**REGIS KOWALSKI:** For a lot of you who don't know me, I'm Reg Kowalksi. I'm part of the Campbell Laboratory. And what I'd like to present today is the efficacy of dropless prophylaxis for preventing endophthalmitis. We were funded by Imprimis through this. And I think a lot of people are now starting to find out about dropless prophylaxis.

As some of you know, and you all should know that we do have a website. The website tells you everything you want to know about opthromic microbiology. There's a lot of good information there, how we culture, susceptibility testing, how to send specimens to the laboratory. So it does just about everything.

When you talk about endophthalmitis rates, I look through the literature and I find that there are so many different rates. But the one I generally find that's generally used is 0.1%. And some people say no, others say yes. But that's what I generally hear. I just saw in the literature not too long ago that someone predicted the various worldwide type, and as they say, it's about 0.265%. Seems a little high to me, but that's what they basically say, I guess if you take the whole world into consideration.

As I said, there's all type of different rates for intracameral cefuroxime in the United States. You can see it's as low as 0.014 with it, 0.31 without it. In Europe, as you know, it's big time cefuroxime intracameral. They have it down to 0.05. And basically, without it they say it's 0.35. But I think the bottom line with all these different rates that there is a whole endophthlamitis prevention somewhere. We just don't know what it is yet.

Now I find cataract prophylaxis is like football. There's all types of defenses. We have the goalline defense, in which we like to use povi-iodine to protect just sort of the outside of the cornea, or we like to go to topical drops. That gives you some protection on the outside but you do get a certain amount of concentration that does get into the anterior chamber. But those bugs, they still get in the anterior chamber, because they use the West Coast offense. So now we go with the anterior chamber injection. That's catching catching on, as you see in the literature.

But there's a new person on the block now, which is the prevents defense. Now we want to inject antibiotics right into the anterior vitreous. And this is what we call dropless injection. And I think there's a lot of interest in it at the moment. But before we go there we did do a study years ago, Campbell Laboratory, in which we tested all the topical antibiotics as far as prophylaxis. And basically what we did was we had groups of rabbits.

Over one hour we gave the drops every 15 minutes, injected five times ten to the four bacteria, which was staph aureus, and then we gave another four drops afterwards. And then after 24 hours we went to find out whether there was endophthalmitis or not. I don't see Ali here, but he would probably like my next statement, which we call the saline Polytrim Cloranfenicol defense. We call that the Cleveland Brown defense, because it really doesn't do anything.

But we also did povidone-iodine, which we gave four drops prior, which you don't do, four drops prior and four drops afterwards. And we did see there was a reduction in endophthalmitis. Also we find gentamicin, if you use gentamicin, it gives this about 50% of time. But we did find that the flora [INAUDIBLE] worked the best. In this study we used the wild-type staph aureus, which was susceptible to everything. We found oflox was actually a little bit better than moxifloxacin. But resistance might make this a little bit different.

So basically one thing I also wanted to point out here is that antibiotics are not antiseptics. So if you believe that you're just going to kill the bugs on the outside, and that's going to prevent endophthalmitis, then you like your povidone-iodine, because that is an antiseptic. All the other and antibiotics, they're concentration-dependant in general. So they have to hit a certain concentration in or order to work. So if you have it there just briefly, it's probably not really doing anything.

And it's my understanding a lot of people use Polytrim now. I don't know why you do that, because it apparently it doesn't work. There's really not a lot of coverage. And it's not very potent. So you may want to consider, you're probably just good surgeons that don't get endophthalmitis if use Polytrim.

Once again, I want to talk a little bit more with the experiment that we did with Imprimis. We wanted to look at dropless prophylaxis after cataract surgery. I'm a surgeon, Dr. Dolly will tell you more about this one. But basically you're injecting an anti-inflammatory and two or one antibiotic right into the vitreous after cataract surgery. And generally the strophulus goes to the transzonal area, or some people I understand it actually does go apart plane injection after cataract surgery.

