Course Name: I Think Biology

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W10L53_Public Health-Malaria (Case study) - Part 1

Welcome back to NPTEL course, I Think Biology. My name is Prachi Gupta and in today's lecture, you will learn about malaria. This week, you are learning about public health and in the first lecture, Dr. Abha Rao already introduced you to public health issues that India is facing currently and then you learned about rotavirus and how its vaccine was developed by Indian scientists.

Today's lecture, we will talk about another life-threatening disease which is malaria. So learning outcomes for today's lecture will be, we will discuss the origins of malaria and how we discovered the pathogen responsible for it and then we will move on to its transmission mechanism, how it originates and how it spreads to humans and then we will discuss the treatment measures and how our understanding of this disease has evolved over time and through all this, you will be able to develop a holistic view of this disease which will give you insights into its history, impact on society and the scientific process that was followed to understand this disease better.

So this lecture will be divided into two parts and in first part, in today's part, we will learn more about its discovery and its transmission and then in the next lecture, we will continue learning more about it.

So how old is malaria? If you thought that malaria is a modern plague, then you are wrong. In fact, ancient scriptures from China show that this disease was prevalent as far as 2700 BC. In different texts, different reasons are given for this disease.

For example, in Chinese texts, it is written that it was caused by three demons and Vedic Indian writings called this disease as “King of diseases" because the symptoms of malaria was very severe. So that's why it was called “King of diseases”. In Greece, the onset of malaria was linked to the appearance of star Sirius.

As you can see, initially, different reasons were given for this disease and given that this disease is old as time, we have made a lot of progress in eradicating it. Even though we have developed some ways to prevent and treat malaria, the battle is far from over.

It is still a major threat to human health around the world. So the very first question is why have I chosen this particular case study about malaria? Why are we talking about this disease? Why is it important to study malaria? So to give you some statistics, globally 200 million people are infected by this disease and from those, 0.5 million results in death. In 2021, 247 million cases of malaria were reported worldwide and from those 6,19,000 resulted in death. In India alone, 12 million people are infected every year and 20,000 people approximately die from malaria.

So as you can see that malaria is still a major threat to human health and society, especially in underdeveloped and developing countries. Millions of people are infected and die because of this disease.

So it's important for us to understand and learn more about its history and the progress of science in understanding it, its transmission mechanism, as well as the ways in which it can be prevented or cured. Being educated in spreading awareness is the first line of defence against this disease. Before we begin learning more about malaria, let's start with what do you know about malaria? I have questions for you to think for a moment.

Maybe you can pause your video here and try and answer these questions on a piece of paper. We'll cover concepts related to these questions in this lecture. And with this exercise, you will be able to track your misconceptions or the concepts that you were not aware about, or you were unclear about, and you can see how they changed at the end of this lecture. Maybe once you've finished writing your answers, you can resume this video and we'll start talking more about malaria. So I hope you have tried to answer these questions.

Let's move on to learn more about malaria. We'll learn more about malaria using a scientific approach. If you remember from the very first week of this course, we introduced you to scientific process, where we told you that how scientists, they come up with a problem and how they come up with a hypothesis and test that hypothesis to reach to a conclusion.

So we'll try and understand malaria from the same scientific process. Different scientists who have discovered the parasite responsible for causing malaria, or who have discovered transmission of malaria, we'll look at it from the lens of scientific process.

So let's begin with the word itself, malaria. Malaria comes from Italian word which translates to bad air. So in early, in early 1800s, there was a prevalent theory called Miasma theory. And according to this theory, diseases were caused by unhealthy or polluted vapours, which rise from the ground or decaying metal. So this theory was finally disproved by the evolution of germ

theory, which states that microorganisms are responsible for transmitting diseases and not any mystic vapour.

So just think for a moment how our understanding of a disease has changed. Earlier in the previous slide, I've talked about people used to think that the disease is caused by a demon or the rise of a star, and then they thought that the disease is caused by a mystic vapor, polluted vapor, and then finally, people evolved their understanding and understood that some diseases are caused by microorganisms and not by any unhealthy vapor.

