HIGH SCHOOL EDITION
Journal of Student Research
Volume 13 Issue 2 (2024)

A Summary of Autoimmune Disease Triggers

Connie Li

Mission San Jose High School, USA

ABSTRACT

Autoimmunity is a condition characterized by an imbalance in the immune system, where the immune system begins to attack the body's tissues, leading to inflammation and damage to organs and tissues. Autoimmune diseases do not have a precise cause and are known for their various triggers. Many studies have been conducted to observe the causes of autoimmunity, but due to the wide variety of autoimmune diseases, it is difficult to study all of them. In this review, we will be discussing the different triggers of autoimmune diseases in general.

Introduction

Autoimmune diseases, such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), multiple sclerosis (MS), and autoimmune hepatitis (AIH), are notorious for their difficult treatability and chronic nature. In these diseases, the immune system, which is designed to protect the body from foreign bacteria and viruses, begins to attack the body's organs because it mistakenly identifies the body's cells and tissues as foreign, [1] resulting in inflammation throughout various parts of the body. Autoimmune diseases vary over a wide spectrum and are differentiated based on how they attack the different organs within the patient's body.

These different autoimmune diseases often target and inflame different organs or parts of the body. For example, multiple sclerosis primarily targets the nervous system, while autoimmune hepatitis affects the liver. Some autoimmune diseases, like systemic lupus erythematosus, can even affect multiple organs, including lungs, kidneys, heart, joints, nervous system, etc. [2].

Many times, autoimmunity begins well before the patient begins to experience any kind of symptoms, causing the disorder to sometimes become life-threatening [3,4]. Understanding the causes of autoimmune diseases is crucial because it can aid the diagnosing process of these diseases and can identify people at risk before the disease becomes life-threatening. It is also essential to identify these underlying mechanisms to develop more effective treatments and therapies that can help modulate the immune response and prevent further progression of the disease. Various causes have been identified as autoimmune disease triggers. External or environmental factors generally trigger most autoimmune diseases, but some are genetically inherited.

Infections

Infections are vital contributors to the development of autoimmunity. Pathogens' main mechanism to induce such conditions is molecular mimicry [5]. This is because pathogens sometimes look very similar to the human antigen tissues [6]. Antigen tissues are receptors found at the surface of the cells. They are crucial to the immune system because their job is to detect and identify foreign antigens in the body [7]. As a result, the body's immune system will begin to attack the pathogens, eventually starting to attack its antigen tissues, which leads to autoimmunity.

The recent SARS-Cov-2 infection is a quintessential example of this phenomenon. Ever since the coronavirus outbreak in 2019, there has been accumulating evidence that connects the SARS-Cov-2 infection with immune dysfunction [6]. Several case studies have shown that after being infected with the coronavirus, patients have been observed to

have developed over 15 different types of autoantibodies [8]. Autoantibodies are antibodies created by the body's immune system that target "self-antigens" which are essentially a patient's own tissues and organs [9]. the SARS-Cov-2's ability to do so is due to its incredible ability to use molecular mimicry to hyperstimulate the body's immune system. This demonstrates how the SARS-Cov-2 infection's link to autoimmunity and inflammation could be classified as ASIA syndrome, a concept of autoimmunity syndrome induced by adjuvants, a concept created by scientists to gather all autoimmune-related viruses and infections [10].

Diet

The gut microbiome is found in the human gastrointestinal (GI) tract and has been gaining more and more attention because it influences human health [11,12]. The gut microbiome comprises intestinal bacteria in the gastrointestinal tract that help maintain immune homeostasis [12]. Diet is a major factor that shapes the gut microbiome, which can lead to the pathophysiology of autoimmunity.

Excessive intake of fat, especially saturated or trans fats, can promote inflammation and obesity. Recent research shows connections between certain fatty acids and their effects on the immune system [13]. For example, the fatty acid, ω-6 polyunsaturated fatty acids (PUFAs) are proinflammatory, and potentially worsen or even trigger autoimmune disorders such as multiple sclerosis [13].

