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Microbial dysbiosis and associated human diseases

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Abstract

Dysbiosis, a disturbance in the normal balance of microbial communities within the body, particularly the gut, is linked to various diseases. The human microbiota is essential for health, aiding digestion, synthesizing vitamins, modulating the immune system, and protecting against pathogens. Dysbiosis can result from factors like antibiotic use, dietary changes, infections, and chronic diseases, potentially leading to or worsening multiple health conditions.

Gastrointestinal diseases are prominently associated with dysbiosis, Conditions such as inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), and colorectal cancer have shown connections to gut microbiota alterations. In IBD, for instance, patients often display reduced microbial diversity and an overgrowth of harmful bacteria, contributing to inflammation and tissue damage. In IBS, dysbiosis may affect gut motility, sensitivity, and immune responses, causing symptoms like pain, bloating, and altered bowel habits.

Beyond gastrointestinal issues, dysbiosis is also implicated in metabolic disorders like obesity, type 2 diabetes, and non-alcoholic fatty liver disease (NAFLD). The gut microbiota influences energy extraction from food, fat storage, and insulin sensitivity. Dysbiosis can promote inflammation and alter metabolic pathways, thus contributing to these conditions. Certain bacterial metabolites, such as short-chain fatty acids (SCFAs), are crucial in regulating host metabolism, and imbalances in their production can impact metabolic health.

Moreover, the gut-brain axis, a communication system between the gut microbiota and the brain, demonstrates the impact of dysbiosis on mental health and neurological disorders. Dysbiosis has been linked to depression, anxiety, and neurodegenerative diseases like Parkinson's and Alzheimer's. Microbial metabolites, including neurotransmitters and inflammatory molecules, can affect brain function and behaviour, underscoring the importance of gut health for mental well-being.

The factors contributing to dysbiosis are varied and complex. Antibiotics, although vital for treating infections, can kill beneficial bacteria indiscriminately, leading to reduced diversity and imbalance. Diet significantly influences the microbiota; high-fat, high-sugar diets can foster the growth of harmful bacteria, whereas fibre-rich diets support beneficial microbes. Gastrointestinal infections can disrupt the microbiota and allow pathogen overgrowth. Chronic diseases, such as autoimmune disorders and cancers, can alter microbial communities directly through disease mechanisms or indirectly through treatments like chemotherapy.

In summary, dysbiosis is a multifaceted condition influenced by numerous factors and linked to various diseases beyond the gastrointestinal tract. Understanding the complex relationships between the microbiota and host health is essential for developing targeted therapies to restore microbial balance and treat dysbiosis-related diseases.

Keywords: Dysbiosis; Gut microbiota; Gut-brain axis. Microbial diversity; Metabolic health

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1. Introduction

The notion of the human microbiome, and its significance in both health and illness, has a lengthy historical background that dates back to the late 1800s and early 1900s [1]. By pinpointing the precise microorganisms that cause infectious diseases, early pioneers like Louis Pasteur and Robert Koch established the foundation for future research [1]. But researchers weren't able to completely understand the intricacy and scope of the human microbiome until the development of sophisticated molecular tools in the late 20th and early 21st centuries [2]. The hypothesis that lactic acid bacteria in fermented milk could extend life by altering the gut microbiota was put up by Nobel winner and Russian zoologist Élie Metchnikoff at the beginning of the 20th century [2] .This was among the first examples of the relationship between microbiome, nutrition, and health. Despite these early discoveries, the research stagnated until high-throughput sequencing methods were developed, allowing for a thorough examination of microbial communities. An important turning point in the study of microbiomes was the establishment of the Human Microbiome Project (HMP) in 2007 [3]. This large-scale project aims to investigate the role of microbial communities in human health and disease, as well as to characterize the microbial populations present at various body sites [3]. The human body contains trillions of bacteria that together encode more genes than the human genome, according to the HMP and other research. These findings have fundamentally changed our knowledge of the microbiome and its vital role in preserving health. [3]

2. Overview of the Human Microbiome

The collection of all microorganisms that live in and on the human body, including bacteria, viruses, fungus, and protozoa, is known as the human microbiome [4] .These microbes live in dynamic, diverse populations that varies greatly amongst individuals and bodily locales [4]. One of the most diverse and densely inhabited ecosystems is the gut microbiome, which is thought to contain about 100 trillion microbial cells [5]. Microbial communities are highly specialized and environment-specific; they are not dispersed randomly The gut microbiome, for instance, flourishes in an anaerobic, nutrient-rich environment, but the skin microbiota is adapted to dry, acidic circumstances [6]. These microbes carry out vital tasks that the human host is unable to do, such as vitamin synthesis, immune system control, and the digestion of complex carbohydrates [6]. Numerous factors, including as genetics, diet, age, environment, and antibiotic use, affect the composition of the microbiome [7]. Extrinsic stimuli have the ability to significantly alter the microbiome, even though it is not highly variable over time; this can lead to dysbiosis [7].

