Host-Pathogen Interaction (Immunology)
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Lecture - 17
Cells of Immune System and its role in Host Defense-Eosinophils, Basophils and Mast Cells

Hi, so in previous session we have discussed about one of very important in immune cell that is neutrophil. Now, in this session, we will discuss about the another immune cell two are present in the blood and one is present in the tissue. So, the two immune cells which is present in the blood is eosinophil and basophils and another is present in tissues mainly present in mucosal surfaces and we call it as a mast cell. So, let us begin with eosinophil.

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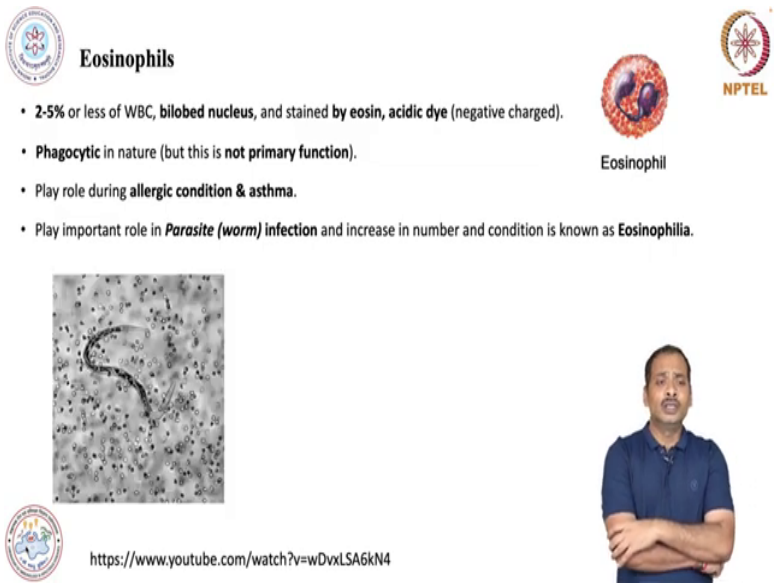

So, eosinophil is a cell which is present in the blood and their number is quite less compared to the of course, neutrophils it is only 2 to 5 percent of total white blood cells. And here you can see that they have a bilobed nucleus and since they have a bilobed nucleus, it is you can easily distinguish under the microscope. And in addition, you can stain with only acidic dyes such as eosin that is why the name is eosinophil.

So, eosinophils basically derived because it can be stained by eosin which is a acidic dye. They are phagocytic, as I have told you in previous session that neutrophil is a main phagocytic, eosinophils are also having some phagocytic activity but they are not so much

phagocytic. It is not primary function. They play a very important role in variety of allergy conditions and in asthma.

So that I will explain you in great detail, along with mast cell, how they are playing a role in a allergy and asthma. And these allergy in the asthma can be life-threatening in some situation. The most important role of this eosinophil is that they protect against the parasite infection, a big parasite infection. And how they are doing? For small microbes, you can understand they can phagocytose, they can be cleared and all those things.

But how the big parasites are dealt by our immune system? And over there the eosinophil is the main player for taking care of this parasite. Basically, what they are doing? They these eosinophils get deposited over the parasites over the surface of parasites and then they damage the parasite. And in that way, that will cause some kind of irritation or something. And basically, when all these things will happen then there is a possibility that there will be a coughing and sneezing.

And when this coughing is sneezing will take place at that time, maybe parasites will be released from the oral cavity this is a one of possibility, it is not the only the thing this is the one way. And this eosinophil number is increased when there will be a allergic condition and a asthma condition in addition, during the parasite infection and there is a one technical term which we call it as a eosinophilia.

There is a increase in number of eosinophils. This eosinophilia is a kind of indication of either allergy or there will be a some parasite infection. So, after that doctor basically prescribed the estimation or quantification of one family of antibody known as IgE. So, after looking at all these results and the doctor can diagnose or predict the individual is having either asthma, allergy or parasite infection, along with another clinical symptoms and another clinical parameters.

Here I have one very short video and it is a very interesting video, you can take a look on this video **(Video Starts: 05:20) (Video Ends: 05:28).** I hope you like this video and this here you can see that this basically the parasite which is a quite big parasite. Over there lot of eosinophils are attaching and then that cause irritation of parasite and that may result to the clearance of parasite.

