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ROTAVIRUS INFECTION: MECHANISMS OF PATHOGENESIS AND STRATEGIES FOR DISEASE CONTROL

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Abstract

Rotavirus continues to be a leading cause of severe, dehydrating gastroenteritis in young children worldwide, even with the availability of vaccines. This review consolidates current understanding of the virus's biology, how it causes disease, and the body's immune defenses against it. We critically assess the development, real-world impact, and persistent obstacles of global immunization efforts. The review also explores future priorities, such as next-generation vaccines and antiviral treatments, which are crucial for moving from control toward eventual eradication of the disease.

Key words

Rotavirus, vaccine, children.

Introduction. For over four decades, rotavirus has been the predominant cause of severe, dehydrating acute diarrhea in young children worldwide. While the World Health Organization's prequalification of oral rotavirus vaccines (ORVs) a decade ago has significantly reduced the global disease burden, achieving universal effectiveness remains challenging. Motivated by the persistent toll of rotavirus, particularly in developing nations, this article provides a detailed examination of the virus's biology, transmission, pathogenesis, host immunity, epidemiology, and vaccination. It also reviews and assesses recent findings on the host, viral, and environmental factors that reduce ORV efficacy in low- and middle-income countries (LMICs) and explores advances in non-vaccine prevention and management strategies.

Rotavirus is a major global pathogen, causing an estimated 258 million cases of diarrhea and between 122,000 and 215,000 deaths annually in children under five, ranking as the third-leading cause of childhood mortality. This burden is starkly inequitable, with the highest mortality rates—approximately 100 deaths per 100,000 children under five—concentrated in ten LMICs.

Despite four WHO-prequalified oral vaccines being used in over 106 countries, rotavirus persists as the leading cause of diarrheal death in children. A critical issue

is the vaccines' lower effectiveness in LMICs compared to high-income countries. This disparity stems from a complex interplay of factors, including host characteristics (e.g., malnutrition, blood group, co-administration with other vaccines), viral factors (e.g., genetic diversity), and environmental influences (e.g., gut microbiome dysbiosis).

Etymology, Discovery, and Basic Virology

First observed in animals in the mid-20th century, rotavirus was identified in children with gastroenteritis by Ruth Bishop in 1973. Thomas Henry Flewett proposed the name "rotavirus" in 1974 due to its wheel-like appearance under an electron microscope, a name officially adopted in 1978. The virus was quickly recognized as a major cause of severe childhood diarrhea, a status it maintains today.

Rotavirus is a member of the *Reoviridae* family. Its infectious form is a triple-layered particle (TLP) that protects its genome of 11 segments of double-stranded RNA. These segments encode six structural proteins (VP1-VP4, VP6, VP7) and six non-structural proteins (NSP1-NSP6). The structural proteins VP4, VP6, and VP7 are key to classifying the virus into groups, subgroups, and serotypes.

Transmission and Environmental Stability

Rotavirus is primarily transmitted via the fecal-oral route through multiple pathways:

- **Direct and Indirect Contact:** The virus spreads easily among children and to close contacts via contaminated hands, surfaces (toys, diaper areas), and objects placed in the mouth. It is highly stable, persisting for weeks on porous and nonporous surfaces.
- **Food and Water:** Contamination can occur through polluted irrigation water, poor hygiene by food handlers, or contaminated storage containers. Outbreaks have been linked to various foods, including vegetables, seafood, and prepared meals.
- **Vectors:** Flies attracted to feces can mechanically transfer the virus to food and surfaces.
- **Zoonotic Potential:** Animal rotaviruses can infect humans directly or through genetic reassortment, with animal reservoirs posing a risk for emerging strains.
- **Waterborne:** The virus is frequently detected in sewage and can contaminate drinking water, leading to outbreaks.
- **Airborne Hypothesis:** Its rapid spread and detection in air samples suggest possible aerosol transmission, though confirmatory evidence on viable virus is still needed.

• Transmission is potentiated by a low infectious dose, extremely high viral shedding in stool, and prolonged shedding from both symptomatic and asymptomatic individuals.

