Open Forum Infectious Diseases

PODCAST TRANSCRIPT

Antibiotics All-Stars Draft: Dr. Paul Sax Faces off with Dr. Rebeca Plank

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Text Intro to Accompany Podcast:

In the fourteenth installment of the Open Forum: Infectious Diseases *(OFID) podcast, OFID Editor in Chief Paul Sax, MD, faces off against Rebeca Plank, MD, MPH, in a game that mirrors a fantasy sports draft, where the players take turns picking the strongest team of antibiotics "players."*

Dr. Plank is an infectious disease specialist with a particular interest in HIV/AIDS and HCV. She is employed at Merck Research Laboratories where she works on late-stage clinical trials and is a part-time associate physician at Brigham and Women's Hospital and part-time assistant professor of medicine at Harvard Medical School.

Podcast Transcript to Accompany Podcast:

Hello. This is Paul Sax. I am the Editor in Chief of *Open Forum Infectious Diseases* and welcome to the next OFID podcast. By the way, it is officially O-F-I-D and not "Ofid," just so you have to know that. Today we're going to do something a little different. I have with me a friend, an ID colleague and a proud native of Jamaica Plain, MA, Dr. Rebeca Plank.

Thanks for having me on, Paul.

So here's what we're going to do. Rebeca and I are going to choose our five favorite antibiotics. We'll each take turns explaining our choices, and it will be kind of like picking a team on the playground or drafting athletes for your pro team. That means if Rebeca picks one, it's no longer available to me, and if I pick one, it's off the board for her. Got it Rebeca?

Yes.

Okay. Now a few other comments before we get started. First, we're limiting ourselves to what are primarily antibacterials today. IV and oral agents are fair game, and we reserve the right to use either the generic or the brand name. Second, we don't need to pick five that necessarily go together well. You can, for example, pick more than 1 beta-lactam, that would be fine.

And then, I should say that I shamelessly stole this idea from the sports writer Joe Posnanski and comedy writer Michael Schur who do this on their own podcast, but and this is really important: I got their permission, that's one. And second, they said that they're never going to do infectious disease topics. So we should be fine.

Are you worried about the legal aspects of what we're about to do?

If we use trade names is there legal implication?

No. You could use generic or trade, but I am the generic police so I may come in and say a few things. Alright, Rebeca. Since you've taken time out of your busy schedule to do this with me, I'm going to let you pick first.

Thanks, Paul. I think that it's not going to surprise you, or I hope not many people listening, that the first draft pick should be definitely be doxycycline.

I have to admit it, it was my first choice too so now it's off the board for me. Why doxycycline?

I love it. It's fun to think about all the different things that doxycycline can treat, but in a practical matter, it is a great agent for tick-borne illness with which we're plagued here [in] New England in the summer and, actually, probably getting close to year-round now.

Indeed.

It's also a great treatment for a lot of sexually transmitted infections. It's a great treatment for skin and soft tissue infections if you suspect MRSA.

Doxycycline is a pretty amazing drug. It's interesting because periodically I communicate with a pediatrician. I'm married to one. She doesn't think the same way about doxycycline that we do. But for ID doctors, it is definitely one of our favorite antibiotics. It's not perfect.

One of the reasons that she may not like it is because tetracyclines in general are contraindicated in children.

Yeah, in young kids. They're afraid of them. There is a whole "pill esophagitis" story, that's no fun.

Right, but there are certain things for which you really need doxycycline. One of the things I like about it—it's like a bucket of Legos, and each Lego brick is 100 milligrams of doxycycline, and depending on how you stack those bricks and how frequently you line them up, you can treat a variety of things.

You know, Rebeca, I have never heard that analogy before. Do tell us more.

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Well, if you think about, for example, someone calls and they say, "I found a tick on myself on Martha's Vineyard. What should I do?"

200 milligrams of doxycycline.

Times one.

Times one, yeah.

Now if they actually had a rash associated with that tick bite then what would you do?

Well, then we treat 100 milligrams twice a day for some duration of time still to be determined.

Right. You either stack the blocks or spread them out, and you can build a lot of different things with doxycycline. Now granted, it's not going to get you out of MRSA endocarditis, and it's not something that you want to treat Gram-negative sepsis with, but it's an extremely useful antibiotic, and regardless of your practice setting, I think it definitely has to be in your arsenal of top five.

Okay, so it's a good choice. I want to say not perfect because of the pill esophagitis, the photo sensitivity, and nausea and queasiness that a lot of people get on it, but still good choice.

My first choice is ceftriaxone.

I think that's a great choice.

