THE EFFECT OF ACUTE RADIATION ON THE NORMAL MICROFLORA OF THE LARGE INTESTINE IN EXPERIMENTAL ANIMALS: RESULTS OF A DYNAMIC STUDY

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Abstract. This study investigates the dynamic impact of acute radiation exposure on the composition and state of the normoflora in the large intestine of laboratory rats. The experiment modeled the consequences of a single 6 Gy irradiation. The obtained data demonstrate significant dysbiotic shifts characterized by suppression of obligate and activation of opportunistic microflora, with subsequent partial recovery by day 30. The results underscore the critical role of gut microbiota in the pathogenesis of radiation injuries and point to potential targets for dysbiosis correction.

Keywords: acute irradiation, gut microbiota, dysbiosis, experimental animals, dynamics, lactobacilli, bifidobacteria, enterobacteria.

ДИНАМИЧЕСКОЕ ИЗУЧЕНИЕ ВЛИЯНИЯ ОСТРОГО ЛУЧЕВОГО ВОЗДЕЙСТВИЯ НА НОРМАЛЬНУЮ МИКРОФЛОРУ ТОЛСТОГО КИШЕЧНИКА У ЭКСПЕРИМЕНТАЛЬНЫХ ЖИВОТНЫХ.

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Аннотация. В настоящем исследовании изучено динамическое влияние острого лучевого воздействия на состав и состояние нормофлоры толстого кишечника у лабораторных крыс. Эксперимент моделировал последствия однократного облучения в дозе 6 Гр. Полученные данные демонстрируют значительные дисбиотические сдвиги, характеризующиеся угнетением облигатной и активацией условно-патогенной микрофлоры, с последующим частичным восстановлением к 30-м суткам. Результаты подчеркивают критическую роль кишечной микробиоты в патогенезе радиационных поражений и указывают на потенциальные мишени для коррекции дисбиоза.

Ключевые слова: острое облучение, микрофлора кишечника, дисбиоз, экспериментальные животные, динамика, лактобактерии, бифидобактерии, энтеробактерии.

1. Introduction. The human body exists in a state of symbiotic equilibrium with a vast and complex community of microorganisms, collectively known as the microbiota. Among these ecosystems, the intestinal microbiota is the most dense and metabolically active, playing an indispensable role not only in digestion and vitamin synthesis but also in the maturation and modulation of the immune system, maintenance of the gut barrier integrity, and protection against pathogenic colonization. This delicate balance, however, is highly susceptible to disruption by external stressors. Ionizing radiation, particularly when delivered acutely at significant doses, represents one of the most potent physical stressors, capable of inducing profound systemic alterations known collectively as acute radiation syndrome.

The gastrointestinal (GI) tract is notably radiosensitive. While the direct cytotoxic effect on the rapidly dividing crypt epithelial cells is a primary driver of the GI syndrome, a growing body of evidence highlights the pivotal role of the commensal gut microbiota in both the development and progression of radiation-induced damage. Acute, high-dose radiation exposure is hypothesized to cause a condition known as radiation-induced dysbiosis—a significant imbalance in the microbial community structure. This dysbiosis is characterized by a decline in beneficial, obligate anaerobic bacteria (e.g., *Bifidobacterium*, *Lactobacillus*) and a concomitant overgrowth of potentially pathogenic, often facultative anaerobic or aerobic bacteria (e.g., *Enterobacteriaceae*, *Staphylococcus*, *Candida* spp.). Such a shift compromises gut barrier function, facilitates bacterial translocation, exacerbates local and systemic inflammation, and can contribute to septic complications, thereby worsening the overall prognosis.

Despite the recognized importance of this phenomenon, detailed longitudinal studies charting the precise timeline of these microbial population shifts following acute irradiation are crucial for a comprehensive understanding of the pathogenetic cascade. Elucidating the dynamics—the rate of decline of protective species, the timing of opportunistic expansion, and the potential for autonomous recovery—is essential for identifying critical windows for therapeutic intervention. Therefore,

the aim of this study was to conduct a detailed dynamic assessment of the state of the autochthonous microflora in the large intestine of experimental animals following a single acute exposure to a sublethal dose of gamma radiation.