Pathogenesis and Mechanisms of Disease

Infection begins when the virus, protected by its stable capsid, reaches the small intestine. The outer protein VP4 binds to host cell receptors, including histo-blood group antigens (HBGAs), whose expression influences individual and population susceptibility to different rotavirus strains. Proteolytic cleavage of VP4 enhances infectivity.

Rotavirus targets and destroys mature enterocytes in the small intestinal villi, leading to diarrhea through three main mechanisms:

1. **Malabsorption:** Villous damage and loss of digestive enzymes impair nutrient and fluid absorption, causing osmotic diarrhea.
2. **Secretory Diarrhea:** The viral enterotoxin NSP4 triggers calcium-dependent chloride secretion and inhibits sodium-glucose transporters, leading to watery, secretory diarrhea. It can also cause secondary lactose intolerance.
3. **Enteric Nervous System Activation:** NSP4 stimulates serotonin release from enteroendocrine cells, activating intestinal nerves to increase motility and potentially trigger vomiting.
4. Although infection is typically localized to the gut, antigenemia/viremia can occur and is associated with more severe symptoms like fever and seizures. Extraintestinal spread and systemic disease are more common in immunocompromised individuals.

Clinical Course and Determinants of Severity

Clinical outcomes range from asymptomatic infection to severe, dehydrating gastroenteritis with vomiting and fever. The incubation period is short (1-3 days), and illness typically lasts 5-7 days. Key determinants of severity include:

• **Host Factors:** Age is critical; severe disease is most common in infants after maternal antibody wanes and before full immunity develops. Malnutrition exacerbates severity and prolongs recovery.

• **Viral Factors:** Virulence is multigenic, involving genes that regulate replication (e.g., NSP1, which inhibits interferon responses), entry (VP4, VP7), and toxin production (NSP4).

Host Immune Response

Innate Immunity: The host detects viral RNA via receptors (RIG-I, MDA-5, TLR3), triggering interferon (IFN) and inflammatory cytokine production to establish an antiviral state. Rotavirus counteracts this via proteins like NSP1, which degrades host interferon regulators. Additional innate defenses involve the

OAS/RNase L pathway and the Nlrp9b inflammasome, which recognizes viral RNA to limit infection.

Adaptive Immunity:

• **Humoral:** Infection elicits neutralizing antibodies (IgA and IgG) against surface proteins VP7 and VP4, which correlate with protection. Local intestinal IgA is a key mediator of immunity. Antibodies against the inner capsid protein VP6 can also provide intracellular neutralization. Repeated exposures broaden the immune response.

• **Cell-Mediated:** CD4+ and CD8+ T-cells are crucial for viral clearance during primary infection. CD4+ T-cells help B-cell differentiation, while CD8+ T-cells directly eliminate infected cells. Pro-inflammatory (Th1/Th17) and regulatory T-cell responses work in balance to clear the virus while maintaining mucosal homeostasis.

REFERENCES:

18. ARTIQOV, I., & ABDULLAYEVA, D. (2025). CHICKENPOX: AMONG YOUNG CHILDREN IN KHOREZM REGION. *Multidisciplinary Journal of Science and Technology*, *5*(3), 678-683.

19. ARTIQOV, I., & ABDULLAYEVA, D. (2025). THE SPREAD OF DIARRHEAL DISEASES IN THE KHOREZM REGION. *Multidisciplinary Journal of Science and Technology*, *5*(3), 672-677.

20. SH, Y. S., YOQUBOV, Q., & NURLLAYEV, R. (2025). FEATURES OF THE COURSE OF THE HERPES TYPE 4 VIRUS IN CHILDREN. *Multidisciplinary Journal of Science and Technology*, *5*(3), 397-402.

21. NURLLAYEV, R., SH, Y. S., & YOQUBOV, Q. (2025). PECULIARITIES OF THE ETIOLOGICAL STRUCTURE OF ACUTE DIARRHEAL DISEASES IN THE CONDITIONS OF THE SOUTHERN ARAL REGION. *Multidisciplinary Journal of Science and Technology*, *5*(3), 403-408.

22. Артиков, И. А., Отажанов, Ш. З., & Садуллаев, С. Э. (2025). ПАТОМОРФОЛОГИЧЕСКИЕ АСПЕКТЫ ДЕТСКОГО ЛИМФОБЛАСТНОГО ЛЕЙКОЗА. *Multidisciplinary Journal of Science and Technology*, *5*(6), 257-264.

