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CHANGES IN THE IMMUNE SYSTEM IN DISEASES OF BACTERIAL ETIOLOGY AND MEASURES TO PREVENT AND ELIMINATE THE CHANGES THAT OCCUR

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Abstract. The development and operation of the mammalian immune system and the commensal microbiota interact in a variety of ways in both homeostasis and illness. While the immune system coordinates the preservation of important aspects of host-microbe symbiosis, the microbiome plays crucial roles in the training and development of significant components of the host's innate and adaptive immune system. Imbalances in microbiota-immunity interactions under specific environmental conditions are thought to play a role in the pathophysiology of numerous immune-mediated illnesses in a genetically predisposed host. Here, we go over the characteristics of microbiome-immunity crosstalk and how it affects both health and illness. We also give examples of the molecular processes that control these interactions in the intestine and other extra-intestinal organs. We discuss how these insights may be applied to the future development of microbiome-targeted therapeutic interventions and highlight some of the current knowledge, obstacles, and limitations in obtaining causal understanding of host immune-microbiome interactions and their impact on immune-mediated diseases. As a result, numerous immune system disorders have been thoroughly examined at different stages of a person's life, along with their dependence on internal and external factors of various kinds, their detailed phenomenological characteristics, the impact of various diseases on the development of immune system disorders, and many other significant aspects of this issue.

Keywords. immunological reactivity, immunostimulation, immunosuppression, immune disease risk factors, immunoregulation.

Introduction. The immune response is the main biological defensive mechanism that protects the body from a variety of dangers, including complex foreign chemicals and microbes like bacteria, viruses, fungi, and parasites. The two main parts of this complex system are inherent and adaptive, each of which serves a different but complimentary purpose. While adaptive immunity demonstrates specificity and immunologic memory, allowing for a more powerful response upon subsequent exposure, innate immunity offers an instantaneous, nonspecific protection against invasive infections or cellular harm. The microbiome is the collective term for the enormous number of microorganisms that colonize the human body, including the skin, gut, and other mucosal regions. Over the past 20 years, research into the collective genomes of bacteria and other microorganisms in this ecosystem—such as fungus, viruses, and parasites—has increased due to the quick development of culture-independent genomic techniques. According to recent developments in microbiome research, the gut microbiome actively influences a number of host functions, including as immunity, metabolism,

