

Post-Antibiotic Gut Microbiota Recovery in the Rumen: Insights into Colonization Patterns, Population Density, and Diversity Dynamics

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Abstract

The post-antibiotic recovery of gut microbiota represents a critical area of research in understanding how microbial communities rebalance and re-establish homeostasis following antibiotic-induced disruptions. Antibiotics, while effective against infections, can cause substantial shifts in gut microbiota, leading to dysbiosis – a state of microbial imbalance that impairs gut health and functions. This recovery process involves multiple complex dynamics, including colonization patterns, population density, and the restoration of microbial diversity. The key factors influencing this recovery are microbial resilience, colonization dynamics, the role of keystone species, competition among microbes, and host-microbiota interactions. Therapeutic strategies, such as the use of probiotics, synbiotics, fecal microbiota transplantation, and alternative antimicrobial therapies, have been explored to aid in microbial recolonization and restore gut functionality. This study aims to comprehensively investigate the mechanisms underlying the post-antibiotic recovery of the gut microbiota. It focuses on understanding how microbial populations reorganize, the role of keystone species in rebuilding ecosystem stability, and the potential of various therapeutic approaches. Additionally, it examines how host factors, such as immune responses and dietary interventions, influence recovery. Insights into these processes will provide critical knowledge for developing strategies to promote healthy microbial communities, improve gut function, and mitigate the long-term impacts of antibiotic treatment on gut health.

Keywords: Antibiotic-induced dysbiosis, colonization dynamics, functional recovery, gut microbiota, host-microbiota diversity, microbial resilience, post-antibiotic recovery

INTRODUCTION

The gut microbiota plays a crucial role in maintaining host health, contributing to essential functions, such as nutrient absorption, immune modulation, and pathogen defence. Antibiotic treatments, while effective in managing infections, often lead to unintended consequences by disrupting the delicate balance of microbial communities. This disruption, known as antibiotic-induced dysbiosis, results in a reduction of microbial diversity and the overgrowth of pathogenic bacteria, which can impair gut homeostasis [1]. Understanding how gut microbiota recovers from such disturbances is essential for developing strategies to restore microbial balance and promote long-term gut health.

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The recovery of the gut microbiota post-antibiotic treatment is a dynamic and complex process. It involves the recolonization of beneficial microbes, the restoration of functional pathways, and the re-establishment of microbial diversity. Several factors influence this recovery, including microbial resilience, the competitive interactions

between different bacterial species, and the role of keystone species that drive ecosystem stability [2]. Additionally, the host's genetic predispositions and immune responses play a significant role in shaping the outcome of microbial recovery. Various therapeutic approaches, such as probiotics, symbiotics, and fecal microbiota transplantation (FMT), have been explored to aid recovery, but the mechanisms underlying their effectiveness remain poorly understood.

This study aims to bridge the gap in knowledge regarding the post-antibiotic recovery of gut microbiota by focusing on colonization patterns, microbial density, and diversity dynamics. A novel aspect of this study is its comprehensive approach, integrating microbial ecological interactions, host factors, and therapeutic interventions. By examining the mechanisms of microbial recolonization, the restoration of functional pathways, and the impact of dietary and immunological factors, this research will provide valuable insights into optimizing strategies for gut microbiota recovery. Ultimately, this work will contribute to advancing therapeutic approaches that enhance microbial resilience and promote a healthy gut ecosystem after antibiotic disruption.

ANTIBIOTIC-INDUCED DYSBIOSIS

Mechanisms Disrupting Microbial Communities

Antibiotics disrupt microbial communities by killing or inhibiting specific bacterial groups, creating ecological imbalances [3]. This disruption reduces the population density of beneficial microbes while allowing opportunistic pathogens to thrive. Understanding these mechanisms enables the development of strategies to repopulate beneficial microbes, restore colonization dynamics, and improve diversity, ensuring the recovery of a resilient and functional gut microbiota.

Effects on Symbiotic Vs Pathogenic Bacteria

Antibiotics do not differentiate between symbiotic and pathogenic bacteria, often eliminating both. This indiscriminate action depletes beneficial species essential for gut health and opens niches for pathogens to dominate [4]. Recovery strategies that target the regrowth of symbiotic bacteria while suppressing pathogenic species enhance microbial colonization, rebuild density, and restore diversity, contributing to long-term gut health.

Long-Term Impacts on Gut Homeostasis

Antibiotic-induced dysbiosis disrupts gut homeostasis, impairing functions, such as digestion, immune regulation, and microbial diversity maintenance [5]. Persistent imbalances can lead to chronic gastrointestinal issues. Strategies that promote the recolonization of beneficial bacteria and enhance microbial density can stabilize gut homeostasis, restore diversity, and support a robust post-antibiotic microbiota recovery process.

Antibiotic Specificity Influences Microbial Shifts

Antibiotics vary in their spectrum and mode of action, leading to different microbial shifts. Broad-spectrum antibiotics cause widespread microbial loss, while narrow-spectrum drugs target specific groups [6]. Understanding these differences allows for tailored recovery interventions that optimize microbial colonization, restore population density, and rebuild diversity, facilitating a more effective and sustainable microbiota recovery.

Recovery Potential of Disrupted Microbial Niches

Antibiotics disrupt microbial niches, creating opportunities for both beneficial and harmful bacteria to colonize. Recovery strategies that target these niches with prebiotics, probiotics, or dietary interventions encourage beneficial microbial regrowth [7]. By filling these ecological voids with beneficial species, microbial density and diversity are enhanced, preventing pathogenic overgrowth and supporting overall gut microbiota recovery.

