Host-Pathogen Interaction (Immunology)
Prof. Himanshu Kumar
Laboratory of Immunology and Infectious Disease Biology
Department of Biological Sciences
Indian Institute of Science Education and Research (IISER) – Bhopal

Lecture – 24
Inflammation Signature of Inflammation

Hi, so, in previous session we have discussed about the cytokines and we have discussed in quite a great length about the cytokines and today we will look at the most important and I will say that the most complex phenomena which is not only associated with immunity, it is associated with a variety of things. So, recent research resulted to the development of this field and it is a huge field.

So, today we are going to talk about the inflammation. So, inflammation is it is a very complex phenomena and if you read more, you will be more confused kind of thing but I will try to shape this session in such a way that you will understand broadly all of this inflammation and inflammation associated signatures and how it will impact the health. So, let us begin with a very simple definition of this inflammation.

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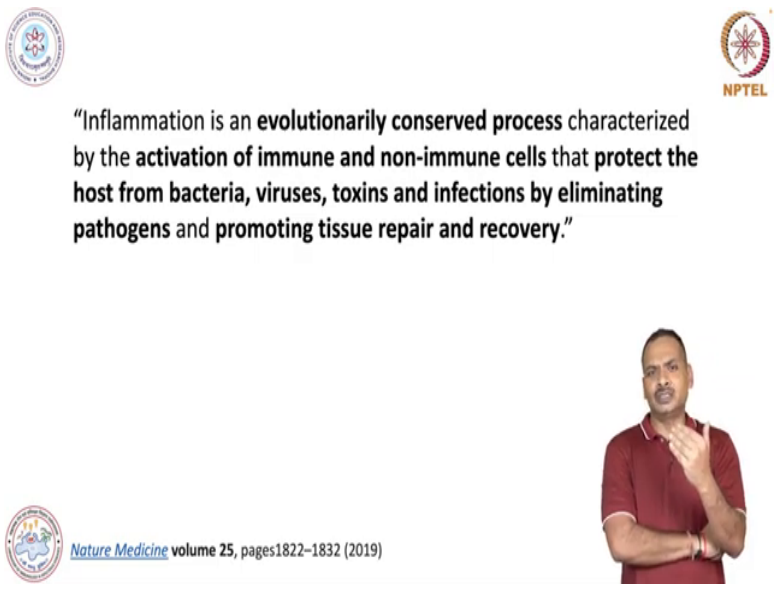

So, it is a evolutionary conserved phenomena or process and it is basically induced by not only immune cell, it is also induced by non-immune cells. So, when I say non-immune cells, it means there are a variety of cells, immune cells. We have learned, there are various blood

cells and there are some immune cell which is residing in the tissues like mast cell but beside all these cells.

Non-Immune cells are also playing a very important role in induction or development of inflammation. So, overall, it is basically driven by the secretion by immune cell as well as non-immune cell and this. This is basically it is a complex, it is not only one kind of molecule or few kind of molecule. There are several kinds of molecules involved in development of inflammation.

So, the basic aim of inflammation which the host is inducing is to protect. It is a kind of alarm system in our body, and so, when, for example, in your house, if somebody evade then there will be a kind of disturbance of all system. And that disturbance result to the trigger of alarm. So, inflammation is also something like that. So, the aim of inflammation is to protect the host from various pathogen.

It could be bacteria, it could be viruses, it could be parasite, it could be the material which is derived from the pathogen like toxins, and the aim is to eliminate this intruder or eliminate this pathogen. This is the one of primary aim of inflammation. Another important the role of inflammation when there is some tissue damage occur in our body. Then, this inflammation is triggered.

For example, if in in your house, if there is some breakdown of something which is not by influence of outside evasion, it is just a normal process or by the individuals in the house. Then that will also cause disturbance that will also trigger the alarm. You will call the person in order to repair that system or to repair the house. So, this basically also promotes the inflammation overall also promotes tissue repair and it also promote the recovery of damaged tissue.

