Abstract

Background: A cytokine is a group of proteins secreted in cells that act as chemical messengers in the immune system. Cytokines can work together to do the role of immune response, but can also act alone or even work against each other, therefore resulting in disease. The thyroid is a small, butterfly-shaped gland within the neck. It is an important hormone gland that plays a major role in the metabolism, growth and development of the human body, but it can be affected by cytokines. Hashimoto's Thyroiditis (HT) is an autoimmune disorder where the thyroid gland is attacked by the immune system.

Scope and Approach: The articles found helped to approach the question of research, which is, "What is the relationship between cytokines and Hashimoto's Thyroiditis. Cytokines enhance the inflammatory response by stimulation of lymphocytes, which results in the production of antibodies and thyroid tissue damage by apoptosis, in particular in HT. Cytokines can modulate the growth and function of thyroid follicular cells in autoimmune thyroid diseases (AITD). They play an important role in the thyroid AITD complications.

Key Findings and Conclusions: Based on the evidence, there is a relationship between cytokines and HT. The evidence suggests cytokines are involved in the pathogenesis of thyroid diseases. They work in both the immune system and directly targeting the thyroid follicular cells (when malfunctioning). Cytokines upregulate the inflammatory reaction through stimulation of both T and B cells, resulting in antibody production and tissue injury.

Introduction

A cytokine is a group of proteins secreted in cells that act as chemical messengers in the immune system. In this way the cytokines "communicate" to stimulate sites of infection, inflammation, or trauma, as seen in Figure 1. Gillaspy (2019) gave a good way to envision it by saying it was like a mailbox. The cell being the mailbox, and the mail being the cytokines. Like how mail works, the person who receives the mail often acts on it. In the same way, cytokines are doing the same thing. The word cytokine, derived from the two Greek words "cyto" meaning cell, and "kine" meaning movement. Cytokines are important when regulating the immune responses. In the immune system, when disruption occurs, one cell affects the actions of other cells by binding receptors.

Cytokines are a large family of molecules that are classified in various different ways. As seen in Figure 1, the word cytokine can be a broad word, which includes other cells. There are many different types of cytokines that include chemokines, interferons, interleukins, and tumor necrosis factor, which each have specific and important jobs. Chemokines are a type of cytokine that calls in cells to the site of infection. Interferons are proteins that prevent viruses from replicating. Interleukins are proteins that regulate immune and inflammatory responses. Tumor necrosis factor plays important roles in diverse cellular events such as cell survival, proliferation, differentiation, and death. According to Mandal (2019), cytokines that can work together to do the role of immune response, but can also act alone or even work against each other, therefore resulting in disease. In mediated actions, however, cytokines are very important to the human body, especially the immune system. The word "meditate" means an intervention between two things in order to bring about an agreement or reconciliation. In mediated actions, cytokines act as the mediator, meaning that they are the "in-betweener".

Hashimoto's Thyroiditis (HT) is an autoimmune disorder where the thyroid gland is attacked by the immune system. The thyroid is a small, butterfly-shaped gland within the neck, as seen in Figure 2. Hashimoto's disease is an autoimmune disorder that can cause hypothyroidism, an underactive thyroid. With this disease, the immune system attacks the thyroid. The thyroid becomes damaged and then can't make enough thyroid hormones that flow throughout the bloodstream. When the immune system produces more antibodies cells, they can attack the thyroid cells, causing thyroid cells to leak hormones, which therefore leads to an enlarged thyroid. As seen in Figure 4, the process on the left is how the malfunctioning of cytokines can resulting in various autoimmune diseases, such as HT.

The immune system is one of the most important systems in the body. This system is a defense system that fights diseases in the body. As seen in Figure 5, there are many parts in the immune system. The immune system recognizes the difference between body cells and any dangerous cells that might cause harm to the body. Therefore, the immune system will destroy this alien cell to be sure it does not cause harm to the body. Even unicellular organisms have immune systems in the form of enzymes. These enzymes protect it from other microscopic things that could hurt that unicellular organism. The defense mechanisms of humans and other eukaryotes, include the ability to adapt over time to recognize specific pathogens more efficiently, which results in immunological memory, according to Medzhitov (2007).

Purpose

The purpose of this investigation is to identify the relationship between cytokines and Hashimoto's Thyroiditis.

