

Malaria Hunters

Dr. Arvind Dubey

Signature tune...fades out

Anthem...fades out

Opening song...fades out

Anchor 1 -*Namaste*, friends. In the last episode of Sunhere Panne you heard that... (recap). In this episode of the radio serial Sunhere Panne we will be talking about a vaccine for Malaria. We will be talking about all the efforts in this direction and about all the Scientists whose research has allowed us to assert with pride that Indians are not lagging behind in this arena of action against Malaria.

Anchor 2-You will be amazed perhaps to know that Malaria and mankind go back more than 50 thousand years. It is speculated that one of the reasons behind the collapse of the Roman Empire was Malaria. In those days, Malaria was often referred to as Roman fever. Actually the word Malaria is derived from two Italian words; Mal and Air...together meaning Bad Air. This goes to show that people attributed Malaria to breathing in bad or dirty air.

Anchor 1 In 1880, when Charles Louis Alphonse Lavaren, a doctor in the French army, first saw *Plasmodium*; the parasite that causes Malaria in a patient, he had no idea that this would be such a huge health problem in the days to come.

Anchor2-In 1907, he was awarded the Nobel Prize for his discovery. Today 90 countries across the world list Malaria as a serious health issue. Malaria affects about 2 crore

people every year; of which about 30 lakh lose their lives to it. Every minute, two children succumb to Malaria somewhere or the other across the world.

Anchor 1 -May God bless Sir Ronald Ross, the Nobel laureate of 1902, who during his tenure at Presidency General Hospital, Calcutta, working with inadequate resources, still managed to demonstrate that the malarial parasite is spread by mosquitoes.

Anchor 2-The undeclared war between Scientists and the malarial parasites has been in existence since the 19th and the 20th centuries –that is ever since the entire life cycle of the malarial parasite was worked out. This purely scientific war has manifest as the medicines against Malaria.

Anchor 1- Unfortunately, it soon became clear that these medicines, so effective against Malaria, seemed to lose their effectiveness against the parasite after a while. This necessitated the search for newer and newer pharmaceuticals products. However, the malarial parasite soon finds a way to render these ineffective too.

Anchor 2-This sparked the new round in the ongoing war against Malaria—the search for a vaccine. A vaccine that would just not stop Malaria in its tracks; but also serve to lessen the impact of the infection as well as prevent it from spreading. We will be hearing about all these advances in this episode of Sunhere Panne...Malaria Hunters.

Music to indicate change of scene...fade out.

Opening Song...fades out

Sounds indicating that it is a room or a chamber in a hospital

Child: I am feeling cold, Mummy. Please get a quilt...a blanket...

Papa: (in stressed out voice): Why are you just standing here...go on...take out a quilt...cover the child.

Ma: I am taking out the quilt...it is just that because winter was over I had put away all the blankets and quilts inside the box bed.

Child: Papa, I am still cold...please wrap me in something warm...(voice is wavering; quaky)

Papa: Yes, my child...here take this quilt and I will put this blanket over it...ok now? Does that make you feel less cold?

Child: No Papa, I am still feeling cold.

Ma: This feeling will not get better so easily...I think it is Malaria. And as soon as the feeling of cold goes away ...the high fever will return with a vengeance....did you call the doctor?

Papa: I called the doctor quite some time back...he should be on his way now.

Ma: Feeling less cold now?

Child: Yes...but my body is aching...I have a headache too.

Ma: The fever is rising...look how the body is shaking...should I massage your head, dear? Where is the doctor?

Door bell rings

Papa; (voice comes from a distance) I'll answer the door...I think the doctor is here.

Ma: Namaste Doctor sahib.

Doctor: Namaste...(after a pause)...lie straight dear... Oh! You are running a high fever.

Child: I was so cold just now.

Dr: Let me see your tongue....Hmm....he has Malaria.

Ma: Ah! That's what I have been saying all along.

