

～Why are allergies increasing?～

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1. Introduction

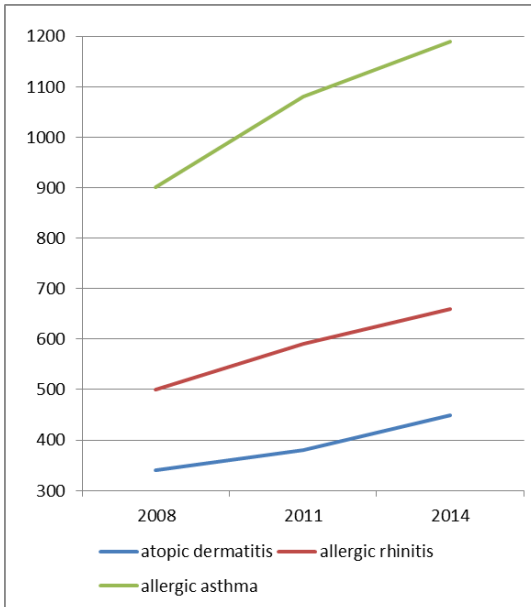


Figure1: the number of people consulting a doctor because of allergic diseases (Source: The Ministry of Health, Labor and Welfare)

Today, there are more kinds of allergen, for instance, pollen, animals, dust, and food. Also, more people are suffering from allergy in developed countries. The number of those people is increasing rapidly. Figure1 shows the number of patients consulting a doctor because of allergic diseases in Japan, over the past 7 years by 3 years (2008-2014). Allergic rhinitis includes hay rhinitis caused by pollen. (The Ministry of Health, Labor and Welfare, 2016)¹. According to this graph, it is shown that the number of those people is an upward trend. Allergy UK said that The World Allergy Organization (WAO) estimates of allergy prevalence of the whole population by country ranges between 10 – 40% (Pawankar R, et al, 2013)².

Then, many serious diseases have been becoming more curable because of the development of medical science and technology, however why are more and more people suffering from allergy?

What could make it hard to improve the treatment for allergy?

This paper will discuss the cause of increasing the number of allergy patients, and the treatment and prophylaxis for allergy.

2. Fundamentals

2.1 Children's food allergy

The number of allergic patients is increasing. They were examined by age groups. The incidence rate of food allergy among children is higher than that among adults. Figure 2 shows the incidence rate among infants and toddlers (their age 0-4) is high. (Quest Diagnostics Health Trends, 2011)³. It turned out that the rate of early age (0-4 years old) greatly higher than that of other age group, and the rate is gradually decreasing when they get older.

Why is the incidence rate of food allergy among infants and toddlers higher than that among adults? Predictable reason is that infants and toddlers don't have sufficient immune system yet compared to adults. As they develop

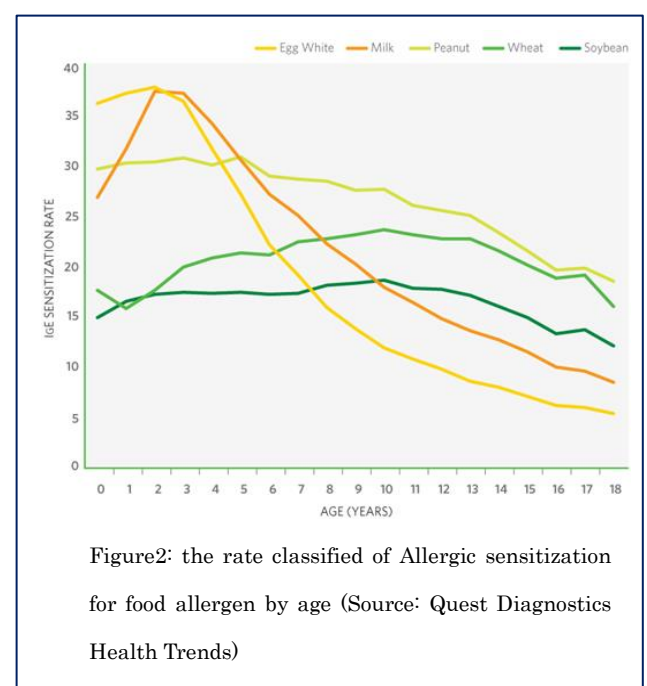


Figure2: the rate classified of Allergic sensitization for food allergen by age (Source: Quest Diagnostics Health Trends)

immune system, they come to have fewer allergies. R. Valiathan, M. Ashman & D. Asthana said that there was significantly higher NK cells (Natural Killer cells) expression (%) in adolescents compared to infants and children (University of Miami - Miller School of Medicine, 2016)⁴. NK cells are essential cells to the innate immune system. In other words, infants and toddlers don't have enough significant cells against allergens.

