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Impact of Gut Microbiota on the Development of Diseases

1. Martyna Michalska
Department and Clinic of Geriatrics, and Internal Medicine Nicolaus Copernicus University in Toruń
Ludwik Rydygier Collegium Medicum in Bydgoszcz, ul. Marii Skłodowskiej-Curie 9, 85-094 Bydgoszcz, Poland
ORCID: 0009-0002-3467-4364
https://orcid.org/0009-0002-3467-4364
martynamichalska1997@gmail.com

2**. Karolina Winiarek**
Department and Clinic of Geriatrics and Internal Medicine, Nicolaus Copernicus University in Toruń
Ludwik Rydygier Collegium Medicum in Bydgoszcz, ul. Marii Skłodowskiej-Curie 9, 85-094 Bydgoszcz, Poland
ORCID: 0000-0001-7305-0613
https://orcid.org/0000-0001-7305-0613
karolinawiniarek97@gmail.com

3. Wiktor Wardyn
Department and Clinic of Geriatrics and Internal Medicine, Nicolaus Copernicus University in Toruń, Ludwik Rydygier Collegium Medicum in Bydgoszcz, ul. Marii Curie-Skłodowskiej 9, 85-094 Bydgoszcz, Poland
wiktor12398@gmail.com
Orcid: 0009-0002-6133-2220
https://orcid.org/0009-0002-6133-2220

4. Cezary Guzowski
Department and Clinic of Geriatrics and Internal Medicine, Nicolaus Copernicus University in Toruń
Ludwik Rydygier Collegium Medicum in Bydgoszcz, ul. Marii Skłodowskiej-Curie 9, 85-094 Bydgoszcz, Poland
ORCID:0000-0002-0022-9943
https://orcid.org/0000-0002-0022-9943
cezary.guzowski@gmail.com

5. Joanna Anna Murawska
Department and Clinic of Geriatrics and Internal Medicine, Nicolaus Copernicus University in Toruń
Ludwik Rydygier Collegium Medicum in Bydgoszcz, ul. Marii Skłodowskiej-Curie 9, 85-094 Bydgoszcz, Poland
ORCID: 0000-0001-7564-938X
https://orcid.org/0000-0001-7564-938X
joanna.murawska94@wp.pl

6. Daria Ziemińska
Department and Clinic of Geriatrics and Internal Medicine, Nicolaus Copernicus University in Toruń, Ludwik Rydygier Collegium Medicum in Bydgoszcz, ul. Marii Curie-Skłodowskiej 9, 85-094 Bydgoszcz, Poland
dziemin98@wp.pl
ORCID: 0009-0001-8240-2593
https://orcid.org/0009-0001-8240-2593

7. Rafał Burczyk
Department and Clinic of Geriatrics and Internal Medicine, Nicolaus Copernicus University in Toruń, Ludwik Rydygier Collegium Medicum in Bydgoszcz, ul. Marii Curie-Skłodowskiej 9, 85-094 Bydgoszcz, Poland
raimer001@gmail.com
ORCID: 0000-0002-1650-1534
https://orcid.org/0000-0002-1650-1534

8. Prof. Kornelia Kędziora-Kornatowska
Department and Clinic of Geriatrics, Nicolaus Copernicus University in Toruń
Ludwik Rydygier Collegium Medicum in Bydgoszcz, ul. Marii Skłodowskiej-Curie 9, 85-094 Bydgoszcz, Poland
ORCID: 0000-0003-4777-5252
https://orcid.org/0000-0003-4777-5252
kornelia.kornatowska@cm.umk.pl

Abstract

Introduction:

Aim: The aim of this article is to review the latest scientific research on the influence of intestinal microbiota on the development of diseases. In this article we will discuss the importance of the intestinal microbiota, the differences in the composition of the microbiota between healthy and sick people and the relationship between the intestinal microbiota and metabolic, inflammatory, cardiovascular and neurodegenerative diseases.

Review methods: A non-systematic review of the scientific literature was carried out according to the following keywords: gut microbiota, dysbiosis, Metabolic diseases, Inflammatory diseases, Cardiovascular diseases, Neurodegenerative diseases, Fecal microbiota transplantation (FMT), Gut-brain axis, Cancer. PubMed was searched and 57 sources published up to 2015 were analysed. It was done to ensure that the knowledge contained in this article includes the most up-to-date information.

Abbreviated description of the state of knowledge: The gut microbiota plays a key role in human health by influencing the development and progression of various diseases. Numerous studies have shown that an imbalance in gut microbiota, called dysbiosis, may be linked to a number of conditions, including gastrointestinal diseases such as inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS), metabolic disorders such as obesity and type 2 diabetes, and even mental health problems such as depression and anxiety. Intestinal microflora interacts with the immune system, modulates inflammation and influences metabolic pathways, which emphasizes its importance in the development of diseases. More research is needed to further elucidate the complex interactions between the microbiota and health and explore therapeutic interventions that target the gut microbiome.

Conclusions: Intestinal microflora is crucial to health, regulating immune, metabolic and neurological functions. Dysbiosis, i.e. disturbance of the balance of intestinal microflora, is associated with diseases such as type 2 diabetes, obesity, inflammatory bowel diseases, allergies, autoimmune diseases and neuropsychiatric disorders. Healthy microflora, influenced by diet, pH and nutrients, are essential for metabolism, immune system regulation and neuronal communication. Recently, scientists have become interested in the possibility of using this knowledge in treatment. Appropriate dietary management, probiotic supplementation and fecal microflora transplantation show promising potential. Future research should focus on elucidating the specific mechanisms by which the gut microbiota influences disease processes and developing targeted therapies to exploit the therapeutic potential of the microbiota.

Keywords: gut microbiota, dysbiosis, Metabolic diseases, Inflammatory diseases, Cardiovascular diseases, Neurodegenerative diseases, Fecal microbiota transplantation (FMT), Gut-brain axis, Cancer

Introduction:

The gut microbiota plays a key role in maintaining human health. More and more research indicates the key role of the intestinal microbiota in regulating the body's immunological, metabolic and neurological functions. Dysbiosis, i.e. an imbalance in the composition of the microbiota, is associated with the pathogenesis of many diseases, such as type 2 diabetes, obesity, inflammatory bowel diseases, allergies, autoimmune diseases, and even neuropsychiatric disorders such as depression and autism.