Although the big parasite clearance is not so easy and you probably know one drug which is quite commonly used by the doctor that is known as it is a quite broad spectrum against a variety of parasites, Albendazole which is used to clear or basically this is a deworming drug and it is a single dose. You just take it in night and then hopefully it will be cleared from the system.

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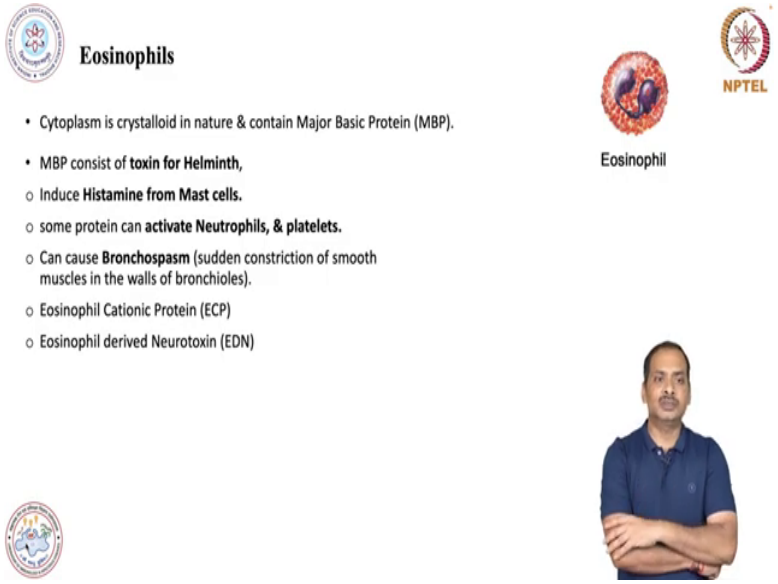

So, eosinophil is basically having this the cytoplasm is a again granular or you can see that it is a crystalloid in nature. And it is basically consists of a major basic protein and what is this major basic protein? It is a basically a toxin to the helminth or big parasite. Helminth like a ~~taenium, solium~~ taenia solium or ascaris one is a flat worm another is a round worm, probably you have studied this thing in class tenth or twelfth or maybe eleventh I do not know.

So, what is this MBP is consists of? Basically, it consists of histamine and this histamine basically induce MBP induces histamine from mast cell. This MBP basically act on mast cell and then this histamine will be released. Some protein can some MBP protein can activate the neutrophils and platelets. MBP can also cause the sudden constriction of smooth muscles in the wall of bronchioles.

Here I told you in previous slide that there will be a sneezing and coughing this is sneezing and coughing is basically triggered by MBP and technically we call it as a Bronchospasm. And it is also consists of eosinophil cationic protein and eosinophil derived neurotoxin. So

basically, they all these components basically act on the parasite and that cause the irritation of parasites.

And all these things may result to the sneezing and coughing and there is a possibility that the parasites will be released from the system.

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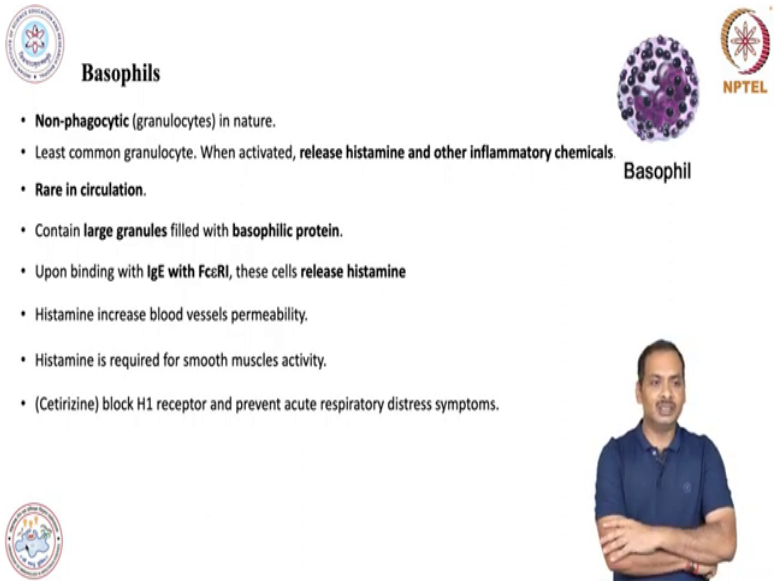

So, this I have discussed about the eosinophil now, we will take the basophils. So, basophils are also very important cells they are absolutely non-phagocytic cells they are they are the granulocyte and their number is also quite less. They also release the histamine, we will discuss about the histamine in little more detail histamine and other inflammatory substances. We will discuss other inflammatory substances in a short while.

