

Anaphylactic Shock: Shocking Error of Immune System!

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ABSTRACT

Activation of immune response is developed in respect to some xenobiotic sensitization, which is supposed to prevent and protect the body from sufferings induced by these xenobiotic. But unfortunately sometime body behaves in a paradoxical manner which misguides the immune system and ultimately turned into a bizarre situation of immune function. One of such response is anaphylactic shock, which is quite fatal if untreated. This review brings insights into the molecular physiology of anaphylactic shock and how some people elicit allergic response to certain substances but not the other. This major catastrophe of the body holds an error of immune system whereas this commentary based review disclosed the synchronization of the unfortunate lessons of the immune system, which makes it a cruel to cause DEATH!

Keywords: Anaphylactic Shock, hypersensitivity, IgE-antibodies

INTRODUCTION

Human body faces a variety of typical (cancer^[1]) to atypical (tropical diseases like leishmaniasis^[2]) diseases and disorders. But certainly some are the issues which seem to be easy in concern but create havoc and ultimately can lead to death. One such example is anaphylactic shock, which is an immediate hypersensitivity type of allergy. The usual allergic response is initiated by the exposure to an antigen, resulted in the synthesis of a particular type of antibody, subsequently cause production of memory B cells and mediate active immunity^[3, 4]. Again re-exposure to the same antigen brings a more powerful antibody response and unfortunately the tuning of immune function disrupts and exhibit immediate allergic reactions especially genetically susceptible persons becomes the victim. Majorly this atypical immune disorder is manifested by the production of type IgE-antibodies. This abrupt increased expression of IgE is proportional to the activation of a

particular subset of helper T cells, activated by the immunogens. Moreover, activated helper T cells release cytokines, which mediate the differentiation of B cells into IgE producing plasma cells. After releasing from plasma, IgE-antibodies circulate in systemic circulation and attached on their Fc portions of connective tissue mast cells. When subsequently the same antigen type invades and attached to the IgE bound to the mast cell, triggers secretion of many inflammatory mediators, including histamine^[5], various eicosanoids, and chemokines^[6-8]. All these mediators initiate a local inflammatory response and allergy^[9]. For example, ragweed pollen induced allergy which cause, mast cells erupt to release mucus, increased blood flow, swelling of the epithelial lining, and contraction of the smooth muscle in surrounding of the airways^[10]. This resulted in symptoms of congestion, running nose, sneezing, and difficulty in breathing. These all symptoms can be usually correlated with IgE

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production^[11]. Allergic symptoms are normally localized to the area of infection but on severity cause severe hypotension and bronchiolar constriction. These events can turn into an immediate hypersensitivity called anaphylaxis which can be fatal due to circulatory and respiratory failure^[12]. Sometimes this immediate hypersensitivity often proceeds to a late-phase reaction lasting many hours, during which vast number of eosinophils elicit chemotactic migration into the inflamed area^[13]. The chemoattractants enlist mainly cytokines which are released by mast cells and helper T cells, on the activated by the allergen^[14]. The normal physiological function of these IgE–mast cell–eosinophil pathway is to keep away those parasites which cannot be phagocytized^[15]. What this all happens at the cellular level, but it can be further explained *via* an example.

This example consists of person and two subsequent encounters with two different allergen shows an example of anaphylactic shock. To this person, wasp never encountered before. After biting, the pumps venom into the skin and within seconds venom starts killing the cells of the localized area, propels the pain. This pain activates the specialized immune cells which are present beneath the skin cells (mast cells). These mast cells shivers, burst and discharge the histamine in corresponds to the venom of the wasp. Released histamine cause vasodilatation of tiny blood vessels in the localized area, consequently there is leakage of fluid from these vasodilated vessels. This fluid flooding the immune cells (antibodies) in the venom affected tissues. Although released histamine has other unpleasant side effects (Hot, red and swollen of that part of tissues). This effect called as “wheel of flare”. However the body makes scanning search for anti-venom (memory immune cells) against wasp venom. As never before the immune system get encountered with the wasp venom so it doesn’t have antibodies which remember the last

encounter with the wasp venom and as a result to develop a rapid immune response against it. Therefore there will be no antibody (anti-venom) against wasp venom into the body. Instead, the body will make them from the scratch. Something again happening at the site of bit, a remarkable process is going on, the wasp venom brings dormant cell, “dendritic cells” to live cells. These cells missioning to carry sample of venom to core of immune system, where antibodies are made, but its complex process that will take several days. But unfortunately sometimes immune system makes wrong antibodies which can cause more harm than good^[16].