2.1. Importance of the Microbiome in Health

A person's entire health and many physiological systems depend on their gut microbiota. It is essential for healthy nutritional digestion and absorption, immune system growth and control, and defence against harmful organisms [6]. The microbiome serves the following important purposes

- Digestive Health - Short-chain fatty acids (SCFAs), such as acetate, propionate, and *butyrate*, are vital for colonic health and give the host energy. The gut microbiota assists in the breakdown of complex polysaccharides and fibres [8].
- Immune System Modulation - By encouraging the growth of regulatory T cells and preserving a balance between pro- and anti-inflammatory responses, the microbiome instructs and modifies the immune system [9].
- Barrier Protection: - Commensal microbes create antimicrobial compounds, compete with pathogens for resources and space, and strengthen the mucosal barrier to avoid infections [10].
- Metabolic Functions - Energy balance, glucose homeostasis, and lipid metabolism are all influenced by the microbiome in the host [11].
- Neurological Impact: - New studies emphasize the gut-brain axis, in which the creation of neurotransmitters, immune response modulation, and neuronal signalling pathways are some of the ways that gut microbiota affect behaviour and brain function [12].

2.2. Causes of Dysbiosis

2.2.1. Antibiotic Use

Antibiotics are one of the main causes of dysbiosis, even though they are necessary for treating bacterial infections. These drugs affect the microbiome broadly because they do not distinguish between good and harmful bacteria [13]. Antibiotic-resistant strains of bacteria can proliferate and microbial diversity can be significantly reduced as a result of prolonged or repeated antibiotic treatment [14]. The gut microbiome is significantly disrupted by antibiotics. Oral antibiotic use releases chemicals into the digestive tract that disrupt the intestinal microbiota [15]. This disruption may result from interactions between the normal gut microbiota and pathogenic and opportunistic bacteria that reside in

the gut [15]. As a result, there is a higher chance of gut pathogen colonization. Antibiotic treatments, whether short- or long-term, may be the cause of the disruption in the healthy microbiome [16].

Table 1 Overview of Common Antibiotics, Their Target Bacteria, Indications, and Side Effects.

Antibiotics	Bacteria	Indication	Side-effects
Amoxicillin	*Streptococcus pneumoniae, Haemophilus influenzae*	Respiratory tract infections	Nausea, diarrhoea, allergic reactions
Ampicillin	*Escherichia coli, Salmonella spp.*	Urinary tract infections, gastrointestinal infections	Rash, gastrointestinal disturbances
Penicillin V	*Streptococcus pyogenes*	Strep throat, skin infections	Allergic reactions, gastrointestinal upset
Methicillin	*Staphylococcus aureus* (including *MRSA*)	Staphylococcal infections	Nephrotoxicity, allergic reactions
Oxacillin	*Staphylococcus aureus*	Staphylococcal infections	Hepatotoxicity, nephrotoxicity
Nafcillin	*Staphylococcus aureus*	Staphylococcal infections	Allergic reactions, nephritis
Cephalexin	*Staphylococcus aureus, Streptococcus pneumoniae*	Skin infections, respiratory infections	Diarrhoea, rash
Cefazolin	*Staphylococcus aureus, Escherichia coli*	Surgical prophylaxis, skin infections	Hypersensitivity, gastrointestinal disturbances
Ceftriaxone	*Neisseria gonorrhoeae, Streptococcus pneumoniae*	Gonorrhoea, bacterial meningitis	Injection site reactions, diarrhoea
Cefuroxime	*Haemophilus influenzae, Streptococcus pyogenes*	Respiratory tract infections, Lyme disease	Nausea, rash
Ceftazidime	*Pseudomonas aeruginosa*	Pseudomonal infections	Seizures, rash
Cefepime	*Pseudomonas aeruginosa, Enterobacteriaceae*	Severe hospital-acquired infections	Encephalopathy, rash
Vancomycin	*Staphylococcus aureus* (including *MRSA*), *Clostridioides difficile*	MRSA infections, C. difficile colitis	Nephrotoxicity, ototoxicity
Daptomycin	*Staphylococcus aureus* (including *MRSA*), *Enterococcus faecalis*	MRSA infections, endocarditis	Muscle pain, eosinophilic pneumonia
Linezolid	*Staphylococcus aureus* (including *MRSA*), *Enterococcus faecium*	MRSA infections, VRE infections	Bone marrow suppression, neuropathy
Gentamicin	*Pseudomonas aeruginosa, Escherichia coli*	Severe gram-negative infections	Nephrotoxicity, ototoxicity
Amikacin	*Pseudomonas aeruginosa, Mycobacterium avium complex*	Severe gram-negative infections, mycobacterial infections	Nephrotoxicity, ototoxicity
Tobramycin	*Pseudomonas aeruginosa*	Pseudomonal infections	Nephrotoxicity, ototoxicity
Ciprofloxacin	*Pseudomonas aeruginosa, Escherichia coli*	Urinary tract infections, respiratory infections	Tendonitis, gastrointestinal upset