Generally, basophils are not so much in the blood, it is a very rare, very few cells you will see in the blood they do present in the blood but they are very few in number. Basically, contain large granules which is basically these granules are packed with some basophilic protein and the basophil is having one receptor which we call it as a Fc, Fc epsilon R1. And this is a receptor for one of antibody known as IgE.

And once this antibody binds on the surface of basophil or eosinophil or later on you will see that this receptor is also present on the mast cell. Once it will bind then that will release the histamine and histamine is small amount of histamine is good but large amount of histamine is having a or it induces the disease-like condition or it is causing immunopathology.

So, histamine basically increases the blood vessel permeability, histamine is also stimulating the smooth muscles activity I will show you in little more detail and how we can block the hisaminetidine. So, probably you may have experience that during weather changes, you are having a sneezing coughing and dripping off water from eyes and nose. It is a clear sign of allergy and generally many people are having this pollen allergy.

So, due to pollen allergy the people is showing this symptom and I believe that most of you may aware that there is a drug known as cetirizine. So, this cetirizine when we take basically this blocks the receptor of histidine sorry histamine not histidine and it prevents the subsequent production of histamine. So, it is a kind of cetirizine is a molecule, a cetirizine or levocetirizine, you have probably heard that molecule.

They basically are the competitive inhibitor of histamine and in that way we feel relieved. But this is a very short-term effect you this effect is not long lasting. So, people around the world or scientists around the world or immunologist particularly around the world they are looking for some more molecule. Because when you continuously take this cetirizine or levocetirizine after sometime you develop a resistance.

So which is not good and that then allergy situation will be much more worst. So, people around the world or around the globe they are trying to find out some novel molecule which can completely cure this thing especially in Japan. Japan has a lot of serious problem due to the pollen allergy; many people are allergic and they have a lot of funding for finding this thing. As from immunologist for immunologist, as well as from plant biologists.

So, for plant biologists they are creating some plants which is not giving this pollen in high quantity so, this is about the histamine and allergy.

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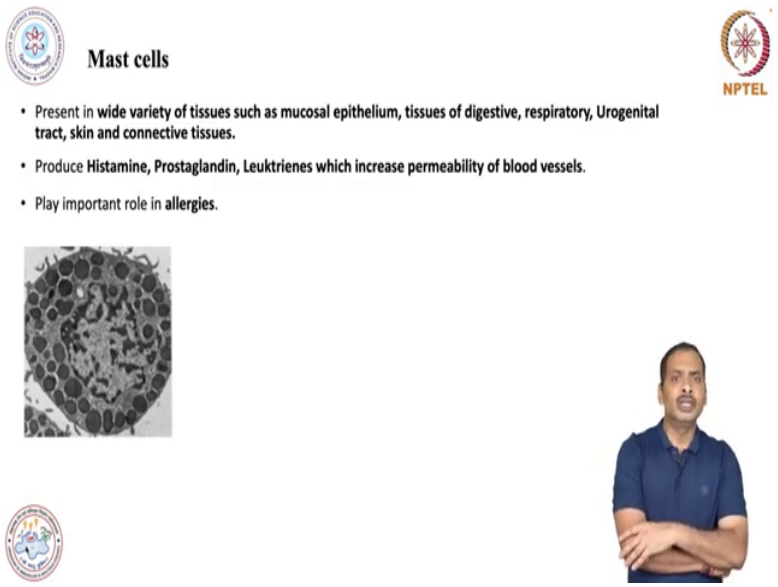

Now, let us move to the mast cells so, mast cells are basically here you can see the electron micrograph of mast cell this is a un-activated mast cell. Here you can see lot of big black dots or black area and these black areas are nothing they are these mast cells are packed with the granules. We will see what is this granules in subsequent slide and mast cell basically present in a variety of this tissues, especially in mucosal epithelium.

And the mucosal epithelium when I say that it means that digestive tract, respiratory tract, urogenital tract, skin and connective tissues. So, all over these tissues, these mast cells are present. And this mast cell basically produce a histamine which we will discuss in more detail in subsequent slide. In fact, after finishing this slide, I will focus on the histamine and this also produce the prostaglandin, leukotrienes.

So, prostaglandin, leukotrienes is basically lipid based or lipid mediator which cause the inflammation, which cause inflammation and it also increases the permeability of blood vessels, it plays a very important role in allergy the mast cells.