The Role of Cytokines in Autoimmune Diseases Such as Hashimoto's Thyroiditis

Kennedy K. Smucker

KALAMAZOO AREA MATHEMATICS AND SCIENCE CENTER

Discussion

The Broad Word Cytokine

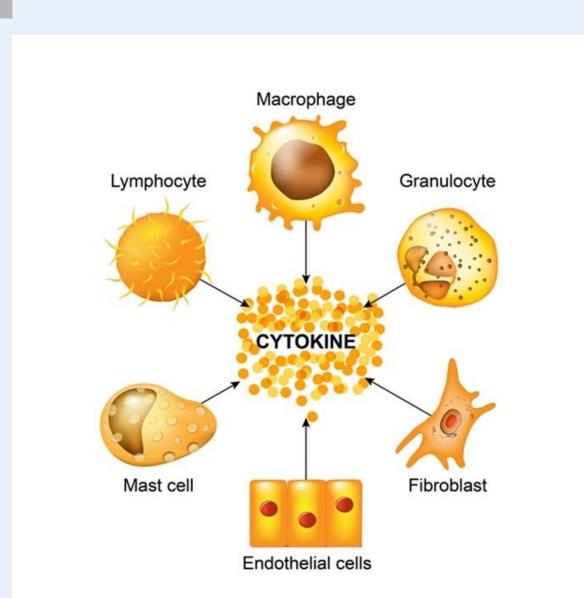


Figure 1: In this diagram, the cytokine is the broader term for all of the smaller cells within. (Designua, 2019)

The Thyroid

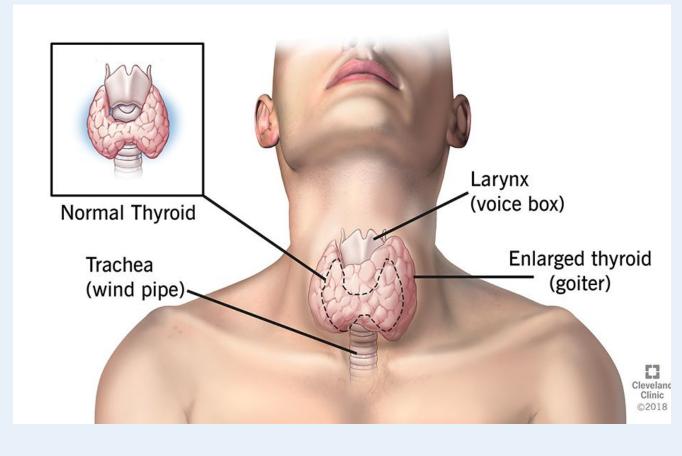


Figure 2: The thyroid is a small, butterfly-shaped gland within the neck. By sending constant amounts of thyroid hormones in the bloodstream, the body can maintain metabolism, health and growth. However, as seen in the photo, the thyroid is enlarged because of HT, and therefore cannot perform the tasks it is meant to do. (Cleveland Clinic medical professional, 2017)

The Thyroid and Cytokines

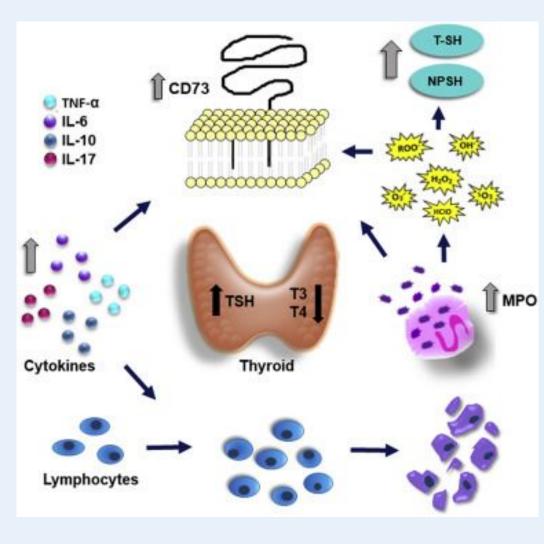


Figure 3: Cytokines enhance the inflammatory response by stimulation of both T and B lymphocytes. This results in the production of antibodies and thyroid tissue damage by apoptosis, in particular in HT. (Baldissarelli, 2019)

