What is the link between atopic eczema and development of an allergy?

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List of abbreviations

Abbreviation	**Definition**
Th	T-helper cell
IL	Interleukin
PTK	Protein Tyrosine Kinase
Ca	Calcium
FCεRI	High affinity receptor of IgE antibody
PGD2	Prostaglandin D2
TNF	Tumor Necrosis Factor
TLR	Toll Like Receptor
AMPs	Antimicrobial Peptides

Abstract

Worldwide, an estimated 4% of people suffer from a food allergy. One of the major risks of this allergy is anaphylaxis, a potential life-threatening hypersensitive acute allergic reaction. During an allergic reaction, immune mediators react severely to an allergen in a IgE mediated or a non-IgE mediated way. Because of this, it is important to find a way to prevent this from happening.

Nowadays, it is known that atopic eczema plays an important role in the development of an allergy. Having atopic eczema as a child, would increase the chance of developing an allergy. Atopic eczema is a skin barrier- or immune dysfunction with two theories about the onset of the disease. In the outside-to-inside theory, skin barrier will break down, because of a filaggrin mutation or dysfunction, causing allergens to infiltrate into body. On the other hand is the inside-to-outside theory, where immune system is dysfunctional because of an increase of Interleukin-4 (IL-4) and IL-13. These will activate T-helper-2 (Th-2) cells and activate the allergic pathway. It is possible that the proportion of IL-4 : IL-12/Interferon-γ (IFNγ) plays a role in the onset of an allergy in people with atopic eczema. After allergens have entered the body via the dysfunctional skin barrier. If the proportion of IL-4 is already higher than IL-12 and IFNγ, because of atopic eczema, the allergic pathway could be activated. A possible therapy to prevent an allergy from developing in children at high risk could be restoring the skin barrier or preventing the skin barrier from becoming a dysfunctional barrier via emollient or moisturizing therapy. Another option would be preventing allergic immune mediators of activation via breastfeeding or prebiotics. Both could pose effective and cheap therapies.

Introduction

An allergy is a hypersensitive response of our immune system caused by antigens, like aerosol allergens, or nutrients in food[1]. Worldwide, approximately 4% have a diagnosed food allergy, added up to the top 3 in the allergy ranking, accompanied by allergic rhinitis and allergic asthma[1–4]. The prevalence of food allergies is higher in women and in Asians, and a variety of symptomatic reactions to these allergies are documented, like hives, anaphylaxis and swelling[1]. Within the food allergies, an IgE mediated allergic response to shellfish is most common[1,5]. These different expressions in allergies are induced by different immunologic mechanisms, the IgE mediated allergic response and the non-IgE mediated allergic response[5].

In case of anaphylaxis, the major risk of food allergy, a severe reaction to an allergen with symptoms like hypotension, shock and bronchospasm will occur with serious life-threatening situations for the patient[6]. Moreover, the most worrying part is that the prevalence of anaphylaxis is rising[4]. Since this is the case, something needs to be done to prevent the prevalence of allergy and thus anaphylaxis and therefore the cause of allergies have to be investigated.

The reason why an allergic reaction appears in one person and not in another person remains unclear, but it is known that the presence of atopic eczema implicates a greater chance of developing an allergy[2]. About 13% of children up to 17 years old will develop atopic eczema[7]. This means that more than 1 out of 10 children is at risk in developing an allergy. Therefore, the cause and the mechanisms of atopic eczema are of interest for the prevention of an allergy. Atopic eczema is also called atopic dermatitis and both are an inflammation reaction in the skin[5]. Normally, allergens can't infiltrate into the body because of the first protection layer, mucus and skin[8]. Mucus catches the allergens you breathe in and makes sure to carry them outside the body. The skin protects the rest of the body from infiltration of antigens. Because of this protection layer, no antigens will infiltrate into the body and no hypersensitive immune response will occur. In atopic eczema patients, the barrier of the skin is dysfunctional and therefore, antigens can infiltrate into the body without any trouble and will be recognised by immune cells. Next to skin barrier dysfunction, inflammation reaction is increased in atopic eczema patients. Therefore antigens will enter the body via the impaired skin barrier and a continuous antigen presence will activate T-helper-2 (Th-2) cells. Isotype switch to IgE antibodies will occur by activated B-cells, which could possibly lead to the onset of an allergy [3].

How the inflammatory response of atopic eczema will precisely lead to the onset of an allergy and if there are possibilities to prevent an allergy for someone with atopic eczema, is of interest in this thesis. In literature, it is claimed that the presence of atopic eczema is a risk factor for the development of an allergy, which would lead to a so called atopic march[2,3]. This means, when someone is already developing one allergy because of atopic eczema, more will follow[3]. This theory is used in a lot of articles, where atopic eczema is claimed to be the problem of the increase of the prevalence of allergies. The problem remains, that little research is done about how atopic eczema could cause these allergies. When the mechanism of atopic eczema and allergies are figured out, opportunities will rise for therapies to prevent an allergy for people at high risk, like people with atopic eczema. Life threatening reactions to an allergy like anaphylaxis could be reduced with these kinds of therapies.

