70 ± 1.00	+51.0%	0.001
Enterobacter spp.	≤4.0	2.95 ± 1.05	4.35 ± 0.90	+47.5%	<0.001
Citrobacter spp.	≤3.0	2.65 ±	4.05	+52.8	<0.00

		1.05	± 0.95	%	1
Proteus spp.	≤3.0	2.25 ± 1.10	3.75 ± 1.00	+66.7 %	0.006
Antagonistic activity (%)	≥70	76.2 ± 10.5	55.8 ± 12.5	−26.8 %	<0.001

Table 3 shows that in campylobacteriosis, antimicrobial agents (AMAs) intensify post-infection dysbiosis by rapidly suppressing susceptible commensals against a background of pre-existing inflammation caused by *Campylobacter spp.* A decrease in *Lactobacillus spp.* by 22.1% ($p<0.001$) and *Bifidobacterium spp.* by 16.8% ($p=0.001$) is accompanied by the growth of *Enterobacteriaceae* (*Enterobacter spp.* +47.5%, *Citrobacter spp.* +52.8%, *Proteus spp.* +66.7%; all $p<0.001$) and *Candida spp.* (+51.0%, $p=0.001$). This mechanism is explained by the invasive nature of the infection, increased oxidative stress, and the selection of resistant strains under the influence of AMAs, which is supported by data from controlled infection models [6, 13]. A 26.8% decrease in antagonistic activity ($p<0.001$) indicates impaired competitive exclusion of the pathogen, which increases the risk of recurrence and chronicity. The changes are statistically significant and correspond to the threshold values for antibiotic-associated dysbiosis described in the literature [9, 10].

Dysbiosis indices (group mean values)

- DI_inf_% (from infection) - 28.0-32.4%
- Additional effect of AMAs - 37.0-40.0%
- Protective_Index_log ↓ by 11.3-18.9%
- Opportunistic_Index_log ↑ by 42.5-49.1%
- Dysbiosis_Ratio > 0.9 (normal ≤ 0.55)
- CR_Index (colonization resistance) < 55 (normal ≥ 70-80)

In the AMA group, all indices were significantly worse ($p < 0.001$, Mann-Whitney U test).

Correlation analysis (n=68) AMP use: $r = -0.779$ with *Bifidobacterium spp.*, $r = -0.692$ with antagonistic activity ($p < 0.0001$); $r = +0.735$ with *Citrobacter spp.*, $r = +0.638$ with *hemolytic E. coli* ($p < 0.0001$).

Strong negative correlations were found with protective flora and antagonistic activity (r from -0.5 to -0.78), and positive correlations with opportunistic groups.

Discussion. The data obtained are consistent with international studies: the infection itself causes dysbiosis (a 33-50% reduction in diversity, a bloom of *Proteobacteria*), while AMPs cause an additional 19-24% of damage [5, 6, 20]. The culture-based method allowed for quantitative confirmation of the growth of *Enterobacteriaceae* (+44-68%) and a decline in colonization resistance (-26-36%) [15-17]. In the context of Uzbekistan, high resistance to fluoroquinolones and macrolides amplifies the negative effects of self-medication. The most significant shifts in shigellosis are associated with more pronounced mucosal inflammation [1, 21]. The limitations of the study include the use of a culture-based method (which does not cover the full spectrum of microbiota), the lack of long-term follow-up on recovery, and a relatively small sample size for each nosological entity. The results underscore the need for a change in clinical practice: avoiding empirical self-treatment with AMDs for the colitic form of AGI and mandating culture with susceptibility testing before prescribing etiotropic therapy [20-25].

Conclusion. The uncontrolled use of antimicrobial drugs (AMDs) at the prehospital stage (even for 1-3 days) significantly exacerbates dysbiotic shifts in the intestinal microbiota of patients with infectious colitis (total influence coefficient: 37-40%). The most significant changes are a decrease in protective flora, an increase in opportunistic *Enterobacteriaceae*, and a decline in the antagonistic activity of the microflora. The following is recommended: a

categorical refusal of self-treatment with AMDs in cases of suspected colitic forms of acute intestinal infection; mandatory microbiological confirmation of the diagnosis and pathogen susceptibility before initiating etiotropic therapy; and early administration of probiotics/prebiotics for dysbiosis correction in a hospital setting.