23. Kadamovna, A. D., Rustombekovich, N. R., Zarifboyevich, O. S., & Ernazarovich, S. S. (2025). COMBINATIONS OF HEPATITIS B WITH PULMONARY TUBERCULOSIS. *Multidisciplinary Journal of Science and Technology*, *5*(5), 60-65.

24. Rustombekovich, N. R., Zarifboyevich, O. S., Kadamovna, A. D., & Ernazarovich, S. S. (2025). THE STATE OF THE ANTIOXIDANT DEFENSE

SYSTEM IN CHRONIC HEPATITIS C. *Multidisciplinary Journal of Science and Technology*, *5*(5), 79-84.

25. Ernazarovich, S. S., Zarifboyevich, O. S., Rustombekovich, N. R., & Kadamovna, A. D. (2025). DYNAMICS OF THE COVID-19 PANDEMIC AND ITS CLINICAL CONSEQUENCES. *Multidisciplinary Journal of Science and Technology*, *5*(5), 85-90.

26. Аскарова, Р. И., & Отажонов, Ш. З. (2020). ТУБЕРКУЛЕЗ НА ФОНЕ СОПУТСТВУЮЩЕЙ ПАТОЛОГИИ. *European Science*, (3), 106-108.

27. Аскарова, Р. И., Атажанов, Ш. З., & Маткурбанов, Х. И. (2019). АНАЛИЗ ПЕРВИЧНЫХ ФОРМ ТУБЕРКУЛЕЗА У ДЕТЕЙ, ПРОЖИВАЮЩИХ В ХОРЕЗМСКОЙ ОБЛАСТИ. *Наука, техника и образование*, (9), 64-68.

28. Ibraximova, H. R., Artiqov, I. A., & Otajanov Sh, Z. (2025). HELMINTH INFECTIONS: CLASSIFICATION, DEVELOPMENTAL CONDITIONS, AND CLINICAL MANIFESTATIONS. *Multidisciplinary Journal of Science and Technology*, *5*(6), 1241-1245.

29. Юсупов, Ш. Р., Отажонов, Ш. З., Артиков, И. А., & Ибодуллаева, С. С. (2025). МИКРОБИОЛОГИЧЕСКАЯ СТРУКТУРА ОСТРЫХ ДИАРЕЙНЫХ ЗАБОЛЕВАНИЙ В ЮЖНОМ ПРИАРАЛЬЕ: РЕЗУЛЬТАТЫ ЭПИДЕМИОЛОГИЧЕСКОГО МОНИТОРИНГА. *Multidisciplinary Journal of Science and Technology*, *5*(6), 237-242.

30. Urinovna, M. O., Kadamovna, A. D., Zarifboyevich, O. S., & Axmedjonovich, A. I. (2025). PUBLIC HEALTH AND EPIDEMIOLOGICAL INSIGHTS INTO THE COVID-19 PANDEMIC. *Multidisciplinary Journal of Science and Technology*, *5*(6), 243-248.

31. Khudaykulova, G. K., & Muminova, M. T. (2025, January). IMMUNOLOGICAL CHANGES IN HIV-INFECTED CHILDREN WITH VIRAL DIARRHEA. In *CONFERENCE ON THE ROLE AND IMPORTANCE OF SCIENCE IN THE MODERN WORLD* (Vol. 2, No. 1, pp. 149-150).

32. Otajanov, S. Z. (2025, January). CYTOKINE LEVELS IN HIV-INFECTED CHILDREN WITH VIRAL DIARRHEA. In *CONFERENCE ON THE ROLE AND IMPORTANCE OF SCIENCE IN THE MODERN WORLD* (Vol. 2, No. 1, pp. 148-148).

33. Худайкулова, Г., Муминова, М., & Отажанов, Ш. (2021). АНАЛИЗ ЭТИОЛОГИЧЕСКОЙ СТРУКТУРЫ ВИРУСНЫХ ДИАРЕЙ У ВИЧ-ИНФИЦИРОВАННЫХ ДЕТЕЙ. *Журнал кардиореспираторных исследований*, *2*(3), 31-34.