The impact of microbiota on human health and disease results from its ability to modulate the immune response, production of metabolites, and interactions with the nervous system via the gut-brain axis. Moreover, the intestinal microbiota may influence the permeability of the intestinal barrier, which is important in the pathogenesis of chronic inflammation.

In this review, we will discuss the latest discoveries on the impact of the microbiota on the development of various diseases, including the molecular and cellular mechanisms that underlie these diseases. The aim of this study is not only to present the current state of knowledge about the intestinal microbiota and its relationship with diseases, but also to indicate directions for future research that may have clinical significance.

The role of gut microbiota in health and disease

The healthy gut microbiota is primarily colonized by bacteria from two major phyla: Bacteroidetes and Firmicutes. These microbial communities establish shortly after birth and evolve throughout the host's life. The overall composition of the gut microbiota is stable, but it exhibits temporal and spatial variations in distribution. The large intestine contains over 70% of all microbes found in the body. When discussing gut flora in the context of disease, it generally refers to the colonic flora [1]. The composition of the gastrointestinal microbiota can be influenced by various environmental factors, such as pH, oxygen levels/redox state, nutrient availability, water activity and temperature. These factors enable different microbial populations to thrive and perform various activities while interacting with their environment, including the human host [2]. Recent research has highlighted the multifaceted functions of these microbial consortia, revealing their critical contribution to nutrition, metabolism, immune regulation, and even neuronal communication. The gut microbiota plays a key role in the metabolism of dietary nutrients, facilitating the breakdown and absorption of compounds that would otherwise be indigestible by the host. This microbial processing not only provides additional energy sources for the host but also produces metabolites critical for immune system regulation [3]. Surprisingly, the gut microbiota also exerts a profound influence on the central nervous system via the "gut-brain axis," affecting a range of functions from basic motor skills to complex behavioral patterns. Microbial modulation of neurotransmitters—including dopamine, norepinephrine, serotonin, and gamma-aminobutyric acid (GABA)—suggests potential therapeutic opportunities for treating neurodegenerative and neuroimmune disorders [4]. Recent studies on the relationship between dietary nutrients, gut microbiota and host immunity underscore the potential for diet-based interventions to modulate immune responses. Such interventions could provide promising opportunities for preventing and treating immune-related diseases, further emphasizing the importance of diet in shaping the gut microbiological landscape and, consequently, the host's immune profile [5].

The composition of the gut microbiota in healthy individuals differs significantly from that in diseased individuals. Reduced diversity or abnormal composition of the microbiota has been linked to various health issues, including inflammatory bowel disease, asthma, and metabolic disorders [2]. These changes can result from factors such as diet, antibiotic use and other environmental influences. For example, a diet high in processed foods and low in fiber can negatively impact microbiota diversity, leading to an increased risk of disease [6].

Intestinal microbiota and metabolic diseases

Obesity, a multifaceted health issue proliferating across the globe, is linked to numerous comorbid conditions, including diabetes, stroke, and heart disease. Recent research underscores the gut microbiota's significant role in obesity's development and progression, orchestrating a complex interplay with genetic, dietary, and environmental factors. Studies indicate that the gut microbiota composition in obese individuals differs markedly from that in lean counterparts, suggesting that microbial dysbiosis may precipitate or exacerbate obesity [7]. Several mechanisms underpin the gut microbiota's influence on obesity. These include modifications in gut barrier function, alterations in the production of satiety-promoting gastrointestinal peptides, and the inflammatory cascade triggered by microbial components such as lipopolysaccharides (LPS). These factors collectively contribute to insulin resistance and increased food intake, showcasing the microbiota's endocrine-like functionality in energy homeostasis [8]. The interplay between gut microbiota, genetics, and dietary patterns profoundly impacts obesity risk. Specific microbial compositions may predispose individuals to obesity by affecting appetite, lipogenesis, and inflammation. Moreover, dietary interventions, including prebiotics, probiotics, and postbiotics, have shown promise in modulating gut microbiota composition, suggesting potential routes to mitigate obesity and its related health issues [9]. A recent review compiling results from 72 animal studies and 15 human trials found that approximately 85% of probiotic supplementation interventions resulted in reduced body weight or fat mass compared to placebo-treated controls. More research is needed to determine whether oral supplementation of pre/probiotic can help combat obesity [10]. There is also significant interest among scientists in whether fecal microbiota transplantation (FMT) can affect weight loss. Numerous clinical trials are being conducted. In one randomized clinical trial involving adolescents who received FMT, no effect on body weight was observed; however, a reduction in abdominal fat was noted [11]. In another study conducted in adults, no significant metabolic effects were observed [12]. One study showed that FMT can improve insulin sensitivity in obese individuals with metabolic syndrome, but wide range of clinical responses is observed [13]. It is believed that FMT may have a positive effect on cholesterol metabolism in obese patients. Additionally, research indicates that CRP, an inflammatory marker that may be elevated due to obesity, can be reduced by FMT. More research is needed to verify this data and the effectiveness of FMT in treating obesity [14].

The microbiome has been linked to the pathophysiology of most chronic diseases, and Type 2 diabetes (T2D) is no exception. Studies indicate distinct differences in the composition of gut microbiota between individuals with T2D and healthy controls, attributing these microbial discrepancies to variations in disease severity and response to treatment.

The potential of probiotics, prebiotics, synbiotics, and fecal microbial transplantation in modulating gut microbiota to improve glucose control and mitigate complications associated with T2D is under investigation [15]. The identification of specific bacterial taxa associated with T2D has provided insights into potential targets for modulating the disease's progression. Studies show that genera such as Bifidobacterium, Bacteroides, Faecalibacterium, Akkermansia, and Roseburia are inversely associated with T2D, while Ruminococcus, Fusobacterium, and Blautia show positive associations. These findings underscore the complex relationship between gut microbial inhabitants and diabetes, highlighting microbial modulation as a promising approach for disease intervention [16].