2.2 Hygiene hypothesis

However, why the incidence rate is continuing to increase? What point is different between in the past and the present? The change of the environment might have caused more people to suffer from allergy recently. Alina Bradford said that being exposed to what many would call unclean conditions is good for a child's immune system. Research has indicated that children who are kept in very clean environments have a higher rate of hay fever, asthma and a wide range of other conditions (Alina Bradford, 2016)⁵.

3. Methodology

To explore this research, a researcher, Dr Ayumi Suzuki at Institute of Infection Immunity & Inflammation, University of Glasgow, UK, was interviewed through the email. She is researching immunology and allergology.

The following questions were asked.

My hypotheses:

By progress in public hygiene, our living environment has become clean. The opportunities to touch microorganisms and bacteria is decreasing and our immune strength is becoming weaker. For this reason, the number of allergic patients is increasing. If we continue to live in a totally clean environment without any microorganisms and bacteria, the types of allergen and the allergic patients will increase.

The incidence rate of food allergy among children is higher than that among adults.

It is because their immune systems are immature considerably compared adult's immune systems. Thus, they react some allergens easily.

My research questions:

- 1) The development of medical science and technology is remarkable, but why are more and more people suffering from allergy?
- 2) Why is the incidence rate of food allergy among infants and toddlers higher than that among adults?
- 3) What should women who are pregnant do in order to prevent their babies from having a food allergy?
- 4) Will it be possible that we could have more types of allergen and more people could suffer from allergy?

4. Results

Dr Ayumi Suzuki's answers:

- 1) **Q1: The development of medical science and technology is remarkable, but why are more and more people suffering from allergy?**

A1: It is said that there are some causes of increase in the number of allergic patients. Three main factors are a change in our living environment, increase stress, and a change in hygiene. It is believed that these

factors are combined to cause increase in the number of allergic patients.

Factor1: A change in our living environment

These days, many people live in condominiums and there is well-equipped heating system. In addition, ventilation and drying of bedclothes are insufficient, consequently our living environment is easy for ticks and mildew to multiply. This is considered to be a cause of increase house dust allergy.

Besides, a lack of vitamin D is considered to cause increase allergy. Recent research shows that vitamin D is effective to control allergy. Synthesizing of vitamin D need sunbathing, however, the opportunities to go out are decreasing, thereby it is considered that people can't take enough vitamin D to maintain their immune balance.

Factor2: Increase stress

There are some epidemiologic researches which said that stress gets worse allergies. However, the molecular mechanism isn't still clarified, thereby it is unclear how stress influence allergies and whether stress directly influence allergy.

Factor3: A change in hygiene

Our living environment come to be clearer, and the opportunities to touch bacteria and virus which we always touch naturally has been decreasing. In order to maintain immune system properly, it is said that the balance of Th1 cell, a cell which works the infection by bacteria virus, and Th2 cell, a cell which is involved in allergy, is really important. Th1 cells have an effect to control Th2 cells. The opportunities to touch bacteria which lead Th1 cells are decreasing, while the opportunities to touch pollens and ticks which can become allergens are rather increase than not change. For this reason, it is considered that Th2 cells can gain an advantage over Th1 cells. The morbidity rate of allergy is higher in an urban district than in a suburban district, and it is higher in developed country than in developing country, therefore the reasons mentioned above are considered.

2) Q2: Why is the incidence rate of food allergy among infants and toddlers higher than that among adults?

A2: Even if people have food allergy, such as milk, soybean and egg, the allergy can be cured as they grow up. It is clear that the incidence rate of food allergy among infants and toddlers is high. 80 - percent of food allergy patients are said to overcome it before they enter elementary school. One of the reasons is the difference of immune system between adults and children. Infants come to eat many kinds of food when they start to eat weaning food, they come to acquire "tolerance" —the immune cells don't attack food. Another reason is the development of digestive system like stomach. The digestive system is still immature, thereby they can't digest food properly and immune cell can recognize food as antigen by mistake.

3) Q3: What should women who are pregnant do in order to prevent their babies from having a food allergy?

