

TPWKY

(This Podcast Will Kill You intro theme)

Erin Welsh

Hi, I'm Erin Welsh and this is This Podcast Will Kill You. I'm back with another bonus episode in our mini series of bonus content that we'll be releasing over the next few months. In case this is the first bonus episode you're tuning into and you're wondering what the heck is going on, I'm using these episodes as an opportunity to explore more about whatever disease or topic we covered in our previous week's episode and also to get to chat with experts about their jobs, their hopes, their dreams, whatever comes to mind. If you've listened to the podcast before you know that I'm kind of a relentless question asker and so instead of just pestering Erin Updyke with all the questions, I'm saving some for these episodes. And so far I've gotten to have some great conversations with people in very different careers studying or working on very different problems. And this week I am so excited to have yet another fun conversation and learn a whole lot more about another topic. So what am I going to be talking about today?

This week really kind of picks up where we left off in our most recent regular season episode which covered a virus of rabbits called the Myxoma virus. If you haven't listened to that episode yet, I would recommend checking it out before listening to this just because there's so much more to that story but I'll give a quick recap here. The Myxoma virus is a type of pox virus that can cause severe disease in some species of rabbits and it became internationally famous back in the 1950s when it was introduced to Australia as part of efforts to control the invasive European rabbit population. What had started out as a handful of European rabbits introduced to Australia in 1859 had within a few decades grown to an absolute ecological and agricultural menace. Entire ecosystems were disrupted, native animals experienced tremendous population declines, many plant species were driven locally or regionally extinct, and huge tracts of land could no longer be used for agriculture.

The introduction of the Myxoma virus did help to drive down or stabilize rabbit populations but over generations the virus lost a bit of its impact as both rabbit and Myxoma virus adapted to one another. The deadly virus was no longer as deadly as it once was and the rabbit was no longer as susceptible as it used to be. So when another lethal virus of European rabbits was identified in the 1980s, the rabbit hemorrhagic disease virus or RHDV, it was explored as another possible form of bio control for rabbits in Australia and RHDV was introduced in the mid 1990s, again helping to keep rabbit populations under control. But the story of rabbits in Australia doesn't end there and neither does the story of the rabbit hemorrhagic disease virus. In 2010, a new type of the virus was discovered in France, the aptly named rabbit hemorrhagic disease virus type 2 and this one doesn't seem limited to just European rabbit populations.

Since its discovery, RHDV2 has spread around the world and has led to concerns for domestic pet rabbits as well as the wild rabbits and hares that are susceptible especially in places which have already seen damaging ecological cascades from RHDV1. So what I really wanted to explore in this bonus episode was these two viruses, RHDV1 and RHDV2. Where did they come from? What effects have they had on rabbit populations? Are they following the same evolutionary patterns as Myxoma virus? How worried should we be? And to help me answer these questions and so many more is Dr. Robyn Hall, veterinary virologist and team leader for the Rabbit Biocontrol Team at CSIRO, the Commonwealth Scientific and Industrial Research Organization which is a government agency in Australia. I am super excited to jump into this interview so I'll just take a quick break here and then we'll get started.

TPWKY

(transition theme)

Robyn Hall

Hi, I'm Robyn Hall, I'm a veterinary virologist and epidemiologist at the Commonwealth Scientific and Industrial Research Organization or CSIRO based in Canberra, Australia. I'm team leader for the Rabbit Biocontrol Team here and I have a special interest in host pathogen interactions, management of invasive species, and viral evolution.

Erin Welsh

Awesome! Thank you so much for taking the time to chat with me today. I am thrilled.

Robyn Hall

Thanks for the opportunity. It's really exciting for me.

Erin Welsh

So in our episode on myxomatosis, Erin and I talked a lot about the long history of European rabbits in Australia and how this invasive species has been incredibly damaging both ecologically and economically. I was wondering if you could bring us up to speed on the current situation with rabbits in Australia. What do we know about the impact that they're still having and where does their continued presence seem to be the most problematic?

Robyn Hall

Back in the 1950s, rabbits were at massive plague proportions throughout Australia and then with the introduction of Myxoma virus, it was incredibly effective in reducing population numbers. But of course populations begin to recover over time and so in the mid 90s RHDV or rabbit hemorrhagic disease virus was released, again with massive declines in rabbit populations. But over time bio controls are not a silver bullet and once more rabbit populations began to increase. And so that led to in 2017 the release of a new variant of RHDV which we call K5 in Australia. And again we're still seeing the impacts from both the K5 release and the arrival of this new virus, RHDV2 in Australia which was not deliberately released but has spread here as it has globally.