Levofloxacin	*Streptococcus pneumoniae, Escherichia coli*	Respiratory infections, urinary tract infections	Tendon rupture, photosensitivity
Moxifloxacin	*Streptococcus pneumoniae, Haemophilus influenzae*	Respiratory tract infections	QT prolongation, liver enzyme abnormalities
Azithromycin	*Streptococcus pneumoniae, Haemophilus influenzae*	Respiratory tract infections, chlamydia	Gastrointestinal upset, QT prolongation
Clarithromycin	*Helicobacter pylori, Mycobacterium avium complex*	H. pylori infection, mycobacterial infections	Gastrointestinal upset, liver enzyme abnormalities
Erythromycin	*Streptococcus pyogenes, Mycoplasma pneumoniae*	Respiratory tract infections, skin infections	Gastrointestinal upset, QT prolongation
Doxycycline	*Rickettsia rickettsii, Chlamydia trachomatis*	Rocky Mountain spotted fever, chlamydia	Photosensitivity, esophagitis
Minocycline	*Acinetobacter spp., Propionibacterium acnes*	Acne, respiratory infections	Dizziness, hyperpigmentation
Tetracycline	*Rickettsia spp., Helicobacter pylori*	Rickettsial infections, H. pylori infection	Teeth discoloration, photosensitivity
Chloramphenicol	*Haemophilus influenzae, Neisseria meningitidis*	Meningitis, severe infections	Bone marrow suppression, aplastic anemia
Clindamycin	*Staphylococcus aureus, Streptococcus pyogenes*	Skin infections, anaerobic infections	C. difficile colitis, gastrointestinal upset
Metronidazole	*Clostridioides difficile, Bacteroides fragilis*	C. difficile colitis, anaerobic infections	Metallic taste, neuropathy
Rifampin	*Mycobacterium tuberculosis, Staphylococcus aureus*	Tuberculosis, MRSA infections	Hepatotoxicity, orange discoloration of body fluids
Trimethoprim/Sulfamethoxazole (TMP-SMX)	*Escherichia coli, Staphylococcus aureus* (including *MRSA*)	Urinary tract infections, MRSA infections	Rash, hyperkalemia
Nitrofurantoin	*Escherichia coli, Enterococcus faecalis*	Urinary tract infections	Pulmonary toxicity, gastrointestinal upset
Fosfomycin	*Escherichia coli, Enterococcus faecalis*	Urinary tract infections	Diarrhoea, headache
Tigecycline	Staphylococcus aureus (including *MRSA), Acinetobacter baumannii*	Complicated skin and intra-abdominal infections	Nausea, vomiting
Colistin (Polymyxin E)	*Pseudomonas aeruginosa, Acinetobacter baumannii*	Multidrug-resistant gram-negative infections	Nephrotoxicity, neurotoxicity

2.3. Diet and Lifestyle Factors

Diet is a major factor in influencing the microbiota. Diets heavy in sugar, processed foods, and bad fats can have a deleterious effect on the diversity and function of microbes [17]. On the other hand, a healthy microbiome is supported by diets high in fibre, fruits, vegetables, and fermented foods [17]. The high-fat, low-fibre Western diet has been associated with dysbiosis and related metabolic diseases. Sleep, stress, and physical exercise are examples of lifestyle variables that affect the microbiome [17]. Due to their negative effects on the immune system and physiological functions of the body, sedentary lifestyles, long-term stress, and poor sleep quality can all lead to dysbiosis [18].

2.4. Environmental Influences

An individual's microbiota is greatly influenced by their living and working environments. Dysbiosis can be brought on by elements like pollution, chemical exposure, and urbanization. Exposure to specific industrial chemicals and pesticides, for example, can alter the gut flora and raise the risk of autoimmune and metabolic illnesses [19]. Furthermore, a correlation has been found between the rise in dysbiosis-related illnesses and urbanization and the alterations in lifestyle that follow, such as less exposure to a variety of environmental bacteria [20].

2.5. Infections

The microbiota can be seriously disrupted by infections, especially those that impact the gastrointestinal system. Unbalance can result from beneficial microbes being outcompeted by pathogenic bacteria, viruses, and parasites [10]. The microbiota of the stomach, for instance, can be dramatically changed by infections with *Helicobacter pylori,* a bacteria connected to gastric ulcers and cancer [21].

Table 2 List of microbiota composition across different body regions**.**

RESPIRATORY TRACT	*ACTINOBACTERIA* *FIRMICUTES* *PROTEOBACTERIA* *BACTEROIDETES*
SKIN	*ACTINOBACTERIA* *FIRMICUTES* *PROTEOBACTERIA* *BACTEROIDETES* *CYNOBACTERIA*
VAGINA	*LACTOBACILLI*
ORAL CAVITY	*ACTINOBACTERIA* *FIRMICUTES* *PROTEOBACTERIA* *BACTEROIDETES* *FUSOBACTERIA*
GUT	*ACTINOBACTERIA* *FIRMICUTES* *STREPTOCOCCI* *BACTEROIDETES* *LACTOBACILLAE* *ENTEROBACTERIA*

3. Types of Dysbiosis

The human body has many microbiomes, each with distinct traits and health implications, which can be impacted by dysbiosis.

3.1. Gut Dysbiosis

The most well-researched and linked to a wide range of diseases is gut dysbiosis. A high diversity of helpful bacteria, including Firmicutes and Bacteroidetes, and a low abundance of pathogenic species are indicative of a healthy gut microbiota [6]. An overabundance of pathogenic bacteria (like *Clostridium difficile*), a decrease in beneficial bacteria (like *Lactobacillus* and *Bifidobacterium*), and a general decline in microbial diversity can all be signs of dysbiosis in the gut [22]. This mismatch can result in persistent inflammation and increased intestinal permeability, commonly referred to as "leaky gut," which can exacerbate conditions like IBD, IBS, obesity, diabetes, and colorectal cancer [22].