Aim of the thesis

How does atopic eczema, immunologically, cause an allergy and how could an allergy be prevented in children with or at risk of atopic eczema?

Key mechanisms in the onset of an allergy

An allergy is a hypersensitive reaction of immunologic mechanisms caused by allergens. To discover what could play a role in the onset of an allergy, underlying mechanisms must be figured out. The pathways of IgE mediated and non-IgE mediated allergic reactions will be discussed below.

Sensitization phase and antigen-specific IgE antibody response

IgE mediated allergy is the most common kind of both types of allergies and will develop in two stages[1]. At first is the stage when the allergen is not yet exposed in the body. At this point, there are no antibodies available yet that recognize this allergen. Therefore, IgE antibodies are thus not specific for this allergen and there will be no reaction to this allergen by an antibody[9–11]. Non-specific IgE will bind to the high affinity receptor of the IgE antibody, FCεRI, but also to monocytes or dendritic cells[9]. Antigens will be carried to the lymph node by the monocytes or dendritic cells, which are both antigen presenting cells[9]. In the lymph node, antigens will be presented to the T-cell. In presence of interleukin-4 (IL-4) and IL-13, the naïve t-cell will transform into a Th-2 cell. This Th-2 cell will activate the B-cell, which will produce antibodies. IL-4, IL-13, basophils and mast cells will activate the immunoglobulin heavy chain, which will produce specific IgE antibodies in the B-cell instead of IgM antibodies[9–11]. This switch is called isotype switch[10].

The second time this allergen enters the body, it will be recognized by these specific IgE antibodies, because it is already present from the first exposure in the body[9]. After binding, IgE antibodies will bind multiple cell types, like mast cells and dendritic cells. The binding to FCεRI initiates mast cell degranulation. Mast cells releases histamine, Prostaglandin D2 (PGD2) and Tumor Necrosis Factor (TNF). PGD2 and TNF recruit Th-2 cells and make dendritic cells migrate to the place of the allergen, which makes the immune reaction more severe[9]. When specific IgE antibodies bind CD23 of the B-cell, more Th-2 cells will be activated by the B-cell[9,10]. Mast cells can produce more IL-4 and IL-13, which increases CD23 expression on B-cells, so it will produce more specific IgE[9] (fig. 1). Eosinophil recruitment is caused by IL-5, a pro-inflammatory cytokine originated from Th-2 cells[12]. The granules of eosinophils are acidophilic, therefore they can bind acidic dyes[12]. One example of the role of eosinophils is in allergic asthma, where eosinophils in mucosa are associated with membrane thickening and secreting profibrotic mediators[13].

Histamine

When IgE antibodies bind mast cells, they will produce histamine the following way. When IgE antibodies bind to FCεRI, activation induces a Protein Tyrosine Kinase (PTK) and phospholipase-C dependent signal. This results in an increase of Calcium (Ca), which ensures that histamine will be released from its granules [14]. Histamine will cause local immediate hypersensitivity, like sneezing and a running nose within a few minutes[15]. Later, when a lot of allergen is present, this phase can be followed up by a up to 9 hours lasting late-phase reaction. Symptoms can stay local like swelling and redness of the skin, but can also become systemic, like a drop in blood pressure and vasodilation[15]. The last two are both aspects of anaphylaxis, which is a major risk for people with an allergy and could be lethal [6].

