Host-Pathogen Interaction (Immunology)
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Lecture - 80
Parasitic Infection – Trypanosomiasis

Hi. So now we are moved to the last session of this course and in this session we will continue the parasite infection. Here in this session, we will discuss about African sleeping sickness or trypanosomiasis. So let us begin.

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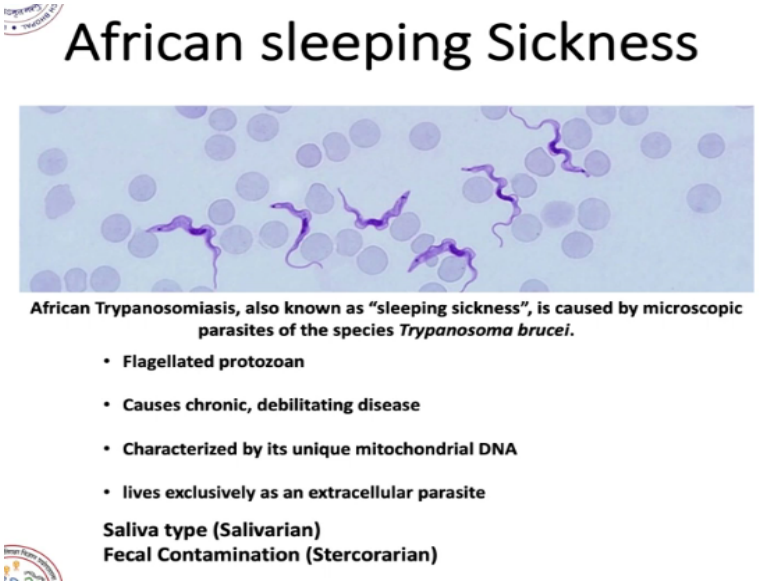

So African sleeping sickness is a basically caused by, here you can see that it is caused by Trypanosoma brucei and here you can see that this blue or violet colour parasite it is a flagellated parasite. It is a flagellated protozoan, causes chronic debilitating disease, debilitating means that the disease which causes you extremely weak that is the meaning of debilitating disease. Characterized by unique mitochondrial DNA.

Lives exclusively as an extracellular parasite. You have seen that this malaria parasites are present in liver cell, they are present in red blood cell, but here it is unlike malaria they are present only in extracellular space. The infection is basically taking place through one arthropod which I will show you in a short while and there are two ways by which this parasite is transmitted inside the human host. One is a saliva type which we call it as a salivarian variant.

So when this arthropod bites, then this releases the saliva and this saliva is loaded with this parasite and this is transmitted to the human host. Another is when they take the blood meal then they take a lot and then they excrete, they release the feces and this fecal material if it is containing this parasite, then this parasite will reach to the human host, so maybe that will cause some irritation.

And this irritation may result to the scratching of that part of the skin and that will cause the translocation of this parasite, stercorarian the technical term is which is used for the transmission of this parasite through fecal contamination.

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So African sleeping sickness is basically transmitted through this arthropod which we call it as tsetse fly, here t is silent just for your information. It is transmitted through tsetse fly which is Glossina species which is found in sub-Saharan Africa. And there are two morphological indistinguishable subspecies of the parasite cause distinct disease pattern in human. One is that Trypanosoma brucei gambiense causes a slowly progressing African trypanosomiasis in western and central Africa. Another is Trypanosoma brucei rhodesiense that causes more acute African trypanosomiasis in eastern and southern Africa.