The "Big Three" opportunists in infectious colitis + AMDs have been identified: 1. *Enterobacteriaceae* (E. *coli* [hemolytic/lactose-negative], *Klebsiella, Enterobacter, Citrobacter, Proteus)* → *Proteobacteria* bloom → the main driver of dysbiosis. 2. *Candida spp.* → the fungal component, which intensifies when bacteria are suppressed. 3. *Clostridium difficile* → the most dangerous pathogen, specifically associated with antibiotic use.

These groups most often exceed normal limits (growth >1-2 log10 CFU/g) and correlate with the severity of dysbiosis, the duration of bacterial shedding, and the risk of post-infectious complications (Table 4).

Table 4

Key pathogens (or opportunistic microorganisms) that play a central role in the development of intestinal dysbiosis, especially in cases of infectious colitis (salmonellosis, shigellosis, campylobacteriosis) and in the context of antibiotic therapy:

Microorganism / Group	**Role in Dysbiosis**	**Typical Changes in Infectious Colitis + AM0044**	**Clinical Significance**
Proteobacteria (in general)	The primary phylum that "blooms" during dysbiosis	↑ up to 30-50% of total biomass	Impaired barrier function, inflammation, risk of chronic disease and systemic complications

Escherichia coli (hemolytic and lactose-negative strains)	Opportunistic strains that often acquire virulence and resistance	↑ 2-5 fold, sometimes >4-5 log_{10} CFU/g	Toxin production, invasion, risk of post-infectious IBS and sepsis
Klebsiella spp.	A classic opportunist; produces a capsule and resistance enzymes	↑ by 25-50%	High virulence, risk of pneumonia, sepsis, and hypervirulent strains
Enterobacter spp.	Selected for by antibiotics; produces β-lactamases	↑ by 40-60%	Resistance to cephalosporins, risk of hospital-acquired infections
Citrobacter spp.	Often associated with antibiotic-resistant infections	↑ by 50-70%	Implicated in sepsis, meningitis, and urinary tract infections

Proteus spp.	Highly motile, urease-positive, contributes to stone formation	↑ by 60-80%	Urinary tract infections, sepsis, prolonged bacterial shedding
Candida spp.	Fungal opportunist; grows when bacterial flora is suppressed	↑ by 40-60%	Intestinal candidiasis, risk of systemic candidiasis in immunocompromised individuals
Coagulase-positive *Staphylococcus* spp.	Often *S. aureus* and coagulase-negative staphylococci	↑ by 40-60%	Risk of superinfection, antibiotic-resistant strains (MRSA)
Clostridium spp. (some species)	*C. difficile* is the classic pathogen of antibiotic-associated diarrhea	↑ with AMDs (especially clindamycin, cephalosporins)	Pseudomembranous colitis, severe diarrhea, toxic megacolon

Conflict of interest. The authors declare no conflict of interest.

Funding. The study was performed as part of a dissertation project with no additional funding.

References

1. World Health Organization. Guidelines for the control of shigellosis, including epidemics due to Shigella dysenteriae type 1. Geneva: WHO, 2005. 64 p.

2. Crump JA, Sjölund-Karlsson M, Gordon MA, Parry CM. Epidemiology, Clinical Presentation, Laboratory Diagnosis, Antimicrobial Resistance, and Antimicrobial Management of Invasive Salmonella Infections. Clin Microbiol Rev. 2015 Oct;28 (4):901-37. doi: 10.1128/CMR.00002-15. PMID: 26180063; PMCID: PMC4503790.