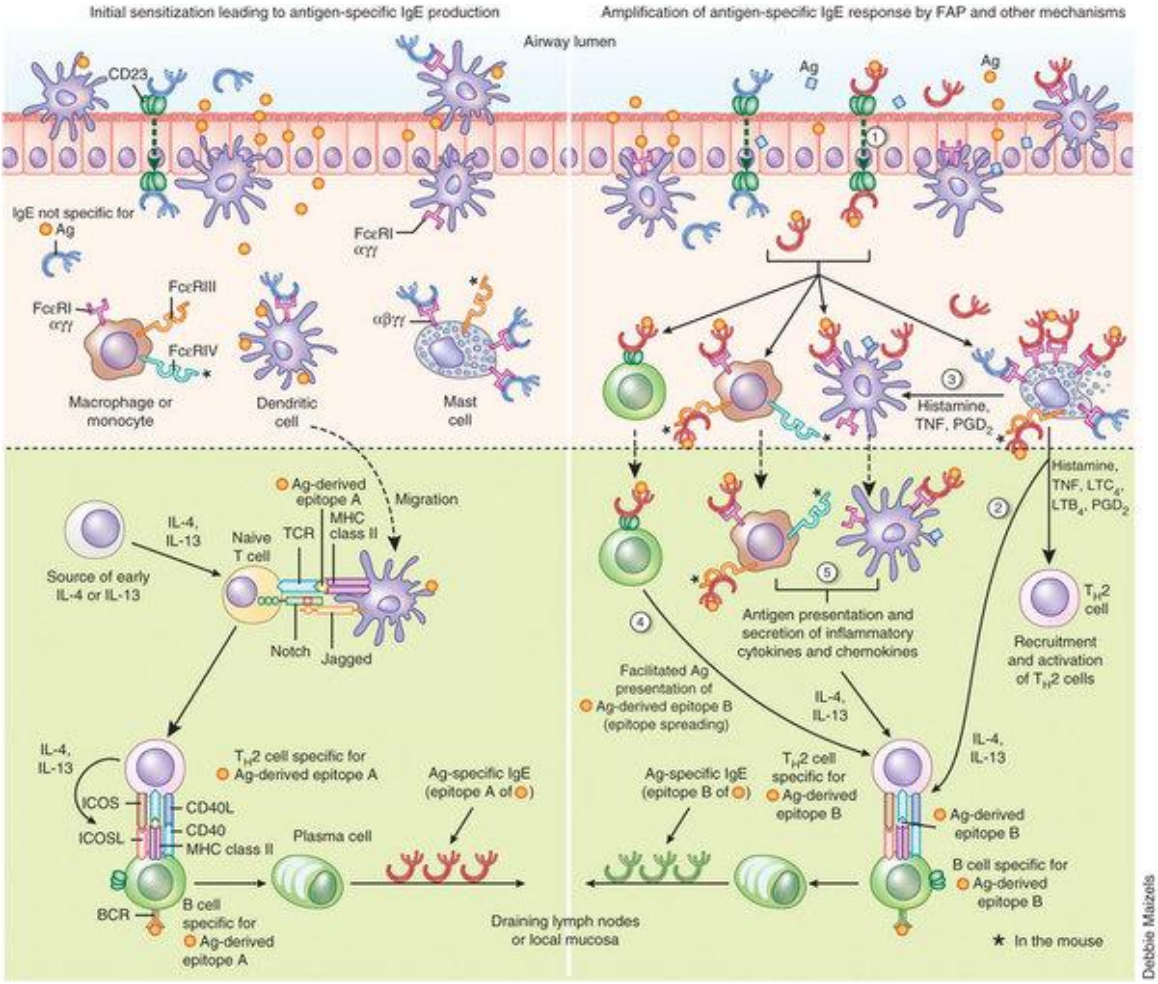

Fig. 1: Pathway of initial sensitization (left) and amplification of antigen specific IgE response by isotype switch of B-cells Is and other mechanisms (right)[9]

Non-IgE mediated allergy

It is very likely that few people with allergies have non-IgE mediated allergy. About this type of allergy, little is known. Like the word says, this type of allergy is not mediated by IgE antibodies, thus not by the Th-2 reaction. It is known that the allergy can be caused by allergen specific lymphocytes [5]. An example of an allergy with this mechanism is contact dermatitis. In this case lymphocytes are activated to transform into Th-1 cells. Another way of causing an allergy is via antibodies with IgG isotype. These antibodies can create immune complexes, which could cause anaphylaxis [5,16]. The last possible non-IgE mediated allergy is serum sickness, at one time the reason for the name allergy, while it is now rarely occurring [5,17].

Immunological aspects of atopic eczema

There are two types of eczema, normal eczema and atopic eczema. For this topic we will discuss atopic eczema, because it is involved in immune activation, just like allergy. Atopic eczema is a skin barrier and immune dysfunction with a prevalence in children up to 17 years old of 13% [7]. This disease is mostly T-cell driven and Th-2 plays the most important role[18]. It is still unclear what causes atopic eczema, and there is probably not one cause. It is known that atopic eczema can also be IgE mediated or non-IgE mediated, also just like an allergy[19]. Nevertheless a lot is still unknown. About the onset of the IgE mediated atopic eczema, 2 theories exist, which will be discussed below.

Outside-to-inside and inside-to-outside theory

The first theory is the outside-to-inside theory, where atopic eczema is claimed to start with genetic defects in the skin barrier, leading to barrier dysfunction and leakage of allergens[18]. Supporters of this theory believe that a Filaggrin mutation or deficiency would cause inflammation and cytoskeletal pathway dysregulation. Filaggrin is the first of the two protecting layers in the skin, laying on the level of the Stratum Corneum (SC) (fig. 2). When this first barrier is dysfunctional, the other one will collapse[18,20].

The other theory is the inside-to-outside theory, which starts with an activated immune pathway that downregulates keratinocyte differentiation, which creates a skin barrier defect. Since a lot of children develop atopic eczema without a Filaggrin mutation or outgrow this disease with the mutation over time, some people support this different theory. In the article of Howard et al., it is described how IL-4 and IL-13, Th-2 cytokines and characteristics of the atopic eczema skin, could lead to keratinocyte differentiation. This would lead to a reduced amount of filaggrin[18,20]. Next to reducing the amount of Filaggrin, inflammatory cytokines, IL-4 and IL-13, would also reduce cell adhesion molecules [21]. On the other hand does Gutowska-Owsiak et al., claim that IL-17a, a cytokine from Th-17, affects keratinocyte expression and reduces filaggrin[22]. This outcome would implicate that more cytokines than only the allergic immune mediators from Th-2 are involved in the onset of atopic eczema.