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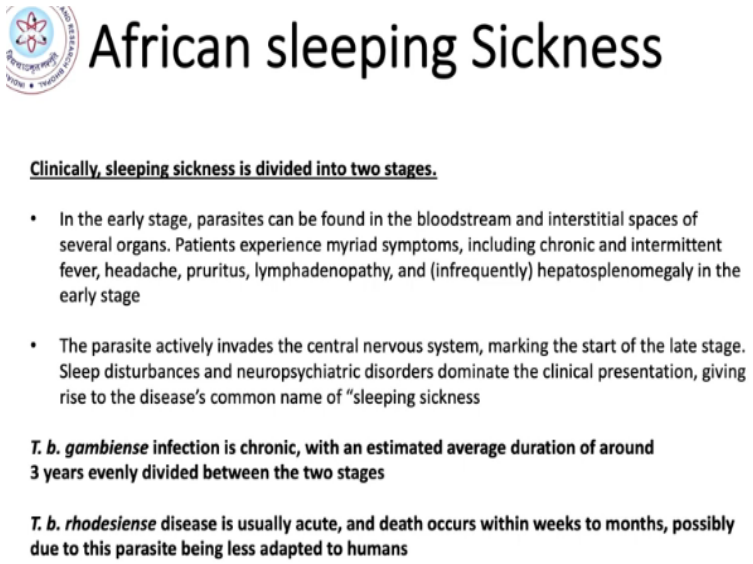

So the clinical symptom **is** of sleeping sickness is divided into two stages. In early stage where you can see that the parasite can be found in blood stream and interstitial spaces of several organs, so there are spaces between the organ, so over there also they may present. The patient experiences myriad symptoms, variety of symptoms include chronic and intermittent fever, headache, pruritus and there is lymphadenopathy and infrequently there will be hepatosplenomegaly in early stage.

The parasite actively evades the central nervous system, this is a complicated situation. So the parasite actively evades the central nervous system making the start of late stage, sleep disturbance and neuropsychiatric disorder. So, basically when they enter in the central nervous system this may cause the inflammation of meninges which we call it as meningoencephalitis. So this can cause the meningoencephalitis.

And this along with the neuropsychiatric disorder dominate the clinical presentation giving rise to disease common name sleeping sickness and basically at this stage there may be a loss of consciousness also in very advanced stage. Trypanosoma brucei gambiense infection is chronic with estimated average duration of around 3 years evenly divided between two stages. Another is Trypanosoma brucei gambiense rhodesiense.

Disease is usually acute and death occurs within a week to months' time, you can understand this is much more dangerous possibly due to parasite being less adapted to the human.

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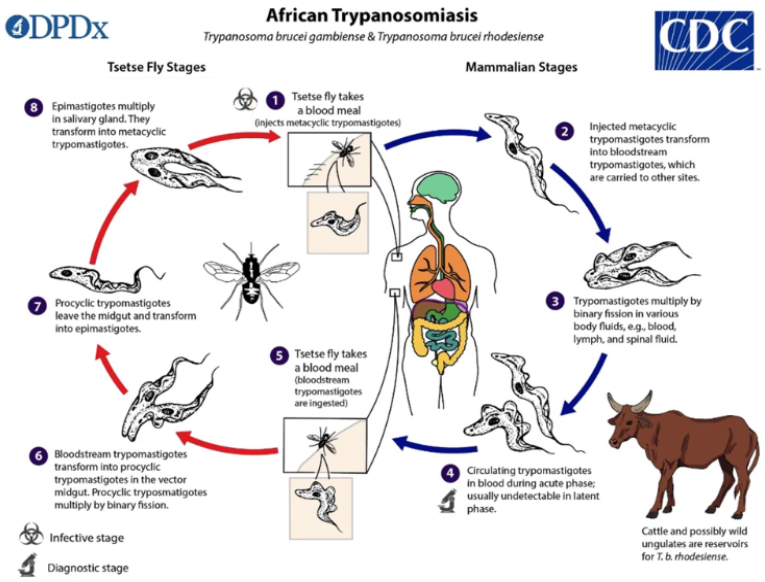

Now we discuss about the life cycle of this African trypanosomiasis. So during blood meal on mammalian host, an infected tsetse fly that is genus glossina inject this metacyclic trypomastigote, here you can see that the insect is injecting this trypomastigote into skin tissue. The parasite enters the lymphatic system and pass into the blood stream. Inside the host they transform into bloodstream trypomastigote.