The drugs through [INAUDIBLE] use things you all know, triamcinolone, alone moxifloxacin, and vancomycin. And then after a while, people said, well let's not use vancomycin. Let's just go with Trimoxi. So basically, we're going to compare these two antibiotics.

Just to give you a little more information, Tyson does give a report in which he used Tri-Moxi-Vanc. He had a fifth of 1,541 cases. He used Tri-Moxi-Vanc instead. He found no endophthalmitis, no horb and no taz. And basically, they're saying that there's an advantage in patient compliance because it's a one shot deal. You don't have to give drops or anything like that.

Now with Trimoxi, you'll find during the clinical trials in the literature, they claim that they had 200,000 to 400,000 patients who you talked to. They passed it around to 500 doctors. But none of that information has ever been published. But they did say on paper, that there were two known cases of endophthalmitis.

So our present stated objectives, we want to test that dropless prophylaxis. Is it effective? Imprimis actually wanted us to do this. And I think one of the things we were also trying to find is antibiotic resistance. Is this is a whole prophylaxis?

So we said, let's challenge dropless prophylaxis with bacteria and a rabbit endophthalmitis prevention model. So basically, what we want to do is we want to use different bacteria. So basically, all we're doing is injecting bacteria into the vitreous and we're treating with dropless prophylaxis.

But what we did in this experiment, we used three different bacteria with varying MICs to moxifloxacin. Vanco works. Vanco's a great drug, which I'll be showing you. But the moxi with the MIC of staph aureus, we used three. One was, it had a 10 micrograms per ml, which was somewhat high. It was one of our highest in our laboratory. We also test staph with two and also with 0.032. And these are all endophthalmitis isolates from our laboratory.

First experiment, basically as I said, we gave 24 rabbits, we injected them with staph whereas they had a MIC of ten to moxi. And eight of these were treated with Tri-Moxi-Vanc. Eight was the Trimoxi, eight was saline. Basically the same experiment, now the bacteria had an MIC of two. We just treated it with Trimoxi and saline. And the last experiment, the MIC 0.32. We treated with Trimoxi and saline.

Now our outcome measures in our experiment, basically, we're looking for clinical presentations of endophthalmitis. Doth We do have a way that we look at it. It works very well.

So basically, it's a slit lamp. We're looking for hypopyon, iritis, AC cells, AC flare, and fibrin. And Dr. Dhaliwal did all these examinations. The grading scale was based on increasing severity from zero to three. And basically, we would just take all the scores and come up with one score. And we finally did it.

In the past, we found that if we have a anterior chamber score of three or greater, that this was considered to be clinical endophthalmitis. And this has worked quite well for us in our models. Another thing we'd like to do is have a clinical impression by the mass observer.

Dr. Dhaliwal had to dress up like the Lone Ranger that day. And basically, we just want to say, do you think this is, as an ophthalmologist, do you think this is endophthalmitis or not. And she just gave her impression. Of course, we want to, if it's endophthalmitis, we want to culture for viable bacteria from the vitreous. I say of aqueous but we didn't do aqueous this time.

So Eric and I just told you, and basically this is the-- I guess this is the meat and potatoes right here. We found that Tri-Moxi-Vanc worked very, very well. We was able to kill bacteria that had a high MIC of moxifloxacin of ten. We did test the other two because the vancomycin is what killed the bacteria. But then we took some that had Trimoxi only. Now we don't have the vancomycin. And we found that it was not effective to a staph [INAUDIBLE] with a high MIC, even one with an MIC of two. But it did quite work with a wild type, which was 0.032. And there's all the stats here. But basically, as you see, the Tri-Moxi-Vanc is better than Trimoxi.

And why do we think that? Well, first the rabbit showed that. But one of the things we don't know and we've actually learned from this experiment, the moxifloxacin has a very short half-life in the vitreous.

We all like moxifloxacin Vigomox because we know we put it topically, it gets into the cornea. It gets in the AC chamber. But we never figured that if we inject it into the vitreous, it wants to come out just as fast as it comes in.