Variations in Dysbiosis Across Antibiotics

Different antibiotics induce unique patterns of dysbiosis based on their spectrum, dose, and duration of use [8]. These variations affect recovery dynamics, with some antibiotics causing deeper imbalances. Identifying and addressing these variations through targeted recovery strategies ensures effective

colonization of beneficial bacteria, rebuilding of microbial density, and restoration of diversity, leading to a healthier post-antibiotic gut.

Resistance Gene Propagation in Dysbiotic States

Antibiotics promote the spread of resistance genes, especially in dysbiotic environments where beneficial bacteria are depleted [9]. Resistant pathogens can dominate, further hindering recovery. Strategies, like phage therapy or precision probiotics, can mitigate resistance gene propagation, fostering beneficial colonization, enhancing microbial density, and restoring diversity, ultimately improving the resilience and stability of the gut microbiota.

Effects on Microbial Metabolic Pathways

Antibiotics disrupt microbial metabolic pathways, including those responsible for producing short-chain fatty acids and metabolizing bile acids [10]. These disruptions hinder microbial colonization and functional recovery. Nutritional interventions, such as prebiotics or postbiotics can restore these pathways, enhancing microbial density, supporting the recolonization of beneficial microbes, and improving diversity, ultimately promoting a functional gut microbiota.

Alterations in Gut Immune Modulation

Antibiotics disrupt the crosstalk between the gut microbiota and the immune system, weakening barrier function and altering immune responses. This impairs colonization by beneficial microbes [11]. Interventions restoring immune-microbiota interactions through probiotics or dietary approaches enhance microbial density and diversity, ensuring a balanced recovery of gut homeostasis and a resilient microbiota after antibiotic exposure.

Role of Microbial Quorum Sensing in Dysbiosis

Antibiotics disrupt quorum sensing, the chemical signaling system that microbes use to coordinate activities. This hampers colonization and microbial balance [12]. Restoring quorum sensing through targeted prebiotics or signaling molecule analogs promotes beneficial bacterial interactions, enhances microbial density, and supports diversity, facilitating the recovery of a well-structured and functional post-antibiotic gut microbiota.

MICROBIAL RESILIENCE

Resilience of Core Microbiota Taxa

Core microbiota taxa exhibit resilience by repopulating disrupted ecosystems due to their ecological adaptability and essential roles in maintaining gut stability. These taxa contribute to microbial density and diversity by filling ecological voids and outcompeting pathogens. Enhancing their recovery through targeted interventions supports the recolonization of beneficial species and stabilizes post-antibiotic gut microbiota dynamics.

Mechanisms Enabling Natural Regrowth

Natural regrowth mechanisms, including competitive exclusion and metabolic specialization, allow microbes to reclaim disrupted niches. These processes promote microbial density and diversity by facilitating the recovery of beneficial bacteria [13]. Understanding and supporting these mechanisms can accelerate colonization, enhance ecosystem stability, and ensure functional resilience in post-antibiotic gut microbiota recovery.

Microbial Biofilm Formation

Biofilms provide structural support and protection for microbes, aiding their survival and recolonization in disturbed environments. Biofilm formation enhances microbial density by creating stable communities that resist external stressors [14]. Encouraging biofilm development promotes the establishment of diverse and resilient microbiota, accelerating the recovery of gut ecosystems after antibiotic treatment.

Thresholds for Ecosystem Resilience

Ecosystem resilience thresholds determine the capacity of gut microbiota to recover from disturbances. Exceeding these thresholds may result in prolonged dysbiosis [15]. Identifying and restoring resilience thresholds through dietary or microbial interventions ensures the recovery of microbial density, colonization of beneficial species, and restoration of diversity, stabilizing the post-antibiotic gut ecosystem.

Role of Dormant Bacterial Spores in Recovery

Dormant bacterial spores resist antibiotic effects and germinate under favorable conditions, contributing to microbial recovery. These spores help recolonize disrupted niches, enhancing microbial density and diversity [16]. Leveraging spore-forming probiotics can accelerate recovery by restoring beneficial species, stabilizing microbial communities, and ensuring functional resilience in the gut microbiota.

Microbial Community Adaptation to New Niches

Disrupted gut ecosystems create new ecological niches, prompting microbial adaptation through genetic and metabolic flexibility. This adaptation facilitates the recolonization of beneficial taxa, enhancing microbial density and diversity [17]. Supporting these adaptations with tailored prebiotics or postbiotics ensures the stabilization of gut ecosystems and promotes sustainable recovery of microbiota after antibiotic treatment.

Influence of Host Genetic Predispositions

Host genetics influences microbial composition and recovery potential by shaping gut environment and immune responses. Genetic predispositions determine the ability of beneficial microbes to colonize and proliferate [18]. Personalized interventions based on host genetics can optimize microbial density, enhance colonization, and restore diversity, ensuring effective post-antibiotic microbiota recovery tailored to individual needs.

Timeframes for Resilient Ecosystem Restoration

Timeframes for gut microbiota restoration vary depending on antibiotic impact and host factors. Recovery strategies can reduce this duration by promoting beneficial colonization, microbial density, and diversity. Understanding these timeframes helps design phased interventions that align with natural recovery processes, ensuring a resilient and functional gut microbiota ecosystem after antibiotics.

Interactions Between Microbial and Host Resilience

Microbial resilience and host resilience are interconnected through immune-microbiota crosstalk and metabolic exchanges. Strengthening host resilience supports microbial recovery by creating a stable environment for colonization and diversity [15]. Interventions targeting both microbial and host resilience ensure improved microbial density, functional recovery, and long-term stability of the post-antibiotic gut microbiota ecosystem.