Gut microbiota and inflammatory diseases

The intricate connection between intestinal microflora and inflammatory diseases has been extensively researched, uncovering a complex interplay that greatly influences human health. The gut microbiota, composed of a diverse array of microorganisms, is crucial in maintaining immune balance and regulating inflammation. Imbalances in this microbial community, known as dysbiosis, have been associated with various inflammatory conditions, including inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), as well as systemic diseases like rheumatoid arthritis and multiple sclerosis [17,18]. The global incidence of inflammatory bowel disease (IBD), encompassing Crohn's disease (CD) and ulcerative colitis (UC), is on the rise. At the core of IBD is a complex interaction among genetic predisposition, the immune system, and intestinal microflora. Research indicates that in conditions like Crohn's disease and ulcerative colitis, the composition of gut microbiota undergoes significant changes. Patients with IBD often exhibit a reduced diversity of beneficial bacteria, such as Bifidobacterium longum, Eubacterium rectale, and Faecalibacterium prausnitzii, alongside an increased presence of pathogenic bacteria like Bacteroides fragilis and Ruminococcus gnavus. These pathogenic bacteria can compromise the mucosal barrier, promote immune dysregulation, and elevate the production of pro-inflammatory cytokines. Such microbial shifts contribute to the inflammation and symptoms characteristic of IBD [19]. In IBD, the intestinal barrier, comprising mechanical, chemical, immunological, and microbiological components, is compromised, leading to increased intestinal permeability and inflammation. This dysfunction is exacerbated by factors such as altered glycosylation in epithelial cells and dysbiosis. Specific pathogenic bacteria, including Escherichia coli and Klebsiella pneumoniae, can breach the epithelial barrier and intensify inflammation. During dysbiosis, levels of short-chain fatty acids (SCFAs) like butyrate, which possess anti-inflammatory properties, are reduced. Additionally, other metabolites such as bile acids and tryptophan derivatives play a role in modulating the immune response. The abnormal immune response in IBD stems from an imbalance between pro-inflammatory and regulatory T cells. Th17 cells, which produce IL-17 and IL-22, are particularly implicated in the pathogenesis of IBD. The gut microbiota can influence the differentiation and function of these immune cells, further connecting microbiota composition to the severity of IBD [20]. Research indicates that probiotics containing Escherichia coli Nissle 1917 (EcN) can inhibit pathogenic bacteria and reduce inflammation. Another promising treatment is fecal microbiota transplantation (FMT), which aims to restore a healthy microbial balance and has proven effective in treating IBD. Additionally, studies have shown that diet plays a crucial role in shaping the intestinal microflora and can influence IBD outcomes [21].

Irritable bowel syndrome (IBS) is a prevalent functional gastrointestinal disorder marked by symptoms such as abdominal pain, bloating, and changes in bowel habits, including diarrhea (IBS-D) and constipation (IBS-C). Affecting 5% to 10% of the global population at any time, IBS significantly impacts patients' quality of life and incurs substantial healthcare costs [22]. Despite its prevalence, the pathophysiology of IBS remains unclear, intertwined with a complex network of genetic, environmental, psychological, and physiological factors. Recently, the gut microbiota has been identified as a crucial element, expanding our understanding toward a more comprehensive perspective of the microbiota-gut-brain axis [23]. Growing evidence suggests that dysbiosis—disruptions in the composition and function of intestinal microflora—is a crucial factor in the development and worsening of IBS symptoms. Dysbiosis is linked to various biomechanical changes, including increased intestinal permeability, inflammation, and impaired motility, all of which contribute to IBS symptoms. These alterations in normal gut flora affect not only local gastrointestinal functions but also have systemic effects, influencing the central and enteric nervous systems and potentially impacting the patient's psychological well-being and quality of life [24]. For instance, patients with IBS often display a unique microbiota signature marked by reduced biodiversity and varying levels of specific microbial taxa compared to healthy individuals. These microbial profiles have been linked to the severity of both gastrointestinal and psychiatric symptoms [25]. Addressing dysbiosis in IBS presents a promising treatment approach, though efforts to modify intestinal flora have yielded mixed results. Dietary interventions, such as the low FODMAP diet, have been shown to influence microbial populations by reducing levels of Bifidobacterium and Actinobacteria and improving symptoms. However, the long-term effectciveness of these interventions remains inconclusive [23]. Pharmacological treatments like rifaximin have demonstrated temporary symptom relief by affecting the gut microbiota, but concerns persist about their long-term benefits and potential adverse effects on microbial communities. Similarly, fecal microbiota transplantation (FMT), which aims to directly restore microbial balance, has not consistently provided long-term relief of IBS symptoms. This underscores the complex role of microbiota in IBS and the necessity for further research [24].

Gut microbiota and cardiovascular diseases

Recent research emphasizes the intricate relationship between gut microbiota and cardiovascular disease (CVD), demonstrating how alterations in gut microbial composition can incite inflammation and drive the progression of various cardiovascular conditions [26]. Dysbiosis has been associated with the pathogenesis of cardiovascular disease, highlighting the gut's substantial role beyond mere digestion. The composition of the intestinal microbiota directly influences local intestinal health and exerts systemic effects that impact cardiovascular risk [27]. Alterations in the composition of the intestinal microflora are linked to numerous pathologies, including atherosclerosis, hypertension, heart failure, chronic kidney disease, obesity, and type 2 diabetes. These changes reduce the metabolic potential of the gut microbiota, significantly contributing to disease development. The gut microbiome functions as an endocrine organ, producing bioactive metabolites that affect host physiology through various pathways, including the trimethylamine (TMA)/trimethylamine N-oxide (TMAO) pathway, short-chain fatty acid pathway, and bile acid pathways.