Thank you. I'm glad that you approve. Once-a-day parenteral beta-lactam antibiotics don't grow on trees, you know, and this is one of only two that we have. The other one is ertapenem. Ceftriaxone is so useful in hospitals, clinics, and the emergency room. We use it for pneumonia, and endocarditis, and meningitis, and gonorrhea. There is no alteration for renal dysfunction. It's got good strep coverage, good Gram-negative coverage. It's really the whole package.

Let's not forget the few drawbacks of ceftriaxone—it doesn't get *Staph aureus* very well.

No. Okay. What is your second choice, Rebeca?

Well, my second choice is just like ceftriaxone. It's levofloxacin.

It's not like ceftriaxone at all. That's a terrible analogy!

It is.

No. If you were taking the modern version of the analogies on the SATs and you said, "Ceftriaxone is to levofloxacin as something is to something," I don't think anyone would get it right because they're not analogous at all.

Here is how they're analogous. They're both once-a-day, they're great Gram-negative agents, have great streptococcal coverage, and levofloxacin has two additional advantages. One is the oral bioavailability is fantastic, and you can't really say the same thing for third-generation cephalosporin.

No, certainly not.

And then the other is that you get the atypicals. They're both recommended for community-acquired pneumonia, but levofloxacin can get the atypicals on its own.

I see some of the qualities that are similar, but I guess just because it's once-a-day, just because it has similar coverage, doesn't make them really very alike at all; I mean, structurally they're totally different. Speaking of structurally, I don't know a lot about medicinal chemistry, but I do know this fact, which is really cool, that ofloxacin preceded levofloxacin and then someone somewhere brilliantly figured out that it was only the L-enantiomer of ofloxacin that had antibacterial activity. So they took out the other side of the molecule and levofloxacin is just the L-enantiomer, and that's why it's got its name "levo" for left, and its "S"—and that's about all the biochemistry I remember.

That is very useful.

Yeah. You can go home tonight and make some up in your lab.

Exactly. I'm glad that you mentioned these other quinolones because if you're going to have an arsenal, I want to say why I chose levofloxacin rather than cipro or moxi.

Sure.

Ciprofloxacin is great Gram-negative coverage, but not such great Gram-positive coverage, and moxifloxacin has great Gram-positive coverage and some anaerobic coverage that levo doesn't have, but importantly no pseudomonal coverage.

Levofloxacin is sort of the nice middle ground of the quinolone antibiotics. I can't let our discussion of the quinolones end without bringing up the big black box in the room, if you know what I'm talking about. The more quinolones we use, the more quinolone toxicity we see. We already knew about all of the rare tendon ruptures, but there turns out that there is this strange, poorly defined neuromuscular chronic syndrome that is bad enough at least that the FDA [U.S. Food and Drug Administration] thought that they should now warn people about it. I think there is some validity to this. For years we used quinolones and didn't really recognize this. Now I think it should be part of our consideration before we prescribe it.

I agree.

There are also historically all these quinolones that were FDA approved and then so toxic they had to be withdrawn from the markets, there's kind of a checkered history. Levofloxacin might be out there and still a very good antibiotic, but it's got some bad relatives.

Alright. My second choice is going to be vancomycin. I confess I'm very ambivalent about this choice. I think of vancomycin as the antibiotic that we all love to hate, but hate to love. Do you know what I mean?

Say more.

Okay. First of all, you can't imagine management of a septic, really sick patient in 2017 without vancomycin because you need to have the gold standard for MRSA coverage, and that's why I chose it so high up on my list. On the other hand, we don't really think vancomycin is that effective of a drug, like if you can use a beta-lactam over vanco you would. Some people already are starting to hint that maybe ceftaroline is

more effective than vancomycin. Maybe that the molecule structure isn't good for treatment of endocarditis or penetrating into abscesses. Maybe linezolid is better for MRSA pneumonia, and of course all antibiotic stewardship programs want to limit vancomycin use.

Last, most importantly, vancomycin levels are a huge pain. You never know, is that really a trough? What is the target concentration you want? And we've pushed the levels higher and higher every year. It's just incredibly annoying. I'm going to take vancomycin as my number two pick, but I do so with ambivalence.

Well, Paul, recently, what about the long-acting MRSA treatments like dalbavancin?

Yeah. Those are amazing drugs, and they are profoundly influenced by the pharmaco-economics of healthcare. A single dose of dalbavancin or oritavancin and you can basically treat a soft tissue infection for a couple of weeks. The problem, though, is that if you give it in a hospital, the cost of that medication all falls under the DRG [Diagnosis Related Group]. There is a lot interest in novel ways of delivering care. I kind of wish we could forget about all that cost stuff, but it does turn out to be critical.