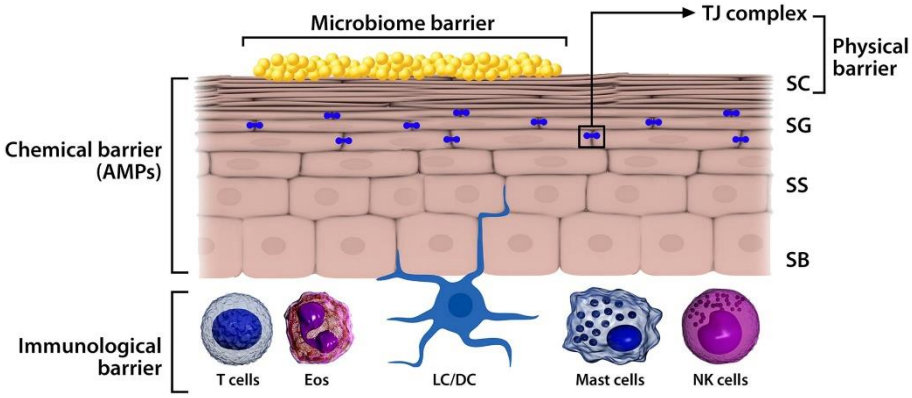

Fig2: The different layers of protection in the skin. In atopic eczema a Filaggrin mutation or deficiency would break down the Stratum Corneum (SC). The Stratum Granulosum (SG), filled with tight junctions follows with the break down, probably because of Il-4 and Il-13. Then, keratinocytes produce, Antimicrobial peptides (AMP's), the chemical barrier. Because of Toll Like Receptor dysfunction in atopic eczema patients, this barrier also breaks down. The immune cells have to protect the body and respond[18].

IgE mediated immune response

After dysfunction of filaggrin, only one of the two layers is left in the skin to protect the inside of the body against allergens (fig 2.). These are the tight junctions, at the level of the Stratum Granulosum (SG). As soon as both barriers stop working, which might be caused by IL-4 and IL-13, keratinocytes try to produce Antimicrobial peptides (AMPs) to strengthen the tight junctions via toll like receptors (TLR)[21]. Unfortunately, TLR's working is reduced in atopic eczema patients causing AMPs not being able to strengthen the tight junctions. This will lead to an infiltration of allergens in the body and an activated immune response[18].

Innate immune system and adaptive immune system both play a major role when this immune response is activated. In every type of atopic eczema, they all play a different role (fig. 3). The first type is nonlesional atopic eczema, where Th-2 is slightly increased. When Th-2 and Th-22 show a major increase and Th-1 and Th-17 a small increase, the type of eczema is acute. Cytokines and chemokines of these T-helper cells further activate and recruit immune cells. While in the acute phase, IL-22 induces hyperplasia and in synergy with IL-17, it reduces filaggrin as discussed above. IL-31 will make the skin itch, which will lead to lichenification of the skin, a thick, leathery and intensely itchy skin, when admitting to the itch and scratching the eczema[23]. After a while, immune cells continue to get further activated in chronic atopic eczema type[23].