So in 1800s, in late 1800s, a person called Charles Laveran, he wanted to understand how malaria is caused. Now we have germ theory, now we know that diseases are caused by germs. So Charles Laveran wanted to understand how malaria is caused.

What he did was he took different blood samples from people who were infected with malaria. So he used multiple samples from various individuals, which were at different stages of malaria, and he took samples even from the people who recently died of malaria. So when he took blood samples from infected people, he observed the presence of pigmented bodies in their red blood cells, and he was able to recognize and describe four different forms of the germ in human blood.

And in the sketch, you can see in figures 7, 8, and 9, there are some filament-like structure, and this led him to predict that this germ was most likely a parasite. So he discovered that malaria is caused by a parasite. And for his work, Laveran was finally awarded a Nobel Prize in Physiology and Medicine in 1907.

So now we know that malaria is caused by a parasite. So this was the beginning of a scientific process which keeps on evolving and understanding the origins of malaria. So now we knew that malaria is caused by a parasite.

Now the next question that science was going to tackle was how do even these microbes enter the human bloodstream? So take a moment to note that how research questions, they evolve building upon the previous work that is carried out in the same area. Someone discovered that how malaria is caused by a parasite. And the next question, so the next research was done by some other scientists who wanted to know how these microbes enter into human bloodstream. So if we can find this piece of puzzle, we will be a step closer to develop preventive measures as well as potential cure for the disease. So this was the beginning of a scientific inquiry.

Then the story begins with Sir Patrick Manson. He was a Scottish physician who was walking in China to understand the transmission of filaria in 1870s. And he discovered that the mosquitoes act as the intermediate hosts or the vectors for the filarial worm. Vectors are the organisms which carry the parasite or the diseased causal organism to the host. So he showed that the worm was transmitted into human bloodstream by the bite of a mosquito which was

carrying the parasite.So his work was monumental in understanding the role of insect vectors in transmitting diseases.

Now his research inspired Sir Ronald Ross. He was a British medical officer who was posted in colonial India from 1880s. And he wanted to see whether mosquitoes were responsible for transmission of malaria as well. And India at that time had one of the highest number of malaria cases making it an ideal place to study the transmission of disease.

So, Sir Ronald Ross, he set out to use the scientific method to understand the how malarial parasites enter the bloodstream. So if you remember from the first lecture, the first step of a scientific process is to make detailed observations. And here are some of the observations or some of the things that we already knew about malaria. Thanks to microscopes, we already knew that malarial parasites resided in liver cells of the infected people. And infected individuals RBCs, red blood cells, they contained pigment bodies which was caused by hemozoin.

Another interesting observation that Ronald Ross made was India, within India, there were some areas where malaria was quite prevalent. And in those areas, he found mosquitoes with dappled wings. So these are the observations, set of observations that he already had. And then he came up with his own hypothesis. He said that mosquitoes serve as vectors for malaria.

So remember, he knew that malaria is a malarial parasite is present in the liver cells of humans. And then in the areas where malaria is prevalent, there are mosquitoes with dappled wings. So he came up with this hypothesis. And he said that belief is growing on me that the disease is communicated by the bite of mosquito. She always injects a small quantity of the fluid with her bite. What if parasites get into the system in this manner? So this is how he began his scientific inquiry.

And keep in mind that understanding the transmission of disease even today is a huge challenge that takes a lot of effort. He was undertaking an important but immensely difficult scientific challenge. Now the question that Ronald Ross was going to tackle was that can mosquitoes carry the malarial parasite? So pause your video here and put yourself in Ronald's shoes. And based on his observations and the hypothesis proposed by him, maybe try and design your own experiment to test these questions of whether mosquitoes carry malarial parasite.

