An old killer-malaria learns new tricks

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SPEAKERS
Maggie Fox, Karen Barnes

Maggie Fox 00:00
Hello and welcome to One World, One Health where we take a look at some of the biggest problems facing our world. I'm Maggie Fox. This podcast is brought to you by the One Health Trust with bite-sized insights into ways to help address challenges, such as infectious diseases, climate change, and pollution. We take a One Health approach that recognizes the planet, the animals, and people living on it and the climate (and) environment are all linked.

Malaria is a big killer; about half the world's population—3.2 billion people risk infection with malaria and 247 million people come down with malaria every year. Malaria killed more than 600,000 people in 2021, (around) two thirds of them (were) young children. Two vaccines can prevent malaria, but they don't work perfectly and only protect people for a limited time. Insecticide-treated mosquito nets also help as do other measures to control the mosquitoes that spread the malaria parasite. But as the numbers show, hundreds of millions of people need treatments for malaria.

There are several different types of drugs used to treat malaria, but the parasites that cause the disease can develop resistance to them. One of the last lines of defense are the artemisinin-based drugs derived from a plant commonly known as sweet wormwood.

Karen Barnes is a Professor of Pharmacology and Founding Director of the Collaborating Center for Optimizing Anti-Malarial Therapy at the University of Cape Town in South Africa. She specializes in the treatment of malaria. Professor Barnes, thanks so much for joining us.

Karen Barnes 01:43
Thank you for having me.

Maggie Fox 01:44
The COVID pandemic has made many people forget about malaria, but it's still, of course, a huge threat. Can you tell us a little bit about how big of a threat it is?

Karen Barnes 01:54

Your introduction summarize very well how big a burden malaria is. And to make things worse, during the COVID pandemic, there was a marked increase in the number of malaria cases, probably about an extra 15 million malaria cases a year and an increased number of malaria deaths in the order of another 60,000 deaths. We know that a child dies from malaria every minute of every day.

And so, I don't think we can allow COVID, as big a problem as it was, to distract us from the important goals of reducing the burden of malaria. We worry that our weakened health systems, the diverted funding from COVID is going to slow our recovery efforts to control and eventually eliminate this disease.

Maggie Fox 02:43
So, what caused this big increase in cases and deaths? Was it the distraction of COVID?

Karen Barnes 02:49
Partly, I think that the health system really struggled with COVID understandably. People were given messaging about if you have fever, flu like illnesses, stay home, don't seek treatment, whereas we know for malaria, we want them to get treatment early before their disease becomes severe, and they are at risk of dying from malaria.

Similarly, to control malaria, we need malaria control programs to be able to reach people in their homes, use insecticides to reduce the numbers of mosquitoes around, encourage the use of bed nets. So, many aspects of the control program were compromised on both sides—on the side of the health systems, but also the community's willingness to participate in those programs totally understandably. But it created a double whammy for the system.

Maggie Fox 03:37
How difficult is it to treat malaria?

Karen Barnes 03:40
Until recently, it was remarkably easy to treat this potentially life-threatening disease. If malaria is diagnosed early enough, it can be cured with only three days of treatment—treatment that can be given at home (tablets or syrups for young children).

However, as you mentioned, the malaria parasite is now learning how to survive the treatments that we have in an increasing number of countries. And this drug resistance can make treating malaria much more difficult.

Maggie Fox 04:11
What causes this resistance?

Karen Barnes 04:14
There's a number of factors that contribute to drug resistance. Most of them relate to how well we use our medicines. So, we know that the artemisinin should never ever be used on their own (and) they should always be used with another medicine. Secondly, we know that resistance develops more rapidly when patients don't get the full dose.

For example, they stop taking the drugs when they feel better even though the treatment hasn't been completed or they get given too low a dose by mistake or to try and save money or they get given a poor-quality medicine that doesn't contain the full dose. So, we must remember how well we need to use malaria treatments and we should only use these life-saving drugs when a malaria infection has been confirmed in a blood test and lots and lots of other illnesses that can cause fever and flu like illnesses.

So, we don't want to be wasting drugs when people don't actually have malaria. Given that imminent threat of resistance, it's really important for all of us to work together now to make sure that the currently available medicines keep working until new drugs are developed. And we think that will still take a few years.

Maggie Fox 05:25
You mentioned this use of artemisinin drugs with other drugs. Is this combination therapy like combining? Would it be combining a quinine-based drug with an artemisinin-based drug?

Karen Barnes 05:35
So, yes, the malaria treatments are currently used in combination. As you mentioned, the artemisinin, which is the fastest acting malaria drug that's currently available, is combined with a longer acting drug that can ------ up any remaining parasites and prevent new malaria infections for a while. And this combination has really been a game changer for malaria patients. And it's a big part of how we were able to reduce the burden of malaria globally since the turn of the century.