And so currently rabbit populations are relatively suppressed comparatively to what they have been in the past but we do still see considerable impacts and these fluctuate on a bit of a boom and bust cycle. When conditions are good, the populations will breed very rapidly and increase in size and if we go into a period of drought then populations can decline again. So the impacts we see are really most obvious in environmentally sensitive areas. So particularly in arid and semi arid zones where rabbits compete with native species for food and shelter and they eat native plants that are already finding it difficult to grow in these arid conditions.

And then of course in agricultural industries as well where they impact crops through grazing, they damage the soil, they compete with livestock for food, and again particularly in drought conditions those impacts are more severe. And rabbits also have some perhaps less considered impacts. So things like they impact our indigenous cultural heritage sites by damaging these artifacts and sacred sites and things and even the impact of reducing the vegetation, that then exposes more soil and the soil can then blow into the fleece of sheep which reduces fleece quality. So there's this really sort of lead on effect, they really have dramatic impacts that are quite wide ranging and both direct and indirect.

Erin Welsh

Our last episode focused on one of the most impactful tools for rabbit control in Australia, of course the Myxoma virus, and we also briefly mentioned the rabbit hemorrhagic disease virus which I cannot wait to ask you more about. But these two biocontrol agents, they're not the only tools used to try to suppress rabbit populations. So can you talk about the other methods that are used?

Robyn Hall

When we talk about a control tool, you really want something that's going to be effective, relatively cheap or easy to distribute, and viruses are really the only thing that we have that are self-disseminating that work on a landscape scale with the existing technologies. However certainly at local levels there are a lot of other tools that can be used. So particularly poisons are used quite heavily, so pindone but also 1080, so pindone is an anticoagulant so it's like rat bait sort of and 1080 is a metabolic toxin. We also focus a lot on habitat removal, so destroying the warrens or if they're harboring in shrubs, removing the shrubbery where possible. Shooting and trapping can be applied on a local level, exclusion fencing has been applied, so where you put up fences that keep the rabbits out but again you have to dig it down and put it up relatively high. And then warren fumigation where you introduce a gas into the warrant to kill them. So all of those other methods, they are very effective at local levels but as you can imagine they're quite labor intensive and certainly we can't use them across the landscape scale of Australia.

Erin Welsh

So now I am so excited because I get to ask about rabbit hemorrhagic disease virus. I read that this is a Calicivirus, what does that mean? Are there other types of Caliciviruses?

Robyn Hall

Yep. I'm very happy to talk about RHDV as well. So yeah, RHDV is a Calicivirus. These are small RNA viruses, so like the coronavirus is an RNA virus as well, it has an RNA genome, but coronaviruses have 30,000 letters in their genetic code whereas these viruses have like 7500 letters, so we call them small RNA viruses. The shell or the capsid that the genome is packaged into is non enveloped, so that means that they're incredibly environmentally resistant. So I think again we hopefully all know now with coronavirus that it doesn't survive particularly long on surfaces and it does use droplets and things like that, it's protected in that moisture droplet environment.

Whereas Caliciviruses, because they're non enveloped, they can survive on surfaces or in soil or something for months. Caliciviruses are pretty common and probably occur in most if not all vertebrate species, although we are really only starting to look at the virus sphere more broadly. But some that you may have heard of would include human norovirus, feline Calicivirus, so it's something that we vaccinate our pet cats for, and then there are Caliciviruses of cows, mice, pigs, chickens, Atlantic salmon. So yeah, it's a big family and the rabbit and hare ones are there as well.

Erin Welsh

How are these viruses transmitted? Or maybe in particular how is RHDV transmitted?

Robyn Hall

A lot of the Caliciviruses are transmitted by the fecal-oral route. So know you ingest them either from a contaminated surface or something like that and then they replicate in the body, they're passed out in the feces, and then contaminate their environment. And so RHDV broadly follows that process. However because again this environmental stability RHDV, can also get picked up mechanically by insects, so particularly carrion flies. The typical lifecycle for an RHDV virus is it's ingested somehow, so either the grass is contaminated and the rabbit eats it or the rabbit sniffs a dead rabbit and gets it in that way or a blow fly comes and lands on the eyelids of a healthy rabbit and deposits some virus there and then the rabbit grooms itself and eats the virus that way. The virus then goes into the gut, enters the animal systemically and causes this major infection that we can talk about in a second and then the rabbit dies typically within 46-72 hours post-infection. So this thing is incredibly, incredibly fast. And then the carcass starts to break down and contaminates the environment and the flies can come in and pick it up and move it between populations.

Erin Welsh

What's going on at the path of physiological level and what's a typical course of infection? What does that look like?