circadian rhythmicity, and nutritional responses, rather than merely acting as a passive bystander [1-5]. The mammalian immune system, which consists of an intricate network of innate and adaptive elements in every tissue, is essential for protecting the host from endogenous disruptions of homeostasis and a variety of potentially dangerous foreign agents. Mammals and their commensal microbes co-evolved toward mutualism and hemostasis from an ecological point of view. In order to prevent commensals from overusing host resources while preserving immunological tolerance to harmless stimuli, such a close association necessitates the appropriate operation of host immunity. However, systemic dissemination of commensal microorganisms, susceptibility to pathogenic invasion, and aberrant immune responses can arise from disruption of the gut microbiome caused by environmental incursions (such as antibiotic use, diet, or changes in geography), impairment of host-microbiome interfaces, or changes in the immune system. Microbiome-immune interactions are linked to a number of "non-communicable" gastrointestinal disorders, such as celiac disease and inflammatory bowel disease (IBD), as well as extra-intestinal disorders, such as rheumatic arthritis, metabolic syndrome, neurodegenerative disorders, and cancer, in addition to controlling infection and commensal spread. The gut microbiota and host immunity have intricate, dynamic, and context-dependent relationships [6-11]. Here, we summarize and illustrate significant recent findings and fundamental ideas that connect the microbiome to immune system development and function. We summarize some of the current mechanistic analyses of complex interactions between the microbiome and immunity in both healthy and ill conditions. Additionally, we go over the difficulties and potential applications of microbiome-targeted approaches in researching the pathophysiology of diseases and creating novel microbiome-related therapies. Since a single review cannot adequately summarize the vast amount of data pertaining to host immune-microbiome interactions, our goal is to present important ideas and instances of these interactions as well as their possible impacts on human health and disease risk. Throughout the review, we make reference to numerous other recent reviews that concentrate on different facets of these developing interactions. In order to prevent pathogen invasion, innate immunity first relies on physical barriers including the skin, mucosal membranes, and protective secretions like tears and saliva. While the complement cascade encourages opsonization and direct lysis of target cells, chemical mediators like lysozyme and defensins break down microbial membranes [12-18]. Neutrophils, basophils, eosinophils, monocytes or macrophages, dendritic cells, natural killer cells, mast cells, and epithelial and endothelial cells are among the cellular components that constantly scan tissues, identify molecular danger signals using pattern recognition receptors, and trigger downstream effector mechanisms. The process of adaptive immunity include the activation of lymphocytes, such as B cells and T cells, which recognize highly specialized antigens through somatically altered receptors. Through opsonization and complement activation, B lymphocytes generate antigen-specific immunoglobulins that either kill infections or aid in their removal. By secreting cytokines that influence B-cell development and boost cytotoxic CD8+ T lymphocyte responses, which eradicate infected or malignant cells directly, CD4+ helper T lymphocytes coordinate immunological activity. Clonal proliferation and the development of immunologic memory, which are essential processes underpinning vaccine effectiveness and long-lasting protection, are characteristics of this arm of immunity. An essential part of innate immunity is inflammation, which responds quickly to epithelial disturbance by attracting leukocytes and releasing cytokines that limit infection and start the activation of the adaptive immune system. Immune specificity regulation is crucial. While insufficient immune activity promotes vulnerability to infection and cancer, disruption of self-tolerance pathways can trigger autoimmune disease [19-24].

The main purpose of the presented manuscript is to provide a brief analysis of changes in the immune system in diseases of bacterial etiology based on the results of reputable scientific papers, as well as measures to prevent and eliminate emerging changes.

Deficiencies in immunity. Affected people are more susceptible to recurring infections and cancers due to immunodeficiencies, which are caused by genetic defects or acquired diseases that impair the ability to produce efficient immune responses. Primary (congenital) immunodeficiencies include severe combined immunodeficiency (SCID), which is characterized by profound impairment of both T- and B-lymphocyte function; chronic granulomatous disease, which is caused by defective phagocytic generation of reactive oxygen species (ROS), which is necessary for microbial killing; and X-linked agammaglobulinemia, which is characterized by an absence of mature B lymphocytes and defective antibody production. The underlying deficiency determines the therapeutic approach, which often focuses on immunological repair and infection avoidance. By delivering foreign antibodies, intravenous immunoglobulin treatment offers passive immunity. By using donor-derived hematopoietic cells to restore immunological function, hematopoietic stem cell transplantation or bone marrow transplantation may be able to treat some illnesses. New gene therapy methods that use lentiviral vectors to repair autologous hematopoietic stem cells have shown promise in treating inherited immunodeficiencies including Wiskott-Aldrich syndrome and SCID, reducing the risk of graft-versus-host illness and donor mismatch. Improving the long-term prognosis requires early detection and well-coordinated interprofessional care [3-13].

Autoimmune conditions. When immunologic tolerance to self-antigens is compromised, the immune system becomes inappropriately activated against host tissues and organs, leading to the development of autoimmune disorders. This dysregulation can appear as organ-specific diseases like autoimmune thyroiditis and type 1 diabetes mellitus, where immune responses specifically target the thyroid gland and pancreatic islets, respectively, or as systemic disorders like systemic lupus erythematosus (SLE), which involves multisystem inflammation and the production of diverse autoantibodies. A complex interplay between genetic predisposition, environmental factors, and deficiencies in immune regulatory pathways is reflected in pathogenesis. Chronic inflammation and increasing tissue damage are caused by imbalances in T-helper cell subsets, compromised regulatory T cell (Treg) function, and abnormal B lymphocyte activation. Immunosuppressive drugs, biologic treatments that target particular cytokines (such as tumor necrosis factor inhibitors), and experimental cellular techniques intended to restore immunological tolerance are the main management methods. Treatment customization based on patient-specific immunologic profiles and disease phenotype is becoming more and more possible because to developments in personalized medicine [5-14].