4 Cytokines Effects on GD and HT

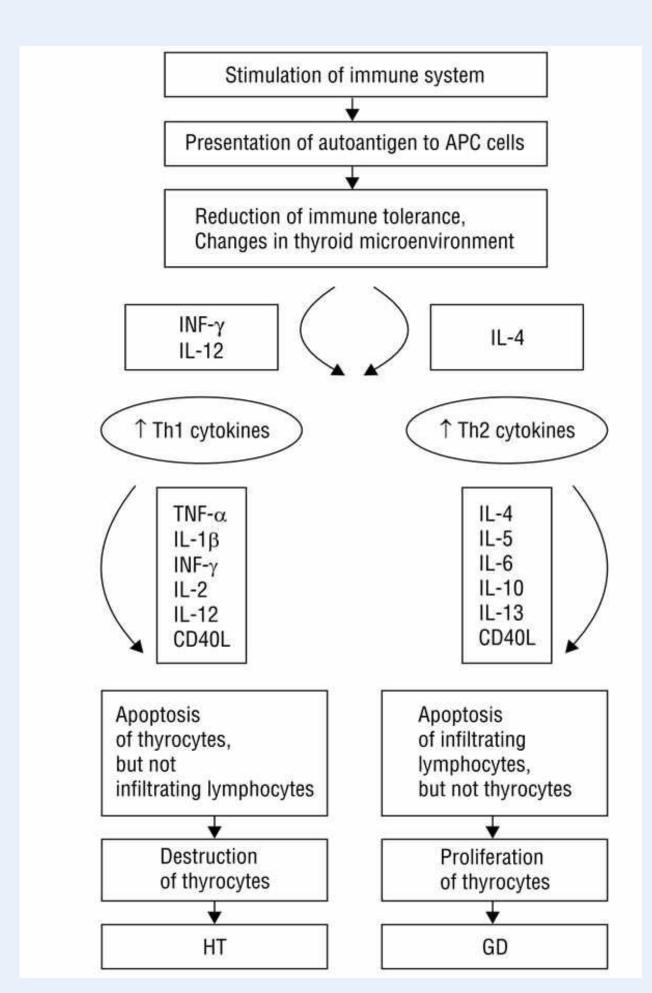


Figure 4:The image above is describing the process of how the wrong amount of cytokines causes apoptosis of thyroid cells which leads to either Graves Disease,(a thyriod disease similar to HT) GD or HT.(Mikó, 2019)

The Immune System

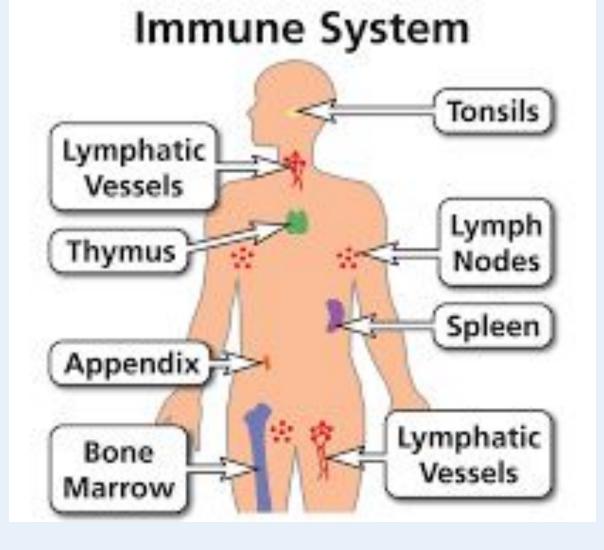


Figure 5: The immune system contains many parts, and each part has a different role that keeps the body ready to fight infections. The immune system is important in in this research because cytokines ar controlled by the immune system.(AIDS info, 2020)