Papa: Malaria! Now, how did he contract this?

Dr: Malaria is spread by the female *Anopheles* mosquito. It is the vector of the malarial parasite, *Plasmodium* and spreads Malaria from the infected to the healthy.

Ma: Doctor, is my child in any danger?

Dr: That is difficult to say categorically just now.

Papa: Whys is that so, Doctor sahib?

Dr: Well, usually Malaria is not a fatal condition...although the patient does suffer from high fever, shivering, body ache...may be vomiting etc.

Ma: My poor child is suffering from all these symptoms...

Dr: The trouble is that infection by one species of *Plasmodium*...*Plasmodium falciparum* to be exact...rather complicates the situation.

Ma: So there is more than one sort of malarial parasite?

Dr.: Well...till date we have found at least 200 different species of which about 11 cause infections in humans.

Ma: How strange!

Dr: Of these, four species cause the most trouble. These are *Plasmodium vivax*, *Plasmodium ovale*, *Plasmodium malariae*, and *Plasmodium falciparum*. In India, most cases of Malaria are due to *Plasmodium vivax* but it is infection with *Plasmodium falciparum* that is the most dangerous.

Papa: *Plasmodium falciparum* ?

Dr.: Yes...it leads to breakdown of blood cells in the body causing anemia and enlarged spleen. If Malaria affects the brain it can lead to seizures and even unconsciousness. It may even pose a threat to life.

Ma: (worried tones) Seizures and unconsciousness...

Dr: Don't worry. Infection with *Plasmodium falciparum* parasite occurs more often in the kids living in Africa. In India, the species *Plasmodium vivax* causes the most infections and it does not lead to such serious conditions.

Papa: God help our child...what should we do now, doctor?

Dr: I am sure your child will recover soon; I have given him the medicines...the fever will subside and he will not vomit any more...and yes. In case the child has fits...or seizures or becomes unconscious rush to the hospital.

Ma: God forbid.

Opening song...fades out

Male Voice (MV) : Malaria can be dangerous. When a female *Anopheles* mosquito sucks the blood from a patient suffering from Malaria, the parasites enter the gut of the mosquito along with the blood. The parasites complete a part of their life cycle in the gut of the mosquito and ultimately reach its salivary glands. Now, as soon as the mosquito bites another person; the sporozoites of the parasite enter the person's blood along with the mosquito's saliva. Along with the blood flow it reaches the liver of the new host. There it multiplies and changes shape too. After a point, these merozoites burst out of the liver cells, destroying the cells in the process. Then they attack the red blood cells. Inside the red blood cells they enter the next stage of their life cycle. They multiply and change shape here as well. This is the schizont stage which gives rise to male and female gametes. They are now in the host's blood ready to take another trip via another mosquito to another human host.....but...what is this...why am I the only one going on talking? Where is my companion? My co-anchor? Where have you vanished? Don't you know there is a programme going on? May you come down with Cholera! May Malaria get you!!

(Female Voice (FV) comes near from afar)---Why are you raving and ranting? Empty vessels sounds the most... why are you cursing me like this?

MV: Why shouldn't I curse you? You disappeared ...simply put all the responsibility of the programme on my shoulders and vanished!

FV: Well curse all you want. I shan't come done with Cholera...not even Malaria!! ---

MV: Why? I mean why not?

FV: I shan't get Cholera because I am careful about what I eat and drink...I maintain high standards of hygiene...that's why.

MV: But why not Malaria?

FV: Malaria? Very shortly, Malaria will not be able to infect anybody...let alone infect me.

MV: How so?

FV: Because a Malaria vaccine is about to enter the markets.

MV: What!! A vaccine for Malaria? Are you sure...there are about 6-7 stages in the life cycle of the malarial parasite, you know.

FV: So?

MV: So, the question is: which stage of the life cycle should the Malaria vaccine target? Plus there is another problem.

FV: And what is that?