Functional Compensation by Residual Microbes

Residual microbes compensate for lost functions during dysbiosis, maintaining essential gut processes. This functional compensation aids recovery by stabilizing microbial communities, enabling recolonization, and supporting diversity. Enhancing the activity of residual beneficial microbes through prebiotics or functional diets accelerates recovery, ensuring resilience and sustainability of the post-antibiotic gut microbiota ecosystem.

COLONIZATION DYNAMICS

Sequence of Microbial Recolonization

Recolonization occurs in a defined sequence where pioneer microbes establish initial niches, creating conditions favorable for subsequent species. This sequence restores microbial density and diversity over

time. Supporting this natural succession with prebiotics or selective probiotics ensures an effective recovery, stabilizing colonization dynamics and promoting a balanced gut microbiota post-antibiotic treatment.

Role of Pioneer Species in Recovery

Pioneer species are the first to colonize the gut post-antibiotics, shaping the microbial ecosystem and promoting beneficial recolonization [19]. These species outcompete pathogens and facilitate the establishment of other beneficial microbes, enhancing microbial density and diversity. Promoting pioneer species through targeted interventions accelerates gut microbiota recovery and ensures a resilient microbial community.

Differences in Microbial Niches in the Gut

Distinct gut regions offer diverse ecological niches, influencing microbial colonization dynamics. Some areas favor aerobic bacteria, while others support anaerobes [19]. Understanding these niche differences aids in designing targeted recovery strategies, optimizing microbial colonization, enhancing density, and fostering diversity, ultimately stabilizing the post-antibiotic gut microbiota ecosystem.

Competition Among Colonizing Bacteria

Microbes compete for nutrients and space during colonization. Beneficial bacteria can outcompete pathogens, establishing a balanced community [20]. Supporting beneficial competition through selective prebiotics or symbiotics ensures microbial density, diversity, and a robust recovery process, reducing the risk of pathogen overgrowth in the post-antibiotic gut.

Temporal Dynamics of Colonization Events

Colonization occurs in distinct temporal phases, from initial establishment to stabilization of microbial communities. These phases influence microbial density and diversity [21]. Aligning interventions with these dynamics ensures optimal recolonization, enhances beneficial microbial populations, and restores a balanced and functional gut microbiota after antibiotic exposure.

Influence of the Mucus Layer on Colonization

The gut mucus layer acts as a protective barrier and a habitat for colonizing microbes. It facilitates the attachment and growth of beneficial bacteria while limiting pathogen colonization [22]. Strengthening the mucus layer through dietary interventions enhances microbial density and diversity, promoting effective recolonization and stabilization of the gut microbiota post-antibiotic treatment.

Role of Ecological Succession in the Gut

Ecological succession in the gut follows a predictable pattern, starting with fast-growing species and transitioning to stable communities. This process enhances microbial density and diversity over time. Supporting succession with prebiotics or strategic microbial supplementation accelerates recovery, stabilizes colonization dynamics, and ensures the establishment of a resilient gut microbiota.

Interplay Between Pathogens and Colonizers

Pathogens and beneficial microbes compete during colonization, influencing microbial dynamics. Beneficial colonizers inhibit pathogens through competitive exclusion and metabolic byproducts [23]. Enhancing this interplay with targeted probiotics or dietary strategies promotes microbial density and diversity, ensuring effective recolonization and stabilization of the gut microbiota post-antibiotics.

Physical Gut Barriers Affecting Colonization

Physical gut barriers, including epithelial cells and tight junctions, influence microbial colonization by preventing pathogen invasion and supporting beneficial bacteria [24]. Strengthening these barriers with nutritional or probiotic interventions enhances microbial density, facilitates colonization, and restores diversity, promoting effective gut microbiota recovery following antibiotic disruption.

Horizontal Gene Transfer in Recolonization

Horizontal gene transfer enables microbes to exchange genetic material, facilitating adaptation and recolonization. This process promotes the establishment of diverse and functional microbial communities [25]. Supporting beneficial horizontal gene transfer through selective interventions enhances microbial density, stabilizes colonization, and ensures a resilient post-antibiotic gut microbiota.

KEYSTONE SPECIES RECOVERY

Identification of Keystone Taxa in the Gut

Keystone taxa are pivotal microbial species that disproportionately influence gut ecosystem stability. Identifying these taxa provides insights into their roles in promoting microbial density, diversity, and colonization [26]. Targeting keystone taxa through probiotics or tailored interventions ensures effective post-antibiotic recovery and restores functional microbial networks.

Roles in Ecosystem Stability and Recovery

Keystone species maintain gut ecosystem balance by regulating microbial interactions and metabolic functions. These species enhance recovery by stabilizing microbial density and diversity [26]. Supporting keystone species through targeted supplementation accelerates gut microbiota recovery, ensuring a resilient and functional microbial community post-antibiotics.

Keystone-Driven Modulation of Diversity

Keystone species drive microbial diversity by creating niches that support various microbial populations. Enhancing their recovery promotes recolonization of beneficial taxa, restoring density and diversity [27]. Interventions focused on keystone species ensure effective stabilization and reestablishment of a balanced gut ecosystem after antibiotic-induced dysbiosis.

Interactions with Other Microbial Species

Keystone taxa interact with other microbes through metabolic exchanges and ecological support. These interactions promote colonization and community resilience, enhancing microbial density and diversity [15]. Encouraging these interactions through dietary or microbial interventions ensures effective gut microbiota recovery and stability after antibiotic exposure.