So, this is a very broad concept of inflammation. It is a more about the positive thing inflammation is needed in order to survive the, for it is important for the survival of individual or the host. But it has a various aspect. So, I will take you to various aspects and then you will learn inflammation is may cause a very detrimental effect to the host.

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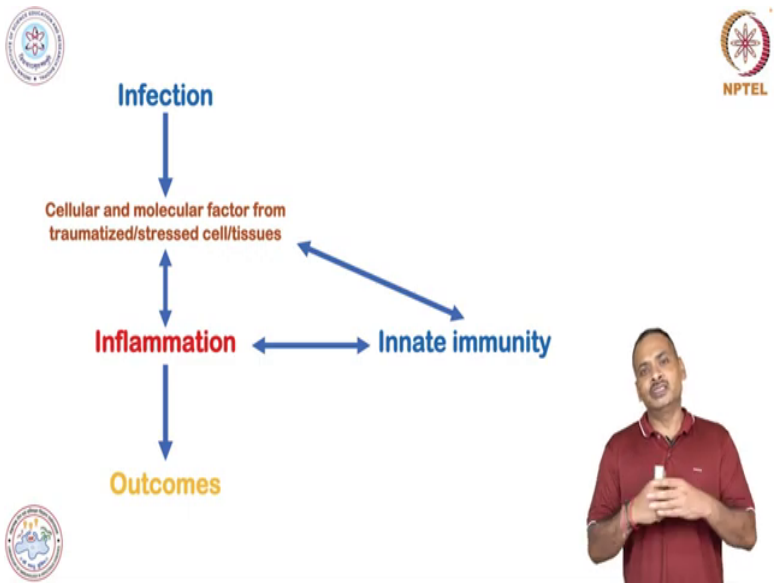

So, here I will take one simple example if the individual is infected by some microbial pathogen or any kind of pathogen then several things will happen. One is that this will damage the tissue, the infective entity will damage the tissue and that will cause the release of some molecular or molecular signatures. So, there are, some molecules which is residing inside the cell. And during education of our immunity those molecules are never exposed.

In that scenario, those molecules which is residing inside the cell they will also act as a foreign material. If the cell is broken by some physical mean, by chemical mean, or anything or by infection. So, in general in our body, when the cell dies then it is a very regulated and very complex process and that process, probably you might know we call it as a "programmed cell death" or a more technical term is "apoptosis".

But if the infection or the entry of foreign pathogen in the host is not appropriate then that will cause some damage of cells. And that will cause release of some molecules which is present inside the cell and these molecules will also act as a foreign molecule. So, when there is entry of pathogen, the two main things are happening, one is entry of foreign biomolecules, number one, number two the release of all those molecule which is hidden from the immune system in the host.

So, those two things basically trigger the innate immune response, the first line of defense which we will discuss in a great length. It will take many sessions about the innate immunity later on. And when this innate immunity is activated, it means there will be a invitation of

some innate immune cells such as macrophages and innate immune responses, will be also induced that is release of some innate cytokine.

For example, IL-6 TNF, IL-1 beta so and so forth. I have discussed in the previous session about the innate immune cytokines, So, overall, what will happen after infection this cell debris or cellular molecules will be released? The pathogen origin molecule will induce and that will activate the innate immune response and that innate immune response basically result to the development of inflammation.

So, this inflammation is in current scenario it is important and it is essential, it is needed. If, for example, if you consider a house and that house does not have any alarm system. So, what will happen that will cause keep on damaging, damaging, damaging and eventually the whole house will damage completely. So, if inflammation is not there then this will be also a detrimental.

So, inflammation here is very important and the outcome will be the elimination of pathogen. And this elimination of pathogen is essential for the survival of host. So, this is a overall concept in immunological point of view. Today, I will also take you more complex things of the inflammation. I will not take too much complex but I will just touch upon all those points.