Here you can see it is trypomastigote, are carried to the other site throughout the body and reach other body fluid like a lymph, spinal fluid, cerebrospinal fluid if you know and continue the replication by binary fission. So, this injected metacyclic trypomastigote transform into bloodstream trypomastigote which is carried to the various sites as I have explained you. It can be present in lymph, it can present in cerebrospinal fluid.

And over there they will go multiple binary fission division. The entire life cycle of this African Trypanosoma is represented by extracellular stages. The tsetse fly become infected with bloodstream trypomastigote when taking blood meal on infected mammalian host, here you can see these are trypomastigotes and taken up by the tsetse fly in fly's midgut. Here you can see now it is in the life cycle in the fly.

In fly's midgut the parasite transforms into procyclic trypomastigote, here you can see that they are differentiating into the procyclic trypomastigote multiplied by binary fission. Leave the midgut and transform into epimastigote. Here you can see this is transformed to the epimastigote. The epimastigote reach the fly's salivary gland and continue multiplication by

binary fission. Here you can see that this is keep on multiplying and making the trypomastigote.

The cycle in fly takes approximately 3 weeks. Rarely Trypanosoma brucei gambiense may be acquired congenitally if the mother is infected during the pregnancy, so this is another new piece of information.

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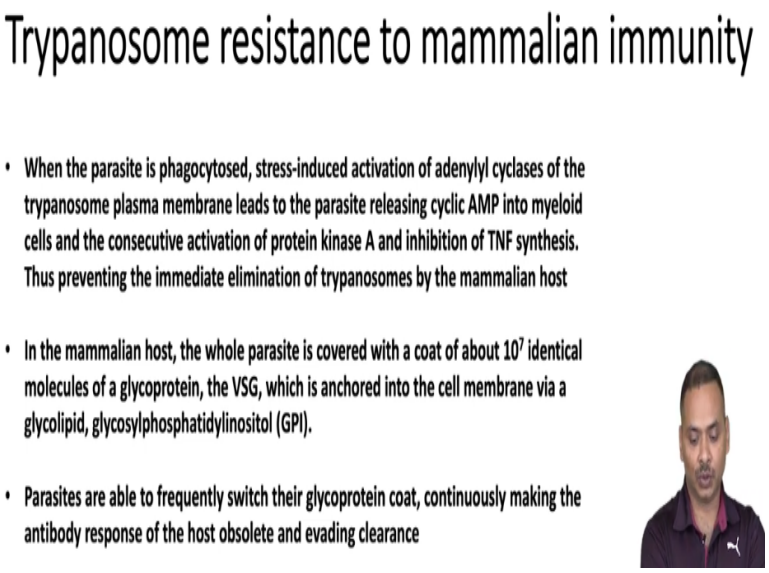

So Trypanosome resistance to the mammalian immunity. When parasite is phagocytosed, the stress induced activation of adenylyl cyclases of the Trypanosoma plasma membrane leads to the parasite release that is cyclic AMP into myeloid cell and consecutive activation of protein kinase A and inhibition of TNF synthesis thus preventing the immediate elimination of Trypanosoma by the mammalian host.

In the mammalian host, the whole parasite is covered with a coat of about 10 to the power 7 identical molecules of glycoprotein which we call it as VSG, this is variant surface glycoprotein, this is very important just remember that thing, which is anchored into the cell membrane via glycolipid and glycosylphosphatidylinositol. Parasites are able to frequently switch their glycoprotein coat, this is very important just follow it, continuously making the antibody response of the host obsolete and in evading clearance. I will explain you in more detail in subsequent slide.