Reintroduction Strategies for Keystone Taxa

Reintroducing keystone taxa through probiotics or microbial transplantation accelerates recovery of microbial density and diversity. These strategies support colonization by filling ecological gaps and stabilizing microbial communities. Designing specific reintroduction protocols ensures a resilient post-antibiotic gut microbiota.

Keystone Species and Microbial Metabolite Restoration

Keystone species produce key metabolites essential for microbial and host health. Restoring these species enhances metabolite levels, supporting microbial density and diversity. Interventions targeting keystone-driven metabolite production accelerate gut recovery, promoting a balanced and functional microbiota ecosystem post-antibiotic.

Keystone Role in Host Immune Modulation

Keystone taxa modulate host immunity by interacting with immune cells and producing bioactive compounds. These interactions enhance colonization and prevent pathogen overgrowth [28]. Supporting keystone species recovery ensures balanced immune responses, stabilizing microbial density and diversity during post-antibiotic recovery.

Keystone Dynamics During Antibiotic Exposure

Antibiotic exposure disrupts keystone species, destabilizing gut ecosystems [5]. Understanding keystone dynamics helps design strategies to protect or restore these species, promoting microbial density and diversity. Targeted interventions minimize long-term impacts, ensuring effective gut microbiota recovery post-antibiotic treatment.

Importance of Rebuilding Microbial Networks

Keystone species act as central nodes in microbial networks, facilitating microbial interactions and ecosystem stability. Their recovery enhances microbial density and diversity by reestablishing functional networks. Supporting keystone-driven network rebuilding ensures a resilient and balanced gut microbiota after antibiotic-induced disruption.

Challenges in Targeting Keystone Taxa Therapeutically

Therapeutic targeting of keystone species is complex due to their sensitivity to environmental factors and interspecies interactions. Overcoming these challenges requires precise interventions that enhance keystone recovery, promoting microbial density, diversity, and colonization. Addressing these challenges ensures effective stabilization of gut ecosystems post-antibiotics.

MICROBIAL COMPETITION

Competitive Exclusion Among Gut Bacteria

Competitive exclusion occurs when beneficial bacteria outcompete harmful microbes for resources and space. This process is essential for recolonization and recovery post-antibiotics by promoting microbial density and diversity [29]. Encouraging competitive exclusion through probiotics or dietary interventions supports the establishment of beneficial microbial populations and prevents pathogen overgrowth during gut microbiota recovery.

Role of Nutrient Competition in Recolonization

Nutrient competition between bacteria shapes gut microbial dynamics. Beneficial microbes outcompete harmful ones for available nutrients, fostering recolonization of beneficial species [29]. Enhancing nutrient availability through diet or prebiotics supports the growth of beneficial microbes, aiding in microbial density restoration and promoting diversity during post-antibiotic recovery of the gut microbiota.

Antimicrobial Peptide Production by Bacteria

Many gut bacteria produce antimicrobial peptides (AMPs) that inhibit the growth of pathogens, contributing to colonization resistance [30]. These peptides help restore microbial diversity by reducing pathogen density, thus supporting the establishment of a balanced microbial ecosystem. Enhancing AMP production through microbial or dietary interventions accelerates recovery post-antibiotics and stabilizes microbial communities.

Influence of Colonization Resistance on Pathogens

Colonization resistance refers to the ability of established gut microbes to prevent the colonization of pathogenic bacteria. This resistance is crucial for maintaining gut stability and restoring microbial diversity after antibiotic-induced disruption [18]. Supporting beneficial microbial populations through prebiotics or probiotics enhances colonization resistance, preventing pathogen overgrowth during post-antibiotic recovery.

Competition Dynamics in Antibiotic-Resistant Bacteria

Antibiotic-resistant bacteria can dominate gut ecosystems after antibiotic exposure, affecting microbial recovery [31]. Understanding competition dynamics between resistant and susceptible bacteria allows for the design of interventions that promote recolonization of beneficial microbes while mitigating the growth of resistant pathogens. This balance restores microbial density, diversity, and stability in the post-antibiotic gut.

Bacteriophages selectively target pathogenic bacteria, promoting a healthy microbial balance. They offer a targeted approach to control harmful microbes without disrupting beneficial populations [32]. Incorporating bacteriophages into recovery strategies enhances competition dynamics, accelerates recolonization, and helps restore microbial diversity, supporting effective gut microbiota recovery after antibiotic exposure.

Effects of Microbial Secondary Metabolites

Microbial secondary metabolites, including bacteriocins and other antimicrobial compounds, play a significant role in interspecies competition. These metabolites help beneficial microbes outcompete pathogens, promoting recolonization and recovery [33]. Encouraging the production of secondary metabolites through specific dietary or probiotic interventions enhances microbial density, diversity, and stability in the post-antibiotic gut ecosystem.

Trophic Interactions Shaping Microbial Recovery

Trophic interactions, such as nutrient exchanges and metabolic dependencies between species, influence microbial recovery [34]. Beneficial microbes support each other's growth through cooperative interactions, promoting overall ecosystem stability. Understanding these interactions and promoting favorable trophic dynamics supports colonization and microbial diversity during gut recovery after antibiotic-induced disruption.

Host Modulation of Microbial Competition

The host modulates microbial competition by influencing gut pH, immune responses, and nutrient availability. This modulation determines which microbes thrive and recolonize post-antibiotics. Supporting host factors, such as immune function or gut environment, through dietary interventions enhances beneficial microbial competition, promoting microbial density, diversity, and stability during recovery.