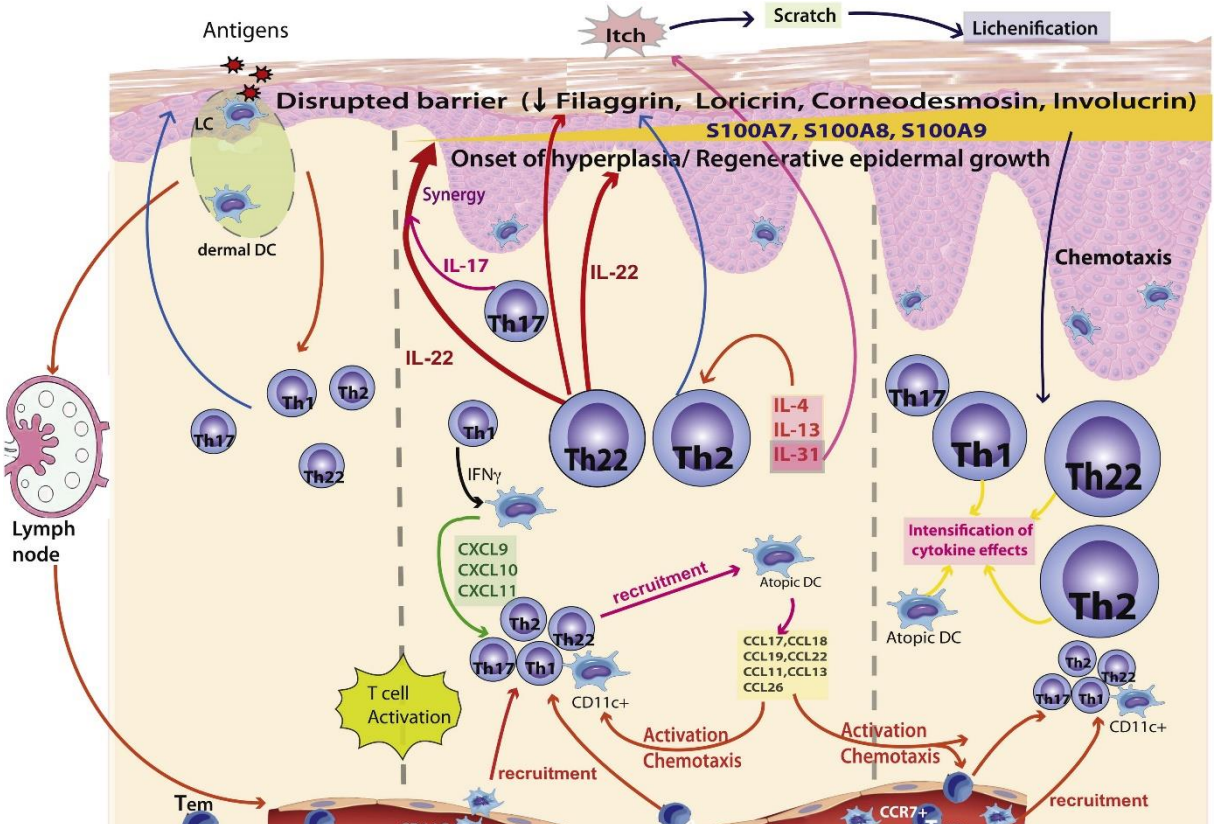

Fig. 3 The three different stages of atopic eczema. Nonlesional stage, with a slightly increased Th-2 and Th-22 (left). Acute stage with a major increased Th-22 and Th-2. Effects of immune mediators are immediate (middle). Chronic stage where activation of immune mediators reinforces themselves for an intensification of effects (right)[23].

Non IgE immune response

It is known that a non-IgE immune response is existent in atopic eczema[19]. Unfortunately, the pathway of this non-IgE immune response is still unknown. To classify atopic eczema, the following checklist was followed. When the patient had: clinical symptoms of allergic diseases, positive skin prick test for allergens, increased IgE or presence of sensitization for allergens, atopic eczema was considered IgE mediated[19]. When the patient had none of these points, it was considered non-IgE mediated[19].

Interestingly, this study showed that a switch from non-IgE mediated to IgE mediated atopic eczema could take place in mostly children up to 3 years old. Also in this study, all non-IgE mediated atopic eczema is switched to the IgE mediated type before children reach the age of 8 years old[19].

How the presence of atopic eczema enhances the development of an allergy in children

In the article of Branum et al. the link between food allergies, atopic eczema and other allergies was investigated[2]. Approximately 27% of people with food allergies had or had had atopic eczema, contrarily only 8% of people without an food allergy had or had had atopic eczema (fig. 4)[2]. Also, the prevalence of other allergies were increased in people with food allergies. Therefore, atopic eczema is very likely a risk factor for the development of an allergy. In normal people exposed to an antigen, a low immune response occurs with a low amount of specific IgG1 and IgG4 antibodies activation [24]. These antigens will activate Th-1 cells, which will cause IFN-y production[25]. In case of an allergy, Th-2 and IgE activation will occur. The reason why naïve T-cells are transformed into a Th-2 cell instead of a Th-1 cell, could be due to one of the risk factors, atopic eczema.