High intake of sodium from salty foods has also been found to be a major dietary trigger in autoimmunity. It has been found that immune cells do not function very well under hypertonic situations, which is the result of high levels of sodium intake [13]. These situations often cause immune cells to display proinflammatory behaviors, as well as activate pathogenic cells such as Th17, which are commonly associated with autoimmunity [14].

Food coloring, a common additive that is added to foods for a more appealing appearance, has been shown to be one of the autoimmunity triggers too. Food coloring often contains a protein called tartrazine, which has been observed in several studies to alter the immune system [15]. This protein often binds to cells and other parts of the immune system such as hemoglobin and red blood cells. At the same time, their presence sometimes triggers an immune response, causing the body's immune system to begin to produce neoantigens to fight off tartrazine. However, this can lead to autoimmunity because these antibodies will begin to attack the tartrazine, but at the same time, they will also attack whatever the protein has bonded itself to as well [15, 16]. This is a crucial discovery because food coloring is found in almost all foods that we consume today.

Stress

The human body comprises many complex systems, including the central nervous system (CNS), endocrine system, and immune system, which work closely with one another [17]. This close relationship has caused many researchers to hypothesize the effects of stress and how it contributes to the presence of autoimmunity. Studies in the past have shown that stress activates the autonomic nervous system, which can often stimulate changes in the body's immunity, these stress factors can range from daily jitters to chronic stress disorders [17].

Inflammation, a major symptom of autoimmunity, has been observed in patients under chronic stress diseases and illnesses. Disorders such as depression and anxiety can cause or increase the production of a protein called IL-6, which can result in an unwanted inflammatory response, especially in middle-aged or older people [18].

In a study conducted by a Swedish research group, they surveyed 1.2 million people who fit into the respective categories: patients with stress-related disorders, matched unexposed individuals (similar to the patients with stress-related disorders, but not affected by them), and full siblings of patients with stress-related disorders. They concluded that the people who had been previously diagnosed with a stress-reparated disorder were at a significantly higher risk of an autoimmune disease. Notably, there were no gender preferences in the susceptibility of autoimmune diseases within the patients who had stress-related disorders. A weak link between the siblings of the patient with stress-related disorders

also showed a potential susceptibility to autoimmunity, which could suggest the role that genetics and early environmental factors might play in the development of autoimmune disorders [19].

Genetics

Eight percent of the human population is affected with an autoimmune disease, of those people, 78% are women [20] which gives rise to the idea that genetic factors may contribute to autoimmunity. Typically, humans are born with 23 pairs of chromosomes, one of those 23 pairs are sex chromosomes, which differ in males and females. This is the same in many organisms, where males have an XY chromosome, while females have an XX chromosome. The significant size difference of the X chromosome and Y chromosome suggests that the X chromosome has more genes because of its larger size. [1]

In a study using mice, Dr. Deborah L. Smith Bouvier and her team injected mice autoantigens that induce experimental autoimmune diseases including, experimental autoimmune encephalomyelitis (EAE) and pristine-induced lupus [21].

EAE and pristine-induced lupus are often used as models in experiments regarding autoimmunity. EAE simulates multiple sclerosis, an inflammatory, demyelinating disease which are also key features represented in EAE [22]. Similarly, pristine is a membrane-activating compound that can produce antigens that lead to immune intolerance, and create symptoms similar to systemic lupus erythematosus(SLE) [23].

They observed the mice's immune response in both the males and females and tested for susceptibility to the disease. It was revealed that mice with the XX chromosome complement were more susceptible to autoimmune diseases than mice with the XY chromosome [21]. Notably, it was also observed that specific genetic backgrounds cause organisms to be affected even more than just gender differences [21].

Conclusion

Autoimmunity is a peculiar area of medicine that causes immune dysfunction within the patient's body and can have various triggers. These triggers vary from person to person and can be both environmental and genetic. The chronic aspect of most autoimmunity makes the diseases difficult to diagnose and treat, especially in later stages.

