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W10L54_Public Health-Malaria (Case study) - Part 2

Hello everyone, welcome back to NPTEL course, i think biology. My name is Prachi Gupta and in this week you are learning about public health. This lecture is the part 2 of the previous lecture where we learnt and talked about malaria. So we will continue talking about malaria and learn more about it. So to give you a recap what we learnt in the previous lecture, we learnt that malaria is a global disease with hundreds of millions of cases reported annually and from those cases thousands result in death. We learnt how our understanding of malaria has changed over time, has increased over time because of the discoveries that made by different scientists.

Now it started with when Leveran showed that malaria was caused by a parasite and not because of some polluted vapors. And building on Leveran's work, Ross and Battista shed light that mosquitoes are the vectors for plasmodium. Plasmodium is the parasite that causes malaria. And then we learnt how the malaria is transferred into human bodies.

How mosquitoes inject the plasmodium into human bodies and how pathogens spreads within the human body and how it reproduces asexually and how it is picked up by another mosquito again in a subsequent bite and the cycle continues. To give you some recap about the life cycle of plasmodium, to summarize, as you can see the first point, the life cycle begins with the bite. A female anopheles mosquito, it injects saliva into the human's bloodstream. And when it bites human, it releases sporozoites inside the bloodstream of human. These sporozoites, they move to liver cells where they reproduce asexually and produce merozoites.

These merozoites from liver, they enter into bloodstream. Now these merozoites which have moved into the bloodstream, they move into the red blood cells. And red blood cells burst open every 2-4 days and this permanently causes damage to the host cell, to RBC and it causes fever. Now some of these merozoites in the RBCs, they develop into gametocytes and this circulates within the bloodstream. So when a mosquito bites this

infected human being, it takes up these gametocytes and these gametocytes now mature inside the mosquito's gut.

They mature into male and female gametes and within the mosquito gut, thousands of active sporozoites they develop inside the oocyst which finally burst open and release the sporozoites. And when this mosquito infects another person, it transfers the sporozoites to that human. So this cycle continues. So now we know from the previous lecture, now you know that malaria is caused by a parasite and the mosquito is the vector of this disease and how the transmission is occurring from mosquito to humans. Now we know that how this disease is spread.

The next part in this scientific journey was to find a cure. So let's see how the cure was developed for this disease. Okay, So in 1920s, quinine which is an active ingredient in cinchona bark, it was isolated from cinchona tree barks from Peru and this ingredient was shown to have effective anti malarial properties. It was effective against malaria and it was used widely. Many variants were also developed using this quinine, this ingredient to fight against different forms of malaria.

But it's important to remember that the disease and the disease causing agents, they evolved with time. So over time and because of the overuse of this quinine based medicines, many drug resistant forms of malaria evolved. Drug resistance is a major problem to public health even today where unchecked use of antibiotics and any other medicines they have led to the evolution of many deadly drug resistant forms of various diseases. Now malaria, once we had this cure for malaria quinine, but malaria became resistant to quinine. These treatments were not as effective and more people were getting infected and they were still die.

Now there was need of developing an alternate cure. So this was in 1920s when we had discovered quinine from cinchona bark of the trees. Even 50 years later, the search for alternate cure continued for 50 years. So for 50 years we were not able to find any alternate cure. In the 1960s, a 20 year war began between the US and Vietnam.

This war was mostly fought in deep humid hot forests of Vietnam. So over half of all the troops that were present in this war suffered from malaria. And this malaria by now was resistant to quinine based medicines. So there was an urgent need to develop an alternate cure. Around this same time, a young up and coming researcher named Tu Youyou joined the Institute of Chinese Materia Medica.

The increased prevalence in deaths caused by malaria caused Chinese government to launch project 523 in the search of a cure for malaria. This project was responsible for

developing an alternative cure and Tu Youyou was appointed as head of this project. So Tu Youyou and her team, they used a unique approach to develop a cure. So Tu Youyou, she screened ancient Chinese medical texts which described cures for diseases that resembled malaria and she went through many such ancient Chinese texts. She and her team, they then experimented with over 640 different recipes they found in these texts.