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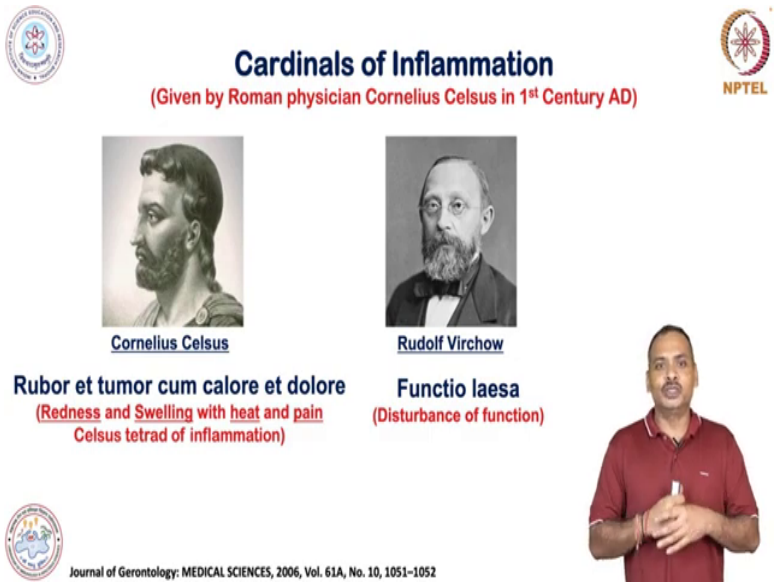

So, this inflammation is a very this is not new. This concept was very old and it is given by Roman physician. His name is Cornelius Celsus and he gave this concept of inflammation in 1st century A.D. It is, it is a very, very, very old concept. And here you can see his his image

Cornelius Celsus and he gave a concept known as it is in Latin word rubor et tumor cum calore et dolore. This is a Latin word, so, do not worry.

I have a English also, so, it means redness and swelling with heat and pain. So, when there will be some inflammation there will be a redness and when this redness will be there it may be associated with some swelling. And this redness and swelling may also associated with that area may be little warm. And all these things will also have some pain. So, this he gave a concept of inflammation.

So, all these four signatures are not essentially present at one time at one side maybe one or two will be there or two or three maybe there or maybe all four will be there. And this concept was further modified or not modified I will say further added by Rudolf Virchow and he gave a concept of "Functio laesa"it means there is a loss of function. When inflammation will be there means when redness will be there, swelling will be there, heat will be there and pain will be there.

Then there will be a loss of function. The function may be change you can understand if there is some inflammation then you may feel loss of appetite which is not the normal function. This is a loss of function. So, this this concept was further added. Besides these four cardinals of inflammation that is redness, swelling, pain and heat and one more is the loss of function.

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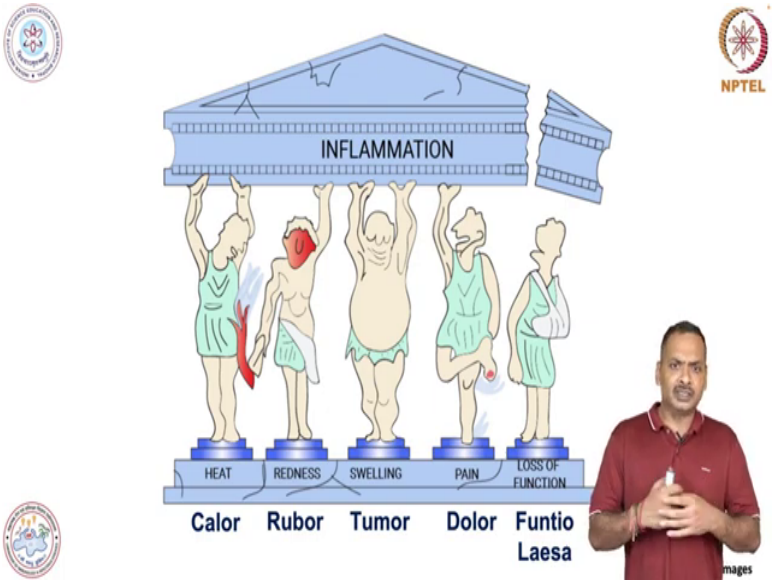

Here I have one very nice a cartoon which explains very nicely with some image here you can see there is a heat, calor there is a rubor that is redness and there is a tumor. Tumor means

swelling and there is a dolor that is pain and there is a funtio laesa that is loss of function. So, this is a overall concept of inflammation. Now, let us look at what is the physiological impact when all these things comes in a individual or in animal.