Additionally, metabolically independent processes, such as those arising from heart failure-related visceral congestion and compromised intestinal barrier function, may contribute to the pathogenesis of cardiovascular disease by facilitating bacterial translocation, systemic circulation of bacterial products, and heightened inflammation [27, 28]. Specific gut microbiota-dependent pathways and their metabolites, such as TMAO and phenylacetylglutamine (PAG), have been demonstrated to impact host metabolism and cardiovascular disease (CVD) risk. Clinical studies have detected high blood concentrations of these metabolites, correlating with an increased risk of CVD events, suggesting a causal relationship. PAG, in particular, has been shown to exacerbate adverse cardiovascular phenotypes by interacting with adrenergic receptors that regulate cardiovascular homeostasis. Recent research underscores the shift in microbiome studies related to CVD from associative to causal, with identified molecular pathways and host receptors playing a pivotal role [29]. The identification of pathogenic mechanisms associated with gut microbiota in cardiovascular diseases has opened avenues for exploring microbiota-targeted therapeutic interventions. Modulating the gut flora through dietary interventions, probiotics, prebiotics, and selective inhibitors of microbial metabolites, such as TMAO inhibitors, holds promise in reducing cardiovascular risk and managing cardiovascular disease. Restoring or maintaining a healthy microbial balance can mitigate inflammation, normalize blood pressure, and enhance lipid metabolism [30]. While these strategies offer new possibilities for preventing and treating cardiovascular disease, they also underscore the necessity for further research to fully comprehend the intricate interactions between diet, microbiota, and cardiovascular health.

Gut microbiota and neurodegenerative diseases

The gut-brain axis represents a bidirectional communication network that integrates the central and enteric nervous systems, linking emotional and cognitive centers of the brain with peripheral intestinal functions. This relationship is mediated through various pathways, including the vagus nerve, immune system, and microbial metabolites, which includes neurotransmitters produced in the gut [31]. In Alzheimer's disease, characterized by plaque accumulation and cognitive decline, multiple studies have reported significant shifts in the gut microbiome composition. Patients with AD often display a decrease in microbial diversity, with an increase in pathogenic bacteria and a decrease in beneficial microbes [32]. Parkinson’s disease symptoms, including motor dysfunctions and neurodegeneration, have a similar connection to gut microbiota alterations. PD patients often exhibit a distinct gut microbiota profile, characterized by an overabundance of certain pro-inflammatory microbes and a lack of protective species [33]. Disturbances in types of bacteria that produce short-chain fatty acids (SCFAs), such as Roseburia and Faecalibacterium, was found in patients with Alzheimer's disease (AD) and Parkinson's disease (PD). Reduced SCFA levels can increase gut permeability and alter gut pH, promoting the growth of opportunistic pathogens like Shigella/Escherichia, which are elevated in both AD and PD. Reduction of SCFA-producing bacteria, can lead to enter circulation normally blocked bacteria and bacterial endotoxins. One such endotoxin, lipopolysaccharide (LPS), a component of the outer membrane of gram-negative bacteria, has been found at elevated levels in the serum of PD patients and in the postmortem brain tissues of AD patients, indicating the involvement of gram-negative bacteria in disease pathology.

Additionally, endotoxins can promote the aggregation of amyloid-β and tau in AD patients and α-synuclein in PD patients, contributing to the progression of these diseases [34]. Produce and modulate neurotransmitters and other neuroactive compounds that impact the brain could alsoprofoundly affect mental health, underlying conditions such as depression, anxiety, autism spectrum disorder, bipolar disorder, schizophrenia, and even influencing the effectiveness and side effects of pharmacotherapy [35, 36, 37]. For instance, decreased diversity and altered proportions of key bacterial groups such as Firmicutes and Bacteroidetes have been identified in individuals suffering from depression and anxiety, indicating a direct link between the gut microbiota composition and these conditions [38]. Furthermore, the potential of probiotics as an adjunctive or preventive treatment for mental disorders highlights the importance of microbial inhabitants in modulating mental health [39]. The exploration of the gut-brain axis has opened new therapeutic horizons, notably in the development of probiotic and psychobiotics (probiotic strains with the potential to benefit mental health). These beneficial bacteria are not limited to improving gut health but are proposed to treating mental and neurodegenerative diseases [40]. Additionally, dietary interventions aiming to modulate the gut microbiota through the inclusion of specific probiotics, prebiotics, and synbiotics hold promise for preventing or ameliorating mental disorders, spotlighting the significant influence of diet on mental health and neurodegenerative disease via the gut microbiota [41].

Gut microbiota and cancers

The composition and functionality of the gut microbiota have been linked to various health outcomes, including the development and progression of cancer. Research has established that significant variances in gut microbiota composition between healthy people and those with cancer can modulate cancer risk and progression. The shift from a healthy to a dysbiotic gut microbiota involves changes in the abundance of specific microbial taxa, reduction in microbial diversity, and emergence of pathogenic bacteria. Studies pinpointing these shifts have identified distinct microbial signatures associated with various cancer types, including colorectal, gastric, and pancreatic cancers [42,43]. These microbial alterations can promote carcinogenesis through different mechanisms, including the induction of chronic inflammation, modification of the tumor microenvironment, and direct and indirect modulation of host cell proliferation and apoptosis. The studies offers a compelling demonstration of how external factors like cigarette smoke can exacerbate cancer risk by modulating gut microbiota. They found that exposure to cigarette smoke led to an increased abundance of "Eggerthella lenta" and decreased levels of "Parabacteroides distasonis" and various "Lactobacillus" species in mice. This dysbiotic shift was linked to increased bile acid metabolites, such as taurodeoxycholic acid, which activated oncogenic MAPK/ERK signaling and impaired gut barrier function, highlighting a direct pathway through which altered gut microbiota can promote colorectal cancer development [44]. Various bacterial species have been identified as key players in cancer development, acting through mechanisms such as DNA damage, immune system modulation, and metabolic interactions. For example, "Fusobacterium nucleatum" has been widely noted for its role in colorectal cancer, promoting cancer through mechanisms that involve inflammatory responses and modulation of the tumor microenvironment [45].