3.2. Dysbiosis of the Skin

The bacteria, fungi, and viruses that make up the skin microbiota are essential for both defending the skin from infections and preserving its health. Skin dysbiosis is associated with a number of dermatological disorders, including atopic dermatitis, psoriasis, eczema, and acne [23]. Environmental contaminants, harsh skin care products, and antibiotics are some of the factors that lead to skin dysbiosis. Inflammatory skin disorders can be made worse by an imbalance in the skin microbiota, which can also worsen immune responses and compromise the integrity of the skin barrier [24].

3.3. Oral Dysbiosis

A varied microbiota found in the oral cavity is essential for preserving dental health. Oral malignancies, periodontal disease, and dental caries are all linked to dysbiosis in the oral microbiota [25]. Smoking, using antibiotics, consuming a lot of sweets, and maintaining poor dental hygiene are all contributing causes [26]. Pathogenic bacteria including *Porphyromonas gingivalis*, linked to periodontal disease, and *Streptococcus mutans*, implicated in tooth decay, can proliferate in the mouth as a result of oral dysbiosis [26]. Additionally, there are interactions between the gut and mouth microbiomes that impact general health.

3.4. Dysbiosis Vaginalis

By preserving an acidic environment, the vaginal microbiota—which is primarily made up of *Lactobacillus* species— plays a critical role in infection prevention. Bacterial vaginosis (BV), yeast infections, and heightened vulnerability to sexually transmitted infections (STIs) can result from vaginal dysbiosis, which is defined by a decrease in lactobacilli and an increase in anaerobic bacteria [27]. Vaginal dysbiosis is caused by a number of factors, such as the use of antibiotics, hormone fluctuations, and certain cleanliness habits [27].

3.5. Dysbiosis

Respiratory Immune system function and respiratory health are maintained by the respiratory tract bacteria. Chronic respiratory diseases such cystic fibrosis, asthma, and chronic obstructive pulmonary disease (COPD) are associated with dysbiosis in the respiratory microbiome. Respiratory infections, environmental contaminants, and the use of antibiotics are factors that lead to respiratory dysbiosis. An unbalanced respiratory microbiome may make people more prone to infections and exacerbate long-term respiratory conditions [28].

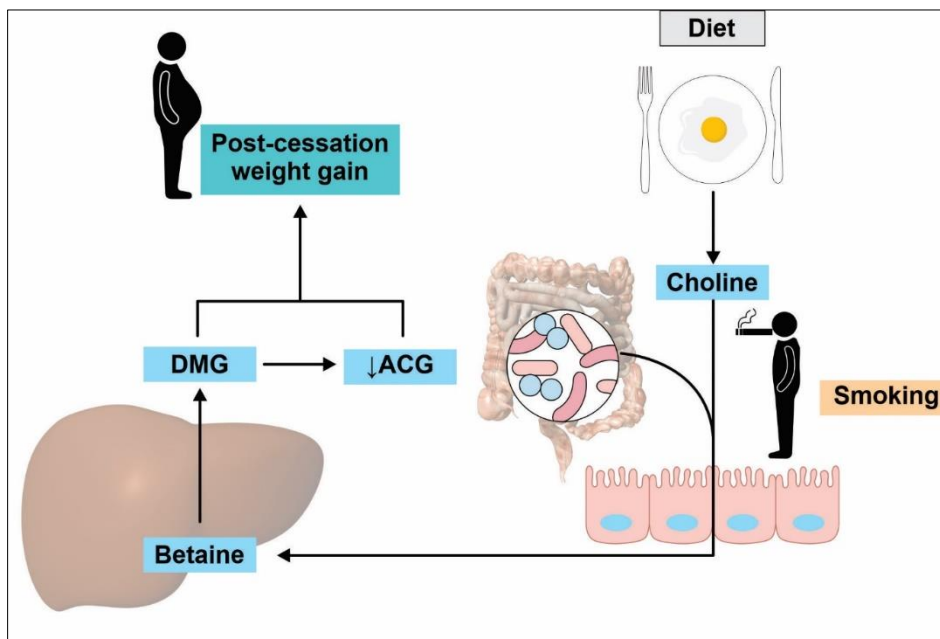## 3.6. Smoking cessation-associated weight gain

Figure 1 Modulation of Weight Gain After Smoking Cessation by the Gut Microbiome.