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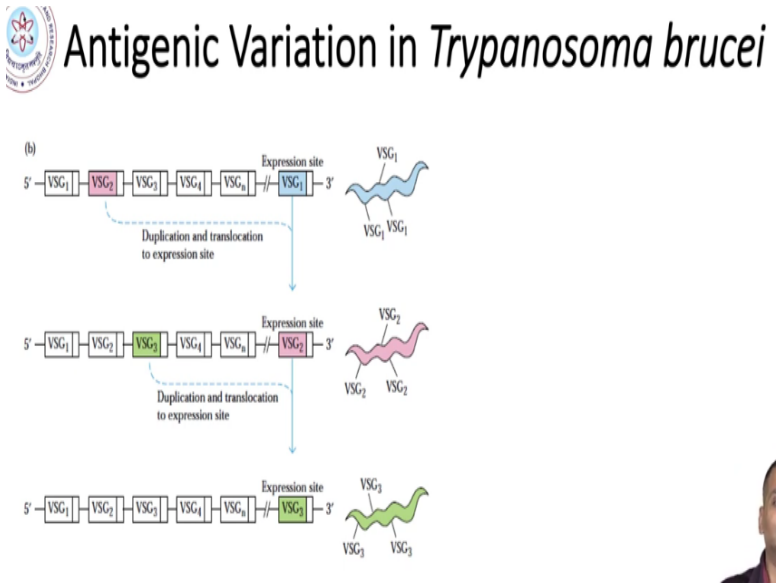

So here I just want to explain you that they have about 1000 to 2000 copies of this VSG protein that is variant surface glycoprotein and at that time only one expresses. So our immune system, here I just want to say that our immune system is quite efficient in clearing this parasite, however our immune system cannot clear 100 percent, still 1 percent will be remained there or a very small fraction will be there.

And that small fraction they will change this variant surface glycoprotein and as I told you they have a 1000 to 2000 copies of this gene. So there will be a translocation of this VSG at expression site and then that previous protein will be replaced. So, in that way they keep on changing the surface, in that way they can very efficiently evade the immunity or antibody mediated immune responses. So this is the strategy by which this Trypanosoma brucei successfully evade the immunity.

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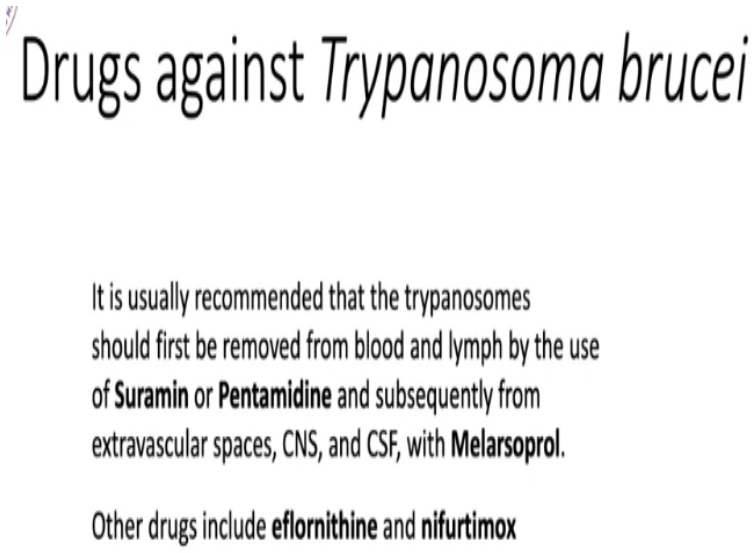

So drugs against Trypanosoma brucei, it is usually recommended that Trypanosoma should first be removed from blood and lymph by use of these are the drug Suramin and Pentamidine and subsequently from the extravascular spaces that is a central nervous system or cerebrospinal fluid with these drugs, here you can see that Melarsoprol. And other drugs include eflornithine and nifurtimox. So these are the drugs against this Trypanosoma.

Here again I am showing a very interesting video which is explaining the life cycle of this parasite in human host as well as in tsetse fly. **(Video Starts: 15:21)** Now here you can see the life cycle in the tsetse fly. **(Video Ends: 20:32)** So with this, I am completing the parasite infection as well as this whole syllabus of host pathogen interaction as well as we have studied the deep immunology.

We have studied innate immunobiology, adaptive immunobiology, organs, various things and I hope you have enjoyed this course and I am looking forward to see that you like this course and it is quite helpful in learning our defense system. Thank you very much.