Robyn Hall

So from the outside you frequently don't see clinical signs which I guess is great from a bio control perspective because the welfare is actually, I mean anything that kills something you don't want to say welfare is good, but it certainly has less impact on the animal than something like say Myxoma virus. So many pet owners, we often hear that, 'Oh it was fine, it was eating the night before. I came in in the morning, it was dead.' And so you often find them still with food in their mouth and so it does happen very quickly and frequently you don't see any clinical signs in the rabbit unless you're sort of taking temperatures every few hours or something.

At the pathophysiological level basically what happens is the virus goes in, it targets the liver, so it starts to replicate in the liver and it causes this massive hepatitis that all the liver cells start to bust open and deliver just pretty much disintegrates I guess. And so that leads to a cytokine storm as such and so you get this massive systemic inflammatory response syndrome, disseminated intravascular coagulation, and circulatory shock and death. And so that sounds all very awful and it is I guess. But it's a fairly typical hemorrhagic fever virus so some people have referred to it as bunny Ebola and things like that. But basically the virus goes in, causes a lot of damage to the internal organs, sets up this massive inflammatory response, and then the body is just overwhelmed.

Erin Welsh

And so is that course of infection, is that fairly consistent across individuals within a population or within a species? And how variable is that across species as well?

Robyn Hall

So RHDV is incredibly species-specific. So there's a couple of different variants of RHDV. RHDV1 was the original RHDV that was first reported in the 1980s and that RHDV1 only affects European rabbits, so there's no definitive evidence that it can replicate in any other species. Then in 2010 a new variant called RHDV2 emerged and what we saw with RHDV2 is that it can also infect other Lagomorph species, so hares or jackrabbits, the Lepus species, and then also the cottontails or the Sylvilagus species. But still people are looking and have looked and there's no evidence of any disease outside of those later Lagomorph species.

Within a species or within individuals, within naive individuals certainly the disease course is pretty typical and we see a case fatality rate upwards of 95-99%. So it is very, very consistent. In animals that have some degree of pre-existing immunity then the infection can look quite different. So you may get prolonged infections, they may get a subclinical hepatitis with jaundice and things like that and then secondary liver disease. But again that sort of depends on the level of immunity. But in naive individuals it's very, very consistent with an extraordinarily high case fatality rate.

Erin Welsh

Where did these viruses come from? What do we know about the origins either of RHDV1 or RHDV2?

Robyn Hall

Yeah. I mean where do viruses come from? That's the question isn't it. (laughs)

Erin Welsh

It is.

Robyn Hall

Certainly when our RHDV1 emerged in the 1980s it was reported in Angora rabbits in China, these rabbits were being bred for fur and they just observed these mass mortality events. So it was pretty clear that something was going on and they identified this virus and later it was found to be a Calicivirus and things like that. So we're fairly confident that it wasn't around beforehand or for a long period of time beforehand because we would have seen these mass mortality events. A couple of hypotheses as to how that virus emerged, it could have been a species jump, so the same thing as Myxoma virus, it's completely subclinical in its natural reservoir host but when it transmits to European rabbits it becomes highly virulent in that species and so that is one hypothesis.

Or it could be recombination. So these viruses recombine so basically different parts of the genome sort of switch in and switch out and that can give the virus different characteristics. And so it could be that if there was a benign Calicivirus present in rabbits which we know rabbits do have several benign rabbit Caliciviruses that just infect the gut, they don't cause that systemic disease, and if that benign virus then acquired virulence either through just standard viral evolution or probably more likely through a recombination event with something, then that could have led to the emergence of this highly virulent rabbit Calicivirus.

Similarly with RHDV2, all known RHDV2s actually contain part of their genome from other rabbit Caliciviruses. And then it's the RHDV2 capsid that's the new part and that gives it the broader host range and things like that. So the capsid is the shell of the virus. And so where those capsid genes came from, again we don't know. Was it just through natural evolution or was it a recombination event with another Calicivirus? So two main hypotheses, cross-species jump or evolution from a benign ancestor.

Erin Welsh

So how did RHDV2 get to be globally distributed? Because it was only found in 2010 but now it has this global distribution. So what do we know about how that happened?

Robyn Hall

That's been the really incredible thing is seeing how RHDV2 has become globally distributed so rapidly. It's really been incredible observing this sort of in real time and a bit horrifying. So again we know that it's an incredibly environmentally resistant virus and so it can survive and remain infectious for months in the environment. And then I think the other thing that's contributed to that is that because there's not a lot of cross protection or immunological cross protection between RHDV1 and RHDV2, RHDV2 very rapidly replaced RHDV1. So I guess the analogy here would be the RHDV2 is the Omicron of rabbit Caliciviruses replacing Delta. And so there was this huge surge in cases because it swept through an effectively naive population, so you had huge case numbers. The virus grows to extremely high levels in infected rabbits and so there was just this massive virus load being shed into the European environment after the emergence and local European spread.