34. Машарипова Ш. АНТИОКСИДАНТНАЯ АКТИВНОСТЬ СЫВОРОТКИ КРОВИ И МАРКЕРЫ СТАТУСА ЖЕЛЕЗИ У БОЛЬНЫХ ХРОНИЧЕСКИМ ВИРУСНЫМ ГЕПАТИТОМ С.

18. Машарипова Ш., Машарипов С. Заболевание печени у больных с ишемической болезнью сердца среди хорезмского региона : дис. – Cardiorespiratory Research, 2021.

19. Машарипов С., Машарипова Ш. Изучение аминокислотного состава фиброина по слоям волокна шелка. – 2021.

20. Машарипов С., Машарипова Ш. Аминокислотный состав фиброина на слоях шелка. – 2021.

21. Хударгенова Д. Р. и др. ЦЕЛЕСООБРАЗНОСТЬ ОТБОРА ЖИВОТНЫХ-ПРОДУЦЕНТОВ ПРИ ПОЛУЧЕНИИ ГИПЕРИММУННЫХ СЫВОРОТОК, ПРИМЕНЯЕМЫХ В СУДЕБНО-МЕДИЦИНСКИХ ЛАБОРАТОРИЯХ. – 2023.

22. Masharipov S., Sh M. DEFINITION OF ETIOLOGICAL DOMINANT STRUCTURES OF NOSOCOMIAL PNEUMONIA. – 2024.

23. Sadullayev, S. E., Artikova, D. O., & Sadullayeva, M. R. (2026, January). STRENGTHENING CLINICAL REASONING IN INFECTIOUS DISEASES. In *Scottish International Conference on Multidisciplinary Research and Innovation–SICMRI 2025* (Vol. 3, No. 1, pp. 19-21).

24. Sadullayev, S. E., Ibragimov, S. J., & Bobojonov, Y. B. (2026, January). IMPROVING CLINICAL PREPAREDNESS AND FIRST AID RESPONSE IN EMERGENCY INFECTIOUS DISEASE SITUATIONS AMONG HEALTHCARE STUDENTS AND PROFESSIONALS. In *International Conference on Artificial Intelligence and Applications (ICAIA)* (Vol. 1, No. 2, pp. 10-13).

25. Jaloladdin o‘g‘li, M. M., & Ernazarovich, S. S. (2025). COMORBID INFECTIONS IN YOUNG CHILDREN: CLINICAL FEATURES AND ANALYSIS OF OBSERVATIONS. *Multidisciplinary Journal of Science and Technology*, *5*(4), 362-366.

26. Машарипова S., & Машарипов S. . (2024). Распространение ветряной оспы и ее профилактика в Узбекистане. *Общество и инновации*, *5*(9/S), 125–130. https://doi.org/10.47689/2181-1415-vol5-iss9/S-pp125-130

27. PROVIDING MEDICAL CARE TO PATIENTS WITH INFECTIOUS DISEASES. (2025). *Multidisciplinary Journal of Science and Technology*, *5*(5), 72-78. https://mjstjournal.com/index.php/mjst/article/view/3371

28. EPIDEMIOLOGY OF EXANTHEMIC DISEASES AMONG THE POPULATION OF KHOREZM. (2025). *Multidisciplinary Journal of Science and*

Technology, *5*(5), 66-71. https://mjstjournal.com/index.php/mjst/article/view/3370

29. КЛИНИЧЕСКИЕ И ИММУНОЛОГИЧЕСКИЕ ОСОБЕННОСТИ ИНФЕКЦИОННОГО МОНОНУКЛЕОЗА У ДЕТЕЙ. (2025). *Multidisciplinary Journal of Science and Technology*, *5*(6), 249-256. https://www.mjstjournal.com/index.php/mjst/article/view/3933

30. Masharipova , S., Karimova, U., & Oltiyeva, H. (2025). RISK FACTORS AND METHODS OF PREVENTION OF NOSOCOMIAL INFECTION. *Общественные науки в современном мире: теоретические и практические исследования*, *4*(2), 67–70. извлечено от https://inlibrary.uz/index.php/zdif/article/view/66205

31. OPPORTUNISTIC INFECTIONS IN THE CONTEXT OF AIDS: A CLINICAL CASE. (2025). *Web of Teachers: Inderscience Research* , *3*(3), 140-144. https://webofjournals.com/index.php/1/article/view/3571