MV: The malarial parasite keeps changing its morphology as well as its antigenic profile.

FV: What you mean is that just like the anti-malaria drug that become ineffective in a few years; the malaria vaccine too will stop working in time.

MV: Quite Right! Shows you decided to exercise your brain cells after all.

FV: Ah well...I have a brain so why shouldn't I use it? Now tell me why don't scientists find a vaccine for each and every stage of the parasite's life cycle?

MV: They have...that is they have made 5-6 types of vaccines.

FV: Ouch! You mean we have to take 5-6 injections just to stay safe from Malaria...and that too multiple times in a lifetime...oh my God!

MV: Yeah...yeah...that is exactly why scientists are looking for a safe and effective vaccine and hopefully they will create such a vaccine one day.

FV: You may think you are a genius but you are actually an idiot.

MV: (Annoyed) Why?

FV: You do not read the newspapers; you have no time to watch TV and the radio you own is broken and hasn't been working for who knows how long.

MV: What does that have to do with anything?

FV: That is why you do not know that Scientists in our country have been carrying out tests on the malarial vaccine that they have developed.

MV: Really!!!

FV: Why should I lie? Haven't you heard of Dr Sanjay Chitnis?

Announcer—Yes...yes...his name was in the news sometime back. Isn't he the person who did his Ph.D. in Physics from IIT but chose to pursue research in Life sciences?

FV: The very same. Dr Sanjay Chitnis. Scientist at the Delhi branch of the International Centre for Genetic Engineering and Biotechnology.

MV: God bless him! This is a matter of great pride for us.

FV: Indeed. He has bolstered national pride. He, along with Prof. Virender Chauhan, Deepak Gaur and many other co-workers has created the PvRII malaria vaccine that is based on Duffy-binding protein; a characteristic protein found in *Plasmodium vivax*.

MV: PvRII?

Plasmodium vivax **reason II**...It is expected that the vaccine will be available in the markets shortly.

- Amen to that.

-It will happen. It will certainly happen. Chitnis and his team have also created a vaccine for *Plasmodium falciparum*. It is called JAIVAC-1.

- JAIVAC-1?

-Yes Sir!!

--So let's introduce our audience to Dr. Chetan Chitnis and his co-workers.

--You? You are going to introduce Dr. Chitnis to the audience?

--Yes. Why not?

--Well you should meet him first, shouldn't you?

--Don't worry. I will meet him and I will introduce him to our audience too.

--Is that a promise?

--A promise it is.

Music. Change of scene...fade out.

Opening song...fade out

Anchor: --We are standing outside the International Centre for Genetic Engineering and Biotechnology.

Sounds of vehicular traffic on a busy road...fades out into the background. The muted sound of traffic remains throughout the scene.

Anchors chat.

--- Friends, as promised we are here to introduce you to Dr. Chetan Chitnis: a famous scientist in the field of vaccine research for Malaria.

--And that is why we are at the International Centre for Genetic Engineering and Biotechnology; Delhi.

--This is where Dr. Chetan Chitnis works and with whom we are going to have a small chat.

Music. Scene change...fade out

Opening song...fade out

- Inside the International Centre for Genetic Engineering and Biotechnology.
...appropriate music
- So friends, here we are: at the International Centre for Genetic Engineering and Biotechnology but we regret the interruption.
- Why?
- Didn't you hear what the gentleman just said...that Dr. Chitnis is not available at the moment?
- Yeah...but he also said...that Dr. Chitnis is expected shortly.
- That's it. That's just it...
- Sir, you are a member of this Vaccine group too. Won't you please speak with us...for our audience's sake...?
- --Yes. Why not?
- --So friends, while we wait for Dr. Chitnis, we take the opportunity to speak with **Dr. X.....**
-

Dr X may be a member of the Vaccine group at the Institute. Or a fictitious character...please use the name of Dr. X in the following conversation.

--Sir, please tell us how the Malaria vaccine story began.