And so then with global travel and globalization, if people walked across the park where a rabbit had died, they pick it up on their shoes and then they travel and take it home and if it gets into a wild rabbit population anywhere then it spreads that way. And I think we saw a similar thing with the emergence of canine parvovirus back in the mid 70s. Parvovirus is also incredibly environmentally resistant and we saw that spread globally within about 6 months actually. So we know that environmentally resistant viruses just through fomite transmission, transmission on shoes and things like that.

I think the other thing that I don't have a lot of data on but I really didn't appreciate I guess so much before RHDV2, how much trade of rabbits and rabbit equipment particularly there are. So I think it could be that if somebody's pet rabbit dies they then put the cage on eBay or something and somebody else orders the cage and then the cage is contaminated. And so again I certainly don't have direct evidence for that but I think it's easy to sell stuff internationally these days and ship stuff and so I suspect that there may be some of that as well.

Erin Welsh

I want to talk about sort of the the impact of RHDV2 in Australia in a minute but I want to first ask about some of these places where RHDV1 or RHDV2 has spread and where rabbits are not considered invasive, where they're just a part of the natural ecosystem. What have we seen in terms of the impact on the local rabbit populations there and what kind of downstream effects have there been on the other members of that ecosystem?

Robyn Hall

The impacts of first RHDV1 and now RHDV2 on rabbit populations in their native home range is really concerning and it's actually caused their threat category to be upgraded in terms of the IUCN Red List. So it really is a major concern for native rabbit populations. And so rabbits are native to the Iberian peninsula, so Portugal and Spain, and there they've certainly observed 60-70% declines in rabbit populations. And then they have also observed similar reductions on their apex predators, so the Iberian lynx and the Spanish imperial eagle particularly because those animals don't have the food source and that then affects fecundity of those populations and so they're not breeding as effectively. And so rabbits really are keystone species in their native environment.

Similarly RHDV2 arrived in the US in early 2020 and we've seen quite dramatic impacts on cottontail and jackrabbit populations in the US. And certainly there are several endangered species over there and so there's quite grave concerns about the impact of RHDV2 on those already threatened populations, likely there will be similar lead on effects on their predators as well. I don't know that the reductions have actually been quantified at this point in the US. And I think the other thing, I've had some conversations with colleagues in the US and they've sort of said, 'We haven't really seen the knockdowns that you've reported in Australia or that was seen in Europe.' And I think that's probably at least partially due to the different ecology of the cottontails and jackrabbits over there. So I believe that they don't form these massive warren systems the same way that rabbits do, the contact densities are probably lower and things like that.

Erin Welsh

A lot of people who are concerned about this are not just concerned about the wild rabbits but also sort of domestic pet owners. Is there anything good on the horizon or is there any good news on the horizon potentially for a vaccine or any sort of control I guess either for both the wild rabbits or people who have domestic pets?

Robyn Hall

Certainly for domestic pets, good news with RHDV or Caliciviruses is that really there's only those two types, so RHDV1 and RHDV2 and the immunity induced if you do have infection or after vaccination is pretty much lifelong, it's a really durable, it's a really strong induction of immunity. And so RHDV2 vaccines have been developed and are available in many parts of the world. And so for pet rabbits if they're vaccinated it's really not likely to be an issue. Unfortunately in Australia we don't currently have an RHDV2 vaccine and that is a problem and something that is being worked on. In terms of wild rabbits I think that's a bit harder. How do you vaccinate wild populations I think is an ongoing concern from multiple disease perspectives. Certainly in the Iberian peninsula they're doing a lot of habitat management to try to help support rabbit populations. They're actually restocking wild populations, so moving animals from high density to impacted areas.

And I think we now know, so in the last couple of years it's clear that maternal antibodies, so if the mom has antibodies to RHDV2 then the kittens will be protected for sort of around an 8 week period. And if the kittens are infected during that time then they don't die, they effectively get vaccinated. And so there was a really interesting paper out recently, they actually spread RHDV2 baits in an enclosed population, in a control population, but they actually spread to baits during breeding periods. And they actually showed that there was a reduction in young rabbit mortality by 1/3 and there were actually more immune juveniles recruited into the adult population. And so I think as RHDV2 becomes endemic and immunity levels increase, that maternal antibody protection will help buffer those impacts on rabbit populations moving forward which is good for native populations but again in Australia it's going to be an issue for bio control.