Weight gain related with quitting smoking Within six to twelve months of quitting smoking, there is often an average weight increase of 4-5 kg. Consequently, poor adherence to smoking cessation is caused by weight increase upon

cessation. Even in situations where calorie consumption was low, a number of studies found that weight increase upon cessation did not significantly affect food intake [29]. Fluhr et al. recently provided evidence that the gut microbiome plays a causal role in weight gain after cessation. It was discovered that the microbiome-driven post-cessation weight gain was associated with improved energy harvest, increased DMG synthesis from dietary choline, and decreased ACG. While ACG reversed the weight gain, DMG dosage negated the effects of antibiotics and caused significant weight gain after cessation. These observations were confirmed by a modest observational human investigation [30].
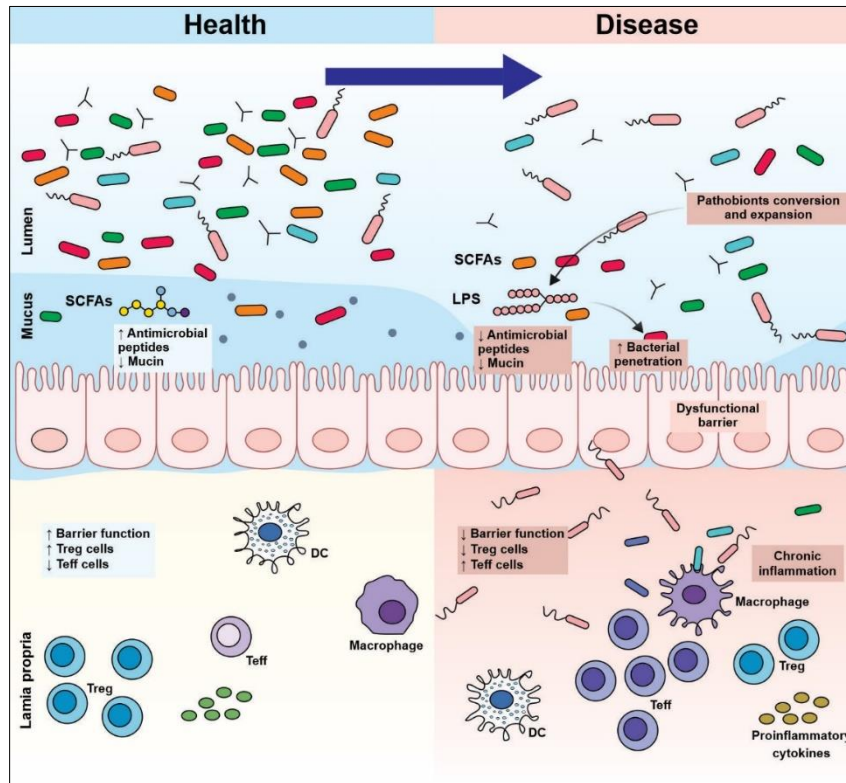

Figure 2 Factors influencing microbiota-associated chronic inflammation in healthy and disease state.

3.7. Dysbiotic vs Normal Microbiota

It is essential to comprehend the distinctions between the normal and dysbiotic microbiota in order to diagnose and treat dysbiosis.

3.8. Regular Microbiome

A varied and steady collection of microorganisms that live in harmony with their host is what defines a normal microbiota. Numerous processes, such as the generation of antimicrobial chemicals, the competitive exclusion of pathogens, and the manipulation of the host immune system, work together to preserve this equilibrium [4]. In addition to helping with digestion, a healthy microbiome also produces vital vitamins, guards against infections, and modulates immune responses [4].

3.9. Dysbiotic Microbiota

Conversely, the microbiota of dysbiotics show decreased diversity, an excess of pathogenic species, and a reduction of beneficial microorganisms. This imbalance has the potential to impair regular physiological functions and hasten the onset of disease [31]. The presence of dysbiotic microbiota can contribute to persistent inflammation and increased susceptibility to infections by producing toxic metabolites, inducing incorrect immune responses, and impairing barrier functioning [31].

3.10. Dysbiosis Mechanisms

The disturbance of the natural microbial balance, or dysbiosis, has a significant impact on a number of physiological functions and is linked to a number of disorders. The processes via which dysbiosis affects the immune system,

inflammation, and metabolism, interacts with the gut-brain axis, influences neurotransmission and neuroinflammation, and involves microbial metabolites and their effects are examined in this area [10].

3.11. Effect on Immune Response and Inflammation

A key factor in controlling the host immune system is the microbiota. An unbalanced immune response resulting from dysbiosis can exacerbate localized inflammation as well as systemic inflammation. Systems of Immunity Modulation The immune system's growth and operation are influenced by the gut flora. It supports the development of immunological tolerance, antibody synthesis, and immune cell maturation [10]. The development of regulatory T cells (Tregs), which are essential for preserving immunological homeostasis and limiting excessive inflammation, is encouraged by commensal bacteria. This equilibrium can be upset by dysbiosis, which results in a rise in pro-inflammatory cytokines and a decrease in Tregs [10].

3.12. Chronic Inflammation

Chronic inflammation, a defining feature of numerous illnesses such as inflammatory bowel disease (IBD), obesity, and cardiovascular disorders, is linked to dysbiosis. For example, dysbiosis in inflammatory bowel disease (IBD) causes the immune system to overreact, which prolongs the inflammation of the gut lining. Prolonged inflammation has the potential to cause harm to tissues, modify gut permeability, and exacerbate dysbiosis [32].

3.13. Natural Immune Reaction

Dysbiosis also affects the innate I mmune system, which is the body's initial line of protection against infections. Toll-like receptors (TLRs) are examples of pattern recognition receptors (PRRs), which identify microbiological components and initiate immunological responses [33]. The signals that these receptors receive can be changed by dysbiosis, which can result in an unsuitable immunological response. For instance, an overabundance of harmful microorganisms may cause TLRs to become overactivated, which would encourage inflammation [33].