The microbiome's function in immune system development. The development of the host's immune system is significantly influenced by early-life colonization of the mucosal surfaces of the mammalian host. Before achieving a more stable adult-like structure at the age of about three years, the microbiota composition exhibits the greatest intra- and inter-individual variability throughout the early years of life, which may be the most crucial events in the teaching of host immunity. However, this "window of opportunity" may also make babies more vulnerable to environmental microbiota invasions, which could have detrimental long-term effects on immunity. Infectious diseases are the primary cause of death for children because of the immune system's immaturity in newborns and babies, which is demonstrated by their heightened vulnerability to several infectious infections. However, prematurely born newborns also often have an increased tendency toward excessive inflammation, as seen by the potentially fatal condition necrotizing enterocolitis [8-15]. The majority of research to date has found no evidence of repeatable microbial colonization already taking place in pregnancy, and it is

generally accepted that the majority of colonization happens after delivery, primarily from the mother's microbiota. This first colonization is influenced by a number of modulators, such as delivery mechanism, which affects the initial microbiota's composition in various bodily habitats. Maternal antibodies given to newborns through breastfeeding are known to provide vital passive defense against infections. Remarkably, a recent study shown that antibody-mediated protective immunity through nursing is driven by the commensal microbiota of pregnant mice. The use of germ-free (GF) animal models provides valuable insights into the molecular causal links between commensal microbiota and host immunity. Early research on GF mice showed that severe intestine abnormalities of lymphoid tissue architecture and immunological activities are linked to the lack of commensal microorganisms.30 αβ and γδ intra-epithelial lymphocytes (IELs) can be strongly produced upon de novo colonization and are considerably lower in GF mice than in conventional colonized animals [16-23].

The immune system and microbiota interact to maintain homeostasis. The intestinal mucosa is the interface for host-microbiota interactions that has been investigated the most. The ability of the intestinal immune system to maintain immune responses against pathogenic infection or commensal intrusion into the sterile body milieu while simultaneously establishing immune tolerance towards a vast and ever-changing wealth of harmless microorganisms is a remarkable feature. The host's immunological reaction to the gut microbiota is strictly confined to the mucosal surface in a healthy state. The intestinal lumen and surrounding structures are separated by a single layer of epithelium. Microbiota compartmentalization is accomplished through a variety of methods. The intestinal epithelium and local bacteria are separated by a thick layer of mucus. The hyperglycosylated mucin MUC2 is the focal point of the mucus barrier [11-16]. However, by imprinting enteric dendritic cells (DCs) in an anti-inflammatory state, MUC2 not only provides protection through static shielding but also limits the immunogenicity of intestinal antigens. One important feature that limits trans-epithelial permeability is tight junctions. Tight junctions and related cytoskeletal proteins are upregulated in response to microbial signals, such as the metabolite indole, which strengthens the epithelial barrier. Antimicrobial peptides (AMPs) and secretory IgA antibodies also preserve the mucosal barrier function (see below). Through processes involving the sampling of gut bacteria for antigen presentation, intestinal DCs are thought to be crucial in the compartmentalization of enteric microbiota [17-22].