Erin Welsh

In our myxomatosis episode we talked a lot about the evolution of virulence which is one of my all time favorite things to think about and how selection pressures are super dependent upon the virus itself and the way it's transmitted, the host behavior, the environment, among many other things. In the case of myxomatosis of course there was this trend towards decreased virulence and then more recently it seems like a few more virulent strains have been you selected for. And then of course genetic resistance among the rabbits played a large role. And so I was wondering what have we seen in terms of any virulence changes of RHDV1 or RHDV2 since these viruses were first discovered? And has there also been any genetic resistance among rabbits?

Robyn Hall

It's such a beautiful example of how each virus is perfectly adapted to maximize its transmission, right. And so Myxoma virus is spread by biting insects and so therefore it requires a live animal to transmit. So it's in the virus' best interest to keep the host alive for as long as possible to maximize the number of biting insects that can feed on that infected animal. And so prolonged disease duration is good, so hence the virus attenuates to become less virulent. In the case of RHDV it's spread from that dead animal, like I said it's that carcass contaminating the environment and being exposed to blow flies that facilitates transmission. And so as long as they die at the peak amount of infectious virus, that's going to optimize transmission. Hence we really haven't seen attenuation of the virus with either RHDV1 or RHDV2 because again maximum transmission occurs by killing that rabbit at that 48 hour mark when the entire liver is just packed full of virus.

And so I know there's been a lot of discussion about that viruses always evolve to be mild and certainly I think this is a classic example of it really depends on the route of transmission. And so in terms of genetic resistance Myxoma virus is a pox virus, so it's a very large DNA virus and so it encodes a whole bunch of genes and I guess that also provides a lot of targets for the host immune system. And so pox viruses have all of these really cool mechanisms of trying to counteract the host immune system and therefore the host evolves to then counteract the counteractions and etc, etc in this really beautiful virus host coevolution. Because Caliciviruses are so tiny they just kind of get in, get it done, and that's it. And so yeah, it's a bit of a different story. There are some studies suggesting the development of genetic resistance in some localized populations to RHDV1 at least in Australia but certainly it doesn't seem to be a major driving force the way that Myxoma virus was.

And again I think that's because RHDV is just so lethal so quickly that there's not really the opportunity to survive. And I think what's really intriguing is the RHDV1/RHDV2 differences here because RHDV1, while it is able to infect young rabbits younger than about 8 weeks of age, it doesn't tend to cause disease in young rabbits, it only kills adult rabbits and that's independent of maternal antibodies. So there's just something about young rabbits that leads them to not develop disease after RHDV1 infection. Whereas that's not true of RHDV2. RHDV2 lethally kills both young and old rabbits. And so in the case of RHDV1 it was kind of a very stochastic or random event, like if you happen to be 5 weeks old when you got infected you survived and if you happen to be 9 weeks old you died.

And so there's not really a strong selection pressure there, it was just sort of a random event whereas with RHDV2 there's not that sort of age differential and so previously just being young enough to randomly avoid dying is not a thing anymore. And so the rabbits that survive RHDV2 infection, if there is a genetic component there, it's potentially likely that there will be a lot more stronger selection pressure for development of genetic resistance to RHDV2 than there was the development of RHDV1. So it's certainly something that people are very keen and actively investigating to try to see how this plays out as RHDV2 becomes endemic.

Erin Welsh

Here in North America and in many other places where rabbits are considered a keystone native species, the arrival of RHDV2 has been met with these alarm bells, like concern for the rabbits, this could lead to a lot of ecosystem collapses. But in Australia where rabbits have been invasive for about 160 years or so, has RHDV2 been seen as a problem or more as a potential solution? And do you think that these differences in perspectives across different countries, do you think that changes the way that research is done or focused on, the different types of research questions into this pathogen?

Robyn Hall

Yeah. So RHDV2 was first detected in Australia and probably arrived in Australia in around 2014 and first detected in 2015. And at that time rabbit populations were certainly increasing and we were actively investigating the release of a new bio control, this K5 variant that I mentioned briefly at the beginning. So rabbit populations were increasing, it was seen to be a problem and population densities were very high. So when RHDV2 entered the Australian rabbit population, as we've observed elsewhere, there was this massive epizootic sweep through. And we saw population reductions based on serological data and spotlight counts and things like that is an estimated 60% reduction in rabbit abundance nationally, 60% population level reduction. So very considerable.

From our perspective, that dramatically interfered with all of the research that has been going on for the K5 release, right, because we put all this modeling and effort into looking at how K5 would behave in the pre-RHDV2 rabbit population. And obviously once RHDV2 swept through, population densities were much lower, they were probably a lot more fragmented. And so the effective reproductive number is totally different in different population conditions. And so there was a very confusing aspect between was this the new bio control that these scientists were talking about and then we're trying to say no, it was a different strain that just spontaneously came in and things like that. So overall perspective, it's dramatically reduced rabbit numbers which has been very beneficial.

