



Research Focus: Panleukopenia outbreak in cats

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Sally Everitt:

Hello, and welcome to this research focus podcast from RCVS Knowledge. During these podcasts, we'll be covering all aspects of veterinary clinical research, from getting involved in research and practice, to discussing published papers and evidence, with particular emphasis on how we can integrate them into our clinical practice.

My name is Sally Everitt and today I'm delighted to be talking to Barbara Glanemann and Karen Humm from the Royal Veterinary College about their involvement in the research into the clinical features and causes of the outbreak of cases of pancytopenia in cats that occurred in the UK in Spring 2021. Barbara is currently associate professor in small animal medicine at the RVC and co-head of Small Animal Internal Medicine at the Queen Mother Hospital for Animals where she spends a majority of her time on the referral clinical service. Barbara is particularly interested in hematological and immune mediated diseases.

Karen is an associate professor of transfusion medicine and small and emergency and critical care. She's the co-head of the emergency and critical care department and director of the Transfusion Medicine Service at the Queen Mother Hospital for Animals. She's also director of the transfusion medicine service. Areas of interest include transfusion medicine, acute kidney injury, and veterinary teaching. Welcome. I'm sure many of our listeners will remember hearing about these cases and even seeing them or wondering if they were seeing them in practice. Perhaps I can start by asking you when you first became aware there was a potential problem. Who wants to start with that?

Karen Humm:

I can go first if you want, Barbara and we'll see how we do.

Sally Everitt:

Okay, thanks, Karen.

Karen Humm:

Yeah, I think what happened was, looking back, it's always easier to see a pattern than when you are in it at the time, but we had a cat that presented with slightly unusual clinical signs of pancytopenia. It's not something we see every day, but then we do see slightly unusual things and obviously at a referral center as many referral centers do, and so those owners didn't actually have lots of money to investigate and so a certain amount was done, but actually, sadly the cat was put to sleep and no

further progression was made. Then another couple of cats came in... Very similar clinical signs and these two were siblings, which was really quite unusual for them both to be presenting in such a similar way and led us to start thinking, "Oh that's odd." And then the cases started to come in actually fairly thick and fast, didn't they, Barbara?

We're seeing increasing numbers every week and actually, what also happened was that not only were we seeing these cases, but actually we get quite a lot of advice calls at the RVC or people ringing us either for advice or ringing us and saying that they would like to refer a case and then ending up not referring it, but we chatted over and therefore we were getting more and more information from people in practice seeing similar cases as well, so although the number of cases we were seeing was unusual, we're also hearing about them as well and that was what really pushed us. Wouldn't you say, Barbara?

Barbara Glanemann:

Yes, absolutely, I think. And the pancytopenia that we saw was just so unusual in the sense that we saw suddenly seven cats within three weeks and usually we see maybe one in every five years. And then as Karen said, we got a lot of calls in from colleagues as well.

Sally Everitt:

Yeah, so once you started seeing these cases, how did you go about the further investigations and then reaching out to the profession rather than just dealing with the advice calls?

Barbara Glanemann:

So, I guess initially, I guess there was a lot of brainstorming going on in the sense of how... First, because for our own cases, what could be the underlying cause, and then we quickly realised we probably would need to get us a bit more demographic information on the background of those cats and that's actually where we started thinking, "Oh, how can we actually collect that information a bit more in a structure, because yeah, Karen was speaking to people, I was speaking to people.

Then of course our colleagues at the Queen Mother Hospital we were speaking to... vets and we all collected a bit of different information, so we created this online survey where we initially very broad and widely asked for a lot of information on the cat's living environment, so household indoor /outer cats; is the cat being kept with other cats together. Then signalment age, breeds, clinical science at presentations, initial clinical pathology findings, like what was the PCV, the neutrophil count and then also, of course, what is the cat fed, what kind of litter was used, any dewormer, vaccinations, any other long-term drugs. Of course was being just coming out of the pandemic, we were asking about Covid within the household just to keep an open mind to see whether we can find a common denominator.

Sally Everitt:

So this was a very broad... What's the living environment of these animals and all the sort of main things you could think about... You know, their food...

Barbara Glanemann:

Exactly.

Sally Everitt:

Infections... Those sorts of things. And how many responses did you get to this questionnaire? Can you remember?

Barbara Glanemann:

Yeah, so I guess the first problem we were facing was how do we publish that service, because we can put a service up on the website, but then how do people know about it? And I guess we tried, so we had a lot of help and that was quite good, because we got in contact with the different professional bodies to provide us with or distribute our survey online with email distribution lists.

