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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

A Hopeful Beginning for Malaria Vaccines

TOWARD MALARIA PREVENTION AND CONTROL

Change and challenge is in the wind as 2008 comes to an end, the same is true when examining this month's ReachMD XM160 special series - Focus on Global Medicine. We take a look at both the changes and the challenges impacting global medicine.

Each year over one million people die of malaria and it's complications. Can malaria ever be eliminated? Is malaria vaccine the answer? You are listening to ReachMD XM160, the Channel for Medical Professionals. Welcome to a special segment - Focus on Global Health. I am Dr. Mary Leuchars, your host, and with me today is Dr. William Collins. Dr. Collins is a Senior Biomedical Research Scientist at the Centers for Disease Control in Atlanta. He has been studying malaria for coming up to 50 years. Today, we are discussing what Dr. Collins describes as a hopeful beginning to malaria vaccine in the fight to eliminate malaria globally.

DR. MARY LEUCHARS:

Welcome Dr. Collins.

DR. WILLIAM COLLINS:

Good day to you.

DR. MARY LEUCHARS:

So, when was the concept of a malaria vaccine first proposed?

DR. WILLIAM COLLINS:

Well malaria vaccine development began probably in 1940s. The early work was done in monkeys, as they tried to develop a vaccine using monkeys and also with mice, but most of the early work was with the monkeys done at the National Institutes of Health. Actually, some work was done in World War II actually to find and make a human vaccine. Some experimental studies were done with humans at that time. But it wasn't very successful and the idea at that time was abandoned at the end of World War II because they had a great

drug, chloroquine was developed as a drug, and at that time with the development of DDT and chloroquine, the two more or less wonder drugs and insecticides, they thought malaria would disappear. They said stop training malariologist, malaria will disappear because we have the perfect insecticide and a perfect drug and actually they did. It was the two great things. Unfortunately, insecticide resistance developed and drug resistance developed. And therefore it was thought then in the recent years, we had to find something else, and then about 25 years ago, the interest became peaked again so we say when some studies in mice showed that you could actually develop resistance against the sporozoite stage, which is the first barrier that you would have. If you could stop the sporozoite, you could stop the disease right away. The people at New York University developed a vaccine using a radiated sporozoite and they could protect mice against infection, and that was the first beginning more or less of an effective vaccine to protect mice. But there is a great leap shall we say from protecting a mouse to protecting a human. Studies then went to monkeys. At the same time, people started working on blood stages and the all the other stages of the malaria parasite, mostly with monkeys and mice, but the thought was that monkeys were the closest thing to people and then the thought was that we could look at all the different stages and find whereabouts we could make vaccines that would protect mice or protect monkeys against infection or against disease and then we could translate that into a vaccine to protect people. So, for the last 20 years, in particular, there has been a lot of work to try and get a vaccine. But the thought was that we could stop the parasite at the very beginning, to stop the sporozoite before it could get into the patient and initiate an infection, that was the first stage, and this vaccine, the vaccine that is being talked about right now, the RTSS vaccine, is the first one that's gone to human trial, this is the vaccine against the sporozoite. Now there are other vaccines that are coming along, shall we say or being looked at against the blood stages, against the mosquito stages and that also have some interest and some promise. But there has always been the hope that if you can stop the parasite before it even initiates an infection, that's the interesting place and the one that would be supported, and this is the vaccine that's now being looked at and being tested. The RTSS is the first one to get extensive human trials and it's against the sporozoite state.

DR. MARY LEUCHARS:

Who is developing the RTSS vaccine?

DR. WILLIAM COLLINS:

The RTSS vaccine originally was developed by studies at the Army. They did some human studies and then it was picked up by commercial company, the SmithKline Beacham, the people who are commercially developing this vaccine, but is being supported by the Gates Foundation and other people who can put money because you have to look out at it from the standpoint is that I don't think anyone expects to make a lot of money out of it. Malaria is the disease of poor people. Most people don't consider it's a vaccine you sell to rich people; it's a vaccine you will eventually give to poor people. Most of the people who have malaria are terribly poor. So, even the development of a vaccine like this, which will eventually probably end up costing a hundreds and millions of dollars to develop, is for people who probably can't afford it in the end anyway. So, it's up to probably government organizations and places like Gates people do it and it's remarkable that a company such as SmithKline Beacham has put so much effort into this. It's really remarkable that they have committed themselves to do this.

DR. MARY LEUCHARS:

How many studies have been conducted using the RTSS vaccine to-date?