A3: There is no report which said that we can prevent children from having food allergy by doing something special. For instance, whether you avoid food which is designated as food allergen is unrelated. It is because the antigen which is included in food isn't transferred from the mother's body to the unborn baby. However, there are some things which mother should care about her baby. As mentioned above, cleaning excessively is not good. Children touch and lick many things. Thereby, they gradually gain immunity to various bacteria and virus, however, these days, parents and nursery school tend to keep clean around children too much. Of course, it is not good to keep the living environment which allergen like a tick propagates easily. However, it is important to not become too nervous. For instance, you need not disinfect children's toys excessively just because they lick, need not wash their hands with soap excessively just

because they put hands in mouth, and need not prevent them from playing in the sand just because they get dirty.

If children have rough skin like atopic dermatitis and eczema, their mothers have to treat it as soon as possible. Recent studies have shown that invasion of allergen from their rough skin brings about having food allergy. For instance, though the children's immunity to eggs becomes tolerance by eating eggs orally, eggs are considered as allergen when eggs adhere to the children's rough skin and is taken into the children's body before children start to eat eggs orally. What parents can do for their children is to do skin care for children properly, not to put food near children and not to touch their children with their hands after touching the food until children can eat various kinds of food.

4) Q4: Will it be possible that we could have more types of allergen and more people could suffer from allergy?

A4: It is unclear whether types of allergen will increase or not. At this time, many substances which is easy to become allergens are already discovered all over the world. However, it can't be denied to increase in types of allergen because there is possibility that another allergen has not been discovered yet. For instance, even if you feel slightly itchy on tongue when you eat food which you rarely eat, almost all people will not go to hospital. They may have allergy against the food, however, it isn't clear whether the food becomes food allergen or not. In addition, there is no way to examine the nature of specific food which have only few reports, and the antigen against the substance. For this reason, probably some food allergens have not discovered yet. In other words, all allergens are not reported. Furthermore, the substance made artificially, not by nature, may become allergen. In the past, an ingredient included in some cosmetic became allergen, and many people show symptoms of exercise — induced wheat allergy. In this way, new allergen may be discovered.

I expect that the number of allergic patients will increase if things are going the way they are. For instance, the number of patients who have atopic dermatitis tends to increase and to make matters worse, it turned out that the risk of child's incidence rate will increase if the parent has atopic dermatitis in the past. For these reasons, the number of patients who have atopic dermatitis continue to increase from now on.

The onset of allergy is greatly involved with the environment. The increase in allergic patients has become social problem, and the living environment and the way to bring up children should be reconsidered. The cause of allergy is complex, the number of patients will not decrease soon. However, if individual can keep in mind to use proper information, try to cure and prevent, the patients may decrease in the future.

Moreover, new treatments and new therapeutic agents are developed. The price of treatment is high and the treatment period is long now. Therefore, it is important to reveal how much the treatment spread into people, and how much the treatment brings large effect.

5. Discussion

Some of my hypothesis can be said to be right. It is because Dr. Suzuki also said that one of the main factors of the increase in the number of patients is that people's immune system became weak due to fewer the opportunities to touch bacteria and virus.

In the past, people lived in the wooden building, raised livestock and raise crops as their food in the environment surrounded by nature. At that time, people didn't disinfect water and crops like today.

However, now people live in building which made of concrete and glass, transfer on the road paved with asphalt and eat food which is disinfected sanitary. Almost all people don't live with their livestock and spray agricultural chemicals on field. The opportunities to touch soil, animals, and nature are very few compared to the past. In addition, there are many products for disinfection and antiviral agent and they are killed many kinds of bacteria and microorganisms. As a result, our immune system has become weak and react against various kinds of allergens excessively. This is also shown by the factor that the number of patients in the town is larger than that in the country.