--How did the idea of a Malaria vaccine originate?

Dr. X.....--Well...it was noted that people who lived in Malaria-prone areas or those who suffered repeated bouts of Malaria often developed a sort of immunity to it.

-Oh! You mean that if the malarial parasite re-entered their bodies they did not develop Malaria.

Dr. X.....--It would not be correct to say that they never (emphasis) developed Malaria. Actually later tests revealed that they could not resist the infection by the malarial parasites but yes, the severity of manifestation of the symptoms was either low or that

Malaria did not develop. The risk of death by Malaria is also quite low in such populations.

---Ah...and so the scientists thought that...

Dr. X (cutting in) Not only this...but when the antibodies recovered from the blood of such people were purified and injected into others, the recipients too developed similar immunity to Malaria.

-- Sir, ...ummm these anti...bodies....?

Dr. X: Actually our bodies have a full-fledged system to defend us against pathogens or foreign elements. This is called the Immune system.

-Immune system?

Dr. X -Yes the immune system. This system is activated immediately when a foreign body...be it a virus, a bacterium or a disease-causing multi-cellular organism enters our bodies.

-- And then...?

Dr. X --The body has many types of cells that work for the Immune system. One of these is a cell that engulfs the invaders and ingests it.

-Our body is simply amazing.

Dr. X Our bodies also manufacture a special type of protein called immunoglobulin that is designed specifically against these pathogenic organisms. These immunoglobins are the raw material for antibodies.

--How do these destroy the malarial parasite or the other pathogens for that matter?

Dr. X Every pathogen carries on its surface certain special types of proteins that we call antigens. The antibodies that the body makes are a sort of mirror image or say a shadow of these antigens. So, the moment the antibody comes in contact with an antigen it locks on ...forming an unit...

--So, in a way the antibody is the direct opposite to an antigen...in its makeup and its characteristics.

Dr. X: Yes and the immune system destroys this unit...effectively destroying the pathogen.

--But Sir, how does this help in creating a vaccine?

Dr. X: Very simply, understand that a vaccine is made up of dead or attenuated pathogens or the antigens associated with them.

--Attenuated...so that it cannot give rise to the disease?

Dr. X: You see, attenuated pathogens actually activate the immune system and the body makes antibodies against them or against the dead pathogens in the same way that it makes antibodies against living pathogens.

--But what about providing safety against diseases?

Dr. X: These antibodies may remain for years...even a lifetime in a person's body...ever ready to destroy the pathogenic antigen against which the body raised it.

---And thus keeping us free from the disease...

Dr. X. That's right.

Sound of footsteps. Khan enters

Khan: I was just passing by and thought I'd just pop in to your cabin. So... what's up?

Dr. X: Nothing much. My visitors are from Akashvani...they had come to meet Dr. Chitnis...

Khan: Oh!

Dr. X. But Dr. Chitnis has gone somewhere... he should be back shortly...so....

Anchor:...so we decided to make good use of the time by talking about the Malaria vaccine.

Khan: Proximity to Dr. Chitnis is making you a celebrity too, Sir.

Dr. X. You are a co-worker too...come in...sit down...oh, and let me introduce you...this is Dr. Khan...a member of our vaccine group...he works on a specific aspect of the preparation of the vaccine....and Khan, as you know, they are from Akashvani.

May use a genuine member from the vaccine group in place of the fictional Dr. Khan; or may use another person in studio interview.

Khan: So what were you discussing?

Anchor: We were talking about how vaccines are made and how a vaccine is being designed for Malaria.

Dr. X. Work on a vaccine for Malaria was begun in 1967 when scientists used radiation on the sporozoites of the parasites and then injected the living but attenuated parasites into some rats.

Khan: It was later found that about 60 per cent of the rats that had received such an injection developed immunity against Malaria.

Dr. X. Computational analyses later revealed that if a mosquito that had been exposed to such radiation, bit a person a thousand times then that person would become resistant to Malaria.