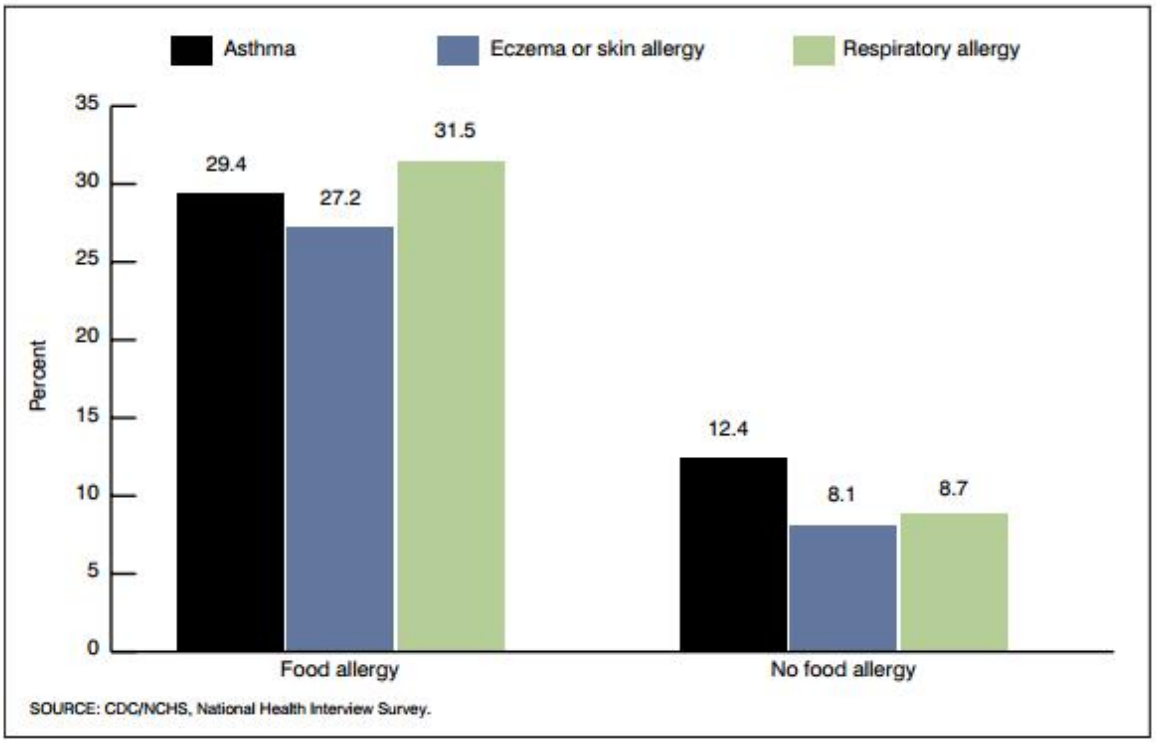

Fig. 4 Research of Branum et al from 2008. People with an food allergy have 4x more allergic asthma, atopic eczema and allergic rhinitis. This gives arguments for the existence of the atopic march. [2]

Hypothesis

There are 2 major reasons I can think of, why atopic eczema could cause an allergy. Normally allergens are not able to infiltrate the body because of the first protection layer, mucus and skin[8]. In atopic eczema, barrier of skin is dysfunctional, causing allergens to enter the body without any trouble[18,20]. Because of this, allergens will be recognized by immune cells, but will not directly lead to an allergic reaction. In atopic eczema patients, IL-4 and IL-13 are increased, which leads us to the next reason.[18,21]. Presence of IL-4 and IL-13 is needed for activation of Th-2 cells from naïve t-cells[21].

During acute and chronic eczema, Th-2 cells are increased. Therefore, IL-4 and IL-13 are also increased, since they activate Th-2. When the dendritic cells present the allergen to the naïve T-cell, Il-4 and IL-13 will make sure it will transform into a Th-2 cell[18,21]. This Th-2 cell binds the B-cell which will produce IgE antibodies instead of IgM antibodies, because of Th-2 activation. An allergic reaction will occur[18].

Supposing that those two reactions are the reasons why atopic eczema could cause an allergy, it is strange that not all patients with atopic eczema suffer from an allergy.
One of the reasons could be, that the proportion of IL-4 : IL-12/IFNγ is of interest. This could be, because IL-4 activates naïve T-cells to transform into a Th-2 cell, which is involved in allergic reactions. IL-12 activates naïve T-cells to transform into a Th-1 cell, which is involved in normal reactions. And IFNγ, a cytokine made by Th-1 cells, prevents naïve T-cells from transformation into a Th-2 cell[15]. I postulate that an allergic reaction would develop if the proportion of IL-4 is higher than IL-12 and IFNγ. Next to this, the skin barrier must be dysfunctional for developing an allergy.
Additionally, eosinophils are increased in allergy and in atopic eczema[12]. In allergic asthma, eosinophils are associated with profibrotic markers, which could also play a role in the dysfunctional skin barrier of atopic eczema[13]. To establish if a correlation exists between the increase of eosinophils and the presence of atopic eczema, more research should be done.

Up to now, only links between IgE mediated allergy and atopic eczema are made. This is logical, because this is the major group of patients, but, I'm wondering if the non-IgE mediated atopic eczema could be a risk factor for a non-IgE mediated allergy[19]. One of the characteristics of non-IgE mediated atopic eczema is that it can and probably will switch to an IgE mediated atopic eczema in childhood[19]. Therefore, non-IgE mediated atopic eczema could only play a role in the onset of non-IgE mediated allergies in children up to 8 years old. Since a lot of allergies develop before children reach the age of 8 years old, non-IgE mediated atopic eczema and allergies could still be a subject of interest. About the consequences of non-IgE mediated atopic eczema, little is known. It could be possible that this type of atopic eczema causes non-IgE mediated allergies, because of the impaired skin barrier and the lack of an IgE mediated immune response[18–21]. But, since no research is done about these types of atopic eczema and allergies, the underlying mechanisms must first be unravelled. Afterwards, a good hypothesis could be drawn about the causes and the consequences of non-IgE mediated atopic eczema and allergies.