However it's certainly a problem for pet rabbit populations because as I said, we don't have a vaccine here. We weren't expecting RHDV2 and so again for that K5 virus, we'd done a lot of research into making sure that the vaccines were appropriate for that release and then RHDV2 swept through and it's having really, really dramatic impact on pet rabbits. And so an RHDV2 vaccine is certainly needed for Australian pet rabbits. In terms of the differences and research focuses between different countries I think really it's all about understanding the pathogen, right. And then you can either use that to your advantage as a biocontrol or to your advantage to counteract its impact. And so I think we're all actually doing quite similar research, it's just how those findings are applied.

Erin Welsh

So the use of bio control is never without controversy. Can you talk about some of the reasons that people are opposed to the use of these rabbit viruses? And is there a possible downside to reducing rabbit populations in Australia?

Robyn Hall

I mean nobody likes killing animals, right? Nobody wants to be killing animals if there was a better way, 100%. So unfortunately with the current technologies that we have, lethal control of invasive species really is the only way to manage that. And you can't go around and surgically sterilize every rabbit in Australia and things like that and even if you do then they're still going to have those environmental impacts in the meantime. But of course, yes, it certainly is controversial. There's a few different reasons why it's controversial. I guess obviously animal welfare particularly, as we said RHDV is very quick and there are minimal clinical signs, although the path of physiology sounds horrific, it's really your organs just pretty much going to organ failure and you die very quickly. So the welfare is way better than something like myxo.



People have raised concerns about releasing viruses, viruses evolve. Will it spread to native species or other species or could it cross species? And certainly I guess with the many decades at least with RHDV1, these viruses appear to be incredibly species-specific and we haven't seen any evidence of infection in non-Lagomorph species. Obviously the impact on domestic rabbits is controversial and for that as we said, we need a vaccine but the vaccines are very effective when they're available. Possible downsides to reducing rabbit populations, I think one thing that's frequently raised is that if you reduce rabbit populations that would lead to predators turning to native species. And again there's been quite a lot of research actually done investigating that and there's been no direct evidence to actually support this prey switching by either feral or native predators in Australia.

And so actually it was the opposite reduced rabbit abundance was shown to actually reduce feral cat and fox abundance and reduce the predation of native fauna because a large population of rabbits supports a large population of these predators. And so just by reducing the number of predators by reducing their food source was actually beneficial but it is something that's quite frequently raised. And then just briefly I think the other thing that perhaps is not so frequently raised by opponents of bio control but for users of the bio control, I guess the efficacy of the agent can be quite variable. So it depends on the virus dose that the animal receives, the level of preexisting immunity, the maternal antibody status, and it really needs to be used at the right times. And so they require a little bit more finesse than something like putting out a poison.

Erin Welsh

So one last question about RHDV2 biology and so on before I get to ask a bunch of questions about you. And that is the impact of climate change. So what do we know or what is thought to be the potential impact of climate change on rabbit populations or on the distribution of these rabbit viruses in Australia?

Robyn Hall

Rabbits are known to be really adaptable, their native range is that Mediterranean ecosystem but they've really managed to adapt to a lot of Europe. There's feral rabbit populations in British Columbia in Canada, they colonized Australia within a 70 year period. So they are really adaptable. And so if the rabbit populations thrive and particularly in adverse environmental conditions, then this is going to really have more impacts on our native plant and animal species. And so for the viruses themselves, as we said they're pretty environmentally resistant but again if we start to see these really prolonged periods of drought, then that's going to probably reduce the environmental burden of these viruses.

And I think we're probably already seeing some of these impacts in terms of the the variability that we've seen over the last few years. So over the last couple of years we've had a La Niña event in Australia, so a lot of warm, wet weather and certainly the last two years we've seen really massive outbreaks of Calicivirus in spring when those fly vectors start to increase. But I would assume that drought may then reduce environmental survival. So there's probably arguments both ways on how that would affect the actual virus but certainly I think rabbits will survive or adapt to climate change a lot more readily than our native species which is a concern.

Erin Welsh

So we're going to take a quick break here and then when we get back, I want to ask you what it's like to work in the rabbit biocontrol program and what a veterinary neurologist does. I'm so excited.

Robyn Hall

Thanks.

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(transition theme)

Erin Welsh

Welcome back everyone. Okay, so I want to know as the team leader on the Rabbit Biocontrol Program, what do you end up doing on a day to day basis? Or maybe it's more accurate to ask you how much does what you do change from day to day?