On the other hand, protective bacterial species such as "Clostridium butyricum" and "Lacticaseibacillus paracasei" exert anti-carcinogenic effects, showcasing the nuanced roles that different gut bacteria play in influencing cancer risk and progression. The integration of gut microbiota insights into cancer treatment strategies marks a promising frontier in oncology. The manipulation of gut microbiota through dietary modifications, probiotics, prebiotics, and antibiotics offers potential avenues for enhancing the efficacy of cancer therapies. A study by Meng and team stressed the importance of investigating the gut microbiota's influence on cancers within the gastrointestinal tract, suggesting that understanding these interactions could lead to novel preventative and therapeutic strategies [46]. Innovations in cancer immunotherapy and chemotherapy underscore the significance of the gut microbiota in modulating treatment outcomes. The work of Cheng-Bei Zhou and colleagues shed light on how gut microbiota impacts cancer immune response and the efficacy of immunotherapy, illustrating the potential of manipulating the microbiota to augment the effectiveness of cancer treatments [47]. Moreover, the exploration of the causal relationship between gut microbiota and cancer through studies like the two-sample Mendelian randomization integrates genetic insights, broadening our understanding of how gut microbiota may predispose to or protect against cancer, offering new angles for intervention [48].

Interactions with microbiota

Dietary habits are a major determinant of gut microbiota composition, exerting a profound influence on host metabolism, immune function, and disease susceptibility. Diets high in fiber are associated with a diverse and stable microbiota, promoting beneficial bacterial strains that contribute to the production of short-chain fatty acids (SCFAs), which have protective effects against obesity and inflammatory diseases. Conversely, the prevalence of processed and ultraprocessed foods in Western diets has been linked to negative alterations in the microbiota, fostering dysbiosis and increasing the risk for metabolic syndrome, obesity, and cardiovascular disease [49]. Dietary habits significantly influence gut microbiota composition, with variations in bacterial strains linked to different dietary intakes impacting fermentative metabolism and intestinal pH. This balance is crucial in preventing the development of pathogenic flora and pro-inflammatory gut microbiota. Studies reinforce the idea that individual dietary habits, such as the consumption of dietary fibers and prebiotics, facilitate temporary modulations of the gut microbiota, showcasing the dynamic interaction between diet and microbial communities [50]. The integration of probiotics, prebiotics, and synbiotics into diets has been documented to differentially restore the abundance of specific gut microorganisms, thus promoting the maintenance of the gut's microbial balance. Probiotics improve the host's health by modulating the gut environment, prebiotics serve as food for beneficial gut bacteria, and synbiotics enhance the survival and efficacy of probiotic bacteria within the gut. The effect is subject to the individual's native gut microbiota composition [51,52, 53]. Antibiotic treatments can drastically alter gut microbiota composition and diversity, leading to dysbiosis. Such alterations may contribute to the development of various health issues, including obesity, inflammatory bowel disease, and increased infection susceptibility. The extent of these changes can vary based on numerous factors such as antibiotic type, dosage, treatment duration, and the individual's health status. Strategies to mitigate these adverse effects, including probiotic supplementation, are essential [54, 55, 56, 57].

Conclusion:

The gut microbiota plays a crucial role in maintaining human health by regulating immunological, metabolic, and neurological functions. Dysbiosis, an imbalance in the microbiota, is linked to various diseases, including type 2 diabetes, obesity, inflammatory bowel diseases, allergies, autoimmune diseases, and neuropsychiatric disorders. This review highlights the impact of gut microbiota on health and disease through its modulation of the immune response, production of metabolites, and interaction with the nervous system via the gut-brain axis.

Research indicates that the gut microbiota, primarily composed of bacteria from the phyla Bacteroidetes and Firmicutes, is established shortly after birth and evolves throughout life. Environmental factors such as diet, pH, and nutrient availability significantly influence the composition and functionality of the gut microbiota. Recent studies have shown that a healthy gut microbiota is essential for nutrition, metabolism, immune regulation, and neuronal communication. The gut microbiota's ability to produce neurotransmitters and modulate the immune system underscores its potential in treating neurodegenerative and neuroimmune disorders.

Diet-based interventions have emerged as promising strategies to modulate the gut microbiota and improve health outcomes. Diets high in fiber promote beneficial bacterial strains that produce short-chain fatty acids (SCFAs), which have protective effects against obesity and inflammatory diseases. Conversely, diets high in processed foods negatively impact microbiota diversity, increasing the risk of metabolic syndrome, obesity, and cardiovascular diseases.

The gut microbiota's role in metabolic diseases such as obesity and type 2 diabetes is significant. Dysbiosis can lead to changes in gut barrier function, production of satiety-promoting peptides, and inflammatory responses, contributing to insulin resistance and increased food intake. Studies suggest that specific microbial compositions may predispose individuals to obesity, and dietary interventions with prebiotics, probiotics, and postbiotics offer potential routes to mitigate obesity and related health issues.

In inflammatory diseases like IBD and IBS, dysbiosis disrupts gut homeostasis, leading to increased intestinal permeability and inflammation. The gut microbiota's interaction with immune cells plays a crucial role in the pathogenesis of these diseases. Treatments such as probiotics, fecal microbiota transplantation (FMT), and diet modifications show promise in restoring microbial balance and improving symptoms.

Neurodegenerative diseases like Alzheimer's and Parkinson's disease are also linked to gut microbiota alterations. Dysbiosis can increase gut permeability, allowing bacterial endotoxins to enter circulation and promote neuroinflammation. The gut-brain axis's role in these diseases suggests that microbial modulation could offer therapeutic opportunities.

In cancer, gut microbiota alterations can promote carcinogenesis through chronic inflammation, modulation of the tumor microenvironment, and direct interactions with host cells. Understanding the gut microbiota's influence on cancer risk and progression could lead to novel preventative and therapeutic strategies, including dietary modifications and microbiota-targeted treatments.

Overall, the gut microbiota's intricate relationship with human health highlights the importance of maintaining a balanced microbial community through diet and lifestyle interventions. Future research should focus on elucidating the specific mechanisms by which gut microbiota influence disease processes and developing targeted therapies to harness the microbiota's therapeutic potential.