Therapies for preventing an allergy for someone with eczema
Since the presence of atopic eczema is a risk factor in developing allergy, an interesting question arises. What if the chance on developing an allergy can be prevented by improving the skin barrier and blocking the inflammatory cascade? Simpson et al. wondered this and investigated if emollient therapy could prevent development of an allergy in neonates at high risk of atopic eczema[26]. This therapy would soften the hard and scaly skin of atopic eczema patients and form a protection layer on top of the fragile skin. In this way, emollient therapy would protect the body from infiltration of allergens and the activation of the allergic inflammatory cascade[26,27]. In this study, neonates at high risk, were determined when one or both of the parents had an allergy, a filaggrin mutation or atopic eczema. Those neonates were randomised and half of this group got the emollient therapy. Results showed that these neonates had a smaller chance in developing an allergy[26].

In the research of Horimukai et al., they did something similar to the research of Simpson et al. In this experiment, moisturizer of the emulsion type was used to prevent allergies in neonates at high risk[28]. A moisturizer is almost the same as an emollient, except that the Statum Corneum gets hydrated in the moisturizer[27]. Also in this experiment, results were very promising. Therefore these therapies could possibly be an easy, effective and safe option in preventing an allergy[26,28].

Because these therapies showed promising results, they hypothesized that exogenous lipids of the emollient or moisturizer therapy would improve skin barrier (fig. 5)[26]. Because this barrier is improved, no allergens will infiltrate into the body, no immune reaction will occur and no allergy will develop[26,28].

One critical note is that this hypothesis assumes the outside-to-inside theory is already verified. For both outside-to-inside and inside-to-outside are a lot of pros and cons. Also did both experiments lack enough time in their experiments. In the research of Simpson et al. and Horimukai et al., neonates were observed for respectively 6 and 8 months[26,28].
I think this time is too short to know for sure that's these children won't develop an allergy. It could also be possible that this therapy extends time before the allergy manifests itself. A research over multiple years should be done to know for sure that emollient and moisturizer therapies reduce the chance of developing an allergy by improving the skin barrier.

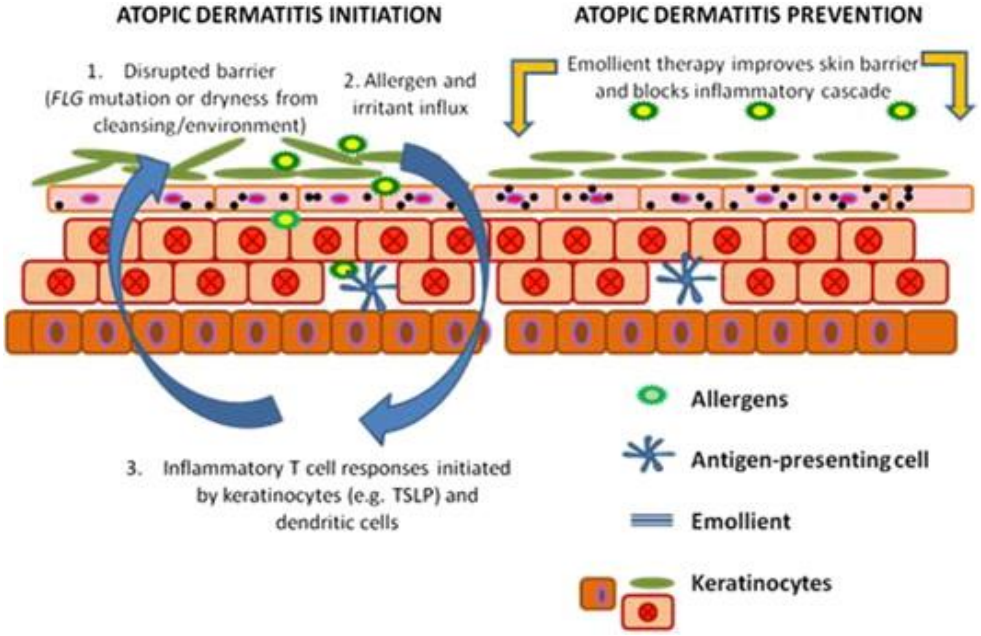

Fig. 5 The theory of the effect of emollient therapy on the atopic eczema skin. Emollient therapy is thought to improve skin barrier and therefore to block the inflammatory cascade [26]

Another interesting question that would pop up is: what if we could prevent the allergic immune response to get activated? Since this is part of the inside-to-outside theory and the second part of our hypothesis, it would be an interesting subject. In the research of Grüber et al., they investigated the role of breastfeeding and prebiotics on young infants up to 1 year old at low risk of developing atopic eczema[29].
In the results is shown that both breastfeeding and prebiotics have a positive effect on preventing the development of atopic eczema with p=0,037[29]. On top of that, IgE antibody serum levels were lower in the breastfeeding and prebiotics group[29]. In this research, they postulate that breastfeeding and prebiotics will reduce the chance of developing atopic eczema and therefore stop the rise of the atopic march[3,29].

Criticism to this research is just like the previous treatment discussed, time. It is not sure that this effect maintains until beyond the first year. To know this for sure, more investigation must be done.