Importance of Niche Differentiation in Recovery

Niche differentiation allows various microbial species to coexist by utilizing different ecological spaces and resources. This differentiation is vital for restoring microbial diversity and ensuring stable recolonization [35]. Supporting niche differentiation through prebiotics or tailored probiotics enhances microbial competition dynamics, accelerating gut microbiota recovery and fostering a diverse, balanced microbial ecosystem post-antibiotics.

DIVERSITY RESTORATION

Recovery of Alpha Diversity Metrics

Alpha diversity refers to the variety of species within a specific microbiota community. Post-antibiotic recovery of alpha diversity enhances ecosystem resilience, microbial colonization, and overall gut health [36]. Interventions, such as prebiotics or probiotics can restore alpha diversity, fostering the recolonization of beneficial bacteria, improving microbial density, and promoting a balanced microbiota after antibiotic-induced disruption.

Dynamics of Beta Diversity Changes

Beta diversity measures the variation between different microbial communities. Tracking beta diversity helps assess the shift in microbial populations during recovery. Restoration of beta diversity is crucial for ensuring ecological stability in the gut. Targeted strategies can accelerate the recovery of microbial populations, aiding in the establishment of a diverse, balanced microbiota post-antibiotic treatment.

Drivers of Microbial Richness in Recolonization

Microbial richness, the number of unique species in the gut, is a key driver of diversity. Factors, such as nutrient availability, environmental conditions, and host immune status influence microbial recolonization [19]. Enhancing microbial richness through selective prebiotics or probiotics promotes gut stability, diversity, and colonization, improving overall gut health post-antibiotic exposure.

Role of Environmental Microbial Reservoirs

Environmental microbial reservoirs, such as soil, food, and feces, serve as sources for recolonization. These reservoirs harbor species that can help restore gut microbiota diversity. Leveraging environmental microbial sources through dietary strategies or fecal microbiota transplants accelerates gut recovery, enhancing diversity and colonization of beneficial species post-antibiotic treatment.

Threshold Diversity Levels for Gut Stability

Threshold diversity refers to the minimum microbial richness required to maintain gut stability. Reaching this threshold ensures effective colonization, resilience, and overall gut health. Strategies to restore and maintain microbial diversity can help achieve this threshold, preventing microbial imbalances and supporting gut recovery following antibiotic-induced dysbiosis.

Challenges in Restoring Rare Microbial Species

Rare microbial species often face difficulty in recolonizing the gut after antibiotic treatment. Their low abundance and niche specialization make them vulnerable to disruption. Targeted interventions, such as tailored probiotics or prebiotics, can support the recolonization of rare species, restoring gut diversity and stability, and ensuring a resilient post-antibiotic microbiota.

Impacts of Low Diversity on Gut Function

Low microbial diversity disrupts gut function, impairing nutrient absorption, immune modulation, and pathogen resistance [37]. Restoration of gut diversity is essential for reestablishing healthy microbial activity. Strategies to enhance diversity post-antibiotic treatment improve gut health, microbial colonization, and overall resilience by rebalancing microbial populations and supporting gut function.

Resilience of High-Diversity Ecosystems

High-diversity microbial ecosystems are more resilient to disturbances, such as antibiotic treatments. These ecosystems provide functional redundancy, where different species can fulfil similar roles. Enhancing microbial diversity through interventions supports gut stability, recolonization, and recovery, preventing the dominance of pathogenic bacteria and promoting overall microbial health post-antibiotic exposure.

Importance of Phylogenetic Diversity

Phylogenetic diversity refers to the genetic differences among microbial species. It plays a crucial role in microbial ecosystem functionality and stability [38]. Restoring phylogenetic diversity after antibiotic treatment helps re-establish functional microbial pathways, enhancing gut microbiota recovery, promoting colonization of diverse species, and supporting microbial resilience in the post-antibiotic gut.

Interventions Enhancing Microbial Diversity Recovery

Various interventions, including probiotics, prebiotics, and dietary modifications, can enhance microbial diversity recovery [7]. These strategies stimulate the growth of beneficial species, promote niche differentiation, and accelerate recolonization. Effective intervention leads to a balanced gut microbiota, improving colonization, restoring microbial density, and ensuring long-term stability after antibiotic treatment.

FUNCTIONAL RECOVERY

Restoration of SCFA Production Pathways

Short-chain fatty acids (SCFAs) are vital for gut health, influencing immune function and intestinal barrier integrity. Post-antibiotic recovery of SCFA-producing microbes enhances gut microbial density, diversity, and colonization. Supporting SCFA production through dietary fiber or probiotics helps restore microbial functionality, benefiting overall gut health and ensuring functional recovery of the microbiota after antibiotic disruption [39].

Re-Establishment of Microbial Gene Expression

Microbial gene expression is central to the functional recovery of gut microbiota. Post-antibiotic, the restoration of microbial gene expression enables key metabolic pathways, such as carbohydrate and protein metabolism. Enhancing microbial gene expression through prebiotics, probiotics, or dietary changes promotes microbial colonization, restores microbial functionality, and supports a balanced gut microbiota, aiding recovery.

Functional Redundancy Among Microbial Taxa

Functional redundancy refers to multiple microbial species performing similar functions. This redundancy ensures resilience and stability during microbial recovery [15]. Post-antibiotic, promoting functional redundancy through diverse microbial populations, strengthens gut microbiota stability and supports recolonization of beneficial species, mitigating the effects of disturbances and enhancing functional recovery of the microbiome.