Furthermore, there is actually an ethnic group whose incidence rate of allergy is really low. They are called Amish, and they live in the northern of Indiana. Many families live on working farms. Almost all Amish families have horse that are used for transportation. A significant percentage drinks raw milks since they were a little child. They do not electricity in their homes. They are always exposed to nature and various kinds of bacteria and microorganisms. A 2012 study of Amish children in Indiana found that only 7 percent had some kind of allergy sensitization, compared to 36 percent of American children as a whole. (Amish children living in northern Indiana have a very low prevalence of allergic sensitization, 2012)⁶

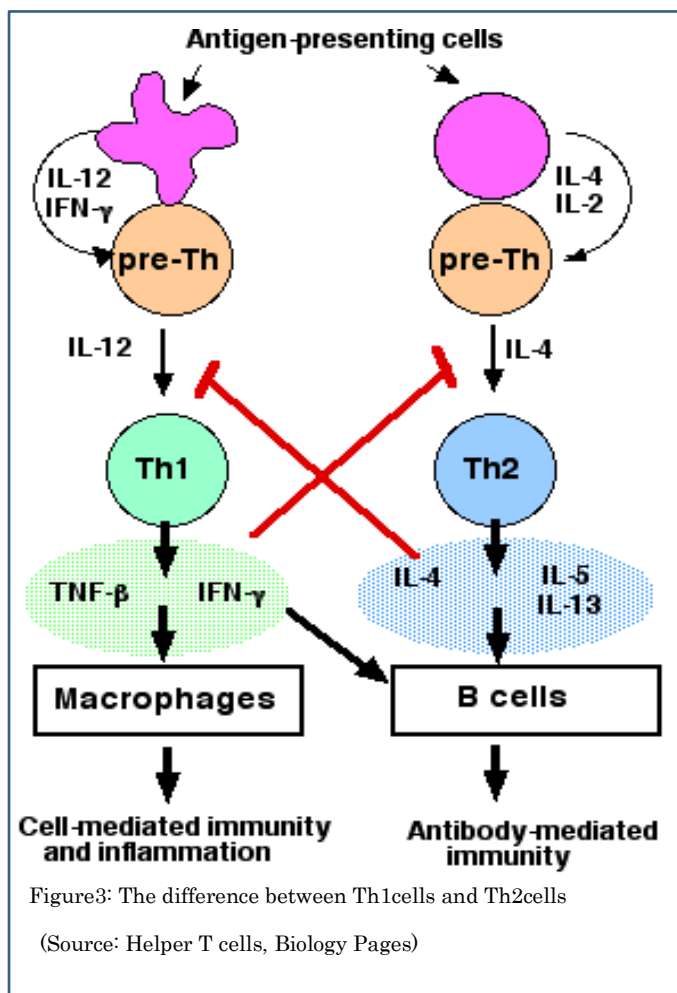
Not making children touch bacteria and microorganisms completely since early childhood can happen children's onset of allergic sensitization. It turned out that these big change in environment in early childhood has affected the increase in the number of allergy patients.

In addition, there are mainly two newly discovers.

First, in order to prevent having allergies, it is important to keep a good balance of Th1cells and Th2cells.

I'm interested in the balance of Th1cells and Th2cells.

(Helper T cells, Biology Pages) 7



Th1 cells

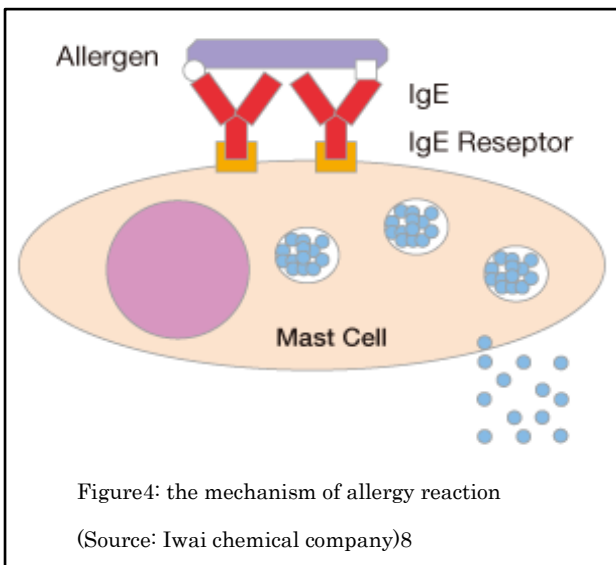
Th1 cells are produced when dendritic cells and pre-Th cells form immunological synapse.

Antigen – presenting cells present antigen to the (IL-12) and interferon – gamma ($\text{IFN-}\gamma$). By these cytokine's stimulation, Th1 cells differentiate from T cells which is called pre-Th cells. Th1 cells secrete $\text{IFN-}\gamma$ and tumor-necrosis factor-beta ($\text{TNF-}\beta$) (also known as lymphotoxin). These cytokines make macrophages and cytotoxic T cells activate, and virus and antigen which in the cells are removed.