Discussion. Numerous pandemic incidents have endangered and killed a great number of people throughout human history. Bacteria like Yersinia pestis were responsible for the deadliest outbreaks. Antimicrobial resistance (AMR) in bacteria is a major global issue that threatens and claims countless lives annually. The goal of the current study was to compile up-to-date information about AMR dangers that has been published in scholarly literature. Antimicrobial resistance, AMR, microorganisms, and Boolean operators were used as descriptors in a review of the literature. The findings demonstrated that antimicrobial-resistant genes and antibiotic-resistant bacteria in organisms are the source of infections brought on by antibiotic-resistant bacteria (ARB) and major infectious disorders. The significance of this subject is emphasized in this review. It clarifies the possibility of recurring infections and how they relate to AMR. It also covers the mechanics and activities of antibiotics as well as the methods by which bacteria gain resistance, emphasizing the significance of the hunt for novel medications, for which peptide research is essential [8-15]. Over the past ten years, a significant amount of research has been done on microbiome-immune interactions, which has improved our understanding of their molecular basis and highlighted the significance of these interactions in influencing a range of immune-related disorders in humans. The development of microbiome-targeted treatment approaches for immune-mediated illnesses is already being accelerated by these discoveries. For

instance, fecal microbiome transplantation (FMT), which has so far been widely used in Clostridium difficile infections, is also considered as a potential treatment in this clinical context with the goal of restoring a healthy microbiome configuration in patients suffering from dysbiosis linked to immune-mediated disease. The characteristics of a "healthy" microbiome, however, are still up for debate. Therefore, the effectiveness of FMT in conditions like IBD is still being assessed, and there are still a number of obstacles to be addressed, such as patient safety and fecal processing optimization. The utilization of "next-generation probiotics," or logically defined microbial consortia, may offer a promising alternative given the limited preventive and therapeutic efficiency of traditional individual probiotics in enhancing human health. New methods are being developed to alter the microbiome more precisely, in addition to approaches that aim to replace a full microbiome. For instance, efforts are being made to use bacteriophage therapy to precisely and selectively deplete specific pathobionts [4,5,11,14]. Given the significant impact of nutrition on the makeup and function of the gut microbiome, diet-based changes in nutrient availability may represent another viable microbiome-modulating strategy. Determining the effectiveness of customized diets, selective diets, or dietary timing manipulation in the treatment of immunological diseases and examining how these diets affect host immune responses may be fascinating. Furthermore, there may be a chance to modify these potentially beneficial compounds (also known as "postbiotics") due to the abundance of microbiome-derived metabolites that are present in high concentrations throughout the gut and in the systemic circulation. In some immunological situations, their supplementation or signaling blockade may provide new opportunities for microbiome-directed therapies. The identification of bioactive metabolites that are crucial for host physiology or linked to immune-mediated disorders may be made easier by chemical genetic screening of gut microbiome metabolites [17-24].

Conclusions. As a result, numerous immune system diseases have been thoroughly examined at different stages of a person's life, along with their dependence on internal and external factors of various kinds, their detailed phenomenological characteristics, the impact of various diseases on the development of immune system diseases, and many other significant aspects of this issue.

The development of these microbiome-based treatments as a whole requires a deeper comprehension of the complicated and complex relationships between immunity and the microbiome. Standardized, rigorous, and objective preclinical and clinical intervention studies are necessary for the successful integration of microbiome-based therapies into clinical practice.

The history of bacteria that have caused pandemics and millions of fatalities is highlighted in this review, which also underscores how crucial it is to confront drug-resistant bacteria, especially the introduction of novel diseases in the context of permafrost thawing due to climate change. Reintroducing these pathogens into the ecosystem increases the possibility of infectious diseases that people and animals haven't experienced in centuries, which could result in outbreaks and worldwide health emergencies.

This review also emphasizes how urgent it is to find new medications to counter these increased risks. In this endeavor, research on peptides—more especially, AMPs—is essential. Because of their broad-spectrum activity and capacity to target resistant bacteria, AMPs present a promising alternative for the development of novel antibiotics and antiviral medicines. To remain abreast of changing microbial dangers and maintain the effectiveness of medicinal therapies, it is essential to investigate AMPs and other novel strategies. All things considered, this analysis emphasizes the need for aggressive scientific investigation and legislative actions to tackle the intricate problems of environmental shifts and the comeback of ancient infections.

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