Recovery of Bile Acid Metabolism

Bile acid metabolism, critical for digestion and lipid absorption, is influenced by gut microbiota. Antibiotic treatment can disrupt microbial-mediated bile acid metabolism, impairing gut function [40]. Re-establishing microbial species involved in bile acid conversion aids in digestive function recovery. Targeted interventions, like probiotics or prebiotics, can help restore bile acid metabolism and overall gut health post-antibiotics.

Impact on Gut Motility and Digestion

Gut motility and digestion are influenced by the composition of the gut microbiota. Antibiotic-induced dysbiosis can impair these processes. Restoration of gut microbiota diversity and functionality after antibiotic exposure can help restore normal motility and digestive efficiency. Supporting microbial growth through diet or probiotics accelerates gut recovery, enhancing digestion and motility post-antibiotic treatment.

Functional Interplay with Host Immunity

The gut microbiota plays a vital role in immune modulation. Antibiotic-induced dysbiosis disrupts this interaction, weakening immune responses [5]. Post-antibiotic recovery involves restoring the functional interplay between the gut microbiota and host immunity. Enhancing microbial diversity and supporting immune-friendly species through interventions can improve immune resilience and recovery, fostering microbial colonization.

Role of Metabolites in Epithelial Repair

Microbial metabolites, such as SCFAs, play a key role in gut epithelial repair. These metabolites enhance gut barrier function and protect against inflammation [41]. Restoring microbial community's post-antibiotic treatment boosts metabolite production, aiding in epithelial regeneration and gut integrity. Prebiotics or probiotics that promote metabolite production support colonization and accelerate recovery, improving overall gut function.

Functional Adaptations During Dysbiosis Recovery

During recovery from dysbiosis, microbial communities adapt functionally to re-establish equilibrium. These adaptations may involve shifts in gene expression, metabolic pathways, and microbial interactions. Supporting functional recovery through dietary or therapeutic interventions accelerates the restoration of microbial density, diversity, and colonization, ensuring the rebalancing of gut functions after antibiotic-induced disruptions.

Recovery of Gut Neurotransmitter Production

Gut microbes influence neurotransmitter production, affecting gut-brain signaling and motility. Antibiotic treatment disrupts microbial populations and reduces neurotransmitter synthesis [42]. Restoring these microbial communities and their metabolic pathways, such as through prebiotics or probiotics, aids in the recovery of neurotransmitter production, improving gut motility, and overall digestive function post-antibiotics.

Integration of Host and Microbial Metabolic Functions

The integration of host and microbial metabolic functions is essential for maintaining gut health and metabolic balance. Antibiotic-induced disruptions in this integration can impair digestion and immune responses. Re-establishing the functional synergy between host and microbial metabolism supports microbial recolonization, restores gut function, and improves overall gut resilience during post-antibiotic recovery.

HOST-MICROBIOTA INTERACTIONS

Role of Gut Immune Cells in Recovery

Gut immune cells, including macrophages, dendritic cells, and T-cells, play a pivotal role in maintaining gut homeostasis [43]. Post-antibiotic, immune cells interact with the microbiota to facilitate recovery, guiding the restoration of microbial populations. Promoting immune function through dietary or microbial interventions can enhance the efficiency of microbial recolonization, improving gut barrier integrity and overall health.

Interaction Between Gut Epithelial Cells and Microbes

Gut epithelial cells form the physical barrier between microbes and the host. Their interaction with the microbiota is essential for recovery post-antibiotic treatment. Restoring the integrity and function of the epithelial layer, through microbial or dietary interventions, enhances microbial colonization and supports gut health. This interaction fosters a stable and resilient microbial ecosystem during recovery.

Modulation of Treg/Th17 Balance During Recovery

Treg (regulatory T-cells) and Th17 (helper T-cells) maintain immune tolerance and inflammation, respectively. Antibiotic-induced disruptions can alter their balance [5]. Post-antibiotic recovery involves restoring this balance to promote gut health. Interventions that support immune modulation, such as prebiotics or probiotics, help re-establish the Treg/Th17 equilibrium, enhancing gut microbial recolonization and immune resilience.

Cytokine Responses to Microbial Recolonization

Cytokines regulate immune responses and inflammation. Following antibiotic treatment, microbial recolonization triggers cytokine responses, which modulate gut healing and microbial recovery. Understanding and influencing cytokine responses through diet or therapeutics can enhance the re-establishment of beneficial microbiota, promoting microbial diversity, colonization, and overall gut function during recovery from antibiotic-induced dysbiosis.

Impact on Gut Permeability and Tight Junctions

Gut permeability and the integrity of tight junctions are essential for maintaining intestinal barrier function. Antibiotic treatments disrupt tight junctions, leading to increased permeability [44]. Restoring microbial diversity post-antibiotic enhances gut barrier function by promoting tight junction protein expression and improving permeability. These processes facilitate better colonization, microbial balance, and overall gut health recovery.

Host Genetic Influence on Microbiota Recovery

Host genetics can influence the composition and recovery of the gut microbiota. Genetic variations in immune regulation, gut permeability, and metabolic processes may impact microbial recolonization after antibiotics. Understanding these genetic influences can guide personalized therapeutic strategies, such as probiotics or diet modifications, to optimize gut microbiota recovery, enhancing colonization and diversity.

Interaction with the Gut-Associated Lymphoid Tissue (GALT)

GALT is a critical component of the immune system, influencing microbial interactions in the gut. Post-antibiotic recovery involves re-establishing GALT functions to support microbial recolonization and gut immunity. Interventions that support GALT health, such as specific prebiotics or probiotics, can enhance the restoration of immune responses, improving microbial density, diversity, and gut homeostasis.