DR. WILLIAM COLLINS:

I don't know how many studies. When you start, even they have gone through mouse studies and human studies, but the studies in Tanzania, which is the first big one that we know about, it got a lot of write up several years ago, showed that it gave about 30% against clinical disease and 40% against new protection. Now the two trials that were just reported this last week at the American Society of

Tropical Medicine and then they are ones that we had an opportunity to review and then doing on Journal Medicine, report better than 50% in both of them against infection. Now this is hard to assess a vaccine when you are also doing control, you know, it's difficult to assess anything when you ethically have to have bed nets and insecticides at the same time. So, there is not a lot of malaria in the area where they are doing their assessment. It's hard to assess a vaccine when at the same time you are having your children sleep under bed nets and you are using control methods such as drugs when every one gets, anyone shows any sign of a disease. But ethically, you must conduct a trial at the same time if you are controlling the same disease you are trying to assess a vaccine. But even under those conditions, it showed that they were getting protection. So that it's really remarkable that in an area where they are having control activities, when they superimposed a vaccine into those areas, they were able to still find that the vaccine was having beneficial effect. Now the next stage III vaccine trial, which is coming up, which will have probably 10 to 13,000 people every child will be sleeping under a bed net at the same time, but, we will hopefully be able to demonstrate that the vaccine is still working. This vaccine is doing what we all hope, everyone hope, will show that if you could stop the sporozoite you can stop infection. If you can stop infection, then you have a beneficial effect. Now, this is designed by using a small piece of protein that's on the surface of the sporozoite. There is another vaccine that is coming along that is using a whole sporozoite, which has been inactivated by being irradiated. Its difficulty is that it needs a cold chain. It has to be used the radiated sporozoites, as they are kept frozen and then the patient is immunized with frozen sporozoites. It has been shown to work in human volunteers, but it's difficulty with that vaccine is that you have to deliver the vaccine under a frozen state, but the thought has always been that frozen sporozoites themselves will have the whole protein. This particular vaccine, RTSS vaccine, is a piece of that thing that has been synthetically produced. It is a 4-amino acid stretch that has been repeated, made chemically repeated.

DR. MARY LEUCHARS:

If you are just joining us, you are listening to a special segment, Focus on Global Health on Reach MD XM160, The Channel for Medical Professionals. I am Dr. Mary Leuchars, your host, and joining me today is Dr. William Collins from the CDC. We are discussing malaria vaccines and their role in eliminating malaria.

Dr. Collins, with regard to the vaccine what's the duration of efficacy of the vaccine?

DR. WILLIAM COLLINS:

Well I don't know if they know how long it will be effective. When you design or when they design the trial, they say the beginning and end of the trial and that was just for logistic reasons of course. You know, it's difficult to say, well we will run a trial for six months, we will run a trial for nine months. We have to find a beginning and an end of a trial. These trials, you know, weren't designed to run to the very end to see, you know, whether the vaccine would run six months to years or not. But most of the thought is on all of these and there are experimental studies, which indicate that this vaccine and all of these anti-sporozoite vaccines are boosted when live sporozoites are introduced so that when a patient or a child out here is fed upon by sporozoites in the field, they will probably be boosted by those sporozoites. So, in the absence of any infection or any malaria in the area, they will probably last anywhere from six months to a year, may be as long as two years. But if there are live sporozoites introduced in which the surface coat, which is of the sporozoite is put in as a booster, then it would last longer. So, experimentally the thought is that in an endemic area, they will last much longer than in a nonendemic area. But experimentally they are designed to last probably in the range of a year to a year a half to two years.

DR. MARY LEUCHARS:

Are there any safety concerns with the vaccine?

DR. WILLIAM COLLINS:

All of these trials, these two trials in particular and the one before have all indicated these vaccines are very safe. They were given in conjunction actually with other vaccines to make sure they didn't interfere with the normal vaccines. The normal expanded program immunization schedule, which was regular childhood immunizations were given at the same time, so it didn't interfere with the normal vaccines, which were been given. The hope is that it will be given along with mesals vaccines and the tetanus vaccines, diphtheria vaccines, and other vaccines that are being given. So, therefore this vaccine was given with other vaccines to make sure that they didn't interfere and that those are the vaccines didn't interfere with it. So, they looked to be extremely safe and they have to have an adjuvant of some sort. The fact is that the small peptide vaccines are ineffective without an adjuvant. That's one advantage possibly of the whole sporozoite vaccine irradiated one that may come along in testing. They may not need an adjuvant, but the small peptide ones absolutely need an adjuvant.

DR. MARY LEUCHARS:

How soon do you think will say this vaccine in clinical use?

DR. WILLIAM COLLINS:

Well this one that they reported on here this RTSS is going to phase III, I think next year, so that at the end of that trial, if it is as successful as these two were, I would image at the end of that trial, you know, probably be ready for widespread distribution. I can't say why we should hold it up any longer.

DR. MARY LEUCHARS:

How close do you think we are to global eradication of malaria?

DR. WILLIAM COLLINS:

That's a problem when you talk about eradication. The Gates Foundation says we should have eradication. But I think elimination from many areas is very feasible. But eradication would mean you eliminate the thing from the world. I don't think you are going to get rid of this particular disease from many isolated areas. That's my personal opinion. But in most of the important areas, it will be brought down.

DR. MARY LEUCHARS:

Well my thanks to you Dr. Collins. We have run out of time. But thank you for being our guest.

DR. WILLIAM COLLINS:

Thank you so much for talking with me. I appreciate it very much.

DR. MARY LEUCHARS:

We have been discussing malaria vaccines in a hope for future eradication of malaria globally. I am Dr. Mary Leuchars. You have been listening to a special segment - Focus on Global Medicine on ReachMD XM160, The Channel for Medical Professions. We welcome you comments and questions through our website at reachmd.com, which now features our entire medical show library, in on-demand podcasts. Thanks for listening.

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