Discussion

It is known that atopic eczema is a risk factor for an allergy and a cause of the so called atopic march[3]. The prevalence of allergies is rising, but it remains unclear how this immunologically happens[4]. This could be due to the complexity and diversity of these diseases. Multiple theories exist about the causes and consequences of atopic eczema, but arguments are contradictory, which makes the theories weaker[18]. This leaves us suspecting that new theories have to be made. In addition, about the role of non-IgE mediated atopic eczema and allergy, little is known[19]. Therefore it is hard to determine what is exactly the cause of atopic eczema, so a treatment can be found to prevent an allergy from developing.

All in all, more research should be done about the following points to uncover the underlying causes and immunologic mechanisms of atopic eczema and allergy, in order to find treatments to prevent development of both.

The cause of atopic eczema

It is still unclear what causes atopic eczema. At the moment, there are two theories, the inside-to-outside and the outside-to inside theory, with both a lot of pros and cons[18]. I believe that preventing is a better option than curing an allergy, but this is only possible when it is known what the cause is. Because both theories have a lot of promising arguments, which are contradictory to each other, an interesting idea could be that the cause of atopic eczema does not have to be one of the two theories. Maybe atopic eczema could be caused by both. Another interesting idea would be that half of atopic eczema patients obtain an allergy caused by the first theory, and other half of the patients, obtain an allergy via the other one. In this way all promising arguments can be right and the disease is more complex than was expected.

IgE mediated and non-IgE mediated

Since IgE mediated allergies and atopic eczema, are the major group, extensive research is done about these subjects. On the contrary, non-IgE mediated allergies and atopic eczema occurs in the minor group. Little is known about the pathways of these kinds of allergies and atopic eczema, therefore the cause and consequences remain unknown[19]. More research should be done to test if non-IgE mediated atopic eczema is a risk factor for non-IgE mediated allergies, because of the impaired skin barrier and the lack of an IgE mediated immune response in both. This should be investigated in children below 8 years old, because afterwards, the non-IgE mediated atopic eczema could be switched to IgE mediated eczema[19].

The reason why atopic eczema is a risk factor for allergies

Also the reason why atopic eczema can cause an allergy is unclear[3,18,21]. I think more research should focus on the proportion of IL-4 : IL12/IFNγ in serum of atopic eczema patients[18,21]. When having atopic eczema, skin barrier is already dysfunctional, so allergens can already enter the body. The only difference between allergic and non-allergic people is the immune reaction[18,19]. Maybe a proportion in cytokines could mean the difference. If the people with a higher proportion of IL-4 to IL-12 and IFNγ develop an allergy, the reason why atopic eczema is a risk factor for an allergy could be uncovered.

Prevention of allergies

Already some research is done to find treatment to prevent an allergy[26,28,29]. I think emollient or moisturizer therapy are already effective, easy and cheap methods to prevent an allergy[26,28]. However, more and extended research should be done about the type of emollient or moisturizer, to uncover the most effective typ for preventing an allergy. The other therapy was breastfeeding and prebiotics[29]. I think the results are very promising for also easy, cheap and effective treatments for preventing atopic eczema and therefore allergy. Emollient and moisturizer treatment assumes the outside-to-inside theory is the cause of atopic eczema[18,26,28]. On the contrary breastfeeding and prebiotics therapy postulate the inside-to-outside theory to be the cause of atopic eczema[18,29]. Both treatments expect a different theory to be true about the cause of atopic eczema, and both show very promising results[26,28,29]. Therefore, it may be possible that our hypothesis about the cause of atopic eczema is right[18,26,28,29]. Namely, it becomes increasingly likely that not one of the two theories is the correct one.

Future perspective

For further research, I would recommend to investigate the proportion of serum IL-4 : IL-12/IFNγ with ELISA in hairless SKH-1/Hr mice[30]. To induce atopic eczema in these mice, three 1-week exposure to ovalbumin can be used[30]. With these mice and this technique, significant differences in the proportion of IL-4 to IL-12 and IFNγ could be established. Afterwards, the link between this proportion and the onset of an allergy could be investigated. In case the IL-4 increased proportion group has significantly more allergies, our hypothesis is verified.

Next to this, research for emollient/moisturizer, breastfeeding and prebiotics therapies should be extended. This research should be done for a period longer than 8 months to know for sure that atopic eczema and/or allergies will express later.

Conclusion

Skin barrier dysfunction, due to filaggrin mutation or deficiency and increase of IL-4 and IL-13 of atopic eczema leads to infiltration of allergens and activation of Th-2, which will possibly cause an allergy. It is likely that the proportion of IL-4 : IL-12/IFNγ plays a role in the onset of an allergy. Emollient/moisturizer therapies, breastfeeding and prebiotics, could pose an effective, easy and cheap therapy for prevention of an IgE mediated atopic eczema or allergy. In case of non-IgE mediated atopic eczema, future studies should unravel if it is a risk factor for a non-IgE mediated allergy.

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