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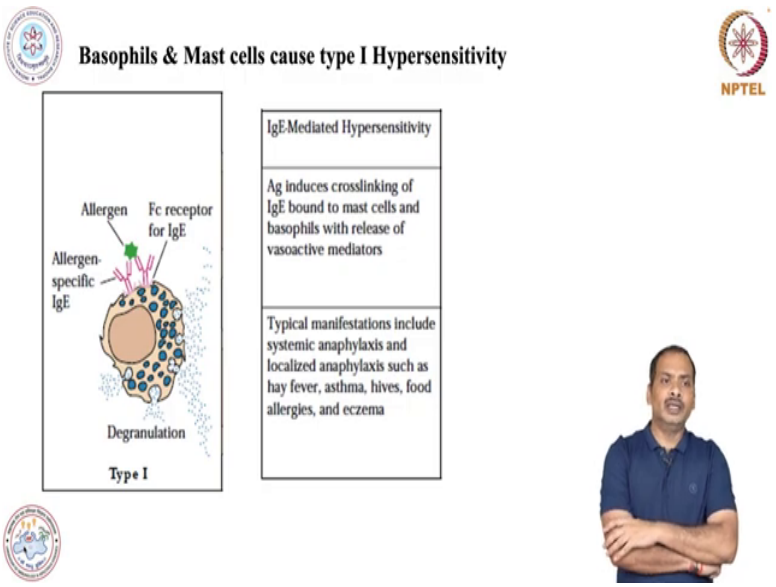

And basically, mast cell and basophil they cause type 1 hypersensitivity and what is type 1 hypersensitivity? It is here you can see this this image here you can see that IgE is binding with the receptor of IgE and then that because the degranulation of a mast cell or basophil and that degranulation basically cause a variety of problems. Here you can see that it is a basically IgE mediated hypersensitivity.

And basically, this causes variety of problems such as eczema. It can cause hay fever, hay fever is nothing it is a pollen allergy the symptom which I have explained earlier. Like watering of eye, watering in nose or respiratory tract, is sneezing, coughing so that is a hay fever this can also cause the food allergy or asthma.

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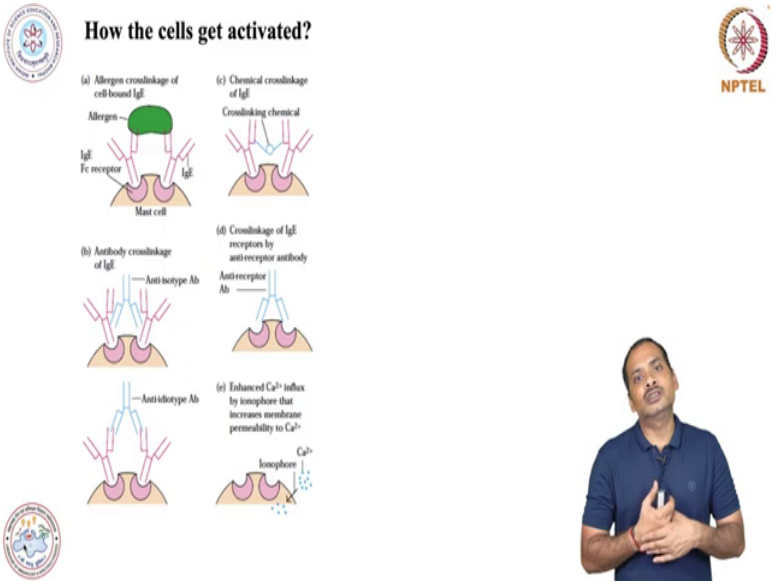

And what happens when these granules are released? So, how this granules are released? Here you can see which I have explained you earlier. So, if the antigen will bind to this antibody then this will cross link the two receptors there will be an increase in number of receptor or clustering of a receptor will take place over the cell. And that will activate the downstream signalling and that will result to the release of this granule.

So, here you can see there are several ways there are some antigen which can trigger this thing. There are some antibody which can cross link these various IgE and then that will increase or that will cause the clustering of receptor and then that will induce the activation of mast cell and release of granules. There are some chemical molecules or antibody, or some ions can also enhance the degranulation of these cells.