How would you go on about designing it? What would you observe? What would be the first thing that you would observe and how? Take some time to think about it, write it down, and then we'll go and learn how he designed his studies and he faced the problem. So don't worry if your design is different than his. It's okay. There are different ways to approach a similar problem. As long as you have logically reasoned your approach and it's relevant to the question you're answering, it's absolutely fine.

So pause here, write your methods, and we'll see how he went on testing his hypothesis. So what he did was he set out to collect mosquito larvae from ponds and culture and he raised adult mosquitoes from them. So this is a caricature of Ronald Ross and who is in hunt of mosquito larvae. And it took him two years of trial and error and finally he was able to culture mosquitoes with dappled wings. He then paid a malarial patient named Huzen Khan to provide a blood meal.

Blood meal is nothing but basically he wanted the mosquitoes cultured by him to feed on this patient, so that the malarial parasite from the patient is transferred to his cultured mosquitoes. Okay and then after feeding the mosquitoes from the blood of this person, he then dissected the mosquitoes and observed them under the portable microscope that he himself invented.

So given that the mosquitoes had a blood meal from the infected individual, what do you think that Ronald Ross would have discovered in the dissected bodies of the mosquitoes? Pause here and think for a moment. Well if you answered that he would have seen the pigmented bodies inside the dissected mosquito bodies then your prediction is correct. And that's what he observed. The mosquitoes were able to take up the malarial parasite from infected individuals.

If you remember Charles Laveran, he had discovered the pigmented bodies in humans and then he discovered pigmented bodies in dissected mosquitoes. So it means that mosquitoes have taken the parasite from the blood meal of the infected human. So he knew that mosquitoes were indeed carrying the malarial parasites but can they infect a healthy individual with it? So to test his next question, he used model organisms which were birds.

He studied avian malaria in birds. So if you remember model organisms are the organisms that has characteristics which makes it useful for studying various processes in the laboratory and they are widely used in scientific research. And we have talked about model organisms in rotavirus lecture.

So Ronald Ross, he used birds as a model organism and he found out that pigmented bodies which were stored in the salivary glands of these mosquitoes, they were released into healthy birds during a blood meal. So he knew that mosquito act as vector for avian malaria.

But what about humans? So the answer came in 1890s by an Italian physician called Giovanni Battista Grassi. He tested and confirmed the discovery in humans. So he built up upon the Ronald's work and he tested his proposed malaria mosquito transmission mechanism in humans. He showed that in a malaria endemic area only humans that were bitten by a female Anopheles mosquito were infected with malaria and not those that were protected against mosquitoes. So he showed conclusively that only female Anopheles mosquitoes, they serve as a factor. So if you remember Ronald Ross found dappled wing mosquitoes which were found in the areas which had prevalence of malaria.

So he confirmed that only female Anopheles mosquito serve as a vector. In malaria endemic

area only humans that were bitten by mosquitoes they fell sick. Those who were protected from mosquitoes they were not infected.

So Ronald Ross, he continued his work after his discovery and developed mathematical models to explore the distribution patterns and tracking the spread of malaria. For his research he was awarded Nobel prize in physiology or medicine in 1902. Battista however he was not awarded the same prize despite his significant contributions.

So take a moment and see we just went on an incredible and exciting scientific journey that started with simple observations and led to a discovery with immense implications for public health. Might make you wonder why is required, what is required to carry out such a process. Here are some of the pictures showcasing some key factors required to conduct science. The first picture here shows you detailed and meticulous notes made by Ronald Ross while he was studying this disease.

Not how immensely detailed they are. Attention to detail is very important and to keep a thorough record for one's work is crucial. So this documentation help in putting all the pieces one has collected and answer the question. In the middle you have a picture of a portable microscope that Sir Ronald Ross designed himself and he used it. He innovated and came up with creative ways to answer the questions he was asking. Critical thinking and critical reasoning is another important skill set in research.

And in the final picture you can see how Ronald Ross his discovery was immortalized and it's in PG hospital where it's written in this laboratory. Surgeon major Ronald Ross in 1898 made the great discovery that malaria is conveyed by the bite of a mosquito.