2. Materials and Methods

The experiment was conducted on 90 mature, outbred white male rats with an average weight of 180-220 g. All animals were housed in standard vivarium conditions with ad libitum access to food and water, in compliance with established principles of laboratory animal care. The rats were randomly divided into two main groups: a control group (n=30), which did not undergo irradiation, and an experimental group (n=60), subjected to a single, total-body gamma irradiation at a dose of 6 Gy using a "Luch-1" apparatus. To enable dynamic observation, the experimental group was further subdivided into 4 subgroups (n=15 each), with animals being sacrificed for sample collection on days 3, 7, 14, and 30 post-irradiation.

Sample collection was performed under light ether anesthesia with strict aseptic technique. Contents from the large intestine were aseptically collected. Quantitative and qualitative microbiological analysis was carried out using the classic method of serial tenfold dilutions followed by plating onto selective and differential diagnostic culture media. The number of colony-forming units (CFU) per 1 gram of material was determined for the following key microbial groups:

- Obligate anaerobes: Bifidobacteria (on Blaurock agar), Lactobacilli (on MRS agar).
- Obligate aerobes: *Escherichia coli* with typical and lactose-negative properties (on Endo agar).
- Opportunistic pathogens: Staphylococci (on Baird-Parker agar), yeast-like fungi of the genus *Candida* (on Sabouraud dextrose agar), *Proteus* spp. (on Ploskirev agar).

Statistical analysis of the data was performed using Student's t-test and non-parametric methods where appropriate. Differences were considered statistically significant at $p < 0.05$.

3. Results

The study revealed pronounced dynamic changes in the composition of the gut microbiota in irradiated animals compared to the control group.

Table 1. Dynamics of Obligate Microflora Indicators in the Large Intestine of Rats after Acute Irradiation (lg CFU/g, M±m)

Group / Time Point	Bifidobacteria	Lactobacilli
Control (n=30)	8.54 ± 0.12	7.92 ± 0.11
Day 3 (n=15)	5.21 ± 0.25*	4.88 ± 0.31*
Day 7 (n=15)	4.05 ± 0.30*	3.72 ± 0.28*
Day 14 (n=15)	6.10 ± 0.22*	5.45 ± 0.24*
Day 30 (n=15)	7.85 ± 0.18	7.20 ± 0.20*

*Note: * - significant difference compared to control (p<0.05).*

As shown in Table 1, acute irradiation led to a sharp suppression of obligate symbionts. A statistically significant decrease in the count of bifidobacteria and lactobacilli by almost 3 orders of magnitude (lg) was already observed on day 3. Maximum suppression was recorded on day 7, coinciding with the peak of radiation-induced enteritis. A gradual recovery began by day 14; however, even by day 30, the lactobacilli level remained significantly lower than the control, while the bifidobacteria count only approached the normal range.

Table 2. Dynamics of Opportunistic and Concomitant Microflora Indicators in Rats after Acute Irradiation (lg CFU/g, M±m)

Group / Time Point	E. coli (typical)	E. coli (lactose-neg.)	Staphylococci	Candida fungi
Control	6.80 ± 0.10	3.50 ± 0.15	2.90 ± 0.12	1.50 ± 0.10
Day 3	5.95 ± 0.20*	5.20 ± 0.22*	4.85 ± 0.25*	3.80 ± 0.30*
Day 7	5.10 ± 0.25*	6.15 ± 0.28*	5.60 ± 0.30*	5.20 ± 0.35*
Day 14	6.40 ± 0.18*	5.45 ± 0.20*	4.20 ± 0.22*	4.10 ± 0.25*
Day 30	6.70 ± 0.15	4.30 ± 0.18*	3.45 ± 0.15*	2.85 ± 0.20*

*Note: * - significant difference compared to control (p<0.05).*

The data in Table 2 demonstrate the opposite trend for opportunistic microorganisms. Their numbers increased progressively, peaking on day 7. The increase in lactose-negative *E. coli*, staphylococci, and *Candida* fungi is particularly indicative of profound dysbiosis and reduced colonization resistance of the intestine. By day 30, a positive trend was observed, but levels of most opportunistic pathogens remained above control values.

