



Insect Hour

Janet Hemingway: The Mosquito Diaries

Transcript

Um, good afternoon everyone. Thank you for joining us today and welcome to this month's Insect Tour. Just a couple of housekeeping notes before we begin. Today's session is being recorded and the recording will be available after the event. If you have any questions during the talk, please pop them into the chat and we'll come back to them at the end of the session. Before we hear from our speaker today, I'd like to share a few updates from the Royal Entomological Society.

First of all, a reminder that Insect Hour takes place on the 2nd Wednesday of every month from 1:00 p.m. to 2:00 p.m. Our next talk will be on the 8th of July and will be given by Deepa Sapati. We have lots of exciting talks planned and more speakers will be announced soon. If you'd like to hear about future talks and register for upcoming sessions, I'd encourage you to scan the QR code on the screen.

Membership is open to anyone interested in insects and entomology, to all of our current members, thank you for your continued support. And if you are not yet a member, membership starts from just £17 per year and students can join free in their first year. We also currently have a 20% discount available for new members, so if you are interested in becoming more involved with the society, please do scan the QR code to find out more. As a member, you'll get access to our entomological library and all of our eight scientific journals. So, you'll also receive discounts on events and publications be eligible to apply for awards and research grants and receive updates to Antenna magazine and our newsletters.

Next slide, please. We are also looking forward to insect week taking place from 22nd to the 28th of June. If you'd like to learn more or get involved as a volunteer, please scan the QR codes on the screen. I'd also like to draw your attention to ENTO26 flagship annual conference this year. It will take place from the 8th to the 10th of September at Cardiff University. There will be keynote speakers, member symposia, workshops and plenty of opportunities to network. Registration and call for abstracts is now open. The abstract deadline is the 12th of June this Friday and the early bird registration deadline is the 3rd of July. So again do scan the QR code and find out more if you are interested.



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We also have several events coming up later this year. These include events organized by our special interest groups and opportunities to hear about current research and developments. So if any of those sound interesting please do scan the QR code and have a look. And finally, if you're thinking about publishing your research, our journals offer high quality peer review, fast turnaround times, open access options, and a global audience. They are a great place to share entomological research and support the wide entomological community.

Now, it's my pleasure to introduce today's speaker, Professor Janet Hemingway. Professor Hemingway is the founding director of ICON and former director of the Liverpool School of Tropical Medicine. She has spent much of her career working on mosquito born disease sus and insecticide resistance and vector control. Her work has contributed to improving mosquito control and public health programs in many parts of the world. Over the years, she has led major international research programs and has also served as an advisor to the Bill and Melinda Gates Foundation on neglected tropical diseases.

Professor Hemingway was awarded a CBE in 2012 for her services to the control of tropical, disease vectors. She's also a fellow of Royal Society and a past president of the Royal Society of tropical medicine and hygiene. Today she'll be taking us through 50 years of mosquito research and some of the biggest challenges in controlling these insects.

We are delighted to have her with us today. So, please join me in welcoming Professor Janet Hemingway. Janet, over to you.

Thank you very much. I'm going to share my screen hopefully. Hopefully that is a full screen for everybody. So thank you ever so much for the opportunity to talk to you a little bit about the 50 plus years that I've had a relationship with this little insect beast. This is an 80s, but I've been working on anophles and other insects.

But I actually started back in 1979, when I was an undergraduate and somebody came to give a talk about mosquitoes. And as a geneticist then I thought why am I going to be working on *Drosophila*? Why don't I work on mosquitoes. So at that point I started working on a mosquito



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called toxin kites revipalpus which is a predatory mosquito that predate on other mosquitoes, and had fun doing that with my undergraduate projects and then moved on in to a PhD on insecticide resistance under the late George Davidson who demonstrated that resistance to insecticides was genetically inherited at that point that deserved a paper in nature.

You need to do a little more than that now to do that, but in 1982 I then went out into the field in Tanzania and that really hit home to me that what I was doing working on mosquitoes was important because it was at that our ability to control these insects. And at the time, my former supervisor had warned me that nobody was really interested in insecticide resistance because there would be a pipeline of new insecticides coming through. So, as we got resistance to one insecticide, we could just switch to the next one. It became very obvious quite quickly to me that that really was nonsense that the target product profile for industry for insecticides had screeched for agricultural insecticides away from the big blockbuster compounds that killed any insect to things that were much more specific and that the new agricultural insecticides that were coming through the pipeline of all the companies were not going to be optimum for controlling mosquitoes.