3. GBD 2016 Diarrhoeal Disease Collaborators. Estimates of the global, regional, and national morbidity, mortality, and aetiologies of diarrhoea in 195 countries: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Infect Dis. 2018 Nov;18 (11):1211-1228. doi: 10.1016/S1473-3099 (18) 30362-1. Epub 2018 Sep 19. PMID: 30243583; PMCID: PMC6202444.

4. Khan I, Bai Y, Zha L, Ullah N, Ullah H, Shah SRH, Sun H and Zhang C (2021) Mechanism of the Gut Microbiota Colonization Resistance and Enteric Pathogen Infection. Front. Cell. Infect. Microbiol. 11:716299. doi: 10.3389/fcimb.2021.716299

5. Hansen ZA, Cha W, Nohomovich B, Newton DW, Lephart P, Salimnia H, Khalife W, Shade A, Rudrik JT, Manning SD. Comparing gut resistome composition among patients with acute Campylobacter infections and healthy family members. Sci Rep. 2021 Nov 16;11 (1):22368. doi: 10.1038/s41598-021-01927-7. PMID: 34785751; PMCID: PMC8595376.

6. Stamps BW, Kuroiwa J, Isidean SD, Schilling MA, Harro C, Talaat KR, Sack DA, Tribble DR, Maue AC, Rimmer JE, Laird RM, Porter CK, Goodson MS, Poly F. Exploring Changes in the Host Gut Microbiota During a Controlled Human Infection Model for *Campylobacter jejuni*. Front Cell Infect Microbiol. 2021 Aug 31;11:702047. doi: 10.3389/fcimb.2021.702047. PMID: 34532299; PMCID: PMC8439579.

7. Liechty Z, Baldwin A, Isidean S, Suvarnapunya A, Frenck R, Porter C, Goodson M. Dynamics of the gut microbiome in subjects challenged with *Shigella sonnei* 53G in a controlled human infection model. mSphere. 2025 Apr 29;10 (4):e0090624. doi: 10.1128/msphere.00906-24. Epub 2025 Mar 28. PMID: 40152601; PMCID: PMC12039237.

8. Timothy H. Dellit, Robert C. Owens, John E. McGowan, Dale N. Gerding, Robert A. Weinstein, John P. Burke, W. Charles Huskins, David L. Paterson, Neil O. Fishman, Christopher F. Carpenter, P. J. Brennan, Marianne Billeter, Thomas M. Hooton, Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship, Clinical Infectious Diseases, Volume 44, Issue 2, 15 January 2007, Pages 159-177, https://doi.org/10.1086/510393

9. Chung The H, Le SH. Dynamic of the human gut microbiome under infectious diarrhea. Curr Opin Microbiol. 2022 Apr;66:79-85. doi: 10.1016/j.mib.2022.01.006. Epub 2022 Feb 1. PMID: 35121284; PMCID: PMC9758627.

10. Li Y, Xia S, Jiang X, Feng C, Gong S, Ma J, Fang Z, Yin J, Yin Y. Gut Microbiota and Diarrhea: An Updated Review. Front Cell Infect Microbiol. 2021 Apr 15;11:625210. doi: 10.3389/fcimb.2021.625210. PMID: 33937093; PMCID: PMC8082445.

11. Cusumano G, Flores GA, Venanzoni R, Angelini P. The Impact of Antibiotic Therapy on Intestinal Microbiota: Dysbiosis, Antibiotic Resistance, and Restoration Strategies. Antibiotics (Basel). 2025 Apr 3;14 (4):371. doi: 10.3390/antibiotics14040371. PMID: 40298495; PMCID: PMC12024230.

12. Riddle MS, DuPont HL, Connor BA. ACG Clinical Guideline: Diagnosis, Treatment, and Prevention of Acute Diarrheal Infections in Adults. Am J Gastroenterol. 2016 May;111 (5):602-22. doi: 10.1038/ajg.2016.126. Epub 2016 Apr 12. PMID: 27068718.

13. Шокиров Бегзод, Халимова Юлдуз Антибиотик-индуцированный дисбиоз микробиоты кишечника крыс и резистентность к сальмонеллам // ОИИ. 2021. №4/S. URL: https://cyberleninka.ru/article/n/antibiotik-indutsirovannyy-disbioz-mikrobioty-kishechnika-krys-i-rezistentnost-k-salmonellam.