Robyn Hall

Yeah. So I think what's really exciting about our team or the research that we do is it spreads quite a few broad areas. So we do animal experimental work, so infection trials and then we do a lot of in vitro work. Caliciviruses notoriously don't grow in cell culture and so we're trying to establish an organoid system for these viruses, so there's some you know molecular biology, there's cell culture, there's animal experiments and then there's field work as well. So we get to go out and sample rabbits in the field which is lovely. And then there's a lot of molecular surveillance and diagnostic testing as well. So we really have broad techniques and are able to do a lot of variable things that keeps life interesting. For me as team leader I'm not really in the lab so much these days which is quite sad but like many sort of PIs I guess I'm working across several projects, working on the next grant, working on the next publication. I'm also a facility veterinarian here so I respond to animal emergencies. And yeah, life's never dull in science I think.

Erin Welsh

Yeah, that's right, you practiced as a veterinarian for a bit and you are still practicing as a veterinarian which is amazing. So can you take me through how you got from veterinarian to veterinarian and veterinary virologist? Lots of 'V's in that sentence but I made it through. (laughs)

Robyn Hall

Lots of 'V's, yeah. Yeah so I was one of those kids who was always curious, always why, but why, but why, but why? And I loved nature, I loved animals and so from a very young age I said I'm going to be a vet and so that's what I did. And I actually thought I was going to be in small animal practice for the rest of my life and I got into small animal practice and I think I found that I wasn't really asking why so much in a day to day basis. There was a lot of routine and there's a lot of other considerations and so that curiosity wasn't satisfied the way I had expected it to be, I guess.

And so to me that lent itself to going back to do a PhD. And when I was applying for PhD programs, looking back everything I applied for was an infectious disease of some sort. And so I'm guessing that infectious diseases piqued my interest somewhere along the line. And yeah, I ended up doing a virology project working on recombinant vaccines for the poultry industry and from there I just fell in love with viruses, they're just so cool and they're so diverse. And heaps of different opportunities have stemmed from that. So after my PhD I worked for a period of time as a diagnostic virologist in one of the state labs and then went back to do a postdoc in rabbit Caliciviruses and like we just talked about, they're so cool, there's so much to do. So I've stayed since.

Erin Welsh

Do you have a favorite virus or bacterium? I'll allow that too. Or parasite.

Robyn Hall

Well I mean I probably have to say RHDV, don't I?

Erin Welsh

(laughs) You don't have to but I would think that that's a very strong contender, yeah.

Robyn Hall

Yes. I just think viruses are also perfectly adapted to their niche, right? And so every single one of them has such a cool story to tell. So I think perhaps one of the coolest ones is syncytin. So syncytin gene which is the gene that allows the development of placenta, right, it allows the cells to fuse which is the basis for placental development. Syncytin is a captured retroviral gene from a human retrovirus, right, and that allowed the evolution of all placental mammals. So I guess I kind of have to say syncytin otherwise I wouldn't be here, whatever virus gave rise to syncytin. And also I would hate to live in a world without my dog.

(laughs) But yeah, viruses have just shaped evolution so strongly and so every single one of them is just amazing. And then there's those Polydnviruses in parasitoid wasps that they inject the virus along with their eggs that suppresses the caterpillar immune response so that the caterpillar immunity system doesn't kill the egg and things like that. And then there's a Microvirus that infects a fungus that infects Rapeseed which turns the fungus from virulent to actually beneficial for the plants and things like that. And so I can't pick one, there's so many cool examples.

Erin Welsh

You just gave some of the most fascinating examples that I don't think I've heard of any of those. And so I am about to go, after this is over I'm going to go on a Wikipedia rabbit hole about every single one of those and I'm very excited.

Robyn Hall

Worth it. Totally worth it.

Erin Welsh

So you work at CSIRO which is a government institution. And what do you think are some of the pros and cons of working at a place like CSIRO versus a university for instance?

Robyn Hall

Yeah. So I think one of the things about working for CSIRO that I really enjoy and that really vibes with my values I guess is the really applied focus. You're doing research because someone or an industry body has said, 'This is important to us, can you look into this?' And so they really applied outcomes that end users really care about, it's really output driven, and you really do get to work closely with stakeholders. So setting the next research agenda, it's like, 'Okay well how do you feel about what we've done so far? Where do we go from here?' So it's a really collaborative approach with the end users which is great.

The flip side of that is that there are really strict milestones and deadlines and there's not so much of the opportunity to sort of just follow the science for the science's sake that perhaps you may get in an academic institution. Similarly it's a lot harder to I guess pivot. So for example with the whole coronavirus situation, I know so many virology labs just completely pivoted to SARS-CoV-2 and obviously that was never going to be an option because the agriculture industry isn't going to, they have a rabbit problem, they still have a rabbit problem. So yeah, the pros and cons, they're both the same side of the coin. It's really achievement focused but then it's a little less curiosity driven, I suppose.