Recovery of IgA-Mediated Microbial Control

Immunoglobulin A (IgA) is essential for microbial regulation and immune defence in the gut. Antibiotic treatments can reduce IgA levels, impairing microbial control [45]. Post-antibiotic recovery involves restoring IgA production and function to manage microbial populations effectively. Interventions, such as probiotics or specific dietary compounds can support IgA-mediated microbial control, promoting recolonization and gut health.

Modulation of Systemic Immune Responses

Antibiotic-induced dysbiosis can lead to systemic immune alterations, affecting overall health. Post-antibiotic recovery of the gut microbiota also involves modulating systemic immune responses. Targeted interventions, such as probiotics or immunomodulatory compounds, can restore immune homeostasis, support microbial recolonization, and improve both local and systemic immunity, enhancing recovery from antibiotic-induced disruptions.

Host Adaptations to Microbial Metabolites

Host cells adapt to microbial metabolites, such as SCFAs, which influence gut function, immune responses, and metabolism [46]. After antibiotic disruption, restoring the production of microbial metabolites is essential for recovery. Supporting these adaptations through targeted microbial or dietary interventions aids in the recolonization of beneficial microbes, improving gut health, and enhancing post-antibiotic recovery processes.

DIETARY INTERVENTIONS

Fiber-Rich Diets for Promoting Microbial Diversity

Fiber serves as a key nutrient for beneficial gut microbes, supporting their growth and metabolic activity. A diet rich in dietary fiber enhances microbial diversity by providing substrates for fermentation, leading to the production of beneficial metabolites like SCFAs [47]. This promotes the recolonization of diverse microbial populations, improving gut health and accelerating post-antibiotic microbiota recovery.

Role of Polyphenols in Enhancing Recolonization

Polyphenols, abundant in fruits, vegetables, and tea, are known to modulate the gut microbiota by promoting the growth of beneficial species. They also exhibit antioxidant and anti-inflammatory properties [48]. Post-antibiotic, polyphenol-rich diets can enhance microbial recolonization by stimulating microbial diversity, supporting the growth of health-promoting bacteria, and aiding gut barrier repair, ultimately aiding recovery.

Fermented Foods as Natural Probiotics

Fermented foods, such as yogurt, kefir, and kimchi, are rich in probiotics that contribute to gut microbiota restoration. These foods introduce live beneficial microbes that enhance microbial density, diversity, and overall gut function [49]. Consuming fermented foods post-antibiotic treatment accelerates microbial recolonization, aids in balancing gut microbiota, and supports immune modulation, thereby aiding in recovery.

Protein and Fat Modulation of Microbial Recovery

Dietary protein and fat intake significantly affect gut microbiota composition. High-protein or high-fat diets can alter microbial diversity, while balanced intake fosters microbial stability [50]. Post-antibiotic, adjusting protein and fat ratios may support the recovery of beneficial microbes by promoting a favorable gut environment for recolonization, enhancing microbial diversity, and functional recovery of the microbiota.

Importance of Resistant Starch in Recovery

Resistant starch is a type of carbohydrate that escapes digestion in the small intestine and is fermented by gut microbes, promoting the growth of beneficial bacteria [51]. Including resistant starch in the diet post-antibiotic treatment aids in restoring microbial diversity, particularly SCFA-producing bacteria. This supports gut health by improving colonization, enhancing the recovery of gut microbiota, and its functions.

Effects of Prebiotic Supplementation

Prebiotics, such as inulin, FOS, and GOS, stimulate the growth and activity of beneficial gut microbes. Post-antibiotic, prebiotic supplementation can restore microbial diversity by promoting the growth of health-promoting species like bifidobacteria and lactobacilli [52]. By enhancing the microbial

niche environment, prebiotics accelerate the recolonization process and restore gut function, supporting a balanced microbiota.

Role of Vitamin-Rich Diets in Gut Repair

Vitamins, especially vitamins A, D, and C, play a crucial role in gut health, immune function, and microbial diversity. Post-antibiotic, a vitamin-rich diet supports gut epithelial repair, enhances immune responses, and promotes microbial diversity. These nutrients help restore microbial homeostasis by fostering a favorable gut environment, aiding in the recovery of disrupted microbial populations.

Plant-Based Vs Animal-Based Dietary Impacts

Plant-based diets, rich in fibers, polyphenols, and prebiotics, typically promote higher microbial diversity compared to animal-based diets [53]. Plant-based diets support the growth of beneficial gut microbes like fiber-degrading bacteria. Post-antibiotic, switching to plant-based diets enhances microbial recolonization, promotes gut barrier function, and aids recovery by fostering a diverse and resilient microbiota.

Influence of Dietary Timing on Microbial Recolonization

The timing of dietary interventions plays a significant role in gut microbiota recovery. Introducing specific nutrients, like fiber, prebiotics, and fermented foods at strategic times, can influence microbial recolonization and functional recovery. Post-antibiotic, proper timing of dietary interventions helps in restoring microbial density, balancing microbial populations, and accelerating the overall recovery process.

Personalized Dietary Approaches for Recovery

Personalized dietary interventions, tailored to individual genetic profiles, health status, and microbiota composition, can optimize recovery. These approaches consider host-microbe interactions, immune status, and microbial resilience. Post-antibiotic, personalized diets can better support the restoration of microbial diversity and functionality, enhancing recolonization and gut health recovery. This ensures a more effective, targeted approach to microbiota restoration.