And so we had almost a 20-y year period I think where resistance to the standard insecticides that we had was clearly building and we had no real new insecticides coming through. There was also an issue with the formulation of the insecticides that we did have. We were spraying them on walls inside people's houses to try and control the insects and the formulations that we had probably if you were lucky lasted for about a month and yet they were only spraying these once every three or six months. So we needed better and longer lasting formulations.

So I and others had been saying to anybody who wanted to listen be it the agrochemical companies or WH or others that somebody needed to start and develop new public health and exercise. The agrochemical companies would tell me that they were never going to do that on their own because there just wasn't the financial incentives to do it. WH and others said it wasn't possible to do that. we were just going to have to manage with what we had.

But in 1998, I was lucky enough to be invited to Seattle as part of a very small group of about 20 people by Bill Gates senior, the father of the Bill Gates that everybody knows. and they



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were at that point thinking about merging two foundations, Bill Senior's Foundation and a Gates Foundation that supported libraries into something that has now morphed into what everybody knows as the Gates Foundation. And as part of that, they were interested in taking on some major public health challenges.

So, they already honed in on malaria and were asking the question of the 20 of us that they flew into Seattle. What would you do to actually improve our ability to control malaria? We were locked in a room there for about three or four days and came up with a strategy document for them that we then passed through and it was clearly up to them what they did with it. But after they had launched the Gates Foundation I went back to them in 2003 and asked them to fund something called IVCC which is the innovative vector control consortium, and that was there to really start and tackle this question of how and with whom should we develop new public health insecticides?

ICC was actually formed in 2005. It took me a couple of years to persuade them to give me the first check for \$50 million, and the check came with a proviso. So I was told I had six months to engage at least one major agrochemical company in helping to develop the new public health insecticides and formulations or they would want their money back and would close the newly established public private partnership.

I managed to persuade the people in buyer to come along and start and work with us, and then shortly after that we had the groups from Senta and I noticed Mark Hoppy was joined us in the audience and Sunumitomo. So we then had a range of different insecticide companies who would start and work with us on the new formulations and screening their libraries of compounds to see whether we could find potentially new public health insecticides that were already there in the chemical libraries that these companies had had. So move forward quite rapidly and this is the current portfolio that we're allowed to put out in the public domain for IVCC.

What you can see there is that we've succeeded in some areas very well. So if you look right at the bottom in terms of the indoor residual sprays there are a whole range of different insecticides there where we've improved the formulations and the standard formulations now



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for IRS really do last for a good 3 to six months when you spray them on the wall. So a big tick in that box in terms of the formulations.

With the active ingredients we had a range of act new activities moving through the portfolio and there are a couple of those there that have made it as far as the development stage. That is still problematic. the market forces are still such that it is difficult for the major ad chem companies to guarantee that they will actually bring these into the market and sell these into the market.

And so IVCC has some of the IP for some of the compounds that have moved through there. Others are still sitting with the companies that have developed those alongside IBCC. The insecticide treated nets when we moved into this area only had pyrethroids on there. We've been instrumental in getting new dual treated nets through into the market that haven't just got pyrethroid on. The first generation had pyrethroids plus praziquantel butoxide. the next generation have other insecticides on those nets and they are now allocating probably about 80 to 90% of the market for bed nets. We looked at spatial emanators and a lot of excitement at the moment about the Johnston and Johnston product that is coming through onto the market as a spatial emanator and also took on trying to validate and improve attractant toxic sugar baits to take through.

So all in all a reasonable success there I think with IVCC. I ran IPCC for the first 15 years and then passed that over to Nick Ham and then more recently to Julian who are taking that forward and it's still operated out of the Liverpool School of Tropical Medicine established as a separate charity and company in its own right but still with a job to do in terms of getting those compounds through to market and really making sure that we actually improve insect control.

And then for a couple of years I concentrated on just finishing off the last things I needed to do as director of the school of tropical medicine before I decided it was time to have fun with the science towards the tail end of my career. And so in 2020 I linked up with friends from industry, academia and the local NHS and set up another product development partnership that I'm currently running which is ICON the infection innovation consortium.



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This is way broader, so I've moved away from just doing vector control, and we're also developing new vaccines, new drugs, new diagnostics, but there is still quite a bit of vector control within that portfolio, and so I just wanted to give you a quick flavour of the sort of thing that we're doing with the new icon consortium which really picks up and takes on some of the gaps that ICC itself are not covering because I didn't want to overlap with their activity. So the icon consortium is actually as I say led by the school of tropical medicine has the University of Liverpool in there. Evitech a big contract use research organization unilver personal care products infect therapeutics which is a small theme. our local NHS trust, LifeArt, which is the spin out from the medical research council in the UK and then more recently MMV, the medicines for malaria venture based in Switzerland has joined the consortium.