3.14. Inflammatory diseases

Dysbiosis is associated with a number of inflammatory illnesses. Changes in gut microbiota composition, for example, have been linked to rheumatoid arthritis (RA). Pro-inflammatory cytokines and autoantibodies can be produced in response to specific gut bacteria, which can lead to joint inflammation and injury [34].

3.15. Relationship with the Brain-Gut Axis

The gastrointestinal tract and the central nervous system (CNS) communicate with each other in both directions through the gut-brain axis. Dysbiosis can obstruct this exchange, impacting behaviour and brain activity [12].

3.16. Signalling of Vagus Nerve

One important channel for gut-brain communication is the vagus nerve. Through modifications to the synthesis of neurotransmitters and other signalling molecules, dysbiosis can modify vagus nerve signalling. For instance, gamma-aminobutyric acid (GABA), a neurotransmitter that reduces brain activity, is produced by specific gut bacteria. Dysbiosis may lower GABA synthesis, which may have an impact on anxiety and mood [35].

3.17. Production of Neurotransmitters

Serotonin, dopamine, and norepinephrine are just a few of the neurotransmitters that are produced and metabolized by the gut bacteria. The availability of these neurotransmitters can be impacted by dysbiosis, which can change behaviour and brain function. For example, the majority of serotonin produced by the body occurs in the gut, and dysbiosis can result in a reduction of serotonin levels, which is linked to depression [36].

3.18. Inflammation of neurons

A number of neuropsychiatric illnesses are linked to neuroinflammation, which is a result of dysbiosis. The immune system and the generation of pro-inflammatory cytokines, which can penetrate the blood-brain barrier and impact brain function, are both influenced by the gut microbiota. For instance, anxiety and sadness have been associated with elevated levels of the cytokine interleukin-6 (IL-6) [37].

3.19. Particular Diseases and Dysbiosis

This section explores the complex interactions that exist between dysbiosis and a range of particular diseases, including autoimmune, cardiovascular, metabolic, neuropsychiatric, and gastrointestinal conditions. Gaining knowledge about the role dysbiosis plays in certain illnesses can help with preventative and treatment methods.

3.20. Intestinal Conditions

3.20.1. IBD, or inflammatory bowel disease

The hallmark of inflammatory bowel disease (IBD), which includes ulcerative colitis (UC) and Crohn's disease (CD), is persistent inflammation of the gastrointestinal system. IBD patients frequently exhibit dysbiosis, which is characterized by a decrease in microbial diversity and an increase in harmful microorganisms including *Clostridium difficile* and *Escherichia coli*. By compromising intestinal permeability, inducing an augmented immunological response, and upsetting the gut barrier, dysbiosis leads to inflammatory bowel disease (IBD). Beneficial bacteria with anti-inflammatory qualities, such as *Faecalibacterium prausnitzii*, are usually reduced in IBD patients, which exacerbates inflammation [38].

3.20.2. IBS(Irritable Bowel Syndrome)

The symptoms of Irritable Bowel Syndrome (IBS), a functional gastrointestinal illness, include bloating, changed bowel habits, and abdominal pain. Studies have linked dysbiosis to IBS, revealing altered gut microbiota composition and decreased microbial diversity.

Patients with IBS frequently have higher concentrations of potentially hazardous bacteria like *Clostridium* and *Streptococcus* and lower concentrations of good bacteria like *Lactobacillus* and *Bifidobacterium*. IBS symptoms may be exacerbated by dysbiosis due to impaired gut motility and increased intestinal permeability. By altering the gut flora, probiotics, low-FODMAPS diets, and antibiotics like rifaximin have been proven to be effective in reducing the symptoms of IBS [39].

3.20.3. Celiac Disease

For those with a genetic predisposition, consuming gluten can cause the autoimmune disease celiac disease. Its pathophysiology is thought to involve dysbiosis. Patients with celiac disease frequently show decreased microbial diversity, with a drop in protective species and an overrepresentation of pro-inflammatory microorganisms. The immune system's reactions to gluten and intestinal inflammation may be made worse by this dysbiosis. Treatment for celiac disease consists primarily of a strict gluten-free diet [40].

3.21. Metabolic Conditions

3.21.1. Obesity

Dysbiosis plays a major role in obesity, a complex metabolic disease. Individuals who are obese usually have a changed ratio of Firmicutes to Bacteroidetes and a reduced microbial diversity. Obesity-related dysbiosis can improve dietary energy absorption, change lipid metabolism, and encourage persistent low-grade inflammation. Certain metabolites produced by bacteria, including SCFAs, can affect how much fat is stored and how much food is consumed. Dietary adjustments, physical activity, and bariatric surgery are among weight loss strategies that can modify the gut flora [41].