Author's contribution

Conceptualization: Karolina Winiarek, Martyna Michalska;
Methodology: Wiktor Wardyn;
Software: not applicable;
Verification: Wiktor Wardyn;
Formal analysis: Karolina Winiarek, Martyna Michalska;
Research: Karolina Winiarek, Martyna Michalska, Wiktor Wardyn;
Resources: Karolina Winiarek, Martyna Michalska, Wiktor Wardyn;
Writing - rough preparation: Wiktor Wardyn;
Writing - review and editing, Karolina Winiarek, Martyna Michalska, Wiktor Wardyn;
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Supervision: Martyna Michalska;
Project administration: Kornelia Kędziora-Kornatowska;
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References:

1. Jandhyala SM, Talukdar R, Subramanyam C, et al. Role of the normal gut microbiota. World J Gastroenterol. 2015 Aug 7;21(29):8787-803. PMID: 26269668; PMCID: PMC4528021. https://doi.org/10.3748/wjg.v21.i29.8787
2. Milani C, Duranti S, Bottacini F, et al. The First Microbial Colonizers of the Human Gut: Composition, Activities, and Health Implications of the Infant Gut Microbiota. Microbiol Mol Biol Rev. 2017 Nov 8;81(4):e00036-17. PMID: 29118049; PMCID: PMC5706746. https://doi.org/10.1128/MMBR.00036-17

3. Adak A, Khan MR. An insight into gut microbiota and its functionalities. Cell Mol Life Sci. 2019 Feb;76(3):473-493. PMID: 30317530. https://doi.org/10.1007/s00018-018-2943-4
4. Strandwitz P. Neurotransmitter modulation by the gut microbiota. Brain Res. 2018 Aug 15;1693(Pt B):128-133. PMID: 29903615; PMCID: PMC6005194. https://doi.org/10.1016/j.brainres.2018.03.015
5. Fan L, Xia Y, Wang Y, et al. Gut microbiota bridges dietary nutrients and host immunity. Sci China Life Sci. 2023 Nov;66(11):2466-2514. Epub 2023 Jun 5. PMID: 37286860; PMCID: PMC10247344.). https://doi.org/10.1007/s11427-023-2346-1
6. Zmora N, Suez J, Elinav E. You are what you eat: diet, health and the gut microbiota. Nat Rev Gastroenterol Hepatol. 2019 Jan;16(1):35-56. PMID: 30262901. https://doi.org/10.1038/s41575-018-0061-2
7. Liu BN, Liu XT, Liang ZH, et al. Gut microbiota in obesity. World J Gastroenterol. 2021 Jul 7;27(25):3837-3850. PMID: 34321848; PMCID: PMC8291023. https://doi.org/10.3748/wjg.v27.i25.3837
8. Gomes AC, Hoffmann C, Mota JF. The human gut microbiota: Metabolism and perspective in obesity. Gut Microbes. 2018 Jul 4;9(4):308-325. Epub 2018 May 24. PMID: 29667480; PMCID: PMC6219651. https://doi.org/10.1080/19490976.2018.1465157.
9. Cox AJ, West NP, Cripps AW. Obesity, inflammation, and the gut microbiota. Lancet Diabetes Endocrinol. 2015 Mar;3(3):207-15. Epub 2014 Jul 22. PMID: 25066177. https://doi.org/10.1016/S2213-8587(14)70134-2
10. Green M, Arora K, Prakash S. Microbial Medicine: Prebiotic and Probiotic Functional Foods to Target Obesity and Metabolic Syndrome. Int J Mol Sci. 2020 Apr 21;21(8):2890. PMID: 32326175; PMCID: PMC7215979. https://doi.org/10.3390/ijms21082890
11. Leong KSW, Jayasinghe TN, Wilson BC, et al. Effects of Fecal Microbiome Transfer in Adolescents With Obesity: The Gut Bugs Randomized Controlled Trial. JAMA Netw Open. 2020 Dec 1;3(12):e2030415. PMID: 33346848; PMCID: PMC7753902. https://doi.org/10.1001/jamanetworkopen.2020.30415
12. Yu EW, Gao L, Stastka P, et al. Fecal microbiota transplantation for the improvement of metabolism in obesity: The FMT-TRIM double-blind placebo-controlled pilot trial. PLoS Med. 2020 Mar 9;17(3):e1003051. PMID: 32150549; PMCID: PMC7062239. https://doi.org/10.1371/journal.pmed.1003051
13. Aron-Wisnewsky J, Clément K, Nieuwdorp M. Fecal Microbiota Transplantation: a Future Therapeutic Option for Obesity/Diabetes? Curr Diab Rep. 2019 Jun 27;19(8):51. PMID: 31250122. https://doi.org/10.1007/s11892-019-1180-z
14. Zecheng L, Donghai L, Runchuan G, et al. Fecal microbiota transplantation in obesity metabolism: A meta analysis and systematic review. Diabetes Res Clin Pract. 2023 Aug;202:110803. Epub 2023 Jun 24. PMID: 37356723. https://doi.org/10.1016/j.diabres.2023.110803
15. Iatcu CO, Steen A, Covasa M. Gut Microbiota and Complications of Type-2 Diabetes. Nutrients. 2021 Dec 30;14(1):166. PMID: 35011044; PMCID: PMC8747253. https://doi.org/10.3390/nu14010166