THERAPEUTIC APPROACHES

Probiotic Strains for Dysbiosis Recovery

Probiotics are live microorganisms that confer health benefits when administered in adequate amounts. Specific probiotic strains, such as *Lactobacillus* and *Bifidobacterium*, can restore microbial balance after antibiotic-induced dysbiosis [5]. By promoting the growth of beneficial microbes and suppressing harmful ones, probiotics support colonization, microbial density, and diversity, facilitating effective recovery of gut microbiota.

Synbiotics Combining Prebiotics and Probiotics

Synbiotics are combinations of prebiotics and probiotics that work synergistically to improve gut health. Prebiotics provide nutrients that stimulate the growth of beneficial bacteria, while probiotics introduce live strains that restore microbial balance [54]. Post-antibiotic, synbiotic therapies promote microbial recolonization, enhancing gut function and microbiota diversity, thus aiding recovery by fostering a stable microbial ecosystem.

Fecal Microbiota Transplantation (FMT) Protocols

Fecal microbiota transplantation (FMT) involves transferring fecal matter from a healthy donor to a patient to restore gut microbiota [55]. FMT is a promising therapy post-antibiotic, particularly for cases of severe dysbiosis. It reintroduces a diverse range of microbes, enhancing microbial recolonization, diversity, and functional recovery. Protocols for donor selection and administration are crucial for maximizing recovery outcomes.

Postbiotics Targeting Microbial Metabolites

Postbiotics are bioactive compounds produced by microbes that exert beneficial effects on the host. These metabolites, such as short-chain fatty acids (SCFAs), support gut health by promoting microbial

growth, immune modulation, and gut barrier integrity [56]. Targeting postbiotics can help in restoring microbial diversity, supporting colonization, and enhancing functional recovery of the gut microbiota post-antibiotic exposure.

Antibiotic-Alternative Therapies

Post-antibiotic recovery can be supported by alternative therapies to restore gut microbiota balance. These therapies include natural compounds, such as herbal remedies or specific antimicrobial peptides, which target pathogenic bacteria without disrupting the entire microbiota. Such alternative therapies help maintain microbial diversity, prevent overgrowth of resistant pathogens, and promote the overall recovery of gut health.

Targeted Antimicrobial Peptides for Pathogen Control

Antimicrobial peptides (AMPs) are small proteins that selectively target and kill pathogens [57]. These peptides can be used as targeted therapies post-antibiotic treatment to control pathogenic bacteria without causing broad disruption to the microbiota. Their use aids in pathogen suppression, preserving beneficial microbial populations, and supporting microbial recovery by promoting a balanced gut environment.

Precision Probiotics for Specific Microbial Recovery

Precision probiotics involve selecting specific probiotic strains tailored to the individual's gut microbiota needs. Post-antibiotic, precision probiotics can aid in recolonizing specific beneficial microbial species that may be depleted. This targeted approach helps restore microbial diversity, optimize colonization patterns, and accelerate recovery by enhancing the stability of the microbiota and supporting gut health.

Phage Therapy Targeting Resistant Pathogens

Phage therapy utilizes bacteriophages, viruses that specifically target bacteria, to control harmful pathogens [58]. Post-antibiotic, phage therapy can be used to eliminate antibiotic-resistant pathogens, without disrupting beneficial microbes. This targeted approach allows for the restoration of a healthy microbial community by eliminating harmful bacteria, supporting recolonization, and enhancing microbial diversity, crucial for effective recovery.

Immunotherapy to Support Microbial Resilience

Immunotherapy can be used to support the host's immune system in restoring microbial balance. This approach enhances immune function, promoting the establishment of beneficial microbes while limiting pathogen growth. Post-antibiotic, immunotherapy can accelerate recovery by improving gut immune responses, supporting the recolonization of beneficial bacteria, and fostering microbial resilience and diversity.

Synthetic Biology for Designing Recovery Microbes

Synthetic biology involves engineering microbes to possess specific traits that aid in recovery. These tailored microbes can be designed to support microbial recolonization, restore diversity, and enhance gut function post-antibiotic [59]. Synthetic biology approaches can optimize the recovery process by introducing beneficial microbes or modifying existing ones to boost resilience and improve the overall health of the microbiota.

CONCLUSIONS

The recovery of gut microbiota post-antibiotic treatment is a multifactorial process influenced by microbial interactions, host factors, and therapeutic interventions. Understanding the dynamics of microbial recolonization, including keystone species, microbial competition, and diversity restoration, is crucial for developing effective strategies to promote gut health. While various therapeutic approaches, such as probiotics and fecal microbiota transplantation, show promise, further research is needed to optimize their application. The insights gained from this study will enhance our understanding of gut microbiota recovery, offering potential solutions to mitigate the long-term impacts of antibiotic-

induced dysbiosis. Ultimately, this work will contribute to improving gut health and developing sustainable strategies for post-antibiotic microbiota management.

FUTURE DIRECTIONS

Future research on post-antibiotic gut microbiota recovery should focus on elucidating the specific mechanisms that drive microbial recolonization and the restoration of functional pathways. Investigating the role of host genetics and immune responses in shaping microbial recovery will be crucial to understanding individual variability in response to antibiotic disruptions. Additionally, there is a need for comprehensive studies exploring the interactions between microbial species during recovery, particularly the role of keystone species in maintaining ecosystem stability. The development of targeted therapeutic strategies, such as precision probiotics, antimicrobial peptides, and phage therapy, warrants further exploration to optimize gut microbiota restoration. Moreover, investigating the long-term impact of dietary interventions and their synergistic effects with microbial therapies will provide insights into sustainable recovery strategies. Understanding the influence of external factors, including environmental and lifestyle elements, will be vital for developing holistic approaches to support microbiota health and resilience post-antibiotic treatment.

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