So that plate is still there. So till now we have learned that mosquitoes are responsible for transmitting malaria. Okay but how exactly does it happen? How does a parasite infect humans and make them sick? Okay so let's learn more about it.

Before going on to understanding the transmission let's learn a little bit about the parasite in the vector. So the parasite responsible for causing malaria is Plasmodium. And Plasmodium is actually a unicellular protozoan parasite and there are some 200 species of Plasmodium genus. But only five species are responsible for malaria in humans. Now vector as you know is an organism which carry the disease-causing microbe from one host to another.

In this case it is mosquito and to be specific it's a female mosquito known as Anopheles mosquito. So anopheles mosquito they act as a vector of malaria and they transmit malarial parasite by biting humans during a blood meal. Now the question that might come to your mind why male mosquito does not cause malaria because male mosquito feed only on flower nectar and they are not the vector of this disease.

And I'd like you to learn and search more about this why male mosquitoes only feed on the flower nectar and why female mosquitoes have to feed on the blood meal.

So here is the picture on the left hand side here is a picture of Plasmodium falciparum. It is the deadliest species of Plasmodium and you can see the pigmented bodies here in the blood smear. And the another picture is of Anopheles mosquito which is known as Anopheles minimus which is enjoying a blood meal from a human.

To start with, so we are saying that mosquito is the vector of malaria. I would like you to take a moment and think about has it ever happened like a government official that comes to your place at the end of the summer they come and ask you if, if you have any coolers at home which still have water or are they being cleaned and closed or there are certain checkups around your area to see if there is no stagnant water. Why is that? Why do we have to make sure that there is no stagnant water at our homes? Okay and some might ask you if you're the tank on the roof of your home or your building is it closed? So I have seen such government officials check up happening in my area.

Most likely you might have also seen it. Why does that happen? Why those people are checking if there is some stagnant water or there is some water in your house or outside your house or near your house? So one of the reasons that they check this is because stagnant water is a breeding ground from mosquitoes. So let's look at the life cycle of mosquito which provides us important insights in controlling the spread of malaria. So mosquitoes they lay their eggs in fresh and non-flowing water. Their larva and their pupa they lead an aquatic life cycle. They have a breathing tube that breaks through the water and allows them to breathe and mosquito life cycle it normally takes two weeks but it can be as short as four days or can go as long as a month.

To develop mosquito larvae they just need 2.5 centimeter of depth in water. So that stagnant water can be a breeding ground of mosquitoes. So now you understand why it is important for us to keep our surroundings clean so that there is no breeding ground for mosquitoes. So these eggs they hatch they went through different stages such as larva which has multiple stages and then there is pupa and then there is the adult mosquito which can cause various diseases and not just malaria there are different diseases which are caused by mosquitoes. So I would like to emphasize how important for us to clean our surroundings and not have any stagnant water being there in our surroundings.

So now let's study in detail how this parasite spread into humans okay and the life cycle of this parasite into the human body. So the very first step as we know is the bite. The bite of the mosquito. Infected mosquitoit bites a human. When it bites a human it releases Plasmodium sporozoites into the body of the human.

So these sporozoites they travel and live inside the liver cells of the humans. Okay now we are

talking about the life stage of the Plasmodium. So this life stage which enters into the humans it is known as sporozoites. So now once inside the human liver cells these sporozoites they start reproducing asexually and asexual reproduction results in merozoites. Okay even during this period now infection has happened the bite has happened these cells are gradually dividing, reproducing asexually and producing merozoites even at this time humans do not show any symptoms, okay.

These myriozoites they are produced as a result of asexual reproduction and then once they are in merozoite form, merozoite life stage they break away from the liver and they enter the bloodstream of humans. Now once they move to blood they move into red blood cells where they undergo many rounds of cell division, asexual reproduction, okay. So these RBCs burst open every two to four days and they're permanently damaged which causes fever. So the initial infection to this stage it takes around 10 to 15 days. So malaria is not detected immediately it takes like 10 to 15 days to get fever and understand that the person might have malaria.