So, what is the functional impact? So, you understood this cardinals of the inflammation.

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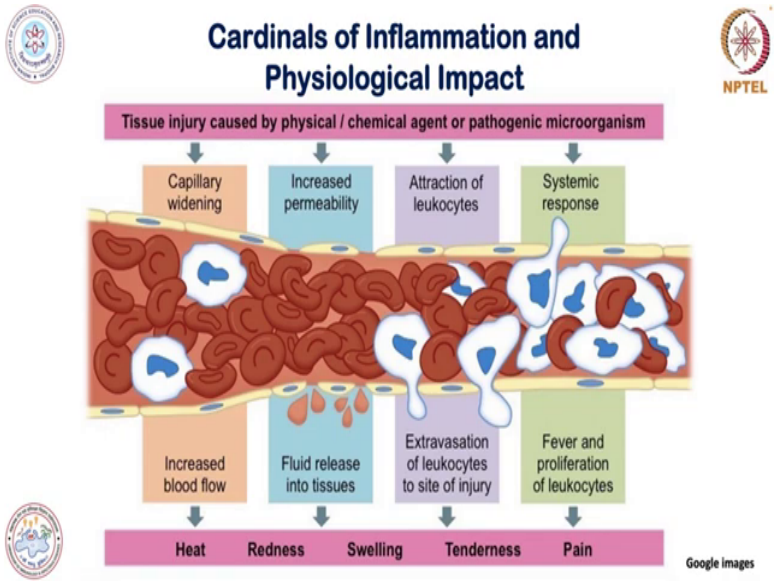

And now, let us look at what kind of physiological changes taking place? Why the redness is there? Why the swelling is there? Why pain and heat is there? So, let us take this heat, so, when there is inflammation then there will be a widening of capillaries. And this widening of capillaries is basically important in order to rush lot of blood at the site of inflammation.

That has a two major thing one is to remove those toxin or pathogen from the site of infection. And it has also to transport these material to the nearest lymph node. So, when there will be a rush of blood at that side then that may generate some kind of heat because of so, widening is basically needed in order to push lot of blood. And that increased blood flow may result to the increase in temperature, local temperature.

Another is a this redness and swelling and basically this is due to the increase in permeability of blood vessels. So, when there will be an increase in permeability of blood vessels then what will happen? The blood cells may come out of these blood vessel because there is increase in permeability, and that that will cause that will cause two things. There is a coming out of blood cell that may include the RBCs, not may that will include the RBCs.

And there will be accumulation of fluid around that area. So that will cause that redness and swelling. So, increase in permeability is linked with redness and swelling. Another is a there will be a attraction of white blood cells at the site of inflammation. And this this will result the movement of these white blood cells out of these blood vessels, and that will cause some kind of tenderness, and this tenderness.

So, when there will be a leukocyte movement from blood vessel to the surrounding tissue. At that time, the ~~team of kinds~~chemokine come in action and these chemokine basically facilitate the movement of white blood cells. And that is very important that will cause a kind of pain. Pain is also important if there will be no pain. For example, you had an injury in your hand, and if there is a no pain then you will keep on doing that work.

And if you will do keep on doing that work then that will cause further severe damage to your hand. So, there are some individual who has some mutations in pain~~,~~ sensors, and those individual are having a very tough time I have seen in in some news scientific news that they, they will not know there is some injury. And that if they will not know then this is a much more dangerous situation because that part may be further more severely damaged.