Anchors: But Dr. Khan, surely this cannot be a process of vaccination.

Khan: You are right, but this thinking did turn scientific attention towards making a vaccine. People started thinking that a vaccine for Malaria may be possible...and work started on many different types of vaccines.

Anchors: Sir, you did say different types?

Khan: Yes...this is because the malarial parasite passes through many different stages in its lifecycle...for example, sporozoites in the mosquito; merozoites that burst out from the host's liver cells; then, trophozoites or the stage spent inside the red blood cells...then male and female gametes.

Dr. X: So different antigenic materials obtained from the different stages were used by different groups, to develop different vaccines.

Khan: The Malaria circumsporozoite protein found on the surface of the sporozoites in the saliva of mosquitoes formed the base for many vaccines. These vaccines could protect a healthy person from Malaria.

Anchors: And what about the vaccines based on the stage inside the red blood cells?

Dr. X: The vaccine based on the stage inside the red blood cells or an erythrocytic Malaria vaccine can prevent an infected person from spreading Malaria.

Anchors: It seems Khan sir, that only if we have vaccines against each and every stage of the parasite's life cycle can we hope to be free from Malaria.

Anchors: ...and if all these vaccines could be combined into one vaccine...that would be the answer to all our problems wouldn't it? The one shot vaccine.

Khan: Yeah...and that is why scientists combined the antigenic materials taken from different stages of the parasite's life cycle to make one vaccine against Malaria.

Dr. X: Apart from this, genetic engineering techniques were used on the expressed protein to make a recombinant vaccine...ours is a similar kind of vaccine, isn't it, Khan?

Khan: Yes. We used genetic engineering to isolate the PvR11 protein from *Plasmodium vivax* to make the vaccine

Dr. X: The first vaccine against Malaria was made using the Malaria circumsporozoite protein expressed by the sporozoite stage of the parasite. However, the level of immunity conferred by this vaccine was so low that it was not even considered for field trials.

Anchor: ...So the first successful Malaria vaccine ...

Khan: Well, it would not be correct to say "Successful" because in reality we are still awaiting an ideal Malaria vaccine. However, the first Malaria vaccine to be clinically tested on human beings was the Patarroyo cocktail vaccine or SPF 66 vaccine.

Anchor: Patarroyo cocktail vaccine, Sir?

Sir: Yes. This vaccine was developed by Manuel Elkin Patarroyo in 1987 and it is called a cocktail vaccine because it uses antigenic materials derived from two stages of the Malaria parasite...the sporozoite stage as well as the merozoite stage.

Khan: Initially the prospects looked bright that this vaccine would stop Malaria in its tracks...but later studies revealed that this was not the case.

Anchor: So, the Patarroyo cocktail vaccine became of historical interest only, is that so Khan Sir?

Khan: Well you could say so in manner of speaking I suppose. But scientists made another vaccine—the CSP Malaria vaccine by combining Malaria circumsporozoite protein with antigenic material derived from the other pathogens. For example, the vaccine made using the Malaria circumsporozoite protein with antigen derived from Hepatitis B virus seems to have great potential.

Dr. X: **MLVac-1** is a vaccine that has been made by using antigenic material taken from all stages of the parasite's life. Trials are currently on...in rabbits.

Khan: I have to admit that, till date, we do not have any vaccine against Malaria that we can use on the public to immunize them...the way we do for many other diseases.

Anchors: What then...Sir?

Khan: Well, scientists began to feel that one vaccine based on the entire life cycle would perhaps never succeed.

Anchor: So what is the next step?

Sir: Scientists are exploring the possibility of using, not the entire antigenic material derived from the parasite, but only, small and significant bits to make the vaccine. These small and significant parts are called sub units and the resultant vaccine is called sub-unit vaccine.

Anchor: I see...sub-unit vaccine.