A Site of Infection in the Skin

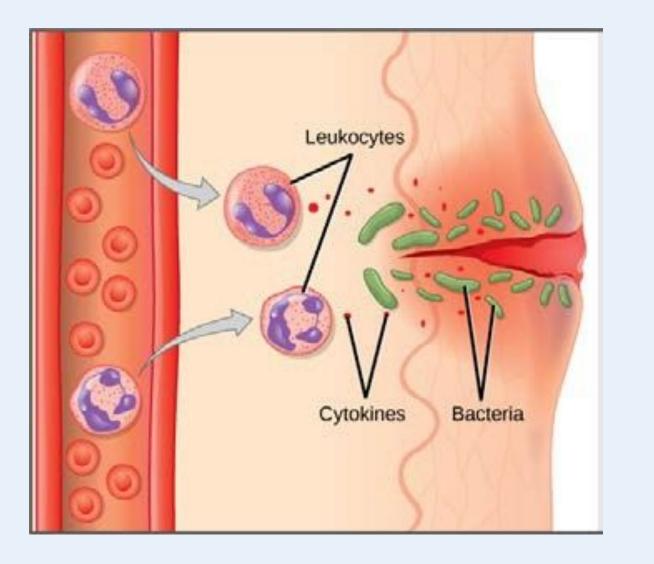


Figure 6: In this image, there is a site of infection, where bacteria is seeping into the skin. In the process of when one cell affects the actions of other cells by binding receptors to their surface, the wound is sensed, and is immediately assisted by cytokines (specifically macrophages and leukocytes). With the help of cytokines, cells know where to go when a wound occurs. (Molnar, 2018)

Conclusions

There is a relationship between cytokines and HT, and the evidence suggests cytokines are involved in the pathogenesis of thyroid diseases.

- Cytokines work in both the immune system and directly targeting the thyroid follicular cells (when malfunctioning).
- The thyroid gland is an important hormone gland that plays a major role in the metabolism and growth and development of the human body, but can be affected by cytokines.
- The thyroid is well known from evidence found by scientists, but the relationship between specifically HT and cytokines is unclear.
- The effect of cytokines is their role in maintaining the balance between health and disease. Cytokines enhance the inflammatory response by stimulation of lymphocytes.
- The production of antibodies and thyroid tissue damage by apoptosis, results in thyriod disorders, including HT.
- Cytokines can modulate the growth and function of thyroid follicular cells themselves in autoimmune thyroid diseases (AITD), playing an important role in the thyroid AITD complications.

Baldissarelli, (2019) concludes that when Th1 cells (promotes cell-mediated immune responses provides defense against viruses bacterial pathogens) produce pro-inflammatory cytokines, this leads to the activation of macrophages and cytotoxic effects. Th2 cells produce cytokines, which can prevent the production of Th1 cytokines. As seen in Figure 3, expression of the response to proinflammatory Th1 cytokines by IFN- γ TNF and IL-1 β (specific types of cytokines) activates thyroid cell apoptosis (Kunz et al., 2009).

Evidence from the researched articles show that cytokines play a crucial role in autoimmune thyroid disease (ATD) through various mechanisms. Cytokines upregulate the inflammatory reaction ny stimulating both T and B cells, resulting in antibody production and tissue injury. Where more research is needed along these lines, there is somewhat of a relationship between HT and cytokines.

References

- 1. Baldissarelli, J., Mânica, A., Pillat, M. M., Bagatini, M. D., Leal, D. B. R., Abdalla, F. H., ... Schetinger, M. R. C. (2019, September 24). Increased cytokine production and oxidative stress are related with purinergic signaling and cell survival in post-thyroidectomy hypothyroidism. Retrieved from Increased cytokines production and oxidative stress are related with purinergic signaling and cell survival in post-thyroidectomy hypothyroidism
- 2. Gillaspy, R. (n.d.). What Are Cytokines? Definition, Types & Function. Retrieved from
 - https://study.com/academy/lesson/what-are-cytokines-definition-types-function.html
- 3. Kunz, Manfred, Ibrahim, & M., S. (2009, October 26). Cytokines and Cytokine Profiles in Human Autoimmune Diseases and Animal Models of Autoimmunity. Retrieved May 22, 2020, from
 - https://www.hindawi.com/journals/mi/2009/979258/
- 4. Mandal, D. A. (2019, February 26). What are Cytokines? https://www.news-medical.net/health/What-are-Cytokines.aspx.
- 5. Medzhitov, R. (2007, October 17). Recognition of microorganisms and activation of the immune response. Retrieved May 22, 2020, from https://www.nature.com/articles/nature06246
- 6. Mikoś, H., Mikoś, M., Obara-Moszyńska, M., & Niedziela, M. (2014). The role of the immune system and cytokines involved in the pathogenesis of autoimmune thyroid disease (AITD). Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/24802739/

Acknowledgements

I would like to thank Mr. Cardwell, Ms. Richardson, and Ms. Chapoton for their support in this process. I would also like to thank many of my peers for helping to review my research. Specifically, I would like to thank Maia Lintner, Mary England, Kendall Conners, Ana Dunfee, Claire Conboy, and Samadhi Attanayaka.