We contacted other specialists in the countries. We used veterinary journal like trade journals to publish it. I think, Karen, if you remember about... We had quite a quick take up off that questionnaire, so we were initially maybe the first day, 10 entries, then the next day we were at 40 hits. Then three days later, we already had 60 cats registered and I think within a week, we had 110 cats registered, so it did spiral quite quickly. And commercial laboratories were very helpful in the sense that if they detected pancytopenia on submitted blood samples, they would put the link on their report, reporting the results out, so yeah, that was quite helpful.

Sally Everitt:

So it shows that you can do it, but there's not a very good formal way of doing it. It sort of depends a bit on the sort of informal networks. I can remember being in practice at the time and we saw one possible cat certainly with severe anemia and you just, at that point, I got the feeling that in the profession, people were hearing about it, but not really understanding what was going on or whether it was something different or not, because we were only seeing individual cats that were dealing with it. So what were your main findings from this questionnaire data?

Karen Humm:

I suppose, I think, the thing with the questionnaire, as Barbara said, we asked about a lot of information and that was because there was a lot of theories being thrown around about what could potentially be going on. We weren't entirely sure the way this... I suppose we have to think of it as almost like an outbreak... Well, it was an outbreak of disease, and so if we think of an outbreak of disease, probably our two main likely issues would be the infectious disease or intoxication, like a novel toxin.

And so we asked about a lot of those and a lot of those aspects that Barbara said about potential sources of toxin, about potential increased likelihood of parameters that could fit with infectious disease, because we asked about infectious disease testing, but also where they, as Barbara said, indoor, outdoor cats... Obviously, if they were indoor and kept solely indoor, we thought infectious was probably less likely, but what did we find? We found a lot of different cats with a lot of different parameters. Barbara mentioned Covid and it was almost surprising how few owners had contact with Covid in the proceeding time, but the common thing that kept coming up was that we had three feeds that were mentioned repeatedly during the survey. Now, not all cats had them by any means, but over 90% of the cats in the survey had three... Had history of being... Ingesting at least one of those three feeds. That was probably the major finding. We got a lot of data, but that was the thing which stuck out in terms of commonality between the cases.

Sally Everitt:

And how... The problem with questionnaire data, especially when you're asking a lot of questions, is how completely people can fill in that data. Were you getting a good amount of data or was there a lot of gaps in your data as well?

Karen Humm:

We got a lot of data and a lot of good data. Definitely. Again, this is what we keep... Whenever we revisit this, Barbara and I... Our big thing is how collegiate the profession was and how much people did for little personal gain, because they really wanted to try and help. And yeah, I think the vast majority of people filled it in completely. What was important to recognize though was that it was a snapshot in time, so often people would give us the information that they knew at that point, so when we had survival data, it was when they filled in the survey. Potentially, some cats did pass away later that were... But they're registered as alive when that survey was completed. And similarly with the food, often, vets were going off a history that they'd taken at the time, and so it may have been that was the food which the owner reported the cat being on at that point, but I think again, neither Barbara and I, having cats, recognized quite how much owners mix and match with their food.

Sally Everitt:

Chop and change, yeah.

Karen Humm:

Yeah, absolutely. Take a bag of food and pour it in a container and then they don't know exactly what it was. Will they feed eight different feeds, that kind of thing, so it was quite tricky. Go on, Barbara, I think, has something to say as well.

Sally Everitt:

Yes, go.

Barbara Glanemann:

Yes and I guess this was also... I guess it was all evolving, wasn't it? Because we would have the first 10, 20 cats registering and then we realized information on diet was maybe sometimes just dry food and so we very quickly filled it in a question saying, is the owner... Would the owner be happy to be contacted for further information, and then we started actually going, so every day we looked at the questionnaire, we also came up with inclusion criteria, so could all cats that were registered really be included in our analysis? Did they fit the picture? And then we were also able then to create and also own a questionnaire that we could really directly send to the owners where we had more questions to verify things on drugs, on diets as well and things like that. So, yeah, it was a lot of evolving work, like day by day.

Sally Everitt:

When people talk about research and suggest that you're going to give them your methodology at the beginning, they forget all of this sort of messy bit that comes along the way and you suddenly realize that it's a bit more complicated.

Karen Humm:

Yeah, I would say to that... Barbara and I have probably done loads of studies between us, but this was one of the hardest to write up, because it didn't fit like a normal study. Like you say, we didn't have a hypothesis and a... Well, I suppose we had a question at the beginning, but actually, it changed as time went on. And what we did change because, as Barbara suggested, it was an iterative process. We were constantly changing what we did. And then things that happened further in the study in inverted commerce happened because of what had happened after we'd done some initial work.