Khan: This uses the processes of genetic engineering to snip out a piece of DNA from any stage of the malarial parasite's life cycle. This bit of DNA is attached to the DNA of another parasite such as Hepatitis B virus. The Hepatitis B virus begins to express the protein encoded in the 'foreign' DNA, which are then harvested to be used for making the malarial vaccine.

Dr. X: Khan, this is why these are called DNA vaccines too.

Khan: You are absolutely right, Sir. The latest vaccine using this technology is the RTS, S recombinant Malaria vaccine. It uses Malaria circumsporozoite protein found on the surface of the sporozoites of the malarial parasite along with the DNA of Hepatitis B virus. This vaccine has been used in field trials in Gambia.

Dr. X: This is the same technique we have used to prepare a vaccine against the species *Plasmodium vivax*.

Anchors: How did you do that, Sir?

Khan: The Duffy binding antigen is found on the surface of *Plasmodium vivax* when it attacks the red blood cells of the host. The Duffy binding protein on the surface of the red blood cells attaches to it and allows it to enter the cell.

Dr. X: The gene responsible for expressing the Duffy binding antigen is situated in the *Plasmodium vivax* region Second or PVRO second of the genome of *Plasmodium vivax*.

Khan: Our group has been able to exploit this region by means of genetic engineering techniques to make a vaccine against *Plasmodium vivax*.

Dr. X: We have received cooperation from two other institutions in our efforts. These are: Programme for Appropriate Technology in Health and the Hyderabad-based biotechnology company, Bharat Biotech international Ltd.

Anchor: How successful will this indigenous vaccine be?

Khan: It is difficult to state categorically but we do have high hopes for its success.

Dr. X: We hope that in the next 5-7 years we will be able to make the Malaria vaccine available to the masses.

Anchor 1: You have indeed done a great job...repaid your obligation to the nation manifold...

Anchor 2: Not only we Indians, but the world owes you a debt of gratitude for this.

Footsteps

Chaprasi enters: Are the visitors waiting for Dr. Chitnis still here?

Anchors (simultaneously): Yes, please.

Anchor: Has he come back?

Chaprasi: Yes. He is waiting for you.

Anchors: OK, we'll come...thank you...both of you...you have given us valuable information

Music...fades out

Opening song...fades out

Anchors: Friends, we have with us today, the famous Malaria researcher, Dr. Chetan Chitnis of the International Centre for Genetic Engineering and Biotechnology.

Dr. Chitnis's interview.

Add here interviews of other members of Dr. Chitnis' group—for example, Prof. Virendra Chouhan, Deepak or other important colleagues.

Suggested questions for Dr. Chitnis:

1. How did you change over from doing Physics at IIT to Life sciences?
2. What was the inspiration behind your work?
3. Please tell us something about your childhood.
4. Where did you get your initial education?
5. What was the status of research when you entered this field and what is it now?
6. Please elaborate a little about your own work.
7. What is Duffy antigen and what is Duffy binding protein?
8. At what stage is the vaccine you have made?
9. What are the results of the trials?

10. What are your expectations from this research?
11. What is your vaccine named?
12. Is it a species specific vaccine for Malaria?
13. You have carried out research against *Plasmodium falciparum* too, haven't you?

Anchor: So...this was another page from the golden album of our history...C.V. Raman, Jagadis Chandra Basu, Chandrasekhar...the legacy continues. Another name has been added to the list of distinguished names.

Anchors: Who knows but the efforts of our scientists may cap all the efforts at trying to make a vaccine for Malaria; that their findings turn out to be the last step in designing an effective vaccine for Malaria.

Anchor: ...and turn out to be that golden episode in scientific discovery the brilliance of which continues to dazzle the world.

The episode you have just heard was dedicated to highlighting advances made in the field of Malaria vaccines and about the contributions of our scientists towards this effort. In the next episode of *Sunhere Panne* we will talk about: (Brief account of next episode).