32. FEATURES OF THE CLINICAL COURSE OF CHICKENPOX IN ADULTS IN THE KHOREZM REGION (UZBEKISTAN). (2025). *Web of Discoveries: Journal of Analysis and Inventions*, *3*(3), 48-52. https://webofjournals.com/index.php/3/article/view/3636

33. МАШАРИПОВА Ш. С. ОСОБЕННОСТИ ЭПИДЕМИЧЕСКОГО ПРОЦЕССА БРЮШНОГО ТИФА В ПРИАРАЛЬЕ //Развитие и актуальные вопросы современной науки. – 2018. – №. 1. – С. 127-131.

34. Машарипова Шохиста Сабировна МОРФОЛОГИЧЕСКОЕ СТРОЕНИЕ ЛЕГОЧНЫХ АРТЕРИЙ ПОД ВЛИЯНИЕМ САХАРНОГО ДИАБЕТА // JCRR. 2022. №1. URL: https://cyberleninka.ru/article/n/morfologicheskoe-stroenie-legochnyh-arteriy-pod-vliyaniem-saharnogo-diabeta (дата обращения: 13.01.2026).

35. Masharipova S. S., Ibrahimova H. R. Matyakubova OU MORPHOLOGICAL CHARACTERISTICS OF THE ARTERIES OF THE SMALL CIRCULATION OF THE CIRCULATION ON THE BACKGROUND OF EXPERIMENTAL DIABETES //THE THEORY OF RECENT SCIENTIFIC RESEARCH IN THE FIELD OF PEDAGOGY. – 2022. – С. 13.

36. Matyakubova O. U. et al. MEASLES DISEASE AMONG THE POPULATION //JOURNAL OF APPLIED MEDICAL SCIENCES. – 2024. – Т. 7. – №. 3. – С. 40-50.

37. Матякубова О., Машарипова S., & Машарипов S. (2024). Clinical symptoms and laboratory features in the course of pneumonia in children according to the Khorezm region . *Современник аспекти паразитологии и актуальные проблемы кишечных инфекций*, *1*(1), 27. извлечено от

https://inlibrary.uz/index.php/problems-intestinal-infections/article/view/32464

38. Матякубова О., Машарипова S., & Машарипов S. (2024). Detection of opportunistic infections in children with hiv infection. *Современник аспекти паразитологии и актуальные проблемы кишечных инфекций*, *1*(1), 28. извлечено от https://inlibrary.uz/index.php/problems-intestinal-infections/article/view/32465

39. OPPORTUNISTIC INFECTIONS IN PATIENTS WITH DIABETES MELLITUS. (2025). *Western European Journal of Modern Experiments and Scientific Methods*, *3*(04), 43-47. https://westerneuropeanstudies.com/index.php/1/article/view/2331

40. Masharipovich M. S. Sabirovna MS TENIOZ KASALLIGI TASHXISLANGAN ALLERGIK FONGA EGA BOLALARNING IMMUN TIZIMINING XUSUSIYATLARI //ЖУРНАЛ ГЕПАТО-ГАСТРОЭНТЕРОЛОГИЧЕСКИХ ИССЛЕДОВАНИЙ.–2022.–№. SI-2.

41. Artikov, I. A., Sadullaev, S. E., Ibrakhimova, H. R., & Abdullayeva, D. K. (2023). *RELEVANCE OF VIRAL HEPATITIS EPIDEMIOLOGY. IMRAS, 6 (7), 316–322.*

42. Sadullaev, S. E., Ibragimov, S. J., Bobojonov, Y. B., Yoqubov, Q. Y., Abdullayeva, D. K., & Khasanova, J. R. (2024). PREVALENCE OF DIARRHEAL DISEASES IN THE REPUBLIC OF UZBEKISTAN. *International Journal of Education, Social Science & Humanities*, *12*(3), 356-363.

43. Ibrakhimova, H. R., Matyakubova, O. U., Sadullaev, S. E., & Abdullayeva, D. K. (2023). *HELMINTISES IN CHILDREN AMONG THE POPULATION IN UZBEKISTAN. IMRAS, 6 (7), 323–327.*