Second story, like wasp venom tiny fragments of dog venom include in the body. Fortunately, this is not the first encounter of the body with this allergen. Unfortunately body made wrong type of antibodies, called IgE-antibody, unlike regular antibody they cling the mast cells which guard the lining of the nose. They will cause trouble. IgE-antibodies here are made against the tiny fragments of dog but are much requiring for large intruders (like tapeworm, and ticks (parasites)). They initiate dramatic chain reaction to blast the parasite away. As now tiny fragments of dog, locks on IgE-antibody which are cling to mast cells, erupt and of pore out their histamine. Blood vessels in nose start to leak (termed as “Local vasodilatation”). The leak contain a fluid escapes a ware of mucus, which would wash any parasite. But there is no parasite is present in the nose. Instead, IgE antibody producing allergy.

Again a question arises why some people are allergic to certain things but not others?

Recently this question was fully understood and the mechanism disclosed the role of childhood of a person. As the seeds were shown in the childhood where all of us in childhood, have the tendency to make antibodies (IgE-antibody). Then through the

exposure of infection, our system, learn how to make regular antibody to protect. But if the body is over-protected from dirt and disease, then immune system never switches at its fullest. Therefore still the body has a tendency to make IgE-antibodies. Half of the population of America and Europe has some sort of allergy^[17].

After 24hrs, wasp sting there is little sign of damage. But the body is already preparing for the next encounter with wasp venom. The dendritic cells carrying venom have now reached a gland in the armpit, where they construct a filter, design to intercept cells which can manufacture antibodies.

Now inside the gland in the armpit an immune cell called B-cells are trapped, it reacts with the wasp venom and starts to clone itself, each clone capable of producing antibody against the wasp venom. The B-cell should make regular antibodies. But is the first one spring into action, it's clear that they made a disastrous error by making IgE-antibody which is intended to made for parasite (tapeworm and for ticks) venom. Now IgE is allergic in nature therefore the body become allergic to wasp venom. The body's immune system is going to over-drive, every second each B-cell clone produces 2000 IgE-antibodies against wasp venom. The IgE-antibody locks over all over places into the mast cells in the body. When they reach a critical level should be allergic to wasps. Body mast cells now become ticking time bombs. Now, again if wasp bit the body^[18]. Thanks!!! To IgE-cells. As mast cells are now thousand times sensitive then the last time stung. Now this can bring most extreme allergic reaction, possibly, "anaphylactic shock"^[19, 20].

Sun-allergy Sun allergy contains U.V light which is able to penetrate inside the skin and may damage to some cell cause mast cells into action sand erupts to produce histamine which

cause locally vasodilation and permits immune cells in a localized area and this whole process cause redding of skin and finally inflammation. 24hrs, body feels uncomfortable. Body feels tenderness. Although the second stung by wasp inject the venom. In just a fraction of seconds, thousands of mast cells erupt.

Even worse is happening when tiny traces of venom surge in blood stream and trigger millions more. And thousands of mast cells erupt all around the places of the body. Excessive histamine number of vasodilation in many blood vessels, fluid pores out from vessel. The fluid sensitive nerve ending, activates nerve ending consequently causing excessive of itching throughout the body!!!...Itching, itching and itching, in response to itch off the stacked parasite. Now the situation is out of control. So much fluid has been lost from the blood stream. Therefore the blood volume is low causing hypotension and ultimately B.P plumps and finally body feeling faint.

Now that is worst because of high levels of histamine, constricts the diameter of the air passage through the nose, bronchoconstriction *via* H1 receptor, this all phenomena is called "anaphylactic shock"^[21-23].

In the refractory response body tries to take a desperate attempt from the respiratory collapse and secretes the adrenaline, physiological antagonist of histamine. Breathing again returns to normal level. But the $T_{1/2}$ of adrenaline is quite short and this terminates the desperate rescue action of the body. But still traces of venom in the blood finding new mast cells triggers. B.P cuts off to ½. Consequently, heart beat increases. The heart tries to fight against a losing battle to pump proper supply of oxygenate blood to all parts of the body. If the situation persists there will be a high probability of cardiac arrest.^[24] Adrenaline (30 times greater than the body produce)^[25]. This

treatment relapses the body to normal in just a couple of minutes. But in case if the person stung again he has to take the adrenaline with him for the rest of the life.

Although recent reports disclosed the cytokine interleukin-33 mediated role in anaphylactic

shock ^[26]. While sphingosine-1-phosphate receptor-2 facilitate its anti-anaphylactic shock activity *via* suppression of Endothelial dependent releasing factor (EDRF) ^[27].

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