16. Gurung M, Li Z, You H, et al. Role of gut microbiota in type 2 diabetes pathophysiology. EBioMedicine. 2020 Jan;51:102590. Epub 2020 Jan 3. PMID: 31901868; PMCID: PMC6948163. https://doi.org/10.1016/j.ebiom.2019.11.051
17. Haneishi Y, Furuya Y, Hasegawa M, et al. Inflammatory Bowel Diseases and Gut Microbiota. Int J Mol Sci. 2023 Feb 14;24(4):3817. PMID: 36835245; PMCID: PMC9958622. https://doi.org/10.3390/ijms24043817
18. Guan Z, Luo L, Liu S, et al. The Role of Depletion of Gut Microbiota in Osteoporosis and Osteoarthritis: A Narrative Review. Front Endocrinol (Lausanne). 2022 Mar 28;13:847401. PMID: 35418947; PMCID: PMC8996773. https://doi.org/10.3389/fendo.2022.847401
19. Qiu P, Ishimoto T, Fu L, Zhang J, Zhang Z, Liu Y. The Gut Microbiota in Inflammatory Bowel Disease. Front Cell Infect Microbiol. 2022 Feb 22;12:733992. PMID: 35273921; PMCID: PMC8902753. https://doi.org/10.3389/fcimb.2022.733992
20. Haneishi Y, Furuya Y, Hasegawa M, et al. Inflammatory Bowel Diseases and Gut Microbiota. Int J Mol Sci. 2023 Feb 14;24(4):3817. PMID: 36835245; PMCID: PMC9958622. https://doi.org/10.3390/ijms24043817
21. Chen L, Wang J. Gut microbiota and inflammatory bowel disease. WIREs Mech Dis. 2022 Mar;14(2):e1540. Epub 2021 Oct 15. PMID: 35266651. https://doi.org/10.1002/wsbm.1540
22. Ford AC, Sperber AD, Corsetti M, et al. Irritable bowel syndrome. Lancet. 2020 Nov 21;396(10263):1675-1688. Epub 2020 Oct 10. PMID: 33049223. https://doi.org/10.1016/S0140-6736(20)31548-8
23. Hillestad EMR, van der Meeren A, Nagaraja BH, et al. Gut bless you: The microbiota-gut-brain axis in irritable bowel syndrome. World J Gastroenterol. 2022 Jan 28;28(4):412-431. PMID: 35125827; PMCID: PMC8790555. https://doi.org/10.3748/wjg.v28.i4.412
24. Canakis A, Haroon M, Weber HC. Irritable bowel syndrome and gut microbiota. Curr Opin Endocrinol Diabetes Obes. 2020 Feb;27(1):28-35. PMID: 31789724. https://doi.org/10.1097/MED.0000000000000523
25. Mamieva Z, Poluektova E, Svistushkin V, Sobolev V, Shifrin O, Guarner F, Ivashkin V. Antibiotics, gut microbiota, and irritable bowel syndrome: What are the relations? World J Gastroenterol. 2022 Mar 28;28(12):1204-1219. PMID: 35431513; PMCID: PMC8968486. https://doi.org/10.3748/wjg.v28.i12.1204
26. Zhou W, Cheng Y, Zhu P, et al. Implication of Gut Microbiota in Cardiovascular Diseases. Oxid Med Cell Longev. 2020 Sep 26;2020:5394096. PMID: 33062141; PMCID: PMC7533754. https://doi.org/10.1155/2020/5394096
27. Tang WH, Kitai T, Hazen SL. Gut Microbiota in Cardiovascular Health and Disease. Circ Res. 2017 Mar 31;120(7):1183-1196. PMID: 28360349; PMCID: PMC5390330. https://doi.org/10.1161/CIRCRESAHA.117.309715
28. Jin M, Qian Z, Yin J, et al. The role of intestinal microbiota in cardiovascular disease. J Cell Mol Med. 2019 Apr;23(4):2343-2350. Epub 2019 Feb 3. PMID: 30712327; PMCID: PMC6433673. https://doi.org/10.1111/jcmm.14195

29. Witkowski M, Weeks TL, Hazen SL. Gut Microbiota and Cardiovascular Disease. Circ Res. 2020 Jul 31;127(4):553-570. Epub 2020 Jul 30. PMID: 32762536; PMCID: PMC7416843. https://doi.org/10.1161/CIRCRESAHA.120.316242
30. Anselmi G, Gagliardi L, Egidi G, et al. Gut Microbiota and Cardiovascular Diseases: A Critical Review. Cardiol Rev. 2021 Jul-Aug 01;29(4):195-204. PMID: 32639240. https://doi.org/10.1097/CRD.0000000000000327
31. Singh MP, Chakrabarty R, Shabir S, et al. Influence of the Gut Microbiota on the Development of Neurodegenerative Diseases. Mediators Inflamm. 2022 Sep 30;2022:3300903. PMID: 36248189; PMCID: PMC9553457. https://doi.org/10.1155/2022/3300903
32. Marizzoni M, Provasi S, Cattaneo A, Frisoni GB. Microbiota and neurodegenerative diseases. Curr Opin Neurol. 2017 Dec;30(6):630-638. PMID: 28906270. https://doi.org/10.1097/WCO.0000000000000496
33. Gomez ABM, Vera VMS, Salluco NFC, Copa JBM. Influencia de la microbiota intestinal en la enfermedad de Parkinson. Revisión. Revista Peruana de Ciencias de la Salud [Internet]. 2023 Oct 15 [cited 2023 Nov 30];5(4). https://doi.org/10.37711/rpcs.2023.5.3.422
34. Solch RJ, Aigbogun JO, Voyiadjis AG, Talkington GM, Darensbourg RM, O'Connell S, Pickett KM, Perez SR, Maraganore DM. Mediterranean diet adherence, gut microbiota, and Alzheimer's or Parkinson's disease risk: A systematic review. J Neurol Sci. 2022 Mar 15;434:120166. Epub 2022 Jan 26. PMID: 35144237. https://doi.org/10.1016/j.jns.2022.120166
35. Flowers SA, Ellingrod VL. The Microbiome in Mental Health: Potential Contribution of Gut Microbiota in Disease and Pharmacotherapy Management. Pharmacotherapy. 2015 Oct;35(10):910-6. PMID: 26497477. https://doi.org/10.1002/phar.1640
36. Pusceddu MM, Del Bas JM. The role of the gut microbiota in the pathophysiology of mental and neurological disorders. Psychiatr Genet. 2020 Aug;30(4):87-100. PMID: 32459708. https://doi.org/10.1097/YPG.0000000000000255
37. Generoso JS, Giridharan VV, Lee J, et al. The role of the microbiota-gut-brain axis in neuropsychiatric disorders. Braz J Psychiatry. 2021 May-Jun;43(3):293-305. PMID: 32667590; PMCID: PMC8136391. https://doi.org/10.1590/1516-4446-2020-0987
38. Xiong RG, Li J, Cheng J, et al.The Role of Gut Microbiota in Anxiety, Depression, and Other Mental Disorders as Well as the Protective Effects of Dietary Components. Nutrients. 2023 Jul 23;15(14):3258. PMCID: PMC10384867. https://doi.org/10.3390/nu15143258
39. Misra S, Mohanty D. Psychobiotics: A new approach for treating mental illness? Crit Rev Food Sci Nutr. 2019;59(8):1230-1236. Epub 2017 Nov 30. PMID: 29190117. https://doi.org/10.1080/10408398.2017.1399860
40. Taheri S, Khomeiri M. Psychobiotics and Brain-Gut Microbiota Axis. Iran J Med Microbiol 2019; 13 (1) :1-13. https://doi.org/10.30699/ijmm.13.1.1
41. Halverson T, Alagiakrishnan K. Gut microbes in neurocognitive and mental health disorders. Ann Med. 2020 Dec;52(8):423-443. Epub 2020 Aug 31. PMID: 32772900; PMCID: PMC7877977. https://doi.org/10.1080/07853890.2020.1808239