And these recipes were derived from both plant and animal sources. So finally they were able to find one particular herb known as QingHao which is a species from genus of Artemisia. This showed promising effects but they were inconsistent. Now Tu Youyou she went back to scriptures and studied them thoroughly and she noticed one peculiar thing. What she noticed was that none of the scriptures mentioned that boiling water or heating the herb was required before administering the drug.

So whatever herbs that have been used so far, they were used after boiling or heating the herb in the water. So Tu Youyou and her team were also doing the same. They were using this herb by heating it in the water, by boiling it in the water. So she went back to these ancient scriptures to learn more about it and here is the picture of this scripture that she found and here is the highlighted part in this which talks about how to administer the drug. And she noticed that there was no mention of boiling or heating the herb before giving it.

Now her team so far had been doing the extraction process which involved high temperatures. So could that be the reason why the effect of the herbs were inconsistent? This was her hypothesis that heating it damaged the active ingredient which has the antimalarial properties. So she decided to test this and she modified the extraction process so that the ingredient could be extracted in relatively lower temperatures and she tested its efficacy against malaria. And yes, she found out that heating was the issue. The ingredients extracted from the modified procedures, they had highly and consistently effective properties against malaria.

So her team finally discovered a potential cure for malaria. This drug artemisinin, it was shown to be 100% effective in mice and monkeys. So usually the process of drug discovery is a long and tedious process. And once the potential drug is discovered, it has to go through a series of experimentations and trials on various model organisms before human clinical trials can even happen and drug can be made to public. So there is a series of events after someone has discovered a drug, it has to go through a clinical trial, it has to go through several model organisms and then ultimately human trials are permitted.

This ensures that the drug is not harmful and it does not have any harmful side effects and it is also effective in humans. So now Tu Youyou and her team showed that

artemisinin is 100% effective in mice and monkeys. But what about humans? Now just remember that this was happening during the time of a war where millions of people were getting affected because of malaria. The Vietnam war and the high infection rates of people involved in the war made it urgent for the cure to be made publicly available. But getting clearance for human clinical trials, it would take a longer time, even years.

So what she did was, Tu Youyou and two of her team members, they tested this drug on themselves and they showed that it is safe and effective. So now once they did that, once the safety was confirmed, the clinical trials were fast forwarded and then the efficacy of the drug was confirmed and it was given to various soldiers. So her work, however, it was not published in English till 1979. So it was unknown to the western world at that time. And later on in 1981, WHO, World Health Organization, invited her to share her findings.

As you can see, Tu Youyou and her team members took a unique approach which paid off in the end. Their cure and its derivatives have helped more than 200 million malaria patients.WHO now recommends artemisinin combination therapy as a first line of treatment against malaria. So for her work, Tu Youyou was awarded the Lasker Award in 2011 and she became the first Chinese woman to win the Nobel prize in 2015. So as you can see her research, it is a unique blend of ancient Chinese texts, pharmacology, traditional chemistry and medicine and it showcases the strength of an interdisciplinary approach to answer scientific questions.

So now this is one of the ways that malaria can be treated. Now we know a drug which helps in curing the malaria. But isn't prevention better than cure? So it's the same for malaria. If we can prevent the disease itself, infection rates will go down and the prevalence of malaria will be reduced. Now we will talk about some measures that can be taken to prevent the spread of malaria and also discuss a case where preventive measures ended up being a problem itself.

So let's see what preventive measures are there to help us prevent malaria. These are very simple preventive strategies that one can take against malaria and I am sure most of us already use it. So for example we use mosquito nets, we use mosquito repellent creams, we apply scented oils. All out most of us use. Other preventive measures are wearing clothing that covers exposed skin against mosquito bites.