So at this stage the RBCs are being infected. Now in RBCs some of the merozoite form of this parasite they develop into sexual form which is known as gametocyte, okay. And this gametocyte it starts circulating in the bloodstream. So now let's say there is an infected individual with malaria and it has gametocyte in its bloodstream, a mosquito let's say might bite this person the mosquito will inject gametocytes, okay. Now these gametocytes they mature in male and female gametes in the mosquito gut. Okay just remember this was sexual stage of plasmodium so these gametocytes now they are inside the mosquito gut and they form male and female gametes, okay.

Now the male and female gametes they fertilize and they form a zygote and this zygote they make their way through mosquito's midgut wall and they form oocyst on the exterior surface. Now thousands of sporozoites develop within the oocyst. Now these oocysts they burst open, which releases the sporozoite which migrate to mosquitoes the salivary glands and the mosquito is now ready to infect another individual through its bite and the cycle continues.

So just take a moment and see even the life cycle of this parasite it's half done in the human and half completed inside the mosquitoes. In mosquitoes they form zygote and which ultimately forms sporozoite and sporozoite sorry sporozoite and sporozoite is the stage which infects the humans and in humans it's forming merozoites and gametocytes.

Okay so different phases of the life cycle of this parasite is occurring in two different hosts. Okay, and the cycle continues the mosquito will infect another healthy individual the same cycle will go inside that healthy individual.

So to summarize the life cycle of the plasmodium,we begin with an infected female anopheles mosquito which inject the saliva into human's bloodstream. These sporozoites they multiply

asexually in the liver cells and they enter the bloodstream through heart and lungs. Now these merozoites they move into RBCs and these RBCs they burst open every two to four days which causes fever and they permanently damage the RBCs.

Then, these some of the merozoites in RBC they develop into gametocytes which circulate in the bloodstream and a mosquito take up those gametocytes in a subsequent bite. Then these gametocytes they mature in male and female gametes in the mosquito's gut and thousands of active sporozoites they develop inside the oocyst which burst open and release sporozoites and the cycle continues.

So this is the summary of the transmission of the life cycle of parasite and the transmission of this parasite from mosquitoes to humans and how humans are infected by the malaria by this parasite. So now some of the symptoms of so now we have a thorough understanding of the origin transmission and infection of malaria.

So let's look at what the disease is capable of. What does the disease, what does this disease do to an infected individual? So the primary symptoms are the periodic fevers with peaks, shivers, headache, vomiting, general muscle pain and in severe cases it may cause anemia, darker bloody urine, respiratory issues and multiple organ failure and it can eventually lead to death as well.

So I have a critical thinking question for you. Why do you think this disease may cause anemia? Just think about it and try and answer this question. Now we know how this disease was being transmitted.

Now we know how this disease is spread in humans. So the next part of the scientific journey was to find a cure. And now the search for the cure begins and in the next lecture we will learn how did we reach to the cure of malaria? What preventive measures can we take to avoid malaria? We'll learn more about this in the next lecture.

To quickly summarize, in today's lecture we talked about how malaria is a deadly global disease with hundreds of millions of cases reported annually and thousands of those reported results in death. And how our understanding of malaria has changed over the years due to the scientific inquiry that different scientists, different researchers did. And Laveran was the person who showed us that malaria was caused by a parasite and not due to some polluted air.

And building on his work, Ross and Battista, they shed light on mosquitoes being vectors for the plasmodium parasite. And then we learned about the transmission of plasmodium parasite to humans. How mosquitoes inject the plasmodium into human bodies where the pathogen spreads and reproduce asexually before being picked up by the mosquitoes again in a subsequent bite and how the cycle continues. So I hope you gained a better understanding of this disease in today's lecture. In the next lecture we will learn about its cure and the treatment and the preventive measures that we can take. Thank you. See you in next lecture.