3.21.2. Diabetes Type 2

Insulin resistance and hyperglycemia are the hallmarks of type 2 diabetes, which is facilitated in part by dysbiosis. Through processes including heightened intestinal permeability, systemic inflammation, and modified bile acid metabolism, dysbiosis can hinder the metabolism of glucose. Patients with diabetes frequently have lower amounts of *butyrate*-producing bacteria, which are crucial for preserving gut health and controlling blood sugar. Blood glucose regulation, improved insulin sensitivity, and the restoration of a healthy microbiome can all be achieved with dietary interventions such high-fiber diets and the use of probiotics and prebiotics [42]

3.22. Mental Health Conditions

3.22.1. Depression

Emerging research indicates that dysbiosis and the gut-brain axis play a major role in the pathophysiology of depression, a widespread mental health condition. By modifying the synthesis of neurotransmitters (such as serotonin

and GABA), affecting immunological responses, and affecting neuroinflammation, dysbiosis can have an impact on mood and behaviour. Reduced microbial diversity and an imbalance in gut flora are common in depressed people [43].

3.22.2. Stress

By means of the gut-brain axis, dysbiosis and anxiety disorders are related. Dysbiosis can impair the generation of neurotransmitters, increase systemic inflammation, and change the function of the intestinal barrier, all of which can have an impact on anxiety. [43].

3.22.3. Parkinson's disease

There is growing evidence that connects the neurodegenerative disease Parkinson's disease (PD) to dysbiosis. Patients with Parkinson's disease (PD) frequently have dysbiosis of the gut, with a decrease in pro-inflammatory species and an increase in beneficial bacteria. The PD hallmarks of neuroinflammation and α-synuclein aggregation can be exacerbated by dysbiosis [45]. It is being investigated as a possible strategy to slow the progression of Parkinson's disease and alleviate symptoms by restoring a healthy gut microbiota through dietary modifications, probiotics, and FMT [43].

3.23. Auto-Immune Conditions

3.23.1. Rheumatoid Arthritis

An autoimmune disease called rheumatoid arthritis (RA) is characterized by persistent inflammation of the joints. Pathogenesis of RA is linked to dysbiosis. *Prevotella copri* is more common in dysbiosis in RA patients, and this is linked to elevated inflammation. Through increased gut permeability, modified immune responses, and molecular mimicry, gut microbiota can impact the development of autoimmunity [44].

3.24. Cardiovascular Diseases

3.24.1. Atherosclerosis

Plaques accumulate in artery walls as a result of atherosclerosis, which causes cardiovascular illnesses. Atherosclerosis is associated with dysbiosis via a number of pathways. Plaque development and advancement can be facilitated by dysbiosis, which can also affect immunological responses, lipid metabolism, and systemic inflammation. *Trimethylamine N-oxide (TMAO)* is one of the metabolites produced by some gut bacteria that is linked to an elevated risk of cardiovascular disease [45].

3.25. Hypertension

High blood pressure, or hypertension, is a significant risk factor for cardiovascular illnesses. New research points to a connection between dysbiosis and hypertension. Blood pressure can be impacted by dysbiosis through immunological regulation, gut-brain connection, and SCFA synthesis. Patients with hypertension frequently have lower concentrations of *butyrate*-producing microorganisms in their bodies [46].

3.25.1. Diagnostic and Therapeutic Approaches

This section explores dysbiosis diagnosis techniques as well as therapy approaches for reestablishing a balanced microbiome. It covers a variety of therapeutic approaches including probiotics, prebiotics, dietary treatments, fecal microbiota transplantation (FMT), and antibiotic medicines, in addition to cutting edge methods like microbiome sequencing and metabolomics for diagnosis.

3.26. Diagnostic Methods for Dysbiosis

3.26.1. Microbiome Sequencing*

Metagenomic shotgun sequencing and 16S rRNA gene sequencing in particular are excellent tools for determining the composition and diversity of microorganisms in different body regions when it comes to microbiome sequencing. By focusing on the 16S rRNA gene, this method makes it possible to identify the different types of bacteria that are present in a sample. It sheds light on the relative abundance and variety of microbes. By sequencing every DNA molecule in a sample, this method offers a thorough understanding of the many microbial species, their functional genes, and possible pathways. It makes it possible to find viruses, fungus, bacteria, and other microbes [22].

3.26.2. Metabolomics

By examining the metabolites that the microbiota produces, metabolomics can provide light on microbial activity and metabolic pathways. Metabolomics methods, such nuclear magnetic resonance (NMR) spectroscopy and mass spectrometry, can detect and measure metabolites in biological materials. This data can highlight metabolic alterations linked to dysbiosis and particular illness conditions. Potential biomarkers and therapeutic targets can be highlighted by metabolomics, which can offer functional insights into the interactions between the microbiota and host metabolism [47].

Clinical Assessments

Diagnostic testing like as blood tests, imaging investigations, and stool tests can also be used in clinical assessments to help diagnose dysbiosis and related diseases. The presence of pathogens, microbial diversity, and inflammatory markers (such as calprotectin) can all be evaluated through stool examination. It is also capable of identifying microbial metabolites and evaluating the effectiveness of therapies like FMT. Blood tests can detect metabolic factors (like glucose and lipids) and inflammatory markers (like C-reactive protein and cytokines) linked to dysbiosis-related disorders [48].

3.27. Treatment Strategies for Dysbiosis

3.27.1. Probiotics and Prebiotics

Probiotics are live microorganisms that, when taken in sufficient quantities, have positive effects on health. They can enhance gut health and aid in the restoration of microbial equilibrium. Pathogenic bacteria are competed with by probiotics, which also produce antimicrobial chemicals, alter immunological responses, and improve the function of the gut barrier. *Lactobacillus*, *Bifidobacterium*, and *Saccharomyces* species are common probiotic strains. It's possible that every strain has unique health-promoting qualities. Non-digestible fibers called prebiotics encourage the development and activity of good bacteria in the digestive system. They nourish probiotics and aid in maintaining a balanced microbiome [49].