So in the previous lecture, we saw the life cycle of mosquito and we saw that mosquitoes they lay eggs in water. Remember? So mosquitoes they breed in stagnant water. So during the rainy season, we should avoid water to collect and if it does collect, we can spray a layer of oil on the water. So this will prevent mosquitoes from breeding.

Lastly one of the effective ways to kill mosquitoes and prevent the malaria are insecticides.

So insecticides are used to kill pest insects and one of the most widely used insecticides is DDT. Dichloro-diphenyl-trichloroethane. It was used during World War II to effectively control malaria and typhus fever among civilians and military troops. So DDT was so famous and popular at one time. Here on the right hand side, you have an image of a Time magazine ad from 1947 which depicts the DDT as a miracle product for widespread use as an insecticide.

As you can see in the headline, it's written DDT is good for me. So this insecticide was quite popular at that time. So it was widely used as a pesticide in homes, forests and agricultural fields. Here is a picture of helicopters spraying DDT over a forest in the USA. And during that time, DDT was also sprayed over entire cities in the USA to kill flies as they were thought to transmit polio.

So at that time, DDT was used on a large scale all over the world. But was it a good solution? In 1962, Rachel Carson, who was an environmentalist from the US, she published a book called Silent Spring. And this book talked about the immense negative effects of DDT on ecosystems. Other studies from across the world also showed that DDT was harmful to humans. It increased the risk of developing breast cancer and disrupting hormonal functions.

So how was DDT negatively affecting ecosystem? Rachel Carson's work, it showed that DDT concentration, it increased with trophic levels, which means that as we go through the food chain, the concentration of DDT was increasing. As you can see in this picture here, DDT here is present in extremely low concentration. This is the DDT in water and then zooplankton take up this DDT and these zooplanktons, they are consumed by small fish and this small fish in turn are consumed by larger fish. By the time this DDT reaches the food chain to a bird, the concentration of DDT has increased from part per billion in water to 25 parts per million in birds. So DDT concentration was increasing with trophic levels, with each trophic level, with top predator like birds, they were being negatively affected by consuming prey, which was exposed to DDT.

And what happened to these birds was, these birds with high levels of DDT in their system, they lay eggs with thin shells and that caused developmental issues and eventually it resulted in decline population of birds. So DDT was not a good solution and it was later on realized by the work of Rachel Carson and we realized how DDT was negatively impacting the ecosystems. So following years of rally, USA finally banned DDT in 1972. But India and several parts of Africa still use DDT as a preventive control.

India in fact is the largest producer of DDT in the world and it produces about 3000 metric tonnes annually.

Mass spraying of DDT It has led to some mosquitoes developing resistant to DDT in several parts of the country. So this was one of the other reasons for me to choosing this particular case study. As you can see this is such an important case study which highlights how an effective solution to prevent a disease can become a problem which had immense health risks, disrupted ecosystem health and was contributing to insecticide resistant mosquitoes. Now we have talked about drugs that were developed against malaria such as quinine, then Tu Youyou later on developed artemisinin and then we learned about the preventive measures such as DDT which became a problem later on. So what could be another potential solution for this disease malaria? So one of the ways we can tackle diseases is that we prevent the disease, another way is to take medication against the disease and one of the other ways is to have vaccinated against the disease.

So vaccines they are an effective preventive measure and they have been proven against variety of diseases such as polio, smallpox and more recently we all have taken the vaccine against COVID-19. So this picture here it shows how a vaccine works where in some form of the disease it is injected in the body and the body detects the foreign entity and it triggers an immune response by creating antibodies. Now the immune system it retains a memory of the infectious agent and it can fight against this disease in any future infections. So despite being such an old disease no effective vaccine for malaria has been developed. Why is that? It is because of the complex life cycle of plasmodium.

As we have learnt the life cycle of plasmodium there are different stages in its life cycle and some of it happens inside a human body and half of it happens in the mosquito. So plasmodium has such a complex life cycle and can produce varying antigen. So this makes it difficult to create a vaccine against this disease. However a potential vaccine called Mosquirix it is a mildly effective vaccine and it has been approved by WHO in 2021. Pilot studies are being carried out in Malawi, Ghana and Kenya to test the efficacy of this particular vaccine.