Erin Welsh

On the podcast we're always talking about one health and how much we love it and how important it is for different fields to work together to consider the whole picture. And so do you feel as though your experience as a veterinarian has given you more of an insight into the one health approach?

Robyn Hall

Yeah, I really do. I think at vet school and in practice you have to have your head both around the individual level, treating the individual animal, but also how that impacts the herd and the population and interspecies level as well. And so I think it's just drilled into us and we've never considered otherwise that how does what I do you here, how is that going to impact the rest of the ecosystem? And again from the veterinary perspective it incorporates nutrition and in terms of large animals that incorporates pasture and so that involves drought because then different weeds will pop up with different climatic conditions and things like that. So I think training as a veterinarian really gives you that broader perspective of the animal but also the environmental and then the human and zoonotic disease picture as well.

Erin Welsh

So can you tell me about a cool project that you're currently working on?

Robyn Hall

So perhaps I may have given away a bit earlier but the whole recombination story has just over the last couple of years really piqued my interest. So as I mentioned, RHDV2 first arrived in Australia probably in 2014 and we've been tracking the genomic epidemiology of these viruses since it arrived. And what we've seen through that genomic surveillance is at least 6 independent recombination events since the arrival of RHDV in Australia and that's just the recombination events that have generated epidemiologically fit viruses, right, not all the viruses that died out. So that's unprecedented or at least I didn't appreciate it prior to that, how important recombination was and then seeing these successive waves of epidemiological replacement by these variants.

And sadly I think it's been superseded now by the coronavirus variants and everybody's like, 'Well yeah, what did you expect?' But for me it was really striking when I saw this with Caliciviruses and I think what's been really intriguing... So among those 6 recombinant variants that have arisen, they all contain almost identical capsid proteins or effectively the spike protein to each other. So it's not immune escape that's driving this epidemiological replacement of these viruses. And so if it's not immune escape, what is it? Because again, there's all this focus on immune escape. And so we recently got funding support for a postdoctoral position to start to try to look into what is driving the epidemiological fitness of these recombinant variants. So which of these non-structural proteins and why? If it's not immune escape, what is going on? And so I think that's really got my interest at the moment.

Erin Welsh

Alright. So I've got one last question for you and that is an advice-seeking question. What advice would you give to someone who is interested in pursuing this type of career? Or maybe what type of advice do you wish you had received when you were just starting out?

Robyn Hall

In hindsight, looking back, I think there's a lot of talk now about this fixed mindset vs. growth mindset type thing and I think as I said I decided from a really early age that I was going to be a vet. And so I guess my whole identity through my school years and then going through vet school and everything was like. 'I'm going to be a vet, I'm going to be a vet.' And that really fixed mindset, I mean it was good obviously, you need to have the drive but it also probably made me pass up or bypass other opportunities that may have popped up along the way. So I think in hindsight if I could have adopted more of a growth mindset instead of this focus on being a small animal practicing veterinarian, it could have looked really different. So I would just say my advice based on that would be to be open to opportunities, have a plan but be prepared to adapt it, be curious. And I think for me it was really important finding out what my values were and as a sort of briefly mentioned, reconciling that practice wasn't satisfying that core curiosity value that is so strong for me and knowing that there's other things out there where you will be a good fit sort of thing. And so yeah, be open to different directions and just be curious.

TPWKY

(transition theme)

Erin Welsh

That was so fascinating. Oh my goodness, thank you so so much Dr. Hall for chatting about rabbits and viruses and evolution. I had such a great time. If you want to learn more about the work that Dr. Hall is doing, I'll link to the project's website as well as a bunch of cool articles related to Dr. Hall's work on the post for this episode on our website, [thispodcastwillkillyou.com](https://thispodcastwillkillyou.com). Speaking of which you can find all sorts of things on that website including but not limited to the sources for all of our episodes, transcripts, our [bookshop.org](https://bookshop.org) affiliate account, our Goodreads list, music by Bloodmobile, links to merch and Patreon, quarantini and placebo recipes, alcohol-free episodes, and so much more. And don't forget to follow us on all of our social media for TPWKY updates.

Thanks as always to Bloodmobile for providing the music for this episode and all of our episodes. And thank you to you listeners. We really love you and appreciate you and I hope you enjoyed this deeper dive, I thought it was super fun. So I hope you did too. And a special thank you also to our wonderful, generous patrons. We love you. We've got another regular season episode coming out next week, covering a whole new topic. So until then, keep washing those hands.