42. Wong CC, Yu J. Gut microbiota in colorectal cancer development and therapy. Nat Rev Clin Oncol. 2023 Jul;20(7):429-452. Epub 2023 May 11. PMID: 37169888. https://doi.org/10.1038/s41571-023-00766-x
43. Park EM, Chelvanambi M, Bhutiani N, Kroemer G, Zitvogel L, Wargo JA. Targeting the gut and tumor microbiota in cancer. Nat Med. 2022 Apr;28(4):690-703. Epub 2022 Apr 19. PMID: 35440726. https://doi.org/10.1038/s41591-022-01779-2
44. Bai X, Wei H, Liu W, et al. Cigarette smoke promotes colorectal cancer through modulation of gut microbiota and related metabolites. Gut. 2022 Dec;71(12):2439-2450. Epub 2022 Apr 6. PMID: 35387878; PMCID: PMC9664112. https://doi.org/10.1136/gutjnl-2021-325021
45. Qu R, Zhang Y, Ma Y et al. Role of the Gut Microbiota and Its Metabolites in Tumorigenesis or Development of Colorectal Cancer. Adv Sci (Weinh). 2023 Aug;10(23):e2205563. Epub 2023 Jun 1. PMID: 37263983; PMCID: PMC10427379. https://doi.org/10.1002/advs.202205563
46. Meng C, Bai C, Brown TD, Hood LE, Tian Q. Human Gut Microbiota and Gastrointestinal Cancer. Genomics Proteomics Bioinformatics. 2018 Feb;16(1):33-49. Epub 2018 Feb 21. PMID: 29474889; PMCID: PMC6000254. https://doi.org/10.1016/j.gpb.2017.06.002
47. Zhou CB, Zhou YL, Fang JY. Gut Microbiota in Cancer Immune Response and Immunotherapy. Trends Cancer. 2021 Jul;7(7):647-660. Epub 2021 Mar 2. PMID: 33674230. https://doi.org/10.1016/j.trecan.2021.01.010
48. Long Y, Tang L, Zhou Y, et al. Causal relationship between gut microbiota and cancers: a two-sample Mendelian randomisation study. BMC Med. 2023 Feb 21;21(1):66. PMID: 36810112; PMCID: PMC9945666. https://doi.org/10.1186/s12916-023-02761-6
49. Perler BK, Friedman ES, Wu GD. The Role of the Gut Microbiota in the Relationship Between Diet and Human Health. Annu Rev Physiol. 2023 Feb 10;85:449-468. Epub 2022 Nov 14. PMID: 36375468. https://doi.org/10.1093/advances/nmy078
50. Bibbò S, Ianiro G, Giorgio V, et al. The role of diet on gut microbiota composition. Eur Rev Med Pharmacol Sci. 2016 Nov;20(22):4742-4749. PMID: 27906427.
51. Li C, Niu Z, Zou M, et al. Probiotics, prebiotics, and synbiotics regulate the intestinal microbiota differentially and restore the relative abundance of specific gut microorganisms. J Dairy Sci. 2020 Jul;103(7):5816-5829. Epub 2020 May 14. Erratum in: J Dairy Sci. 2020 Dec;103(12):12159. PMID: 32418689. https://doi.org/10.3168/jds.2019-18003
52. Upasana. Application of Probiotics, Prebiotics and Synbiotics in Maintaining Gut Health. IJND [Internet]. 2022 Jul. 13 [cited 2024 May 21];59(3):388-97. https://doi.org/10.21048/IJND.2022.59.3.29516
53. Jung HY, Kim KW. An Evidence-Based Review of Probiotics and Prebiotics. Sci Insights [Internet]. 2022 May 30 [cited 2024 May 21];40(6):527-31. https://doi.org/10.15354/si.22.re055
54. Yang L, Bajinka O, Jarju PO, et al. The varying effects of antibiotics on gut microbiota. AMB Express. 2021 Aug 16;11(1):116. PMID: 34398323; PMCID: PMC8368853. https://doi.org/10.1186/s13568-021-01274-w

55. Nurgaziyev M, Sergazy S, Chulenbayeva L, Nurgozhina A, Gulyayev A, Kozhakhmetov S, Kartbayeva G, Kushugulova A. THE EFFECTS OF ANTIBIOTICS ON THE GUT MICROBIOME AND THE IMMUNE SYSTEM (Review). Georgian Med News. 2020 Jun;(303):167-173. PMID: 32841200.
56. Ianiro G, Tilg H, Gasbarrini Antibiotics as deep modulators of gut microbiota: between good and evilGut 2016;65:1906-1915. https://doi.org/10.1136/gutjnl-2016-312297
57. Kesavelu D, Jog P. Current understanding of antibiotic-associated dysbiosis and approaches for its management. Ther Adv Infect Dis. 2023 Feb 24;10:20499361231154443. PMID: 36860273; PMCID: PMC9969474. https://doi.org/10.1177/20499361231154443