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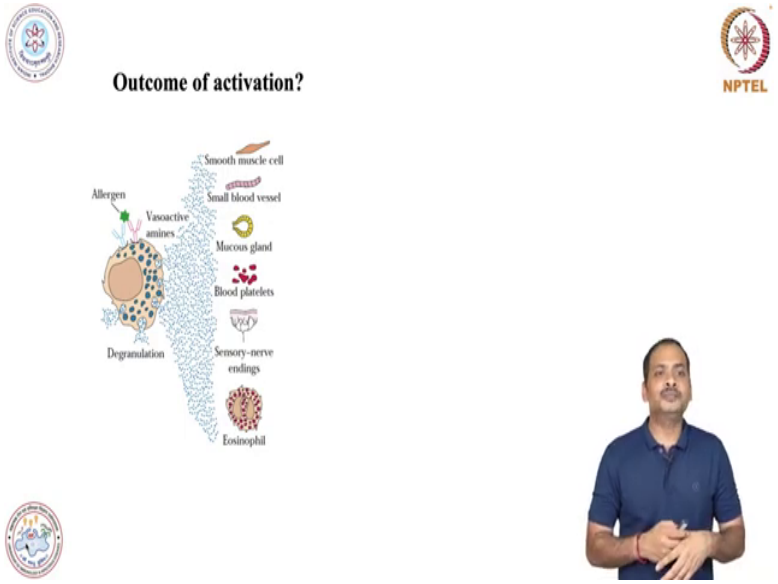

And when the degranulation happen, what will happen? Basically, they will cause variety of things such as this will act on the smooth muscles, contraction of smooth muscles. This will also act on blood vessel this will also act on mucous gland. So, when it will act on mucous gland the mucous gland will start making lot of mucus that is why there is a watering from eyes or from nose and all those things.

This will also act on blood vessels, they also act on sensory nerves you feel very irritated and this can also act on eosinophils. So basically, all these things results to the various degree of complication, it depends on the amount of allergy.

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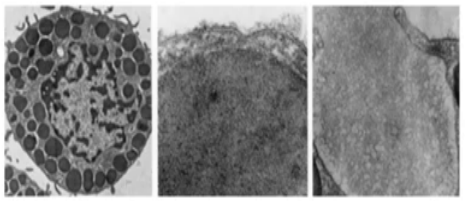

So, basically degranulation, when degranulation happens here you can see a very nice electron micrograph in middle panel you can see that the cell is having a lot of granules and after activation of this mast cell the all granules are all this vesicles are empty. So, this is a very nice electron micrograph and you can notice the degranulation also.

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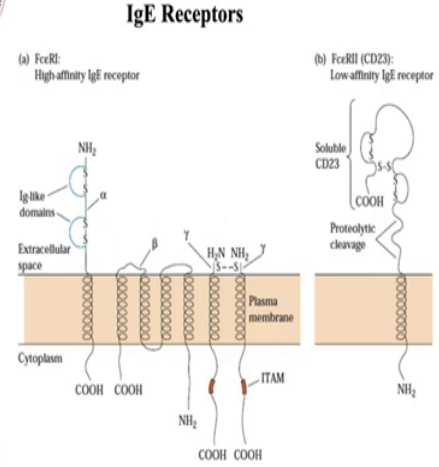

How basically, the things work? So, when the IgE comes so, IgE is an antibody which is generated against antigen and once the IgE comes, we will not discuss how the IgE is coming. Right now you can understand there is a antibody known as IgE, generated against some weak antigen. So, this antibody will be synthesized and once this antibody is synthesized they can act on these cells mast cell, eosinophil, basophils.

And there are two kinds of receptor, one is Fc epsilon R1, here you can see and another is Fc epsilon R2. So, Fc epsilon R1 is a high affinity receptor as you can see and another is the low affinity receptor and when they will bind the antibody will bind and then antibody will be cross link then there will be a clustering. And here you can see that the high affinity receptor has also additional membrane protein.

This is a receptor complex and then that can activate the signal and cause the degranulation. On another end Fc epsilon are two receptors they are kind of they can be released in the circulation after proteolytic cleavage and then that will not cause so, severe degranulation of these cells. So, this receptors plays a very important role in degranulation of these cells.