However, quinine was never chosen for these combinations as it's really not an ideal drug. It causes lots and lots of side effects and needs to be taken for at least a week. Because it causes side effects, people find it really hard to keep going. So instead, we've combined the artemisinin with other drugs that are better tolerated and only need three days of treatment.

But now that artemisinin resistance has become a real problem for us, it's threatening the effectiveness of these artemisinin-based combinations that are the backbone of all of our current treatments, both for uncomplicated malaria and for severe life-threatening malaria.

Maggie Fox 06:46
How worrying is it that artemisinin resistance is now being seen in parts of Africa?

Karen Barnes 06:53
This situation is very very worrying indeed. As you mentioned, at least 95% of cases and deaths from malaria occur in Sub-Saharan Africa. So, the impact of our drugs becoming less effective is going to be much greater here than in areas like Southeast Asia or South America where malaria cases are far fewer. Many African countries have detected malaria parasites with the mutations associated with artemisinin resistance, which means that the rate at which the artemisinin can kill those parasites is significantly slowed.

We are also starting to see reports from studies where more than 10% of patients are failing the first-line artemisinin-based combination treatment. And this 10% threshold is used by the World Health Organization to indicate when a change in malaria treatment policy is needed. But because the artemisinins are the best option that we have, that change is not so easy to effect.

And we have to look at multiple strategies to use medicines in more effective ways to control or prevent deaths from malaria while we wait for the development of new drugs.

Maggie Fox 08:10
What would some of these strategies be?

Karen Barnes 08:13
So, we thought it was a major advance 20 years ago to be using two medicines together instead of just one medicine on its own like we used to with things like chloroquine. And now we know that maybe that's not going to be enough. We need to use perhaps a third medicine in the combination treatment or we should be using multiple different combinations of artemisinin with different partner drugs either alternating them over time, over place, different age groups getting different drugs, so that the parasite that's not killed with one drug will be killed by the other drug.

We also need to combine that with efforts to really really limit the transmission of malaria—whatever we can do to prevent malaria to stop ongoing transmission to reduce the mosquito burden. All of that will stop the spread of resistance to places that really really cannot afford to have failing artemisinin combinations.

The history that makes us all wake up in the middle of the night and fear dire consequences about losing the artemisinin combinations is that when we started to get to high levels of chloroquine resistance at the end of the 1900s, there was a two-to-three-fold increase in hospital admissions and deaths from malaria. And in some areas, they found a six fold increase in malaria deaths. And that really shows you that millions of deaths can result if we don't keep on top of the malaria situation and keep using our medicines in a way where they can remain effective.

Maggie Fox 09:48
You're working with a number of groups to try to coordinate these changes in treatments. Can you tell us a little bit about that?

Karen Barnes 09:54
Certainly. I think one of the joys of the malaria community is that, I think because it's a poverty related disease, is a natural tendency towards collaboration and partnerships. Artemisinin resistance emerged first in Southeast Asia. And so, those of us sitting in Africa have been watching for a long time worrying about what's going to happen when the resistance gets here. And we've built up strong links with people that developed experience in Asia.

We've now also got links with people in East Africa where the bulk of artemisinin resistance seems to be reported so far, and we've built a consortium to link together the malaria programs and the scientists that can support them in southern and East Africa with those in Europe and in Southeast Asia, who are

going to help us tackle drug resistance in this region and really do everything we can to prevent it from having a very very heavy burden that was caused by chloroquine resistance.

Maggie Fox 10:58
Will the new vaccines make any difference?

Karen Barnes 11:01
Indeed. I think to tackle malaria, we need a full toolkit. We need vaccines, we need drugs, we need insecticides. And after decades of development, we finally have two vaccines that are considered effective and safe. One (has been) very newly announced; it still hasn't gone through the hoops of being accredited by the World Health Organization. One that was accredited a couple of years ago. And these should reduce the burden of malaria.

They should be able to prevent malaria cases and they should prevent hospitalization from malaria. And then that will put less pressure on the treatments for malaria because there should be fewer cases. It will, however, take some time before the vaccines reach their full impact. It takes a while to roll out a new vaccine.

The COVID pandemic definitely detracted manufacturers from making vaccines for anything other than COVID. So, we haven't got a great supply of the first vaccine yet. Hopefully, the second vaccine being accredited will increase supply and by the time they're rolled out, they will join our fight to reduce the burden from malaria. However, even then, we will continue to need effective drugs to cure malaria patients and effective insecticides to kill the mosquitoes that transmit malaria.

Maggie Fox 12:20
That was very informative, Karen. Thank you so much for joining us.

Karen Barnes 12:25
My pleasure. Thank you for having me on your show.

Maggie Fox 12:29
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Ramanan Laxminarayan 12:47
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