And so basically, we have a very short life of moxifloxacin. Vancomycin, the half-life is 25.1 hours. It really stays there for a long time. And actually in humans, they've shown it could be up to 56 hours. So we have a good drug that stays or it kills gram positive. That's a very good drug.

So for our first experiment, this experiment, if you're using Tri-Moxi-Vanc, at time zero, the moxifloxacin concentration is about 50 micrograms per ml. As you see vanco's, 468. It could go to three half-lives. We're already down to 5.86. But the MIC is ten, so that sort of give you an idea that that MIC is not staying high enough and moxifloxacin is a concentration dependent antibiotic. So it needs that high concentration in the work. And basically what we found here, this is probably why Trimoxi didn't work in our model, just because it couldn't sustain those high concentrations in the vitreous.

So how important is it? I just told you a bunch of numbers. What do these numbers mean? So basically, I just told you the Trimoxi does not cover an assay with MIC of two. But it does cover a 0.32. Theory So if you look at the MIC 90, something that we do in microbiology, the MIC 90 is the concentration that will cover 90% of the bacteria.

In our laboratory, you can see, that MRSA, MSSA, MR-- [INAUDIBLE] like [INAUDIBLE] staph, and also with CNS, these are all very, very high. It's not going to cover these bugs. And these are the bugs we find in endophthalmitis.

If you look at other people's studies, like Penny Asbell, She does an ARMOR study. You probably heard that at the meetings. Once again, she has very, very high MIC.

So there's a great indication that Trimoxi is not going to be a good drug for these are holes and there's problems with using Trimoxi as a dropless prophylaxis.

So thoughts and conclusions. Well, bacterial as antibiotic resistance could be a whole cataract prophylaxis. That basically makes sense. If it's highly resistant and you don't have enough drug there for a long enough time, it's not going to work. We did find dropless Tri-Moxi-Vanc as more efficacious than dropless Trimoxi for preventing staph or as endophthalmitis. And this is probably the same thing with gram negatives and coagulates negative staph. And staph with elevated MICs to moxi developed endophthalmitis in our rabbit model when administered dropless Trimoxi.

So we've got to know our limitations with our model. First thing, is there a correlation between rabbit studies and actual clinical situations? Many times, no. But I think we have enough here to show that basically, all we're doing is injecting a bacteria, injecting an antibiotic, and we're just seeing if there's good treatment there.

So there's a possibility as the experience of-- another thing I'm going through when I'm looking at this, looking at prophylaxis-- is the experience of surgeons in clinical studies, a prophylactic measure in itself and thus, a confounding factor. Chances are you're all very good surgeons. And more or less, if you're using Polytrim, that's not doing anything. And yet you're still not getting endophthalmitis.

So when you see these big studies, there's just no bugs there to kill. So of course it's going to work. And I think that's why I say in my fourth point here is, is it surprising that injecting antibiotics into a sterile vitreous would prevent endophthalmitis. So I think there's problems with the clinical studies itself. And we actually need to do rabbit studies to at least come up with some ideas of whether prophylaxis really works.

And the other thing I sort of figured when I was questioned by the companies, basically, would endophthalmitis be prevented using the Trimoxi if 5,000 CFU of staph aureus was injected after they did surgery. Right? So you did cataract surgery. You gave Trimoxi and then inject 5,000 staph aureus. Of course, you're not going to do that. But would it be prevented? And the answer is, I don't think it would. More or less, it's not going to.

But I think another thing from our study that I've thought about, there's been some thinking that maybe we should start using moxifloxacin as an antibiotic for endophthalmitis therapy. And I think our data here shows that would possibly be a disaster. Might work sometimes, but more or less, since we know we're getting higher MICs to the fluoroquinolones, and then you have endophthalmitis. And then you inject the moxifloxacin, it's not going to keep that high concentration there. So it may not work as well. So that's just another thought that came out of our study.