Th2 cells

Th2 cells are produced when antigen – presenting cells present antigen to the receptor of T cells. Antigen – presenting cells secrete interleukin 4 (IL-4) and interleukin 2 (IL-2). By these cytokine's stimulation, Th2 cells differentiate from pre-Th cells. Th2 cells secrete IL-4, interleukin 5 (IL-5) and interleukin 13 (IL-13). These cytokines make B cells activate, and

promote the synthesis of the antibody which is called immunoglobulin E (IgE antibody). When IgE antibodies adhere to the receptor of mast cells and allergens combine with IgE antibodies, mast cells release chemical substances such as histamine. When these histamines combine with IgE receptor, allergy reaction, itch and inflammation appear.



Th1cells and Th2cells control each other in order not to let either Th1cells or Th2cells react excessively. $\text{IFN-}\gamma$ which is secreted by Th1cells prevent formation of Th2cells. IL-4 which is secreted by Th2cells prevent formation of Th1cells. (This is shown as red arrows in Figure3) When Th1cells decrease and Th2cells increase excessively, some allergic reaction appears.

The opportunities to touch bacteria and virus decrease these days. By examining these findings, that fewer opportunities make it difficult for Th1cells to be stimulated and the control of Th2cells become weaker. As a result, the immune reaction of Th2cells became excessive and also lead to the allergic reaction appear. It is important that Th1cells and Th2cells stimulate and control each other, and keep immune balance.

Second, infants come to have allergy against the food by taking it through the rough skin before they are able to eat the food orally.

Allergy aren't inherited from parents to children. It turned out that it is important the skincare of children during the time between the birth and when they are able to eat various kinds of food. Infants come to acquire the tolerance by taking first food through their mouth. Tolerance is the prevention of an immune response against a particular antigen. For instance, the immune system is generally tolerant of self-antigens, so it does not usually attack the body's own cells, tissues, and organs. However, when tolerance is lost, disorders like autoimmune disease or food allergy may occur. (National Institute of Allergy and Infectious Diseases)9. Thanks to the immune tolerance, our immune system doesn't consider food as foreign body. However, the tolerance against the food which entered through the rough skin isn't create well. Infant's immune system makes the antibody against the food by taking it through their rough skin. Parents must not their baby to approach allergens. For instance, an infant developed atopic dermatitis before he comes to be able to eat various kinds of food. If his mother touch with her hands after touching eggs his affected parts, a possibility that he develops egg allergy is high. Nonetheless, it is similarly presumed that if parents make too clean environment which like mentioned by Dr Suzuki in the process that infants and toddlers gain their tolerance, there is possibility not to be able to gain the tolerance against allergens for them. Besides, their children's immune strength will become weak and they react allergens easily. There is no concrete criterion of cleanliness, and therefore it is really complex and difficult problem. Further consideration will be needed to yield any findings about the concrete measures.

I estimated a possibility of the increase in the types of allergens and the number of allergy patients from now

on.

Dr Suzuki mentioned that there is no scientific basis that suggest the types of allergen will increase, however, there is a possibility that the substances made artificially, not by nature may become allergen.

By the development of science technology, it is considered that new food made by variety improvement, and new components which is included in new cosmetic and soap may become new allergen. New substances and commodities must be developed more. However, these may create a risk. The researcher who create new substances and commodities have duty to examine them many times and to notify people of the risk. Anybody has possibility to depend allergy of new substances and commodities newly, even if you don't have allergy now. It is important to have the consciousness which they have possibility to depend new allergy. In addition, Dr Suzuki mentioned that the number of allergic patients will increase if things are going the way they are, however, our living environment and the way to bring up children are reconsidered and the patients may decrease in the future.

6. Conclusion

The cause of increase in the number of allergy patients is not only one, really many factors are complicated in this research, for instance, a change in our living environment, a change in the way to bring up children, and our body's mechanism. It is almost impossible to eliminate all cause of allergy. I thought that it is necessary to let people know proper information about the treatment and prophylaxis for allergy more. It is presumed that many people don't know the information such as the invasion of allergen from infant's rough skin before they eat the food orally brings about having food allergy. With the proper information, it is considered that the number of allergy patients can decrease by changing gradually our living environment and way to bring up children.

I suppose that the long-term research of allergy is necessity and the future issue is finding the cause and efficient treatment of allergy. I believe that this paper will be chance to examine this problem.

7. Reference

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