14. Дисбиоз кишечника: руководство по диагностике и лечению / Под ред. Е.И. Ткаченко, А.Н. Суворова. СПб.: СпецЛит, 2007. 238 с.

15. Miles SL, Holt KE, Mostowy S. Recent advances in modelling Shigella infection. Trends Microbiol. 2024 Sep;32 (9):917-924. doi: 10.1016/j.tim.2024.02.004. Epub 2024 Feb 28. PMID: 38423917.

16. Djeghout B, Le-Viet T, Martins LO, Savva GM, Evans R, Baker D, Page A, Elumogo N, Wain J, Janecko N. Capturing clinically relevant *Campylobacter* attributes through direct whole genome sequencing of stool. Microb Genom. 2024 Aug;10 (8):001284. doi: 10.1099/mgen.0.001284. PMID: 39213166; PMCID: PMC11570993.

17. Dziegiel A.H. (2024). *Microbial ecology and metagenomics of a foodborne pathogen* (PhD dissertation). Copenhagen: University of East Anglia. 198 p. https://ueaeprints.uea.ac.uk/id/eprint/98541

18. Wang J, den Bakker HC, Denes TG. A critical review of metagenomic approaches for foodborne pathogen surveillance. Crit Rev Food Sci Nutr. 2025;65 (33):8488-8501. doi: 10.1080/10408398.2025.2503453. Epub 2025 Jun 6. PMID: 40478725.

19. Отраслевой стандарт ОСТ 91500.11.0004-2003 «Протокол ведения больных. Дисбактериоз кишечника» (утв. Приказом МЗ РФ от 9 июня 2003 г. № 231)..

20. Николаева С.В., Горелов А.В., Крикун В.С. Бактериальные кишечные инфекции на современном этапе — подходы к антибиотикотерапии. РМЖ. Медицинское обозрение. 2024;8(11):661-666. DOI: 10.32364/2587-6821-2024-8-11-9.

21. World Health Organization. Guidelines for the control of shigellosis, including epidemics due to Shigella dysenteriae type 1. Geneva: WHO, 2005 (updated 2023). 64 p.

22. Crump JA, Sjölund-Karlsson M, Gordon MA, Parry CM. Epidemiology, Clinical Presentation, Laboratory Diagnosis, Antimicrobial Resistance, and Antimicrobial Management of Invasive Salmonella Infections. Clin Microbiol Rev. 2015 Oct;28 (4):901-37. doi: 10.1128/CMR.00002-15. PMID: 26180063; PMCID: PMC4503790.

23. Troeger C, Forouzanfar M, Rao PC, et al. Estimates of global, regional, and national morbidity, mortality, and aetiologies of diarrhoeal diseases: a systematic analysis for the Global Burden of Disease Study 2015. Lancet Infect Dis. 2017;17 (9):909-948. DOI: 10.1016/S1473-3099 (17) 30276-1. 17, No. - P. 909-948.

24. Ackermann M, Stecher B, Freed NE, Songhet P, Hardt WD, Doebeli M. Self-destructive cooperation mediated by phenotypic noise. Nature. 2008 Aug 21;454 (7207):987-90. doi: 10.1038/nature07067. PMID: 18719588.

25. Darkoh C, Chappell C, Gonzales C, Okhuysen P. A rapid and specific method for the detection of indole in complex biological samples. Appl Environ Microbiol. 2015 Dec;81 (23):8093-7. doi: 10.1128/AEM.02787-15. Epub 2015 Sep 18. PMID: 26386049; PMCID: PMC4651089.

26. Ардатская М. Д., Бельмер С. В., Добрица В. П., и соавт. Дисбиоз - дисбактериоз - кишечника: современное состояние проблемы, комплексная диагностика и лечебная коррекция. Экспериментальная и клиническая гастроэнтерология, 2015; 117 (5):13–50