So, pain is or tenderness is important. So, another is the systemic response so, when all these things will happen that will result not only the pain then that will also increase the body temperature. There will be a fever and when all these things will happen then the lymphocytes or leukocytes. More leukocytes will reach at the site of infection or at the site of inflammation more appropriately inflammation and that will cause a kind of battle~~metal~~ kind of situation.

They will secrete lot of inflammatory mediators which I have explained you in cytokine. For example, there are IL6, TNF and if you remember the non-cytokine bioactive molecules like prostaglandin, leukotrienes~~lupton~~, thromboxin, all these are lipid body mediators. All these things will cause inflammation and I have told you that there are some drugs, for example aspirin and ibuprofen.

They basically inhibit some enzymes known as cyclooxygenase and then you feel relief from the pain. So, this is a physiological impact of all these five signatures. Here we have discussed four signature and that result to the loss of function.

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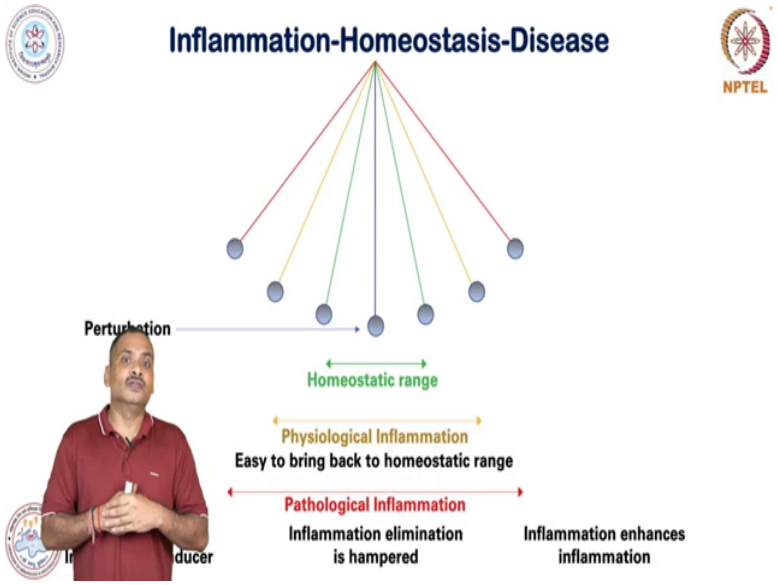

So, now, let us look at so, I have explained you that inflammation is important. It is very important in order to overcome the infection and it is also very important for repair of tissue, repair and recovery of that tissue. So, but there is a limit of inflammation, so, there is a very strong correlation between inflammation, homeostasis and disease.

So, let us look at that. So, inflammation is if it is within a within a range if the inflammation is acute for short duration, there will be a pain and all those things but it is good. It will repair the tissue and then everything come in a centre line. Center line here you can see I am trying to explain this phenomena by this simple schematic. So, there is a homeostatic range so, there is a perturbation by say infection or injury or whatever.

And this perturbation will push the normal homeostasis to the end and that will be within a range it is acute and soon it will come down and then the individual or the host will feel better. So, this is a within a homeostatic range but there is some situation in which the inflammation is keep on persisting. And then it is very difficult to bring back to the normal situation, and that we call it as a physiological inflammation.

And however, if you take some drug or some, if you wait or take a rest or something then it will come back to the normal range. So that we call it as a physiological inflammation and then there is a one more range which we call it as a pathological inflammation. So, pathological inflammation is a much more kind of fatal. So, in that scenario, what is happening there will be a persistent of inflammatory, inducer.

But inflammatory inducer means the molecules or the substance which is causing inflammation they will be remain present. In above two cases, it is the inflammatory material is there but due to inflammation those things are removed. So, the individual is under the homeostatic range. But here when the inflammatory substance is remain in the tissue or in the system then that will cause or that may result to the pathological inflammation.