3.27.2. Dietary Interventions

The microbiome is significantly shaped by diet. Nutritional changes have the power to alter the makeup and activity of microorganisms, fostering a favorable gut environment. High-fiber diets encourage the development of good bacteria that ferment dietary fiber into short-chain fatty acids (SCFAs), which are advantageous for metabolism and have anti-inflammatory properties. Low FODMAP diet limits the intake of fermentable carbohydrates, which can aggravate symptoms in disorders such as IBS [50].

3.27.3. Fecal Microbiota Transplantation (FMT)

In order to treat illnesses associated to dysbiosis and reestablish a healthy microbiota, FMT entails transferring fecal material from a healthy donor to a recipient. FMT is most frequently used to treat antibiotic-resistant recurrent *Clostridium difficile* infection (CDI). Moreover, it has demonstrated promise in treating metabolic disorders, IBS, and IBD [51].

3.27.4. Emerging Therapies and Interventions

1. Postbiotics and Metabolite-Based Therapies: Probiotic bacteria create bioactive substances called postbiotics, which may be used to treat illnesses linked to dysbiosis. Extracellular vesicles, bacteriocins, and SCFAs are examples of postbiotics that have metabolic, immunomodulatory, and anti-inflammatory properties. Metabolite-based treatments are becoming more and more popular as cutting-edge treatments for inflammatory and metabolic diseases. These treatments target certain microbial metabolites, such as bile acids, polyphenols, and indole derivatives [52].

2.Gut-Brain Axis Modulation: Probiotics with neuroactive qualities that have the potential to affect mental health and brain function are known as psychobiotics, thanks to developments in the manipulation of the gut-brain axis. Psychobiotics have the potential to treat depression, anxiety, and cognitive impairment. Examples of these strains are those that produce GABA or serotonin precursors. Dietary strategies that are specifically targeted, such the ketogenic and Mediterranean diets, may also influence the gut-brain axis and enhance neurological outcomes [53].

3. Microbiota-Targeted Drug Delivery: The goal of advances in microbiota-targeted medication delivery systems is to reduce side effects and maximize therapeutic efficacy. Targeting dysbiotic bacteria populations or delivering bioactive substances to the gut mucosa can be achieved through the use of site-specific medication formulations, microencapsulation technologies, and delivery platforms based on nanoparticles. This method maximizes therapeutic advantages while enabling precise control of the gut flora [53].

4. Microbiome Engineering and Synthetic Biology: Synthetic biology techniques and microbiome engineering enable the creation of unique microbial communities with specific roles. Probiotics that have been engineered have the ability to perceive their surroundings, release therapeutic payloads, and engage in controlled interactions with host cells. It is possible to engineer synthetic microbial consortia to carry out intricate metabolic processes, generate bioactive compounds, or alter host immunological responses. These creative approaches open the door to customized microbiome therapies in the treatment of illness [54].

4. Conclusion

We have examined the definitions, causes, mechanisms, associations with other diseases, diagnostic techniques, therapeutic approaches, new research findings, and future directions of dysbiosis in this thorough examination of the condition and its effects on human health. Let's review the main ideas covered and emphasize the importance of comprehending and treating dysbiosis, as well as the implications this has for next studies and therapeutic applications.

Comprehending and managing dysbiosis is extremely important for multiple reasons:

- Precision Medicine and Personalized Care: - The necessity of customized medicine strategies that take into account each patient's unique microbiome composition, genetic susceptibilities, disease phenotypes, and response to treatment is highlighted by dysbiosis. Customized treatments have the potential to enhance therapeutic results and elevate patient care.
- Preventive Health Strategies: Early detection and intervention for dysbiosis can facilitate preventive health strategies, such as targeted dietary interventions, lifestyle modifications, and microbial modulation therapies. The risk of acquiring related diseases can be reduced by treating dysbiosis as soon as it appears.
- Therapeutic Innovation: Research on dysbiosis stimulates the creation of innovative therapies, including microbial consortiums, microbiota-targeted drug delivery systems, engineered probiotics, and postbiotics. These cutting-edge methods provide least intrusive, efficient, and focused therapies.
- Interdisciplinary Collaboration: Multidisciplinary cooperation amongst microbiologists, immunologists, geneticists, physicians, bioinformaticians, and pharmaceutical researchers is essential for the study of dysbiosis. Comprehensive treatments for diseases associated with dysbiosis can be created by utilizing a variety of resources and areas of expertise.

In conclusion, dysbiosis is a complex issue with wide-ranging effects on human health. Enhancing our knowledge of dysbiosis mechanisms, utilizing novel therapeutics, adopting personalized medicine strategies, and encouraging cooperative research endeavours can pave the path for revolutionary developments in the management of dysbiosis and the prevention of disease. To fully achieve the potential of microbiome health in enhancing global health outcomes, a collaborative effort involving academics, physicians, policymakers, and the scientific community at large is needed.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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