Sally Everitt:

Yes, of course. So having got the questionnaire, you got the idea that there... Some feed might be involved in some shape or form and I suppose when you start thinking about feed, you're looking at either deficiencies or intoxications. How did you then start to narrow that down? Because that's how we very slightly narrowed it to one possible area. It still doesn't tell you particularly what to look for.

Barbara Glanemann:

So how did we narrow this down? I think we did try to narrow it down by talking to loads of people that have more expertise than us in those fields. We spoke to a lot of toxicologists within the UK, outside of the UK, just to get really as much input as possible. And then of course, we were also relying on the help of the food companies, of the official government bodies, to help us with analyzing those samples as well, because I guess we have done our own analysis, but I guess we were a bit restricted in what we could do on those as well. So yes, I think it was just a very large corporation of many, many people together, yeah.

Sally Everitt:

It's really nice to hear that that can come together. Can you just explain a bit more about when did the idea of mycotoxins and looking for specifics come into that? Because there's still a lot to narrow down there.

Karen Humm:

Yeah, I think, yeah, definitely, and as Barbara said, we were getting a lot of input from a lot of people and as I said at the beginning, there were lots of theories flying around and lots of people suggesting lots of things. Once we realized there was potentially a food component to it, and as we described to colleagues and people we didn't know actually, who offered to help and toxicologists particularly, when we described what we were seeing, mycotoxin just kept coming up as a possible cause, so that was something that many people suggested to us, so although it was something I really didn't know anything about and not something I would've come up with myself, when we described the symptoms and we said it was a potentially food related issue, that was something that many toxicologists suggested. And so that was what pushed us towards testing and particularly for those specific mycotoxins. Yeah.

Sally Everitt:

So we've started to get an idea. We've found that there are some mycotoxins in there. I seem to remember that the recalls on the food went out really quite quickly after that, from my memory. Was that your finding at all or was there any need to push them to do that?

Karen Humm:

Well, actually, the recall was done before a clear understanding of what the actual cause was. That was certainly before any testing was done of the food with results coming back, because that takes a certain amount of time. But as Barbara said, the survey came out and we started to get more and more cats and we could see this link and it would never be proven that it was causative, but there was a link between these two feeds and the cats... Then yeah, there was definitely a response and it came to head fairly quickly and over a weekend, things progressed quite quickly.

Sally Everitt:

Okay, and do I remember reading the paper that the three foods were actually being produced in the same factory... That it was at a factory level there was an issue?

Barbara Glanemann:

Yes. Exactly, so initially, we established that there were three brands that were always, or were very frequently popping up and they were not necessarily brands that you would think were the most commonly sold, so it's just like coincidence that there are popping up, and then again, it was evolving over days and a week that actually we started talking to these different brands of food and then it came out that actually the common denominator they had was that they were all produced at the same factory. Yeah.

Karen Humm:

And then once we found that, we felt much more... Much better, because we had three very separate, and again, I've learned a lot about the food. But yeah, these three very different brands that I would never have known were all made in the same place, but once we found that, we felt a lot more, because before we were looking for one source and one brand and we'd say, "Oh look, this brand keeps coming up." But actually, it's only say, 50% of the cases and that was confusing us, but once we could link those three brands, things became a lot...

Sally Everitt:

It started to be.. it sounds like a plausible hypothesis that could account for it and there could be other places that were contaminated as well, presumably. Presumably, factories get contaminated by ingredients or something like that. I mean, you might never get to the bottom of it. It's absolutely fascinating to listen to how this has come together and what strikes me is how many different people had to be involved to have an input for this to work. What do you think?

Karen Humm:

Yeah, I should just say this, Sally, actually, just because this is particularly literature specific, I think we quite frustrated our journal with the number of acknowledgements we asked for. They did ask us to... Whether we actually needed them all. And if anyone does go and read these papers, I really would say, "Please do something. Look at the acknowledgements." Because each and every person listed very much deserves their place and they didn't get all of the ships. They got acknowledgements, but we were asked whether they were really necessary and we felt they definitely were, at least for those people.

Sally Everitt:

Yeah, no, I can see that. Having listened to this. This is not your average research project. This is something that developed. I suppose where we get to now is, having been through all of this, what would be your wishlist for the future, for the profession? Heaven forbid that these sorts of things will happen again, regardless that we have... We obviously came together and it worked remarkably well on this occasion, but do you think there are things that we would benefit from putting in place so that we've got a way to deal with this in the future?