Table 3. Changes in the Ratio of Major Microbial Groups (Dysbiosis Indices)

Group / Time Point	**Anaerobes/Aerobes Ratio**	**Lactose-Negativity Coefficient (LNC)**
Control	1.85 ± 0.05	0.51 ± 0.03
Day 3	0.12 ± 0.01*	0.87 ± 0.05*
Day 7	0.05 ± 0.01*	1.21 ± 0.07*
Day 14	0.45 ± 0.03*	0.85 ± 0.04*
Day 30	1.10 ± 0.04*	0.64 ± 0.03*

*Note: * - significant difference compared to control ($p<0.05$). The dysbiosis index was calculated as the sum of lg bifido- and lactobacilli divided by lg E. coli. LNC = lg lactose-neg. E. coli / lg typical E. coli.*

Table 3 summarizes dysbiotic shifts through integral indicators. The sharp drop in the anaerobes/aerobes ratio by 30-40 times on day 7 and the significant increase in the lactose-negativity coefficient confirm the severity of the microbial imbalance. Partial recovery by day 30 did not lead to complete normalization of these key indices, indicating the long-term nature of post-radiation dysbiosis.

4. Discussion

The results clearly illustrate the pathogenetic dynamics of radiation-induced intestinal dysbiosis. The initial phase (days 3-7) is characterized by a catastrophic decline in obligate anaerobes—bifidobacteria and lactobacilli, which are the most radiosensitive components of the microbiocenosis due to their strict anaerobic nature and complex metabolic requirements. This creates an "ecological vacuum" and leads to a sharp decline in the colonization resistance of the mucosal barrier. The vacated ecological niches are actively occupied by opportunistic

microorganisms, as confirmed by their exponential growth. The peak of disturbances on day 7 correlates with the clinical picture of acute radiation syndrome, manifesting as severe enterocolitis, diarrhea, and a high risk of endogenous infection.

The recovery phase (days 14-30) is slow and incomplete. Partial recolonization by obligate microflora is likely associated with reparative processes in the intestinal epithelium and the adaptation of surviving strains. However, the persistently elevated levels of lactose-negative *E. coli*, staphylococci, and the incomplete recovery of lactobacilli indicate long-term alterations in the ecosystem. This aligns with literature suggesting that radiation exposure can cause persistent changes in microbiota composition, affecting host metabolism and immune status even after clinical recovery. The disturbance of key indices, such as the anaerobe/aerobe ratio, is a reliable marker of dysbiosis severity and can be used to assess the efficacy of probiotic or other corrective therapies.

5. Conclusion

In conclusion, this dynamic study convincingly demonstrates that acute radiation exposure at a dose of 6 Gy induces profound and persistent disturbances in the normal microflora of the large intestine in experimental animals. These changes are phasic: the acute period features total suppression of symbiotic flora with a compensatory overgrowth of opportunistic representatives, while the later period shows incomplete and delayed recovery of the original balance. The identified patterns underscore that intestinal dysbiosis is an integral component of radiation injury pathogenesis and may significantly contribute to the development of complications. These findings justify the necessity of including measures to correct intestinal microbiocenosis (e.g., application of probiotics, prebiotics, metabiotics) in the comprehensive treatment scheme for radiation injuries, with such correction ideally initiated as early as possible to mitigate the peak dysbiotic disturbances. Further research should be directed towards studying the efficacy of various biocorrective agents in the context of acute radiation exposure.

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