Back in 2020, the UK government gave me 18.6 million to set that up, and we got a further 6.6 million from the European Union. Today, the portfolio that we're running is worth just over 360 million and we're working with a couple of hundred companies. We've got 36 products through to market. But in terms of the entomology, we're really working at the back end of that activity where you've got your product and you want to see how well that product is working. And so there were two obvious areas there that I wanted to tackle.

Because when the companies got their new bed nets in particular to the point that they wanted to sell them, who at that point said you had to do three large randomized control trials before they would validate those nets in a format that the companies could sell them. And the cost of doing those trials was enormous. and the data that you got from them if you tried to run those trials against a background of a country that was already doing its own malaria control was very patchy. So it really wasn't working and the products had stalled at that very late stage. These are just where the companies are that we're working from icon.

So scattered across the world it's a global sort of activity that we've got running. So what I wanted to do then was actually think could we look at novel methods of doing the randomized control trials for the assessment of bed nets and compare the efficacy of different nets under different conditions. So we set up in Uganda where they clearly got very high malaria transmission where we knew the ministry of health very well and we were linked up with the local research organizations in Uganda and we then got give well and against malaria



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foundation to work with us. So they were providing the bed nets and the ministry of health agreed that they would actually distribute them across the whole of Uganda in the pattern that we requested so that we could actually embed the randomized control trial in the operational activity of the country itself.

Effectively it was the world's largest randomized control trial. We were able to show then at scale that the PBO treated nets in areas where we had high levels of pyrethroid resistance were significantly better than the pyrethroid nets alone and the level of data that we got from that trial it's now published in the Lancet was such that Uganda and all of the countries around went back to WHO and said this is one trial but it is of such scale and if you look at the different areas of Uganda comparing high and low transmission where you've got different mosquito species that you WH now need to put in a recommendation for the use of these nets. It transformed the net market such that the PBO nets could then be bought by global fund and others that needed that WH recommendation.

And the benefit of that was that it was about a fifth of the cost of doing the control trials that WH had actually requested and the data quality was better. So we're now using that model and we've simplified it further. We have three ongoing randomized control trials actually in the Democratic Republic of Congo comparing some of the new nets that are coming through and some of the different PBO nets and different chlorfeniramine mix nets against each other to see how well those are performing in different areas in areas of high transmission.

Alongside that, we really wanted to know what was going on with the formulation of the insecticides on the nets. Because if you actually looked at the rate at which you lost the insecticide from the chemical analysis then that differed depending on the sort of nets that you were looking at. So the data you've got here is just comparing permanent 2 and permanent 3. They start at different concentrations of py of deltamethrin, and if you look at what happens with the unused net, which is the orange line at the top, then the insecticide stays quite happily on the net for 3 years. If you look at what happens to it as the net gets used operationally, then that insecticide concentration, it declines quite significantly.



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An improvement between the permanent 2 and permanent 3, but still quite a big rate of decline, and then if we looked at what was going on with the pipinobutoxide on those same permanent three nets, you can see from the graph on the right hand side that as you use the net, the rate of pepperontoxide decline was more substantial than the decline rate of the pythroidid itself.

So still some work to be done on the formulation. We also looked at different kinds of nets. So this is a different net manufacturer and the dotted lines show you the optimum concentration that they're aiming for of both the alpha cyclomethrine which is the green line and the pepperonut which is the orange line. You can see even at baseline these nets were underdosed by the time they got out to the field with the PBO and that PBO declined very dramatically over time.

So we actually looked then at what was going on the surface of the nets, things very different depending on the net. So some of the nets, these are the permanets. You could see that the insecttoide was crystallizing onto the surface of the net and the PBO was co-crystallizing along with the pythroidid, but you would lose the PBO from those crystals much quicker. If we looked at what was going on with the Verolins and some of the others, we were not getting co-crystallization on those nets. So the surface chemistry is different. So we are at the moment just comparing how well those nets work operationally in the field. I'm now going to switch t and move on to the indoor residual spray side of the activities.

This is just some data from India that basically modeled out and it's actually for visceral lucrinasis that you needed to get a constant 60% coverage with indoor residual spraying at the right target dose of insecticide to be able to get control of visceral leucanis across India within different provinces and what we were able to demonstrate working in India over a period of time was that that dosage really wasn't being hit. So, the coverage claims were high, but the optimal dosage of things exercise on the walls was nowhere near where it should be, and I'm going to skip that from time.