Karen Humm:

You start, Barbara. I'm good.

Barbara Glanemann:

No, I'm not sure if I'm good to start. Yeah, I think now, two years down the line, everything looks quite ping, doesn't it? So I think it was just very difficult to get the word out in the sense of like, "Who do you approach?" That you can really make sure that everyone hears about it and that we can act as quickly as possible, and it might be just us. We should definitely be aware of, but we were not, because it's not our day-to-day work. We dealing with the individual patient in front of us, and I think that was quite difficult, so like a system in place where there's more an automatic process in place if something similar happens. That, I guess, would be quite nice to have.

Sally Everitt:

And I suppose we've got a couple of different levels there, because they're contacting the profession, but they may also, particularly with something like food, because it may also be a matter of contacting the public and the people who are feeding things.

Barbara Glanemann:

Exactly, and then also, I guess, I think as soon as it was clear that we looked for food-borne something, then we did now... We needed to speak to the Food Standards Agency, but before then, who do you approach if you don't know yet? And then yeah, as you say, it's different levels. One is the profession, but then it's the public, the owners, because I guess many, many owners were feeding the food, not being even aware of... We even had a set case just recently where the owner capped the food, unknowingly, got a new cat into the household and started that food bag again, and now the cats affected two years down the line, just because they were not aware, so...

Sally Everitt:

Karen, what do you think?

Karen Humm:

No, I was going to say, like in Australia, there's a system where they... that I think we've talked about in... They want to know we talk about in the paper that... Of notifying, that vets can use to notify about these concerns, and I think that would be really beneficial here.

I also think it would be great if some pet food companies do test for mycotoxins, but not all of them, and I think it'd be great when we spoke to people about mycotoxins and industry experts, they seem to suggest, and I'm more aware now when I see things in the news... they seem to suggest this is a growing issue and will become more of an issue, certainly in terms of food security, and as issues become with climate change, more of a concern that there will be more of these problems, so I

think, yeah, testing for mycotoxins, having a better alert system. And I know what you say, Sally, it does seem like things work quite well, but actually, hundreds of cats died. At least hundreds. We don't even know. It could have been more. We've only got what we recorded in our database, but there will be hundreds more that weren't recorded, because people didn't know.

We tried our best to do outreach and get people aware of the problem, but either people didn't have time to fill in database or just didn't know about it. So I think actually, it was horrific. And so, again, when we looked and looked at other things, not necessarily in the UK, but there'd been a few things in the UK, but in other countries there's definitely been pet food issues like this. And particularly actually a few in Australia, which is probably why this system exists there.

And so learning from those, because as vets, we often promote and sell pet foods. We want to be able to go there and talk about the danger of maybe homemade diets, and definitely, again, Barbara and I have seen that. We've seen pets on homemade diets that have become very sick from them, so we want to make sure that we can help keep that industry as safe as possible...

Sally Everitt:

Survival.

Karen Humm:

... to do it as well. These people... Everyone involved really wants to do the right thing in inverted commerce. Everyone involved... We had involvement with, in the pet food industry. They're not out to make a quick buck. It's not that they don't care. They really want to do as best they can and so, always trying to improve that system, I think.

Sally Everitt:

Well said. We've got some surveillance with things like Vet Compass and SAVSnet, but they're looking at such a big population level. They're not going to pick up the individual or very small numbers of cases, at least not until it's got out of hand, so there's sort of a reporting system of something a bit like medicine's reporting and things like that.

Karen Humm:

We have for the VMD, because yeah, you're right.SAVS did help us. We got in touch with them, but because, actually, the search terms were so generic in general. There were two and it was like you say, it was... Although it was lots of cats involved actually... It was in the noise, it was hard for them to see anything, so it was super helpful and also it's almost a bit too late by the time they can see stuff. It would have to be so big.

Sally Everitt:

Yeah, so early reporting and ways of getting this information out to the profession and the public, so that everybody goes to one place or knows where there is somewhere and those things can get out. That's absolutely brilliant. Was there anything else you want say before we finish. Have we missed anything? Any burning points that we haven't brought out so far?

Karen Humm:

I don't think so.

Barbara Glanemann:

No. No, I think we've covered most of it.

Sally Everitt:

Well, thank you both very much. It's been a really interesting discussion and given me much greater insight into the number of different parts that had come together to enable this research to successfully establish the cause in these cases. If anyone would like further details of the study, we'll provide links to the published papers on the website.

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