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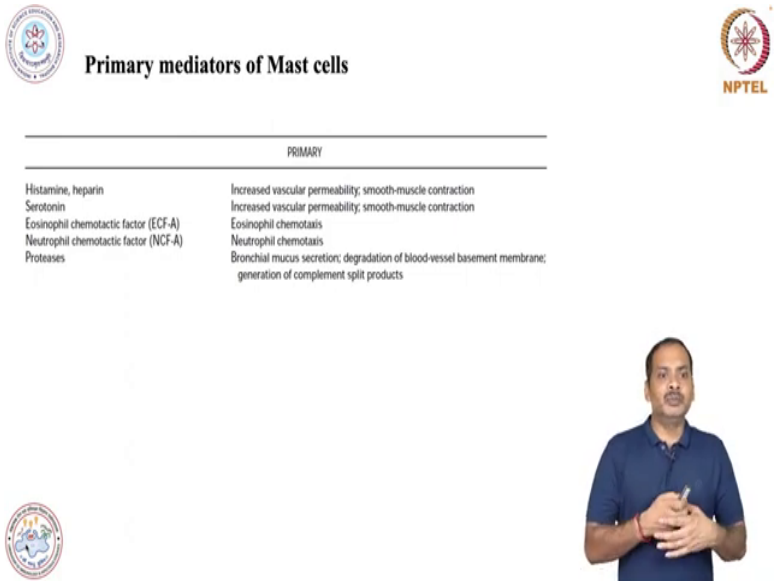

These are the few primary mediators, the granules which you have seen it contains a like a histamine, heparin which basically increases the vascular permeability, cause muscle contraction. Similarly, serotonin also occurs the same thing, eosinophil chemotactic factor they cause the invitation of eosinophil at the site of mast cell degranulation which we technically call it as a eosinophil chemotaxis.

This will also cause the invitation of neutrophils which is the factor which is responsible for chemotaxis of neutrophil is neutrophil chemotactic factor. There are some proteases, some this granule contain some proteases. So, these are the primary component and primary function of these granules.

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Secondary mediators of Mast cells

SECONDARY	
Platelet-activating factor	Platelet aggregation and degranulation; contraction of pulmonary smooth muscles
Leukotrienes (slow reactive substance of anaphylaxis, SRS-A)	Increased vascular permeability; contraction of pulmonary smooth muscles
Prostaglandins	Vasodilation; contraction of pulmonary smooth muscles; platelet aggregation
Bradykinin	Increased vascular permeability; smooth-muscle contraction
Cytokines	
IL-1 and TNF-α	Systemic anaphylaxis; increased expression of CAMs on venular endothelial cells
IL-2, IL-3, IL-4, IL-5, IL-6, TGF-β, and GM-CSF	Various effects

There are some secondary also, there are several factors which basically make the system very vulnerable or very immune active location. So, with all this primary and secondary granules, we can it will basically cause a hyper immune response that is why we call it as a type 1 hypersensitivity. It is a very high immune response are there and all these things are basically mediated by primary and secondary molecules.

Here you can see the secondary molecule and this if we do not control then that will result to the very fatal condition, it may take the life also.

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Drugs to prevent Type I Hypersensitivity

Drug	Action
Antihistamines	Block H_1 and H_2 receptors on target cells
Cromolyn sodium	Blocks Ca^{2+} influx into mast cells
Theophylline	Prolongs high cAMP levels in mast cells by inhibiting phosphodiesterase, which cleaves cAMP to 5′-AMP*
Epinephrine (adrenalin)	Stimulates cAMP production by binding to β-adrenergic receptors on mast cells*
Cortisone	Reduces histamine levels by blocking conversion of histidine to histamine and stimulates mast-cell production of cAMP*

So, there are some drugs which is commonly used for controlling this type 1 hypersensitivity like antihistamine which blocks the histamine receptor. Because once the histamine is produced again, it will bind to the histamine receptor and then that will trigger again

production of more histamine it is a kind of positive feedback loop. So, if we block this this positive feedback loop and the one molecule that is cetirizine and or levocetrizine then we can control.

There are some molecule like a cromolyn sodium which is a blocker of calcium ion influx in the in the mast cell. If we use then we can reduce the inflammatory condition. Theophylline which basically act on cAMP. So, if you look at this signalling pathway, it is a quite complex, I did not discuss here so, this molecule is also used. Another molecule you which we use in very severe cases is the epinephrine.

Epinephrine is a it is a very effective basically, it increases the amount of cAMP in the mast cell and then this will be the production of histamine is reduced. In ~~inverse~~worst scenario, one can use the cortisone, cortisone is basically steroid and basically they are the dampers of immune responses and it reduces the histamine production. With this I will stop here and in in next session, we will take another cells such as dendritic cells, macrophages and so on. Thank you, thank you very much.