And how it is possible? One is that inflammation whatever inflammation is induced, it is kind of inflammation. Basically, could not clear those material this is one possible reason. Other is basically the inflammation material, basically activate the inflammation and then that will also produce some inflammatory system and this is kind of positive feedback loop. So, due to that the inflammation will be remain.

I probably you it is difficult to understand. I will give you one simple example. For example, there is a some disease, autoimmune disease. Let us take a disease of some joint. Over there, there is a destruction of some tissues which is present in the joint. I am telling you in a very simpler way. I am not using the technical term I am basically talking about the arthritis.

So, basically over there, the at the joint there will be a tissue and this tissue is keep on damaging and then this is keep on releasing. And this is inducing inflammation and this inflammation is further exacerbating~~observating~~ this tissue damage and then that will inducing the inflammation. So, this is kind of positive loop and it is very difficult to remove that tissue. Because if you remove then it the system will collapse.

So, this kind of situation result to the pathological inflammation. That will that will cause some kind of disease like arthritis. There are so many diseases particularly autoimmune diseases.

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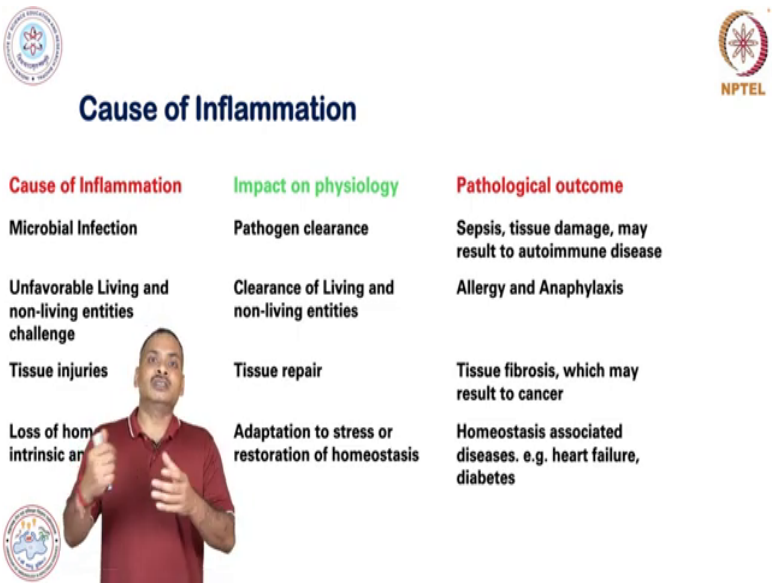

Now let us look at the cause of inflammation there I have told you but here I am giving you in a very tabular or content form. So, one is, it could be the microbial infection. We have discussed in a great length in this session. Another could be a unfavourable living and non-living and entities. Unfavourable living means all microbes are not pathogen but some microbes are pathogen.

And some are non-pathogenic if those non-pathogenic microbes basically somehow reach to the system and that may also cause inflammation. This is a about the living entity and non-living entity it is very easy to understand there are for example, the pollutants this is a non-living but they do curse the inflammation. So, if the host is challenged by these living or non-living entity then that will also cause a inflammation.

Tissue injury, tissue injury is a one of very common for example, you take your hand in a perfect, clean condition. Perfect clean condition means you sterilize your hand by say these days people know the 70 percent ethanol which is used for the sterilization. So, you clean your hand by 70 percent ethanol and you clean a blade with 70 percent ethanol. So, now, whole system is clean.

And if you make a cut that will cause also inflammation over there, there is a no pathogen, there is no for an entity. But that tissue damage will also cause the inflammation. So, this can also cause inflammation and there is a loss of homeostasis by intrinsic or extrinsic factors. So, intrinsic factor is, for example, there is a signaling pathway which induces the inflammatory cytokine and this signaling pathway has also some negative regulators.