Let's learn about malaria in India. India's geoclimatic condition provides a conducive environment for various mosquito species to breed and thrive. They are responsible not just for malaria but a variety of diseases such as filaria, dengue, chikungunya and so on. And lack of awareness and diverse environmental conditions as well as increased temperatures caused by climate change they have contributed to increase in malaria incidence in our country. According to one World Malaria Report in 2019 by WHO, it showed that 58% of all malarial cases in Southeast Asia they were reported from India. But over the years India has taken big strides in the management and prevention of this

disease.

Now in India there are about 9 species of Anopheles musketos which are known to transmit 3 plasmodium species which is P. falciparum, P. vivax, P. malariae. So among these 3 plasmodium species P. falciparum is the most common parasite and Anopheles culicifacies is the primary vector. Now this map here shows the prevalence of malaria incidence based on different species of vectors in parasites. Here you can see the yellow and red regions are the states with high incidence of malaria. And we can see that different vectors and different parasites are responsible for the transmission of disease in different parts of the country.

Odisha, Chhattisgarh, Jharkhand, Meghalaya and Madhya Pradesh. They account for about 45% of the total number of cases in the country. Now India has a long history with this disease malaria. In 1947, about 20-25% of Indian population was infected by malaria and resulted in 0.8 million deaths per year. By 2017, India was one of the top 5 countries with malaria cases. However in 2019 we saw the reduction and the reduction was almost by 49% in the reported cases compared to 2017. As you can see here in this graph, it shows the immense reduction in incidence and death due to malaria over the last two decades. In fact the government has planned to eliminate malaria completely by the year 2030. Now in this lecture we have learned how human action it affects the natural world at many levels.

And nature in turns affects our lives. We learned like human actions such as DDT, how is it affecting the natural world and how that natural world is affecting our lives. So addressing the problem of malaria is not really straightforward. The malaria prevention it requires people from different professions, many different professions such as from physicians and public health specialists to urban planners and climate scientists. And it is important to note that the malaria parasite and the vector can evolve resistance to drugs or insecticides and such resistance can cause enormous damage to the environment. So solutions for preventing malaria also have to be country specific or region specific, keeping in socio-economic challenges in mind as well as one solution does not fit all the problems.

So to summarize today's lecture, we looked at how Tu Youyou, she used a unique blend of ancient Chinese knowledge, pharmacology and modern science techniques to develop a cure for malaria. This was the cure that she developed and then we studied about the preventive measures that can be taken against malaria. And sometimes seemingly simple solutions, they can cause unrelated problems. And DDT was an effective tool against the spread of malaria. However, Rachel Carson showed the negative impact this DDT has on ecosystems.

And in India and parts of Africa, this DDT is still being used and has led to evolution of resistance in mosquitoes against it. Then we learned about the vaccine. We are still researching and developing an effective vaccine against malaria and recently in 2021, very recently, a mildly effective vaccine was approved by WHO. Then we studied and we learned about the prevalence of disease of this particular disease in India.

And we saw how India has progressed in tackling malaria. India has made significant strides in its fight against malaria with lower and lower cases and deaths reported every year. However, factors like lack of awareness and climate change, disease resistance, they still are a major hurdle in India's aim to be malaria free. So learning more about malaria, a public health issue, we saw the work of various scientists, such as Leveran, Ross, Battista, Tu Youyou, and Rachel Carson, and the scientific process and the scientific inquiry and the efforts that goes into it. So through this lecture, I hope you have an appreciation for the scientific process and how one can go about tackling various problems using this approach. So now let's go back to the questions we went through at the beginning part one of this lecture.

Pause the video and now try answering these questions and see how your understanding of the disease has changed from the beginning of the lecture. So I hope you enjoyed learning about this deadly disease and how scientists work to develop ways to fighting and managing this disease. Thank you.