Most autoimmune diseases currently do not have treatments that can fully cure the diseases, but just use immunosuppressive medications and therapies to calm down the inflammation and further progression of the disease. However, this can increase patient's risk of other viruses and infections, putting them in a more vulnerable position to becoming sick [24].

By identifying and understanding the triggers of autoimmune disorders, researchers can further develop new treatments that can hopefully treat or even cure patients of autoimmunities, lowering the risk of the medications [3]. Researchers are still continuously exploring the topics of immunology to truly comprehend the complex process involved in autoimmunity, with the ultimate goal of diagnosis, management, and treatment of these challenges and often debilitating conditions.

Acknowledgments

I would like to thank my mentors, Ling Meng, Yan Li, Daisy Li, and Dai Li for supporting and guiding me throughout this project. I could not have done it without them.

References

Angum, F., Khan, T. M., Kaler, J., Siddiqui, L., & Hussain, A. (2020). The Prevalence of Autoimmune Disorders in Women: A Narrative review. *Cureus*. https://doi.org/10.7759/cureus.8094

Wang, L., Wang, F. S., & Gershwin, M. E. (2015). Human autoimmune diseases: a comprehensive update. *Journal of Internal Medicine*, *278*(4), 369–395. https://doi.org/10.1111/joim.12395

Rosenblum, M. D., Remedios, K. A., & Abbas, A. K. (2015). Mechanisms of human autoimmunity. *Journal of Clinical Investigation*, *125*(6), 2228–2233. https://doi.org/10.1172/jci78088

Khan, M. F., & Wang, H. (2020). Environmental exposures and autoimmune diseases: contribution of gut microbiome. *Frontiers in Immunology*, *10*. https://doi.org/10.3389/fimmu.2019.03094

Huang, X., Huang, X., Huang, Y. H., Zheng, J., Lu, Y., Mai, Z., Zhao, X., Cui, L., & Huang, S. (2023). The oral microbiome in autoimmune diseases: friend or foe? *Journal of Translational Medicine*, *21*(1). https://doi.org/10.1186/s12967-023-03995-x

Vojdani, A., Vojdani, E., Rosenberg, A., & Shoenfeld, Y. (2022). The role of exposomes in the Pathophysiology of Autoimmune Diseases II: Pathogens. *Pathophysiology*, *29*(2), 243–280. https://doi.org/10.3390/pathophysiology29020020

Magaki, S., Hojat, S. A., Wei, B., So, A., & Yong, W. H. (2018). An introduction to the performance of immunohistochemistry. In *Methods in molecular biology* (pp. 289–298). https://doi.org/10.1007/978-1-4939-8935-5_25

Dotan, A., Muller, S., Kanduc, D., David, P., Halpert, G., & Shoenfeld, Y. (2021). The SARS-CoV-2 as an instrumental trigger of autoimmunity. *Autoimmunity Reviews*, *20*(4), 102792. https://doi.org/10.1016/j.autrev.2021.102792

Elkon, K. B., & Casali, P. (2008). Nature and functions of autoantibodies. *Nature Clinical Practice Rheumatology*, *4*(9), 491–498. https://doi.org/10.1038/ncprheum0895

Halpert, G., & Shoenfeld, Y. (2020). SARS-CoV-2, the autoimmune virus. *Autoimmunity Reviews*, *19*(12), 102695. https://doi.org/10.1016/j.autrev.2020.102695

Qiu, C., Caricchio, R., & Gallucci, S. (2019). Triggers of autoimmunity: The role of bacterial infections in the extracellular exposure of lupus nuclear autoantigens. *Frontiers in Immunology*, *10*. https://doi.org/10.3389/fimmu.2019.02608

Thursby, E., & Juge, N. (2017). Introduction to the human gut microbiota. *Biochemical Journal*, *474*(11), 1823–1836. https://doi.org/10.1042/bcj20160510