So, if there is a loss of this negative regulator, a loss of gene or whatever way. So, if there is a loss of this negative regulation of the pathway then that is also causing a persistent inflammation and that will result to the various complications, extrinsic factor could be this. This could be a tissue injury or this could be some physical impact. Physical impact means temperature or some pressure or something or the extrinsic factors is numerous.

I will talk in maybe in next session. What are those extrinsic factors? Maybe psychological, there is a neurological, there are environmental everything comes into extrinsic factor. Now, what is the impact on physiology? So, if there is a microbial infection then the pathogen will be clear. And if the pathogen will be not clear then that will result to the physiological or pathological kind of situation.

That result to the disease that result to the pathogenesis or pathological problems. And what could be this then, this could result to the some kind of sepsis, tissue damage may result to the autoimmune disease development of some autoimmune disease. In case of unfavourable living and non-living entities. The impact on physiology will be the clearance of that living or non-living entities.

So, for example, if the worker is working in a cement factory that cement particles are non-living entities, so, we do have some system in order to remove these particles. We secrete lot of mucus and this mucus may throw the that cement particle but if it is not removed then that may result to the complex that result will be very complex that may result to the development of some kind of disease, particularly allergy.

So, you may know that the people are allergic to the dust. So, this is also a result of inflammation. Allergy or anaphylaxis, anaphylaxis and allergy is a quite similar. It is a different levels of hypersensitivity, so that will result to that. And tissue in case of during tissue damage. So, it is not only cut sometime, for example in your if you have some dental problem so, sometime when you eat after eating, you will feel pain in your gums. So that is also a kind of tissue injury.

So, tissue injury is a one of a very important cause of inflammation and the impact on physiology will be the tissue repair and the pathological thing will be the fibrosis of tissue.

And this fibrosis of tissue is a may result to the very dangerous consequences that may result to the development of cancer. So, probably you might have heard that in TVs or radio or various media that the doctors or the government suggest that do not chew these various things like gutka and all those things.

Because those are the inflammatory things they will keep on inducing inflammation and that inflammation result to the fibrosis of some tissues and that fibrosis may result to the cancer. So, those are not good things. Another is a like a loss of homeostasis by intrinsic and extrinsic factors. So, basically one way is that host will adapt with that stress or basically, they will make some changes in order to bring the homeostasis ~~your stresses~~.

So, this is a physiological impact but if it is not resolved then that may cause to the I mean that will cause the disturbance in homeostasis and this persistent disturbance in homeostasis may result to some complicated consequences. For example, that will result to the development of metabolic diseases like cardiac associated diseases like glucose metabolism associated diseases like diabetes and all those things.

So, here I gave you a kind of complete picture about inflammation, how inflammation is induced? And what is the impact of this inflammation in physiology? And if inflammation is not resolved then what is the pathological impact? How this will result to some disease or that may result to disease?

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So, there is a one term known as sterile inflammation. This is quite commonly used in these days, so, this is sterile inflammation can be a biological. Biological factors are responsible, for example, if some problem in IL-6 a production pathway. As I told you if there is a some loss of some negative regulator then IL-6 will keep on producing in the host and that will cause a persistent inflammation here there is a no infection.

So, that therefore, we call it as a sterile inflammation or there is a some tissue factor which is released from the tissue and that will keep on inducing inflammatory cytokine, so that will also cause a sterile inflammation. There could be a social and psychological factor. This has a huge range and these days you understand, there is a like a stress, different kind of stress, physical, mental stress that will also cause the inflammation.

However, those inflammation is not very well understood. What are the substances? How much the role of cytokine is there in that kind of inflammation? So that is also result to the sterile inflammation. There will be an environmental factor some, for example, extreme heat or extreme cold. That will cause some tissue damage and that may result to the sterile inflammation.

So, here I gave you all views of the or overall view of the inflammation and I hope you understood in next session what I will do? I will take some of the cytokines more immunological associated and I will also discuss about some systemic, chronic inflammation and their impact on human health. Thank you. Thank you very much.