So, one of the issues there was quality assurance. WHO suggested if you wanted to quality assure what you were doing for indoor residual spraying you should take susceptible insects, put them in a cone, put them on the walls of the house and see whether they died in in a time



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period. Nobody really does that because you'd have to raise susceptible insects. You'd have to move them to the field site. You'd have to run at the assays there.

The WHO also suggests that you put a filter paper on the wall and when the spray team goes around they'll spray the filter paper as well as the wall. Then you can go and collect the filter papers. You can do HLC analysis on the filter papers and see whether you've got the target dose. Well, that's fine, but the spray people see the filter papers. They overdose the filter papers. You take the filter papers off the wall, you send them back to the lab to do the HLC, and a month later you get the results back. and that's too late to do anything sensible about it if you're under or oversprayed within the system.

So, as part of the program, we decided we wanted a simple sensor that we could actually take into the field to actually measure insecticide concentrations on the walls themselves. And so, the handheld detector that you can see here has a simple simple traffic light. If you get a green light, then you're at the right target dosage. If you've got a red light, you're overdosed. If you've got a yellow light, you're underdosed or there's no insecticide there, and that works within 5 seconds. So, the spray supervisor can go around and check exactly what is on the walls. We set this up for alpha cythrine going through various iterations. So, the picture on the left is the first detector we had.

We now have a much smaller handheld detector that operates on a couple of A4 batteries, and we've been funded by the Gates Foundation and others to expand the range of this so that we can not only use this for alpha cythrine, but for all the newer insecticides that are there for the indoor residual spray programs. So the final device is actually going out to Nepal this year and this is the picture of the device here on the left for them to do the final validations and see how long it takes them to break it using it operationally over the course of a couple of years, but we now believe we have a quality assurance system for being able to measure insecticides on different surfaces independent of what the house surface is. Having got the technology working for that we got challenged to see whether we could do something on the paracetology side.



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And so it struck us that we could use the same technology for actually trying to measure microfalaria or malaria parasites in blood without needing physically to take a blood sample. Now that's important if you're looking at the lymphatic variasis program because there they're going and taking blood samples in the middle of the night to try and determine whether they've got elimination of the disease, and so we set about designing a wearable sensor again through various stages. The stage four here which is right over on the right hand side is just something that you can strap on for the arm.

It's still bigger than we would like it. It works. We've got field data showing that it's operational, but if you've got to sleep with that on, it tends to get shuffled around a bit. So right now in the lab, we're turning that into something that is about a hundredth of that size, and it's almost like a patch that will go onto the arm that you can wear and then download the data.

And again that will be tested out in Nepal and out in India in about 18 months time to see whether we can change the way that we can monitor how well we're controlling some of these vector-borne diseases, and then finally in this real whistle stop tour, I've got used to working at scale with different things, but everybody is getting really excited about what you can do with AI, robotics, machine learning. We've put been putting the AI and machine learning into the devices that you've just seen in terms of those diagnostic detectors, but we decided we could actually take this a stage further in terms of what we were doing by way of the design and development of new drugs, new vaccines, new potential insecticides as we're going through.

So we've just raised 20 million pounds to set up a large category 3 infection research laboratory at the school. It will be open in September and it's the first of its kind operating at that size and scale. It'll be able to handle all of the vector-borne parasites, viruses and the human organoids linked up with those and mosquito tissues linked up with those in a self-contained modular system. So that I think will be an exciting way of going forward that we hope will speed up some of the activities that we've got ongoing with colleagues around the world who are interested in developing some of these new technologies. So I haven't been keeping track on time.

I'm hoping I've roughly kept a time with that whistle stop tour, but I hope I've given you a feeling of the way that a career in entomology can take you.



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So back in 1979 when I started my first work on the predatory mosquito, I had no idea that it would take me to the places that it's taken me and to be able to work with some of the people and technologies that we have over many many years. But it's been a great time to be involved in control of some of these insects.

We still haven't got there. Malaria is still a problem. It's still less of a problem than it was when I first started. but no child should really die of malaria and we still have half a million of them each year dying and those numbers are starting to go up again. So we need to make sure that the technology that we got is deployed. It's deployed well, and that we're actually keeping pressure on the international communities to take these through and make sure that we actually control these diseases.

I love the mosquitoes. I'd rather they didn't transmit the disease, and if we can get to that point where we can live happily with them, and they're no longer killing large numbers of children across Africa and Asia, then I think all of us will be happier for that. So, thank you for your attention.

More than happy to take any questions on some of the activities that have been ongoing over that time.