Jörg, S., Grohme, D. A., Erzler, M., Binsfeld, M., Haghikia, A., Müller, D. N., Linker, R. A., & Kleinewietfeld, M. (2016b). Environmental factors in autoimmune diseases and their role in multiple sclerosis. *Cellular and Molecular Life Sciences*, *73*(24), 4611–4622. https://doi.org/10.1007/s00018-016-2311-1

Kleinewietfeld, M., Manzel, A., Titze, J., Kvakan, H., Yosef, N., Linker, R., Müller, D. N., & Hafler, D. A. (2013). Sodium chloride drives autoimmune disease by the induction of pathogenic TH17 cells. *Nature*, *496*(7446), 518–522. https://doi.org/10.1038/nature11868

Vojdani, A., & Vojdani, E. (2021). The role of exposomes in the pathophysiology of autoimmune Diseases i: Toxic Chemicals and food. *Pathophysiology*, *28*(4), 513–543. https://doi.org/10.3390/pathophysiology28040034

Zhang, G., & Ma, Y. (2013). Mechanistic and conformational studies on the interaction of food dye amaranth with human serum albumin by multispectroscopic methods. *Food Chemistry*, *136*(2), 442–449. https://doi.org/10.1016/j.foodchem.2012.09.026

Glaser, R., & Kiecolt-Glaser, J. K. (2005). Stress-induced immune dysfunction: implications for health. *Nature Reviews Immunology*, *5*(3), 243–251. https://doi.org/10.1038/nri1571

Glaser, R., Robles, T. F., Sheridan, J. F., Malarkey, W. B., & Kiecolt-Glaser, J. K. (2003). Mild depressive symptoms are associated with amplified and prolonged inflammatory responses after influenza virus vaccination in older adults. *Archives of General Psychiatry*, *60*(10), 1009. https://doi.org/10.1001/archpsyc.60.10.1009

Song, H., Fang, F., Tómasson, G., Arnberg, F. K., Mataix-Cols, D., De La Cruz, L. F., Almqvist, C., Fall, K., & Valdimarsdóttir, U. (2018). Association of Stress-Related Disorders with subsequent autoimmune disease. *JAMA*, *319*(23), 2388. https://doi.org/10.1001/jama.2018.7028

Fairweather, D., Frisancho-Kiss, S., & Rose, N. R. (2008). Sex Differences in Autoimmune Disease from a Pathological Perspective. *The American Journal of Pathology*, *173*(3), 600–609. https://doi.org/10.2353/ajpath.2008.071008

Smith-Bouvier, D. L., Divekar, A., Sasidhar, M. V., Du, S., Tiwari-Woodruff, S. K., King, J. K., Arnold, A. P., Singh, R. R., & Voskuhl, R. R. (2008). A role for sex chromosome complement in the female bias in autoimmune disease. *Journal of Experimental Medicine*, *205*(5), 1099–1108. https://doi.org/10.1084/jem.20070850

Constantinescu, C. S., Farooqi, N., O'Brien, K., & Gran, B. (2011). Experimental autoimmune encephalomyelitis (EAE) as a model for multiple sclerosis (MS). *British Journal of Pharmacology*, *164*(4), 1079–1106. https://doi.org/10.1111/j.1476-5381.2011.01302.x

Yun, Y., Wang, X., Xu, J., Jin, C., Chen, J., Wang, X., Wang, J., Qin, L., & Yang, P. (2023). Pristane induced lupus mice as a model for neuropsychiatric lupus (NPSLE). *Behavioral and Brain Functions*, *19*(1). https://doi.org/10.1186/s12993-023-00205-y

Rosenblum, M. D., Gratz, I. K., Paw, J. S., & Abbas, A. K. (2012). Treating Human Autoimmunity: Current practice and future Prospects. *Science Translational Medicine*, *4*(125). https://doi.org/10.1126/scitranslmed.3003504