Yeah. I noticed that the MRSA Treatment Guidelines haven't been updated since 2011.

Yes, long overdue. Alright. That's my second choice. Go ahead onto choice number three, Rebeca.

Yes—my third choice is amoxicillin clavulanate.

Really? An oral choice, just oral, at least in this country.

At least in this country, yes.

Interesting. Explain.

Well, there are a few reasons why I think it's important to have this drug in your arsenal. The first one is that it's got anaerobic coverage, which I really didn't have great anaerobic coverage with my previous two choices. The other thing is that it has a pretty broad range including enterococcus, which I was also missing with my previous choices. I wanted to add those two components.

Amox-clav is probably the best of the oral beta-lactams. It's got the great, as you mentioned, anaerobic coverage and the Gram-negative coverage, and it's got good *Staph aureus* coverage. I will just say parenthetically, again, that if the pediatricians were playing this game, they would choose amoxicillin, amoxicillin, amoxicillin as their number one, two, and three. But probably the next choice would be the amox-clav.

I'm going to move on now to my third choice, which is an IV and an oral, and it's metronidazole. Metronidazole continues the theme that you just started about anaerobic coverage, and it really gives it some oomph because, aside from a few isolated case reports from South Asia, you basically don't see much in the way of anaerobes getting resistant to metronidazole, which is really amazing, because we've been using it for this purpose for decades. It penetrates well into abscesses. It's pretty safe. Occasionally, people can get kind of loopy on it, but most of the time they tolerate it well. It does give people that funny taste in their mouth, but it allows us to use that great word that describes taste disturbance: dysgeusia.

I love saying dysgeusia. And the other thing I love about metronidazole of course is that one of my colleagues—she's married to a gastroenterologist and they had a pet bird for a while—What do you think this ID doctor and gastroenterologist called their pet bird? They called this pet bird Flagyl. There is almost nothing better than that, a pet bird named Flagyl, don't you think?

Well, it does present a certain Venn diagram of infectious disease and gastroenterology.

Yeah. I was telling that to someone the other day who's not quite as medically sophisticated as you and I are, and she had no idea why that was funny. I think it's funny. In fact, when I get a bird, I'm naming it Flagyl, and I'm not even married to a gastroenterologist.

I think you should name your bird Augmentin, actually.

That's a terrible name for a pet. Alright.

Actually, I have a question for you about metronidazole, if you don't mind. Because I frequently will recommend metronidazole when anaerobic coverage is needed rather than clindamycin and some people think that clindamycin has some advantages clinically. Are you in a situation where specifically anaerobes, you would choose clindamycin over metronidazole?

There is this lore—I think it's promulgated by the oral surgeons and head and neck surgeons and the like—that clindamycin is more effective than metronidazole. I don't know where they get that. I will tell you that in vitro we now know that anaerobes are becoming increasingly resistant to clindamycin. I do also know an oral surgeon who, after using clindamycin for years for her patients, had one of her patients develop life-threatening *C. diff*, required a colectomy, and she no longer uses the drug at all. I'd say there are a lot of reasons when treating anaerobes to use metronidazole. Now if you're using clindamycin as a protein synthesis inhibitor in people with toxic strep syndrome, that's different, but I think for anaerobe coverage in general, metronidazole is better. That's my strong opinion on that one.

Yeah. That's my question.

One other thing, for educational purposes, you really have to tell your patients not to drink alcohol. They can get pretty sick if they drink alcohol while taking metronidazole, bad news, you get that disulfiram effect.

Speaking of avoiding alcohol and metronidazole, this was a terrible story of a friend of mine who got a very thorough dental cleaning prior to a wedding, their own wedding. And because of the thoroughness of the dental cleaning, they thought it was

prudent to take clindamycin following this, and they ended up getting *C. diff* right before the wedding. Now this person is on metronidazole, and that's a tough spot to be in with all those champagne toasts et cetera that are going to take place at the reception without a doubt.

I'd say that's a tough spot to be in regardless of the toasts, but the whole thing could have been avoided if that dentist had used say penicillin, or amoxicillin, or amox-clav after the tooth cleaning. He or she didn't have to use clindamycin. Alright. Next choice, Rebeca.

This is my number four. Glad I snagged before you did, meropenem.

It's definitely on my list. In fact, it was next on my list. You took it.

Just in time. But I have to say, I struggle a little bit with this choice because I thought that I could choose meropenem, or cefepime, or piperacillin-tazobactam.

Yeah. Those all three fall into that category of the "big guns antibiotics" that broad-spectrum, incredibly sick patients, nosocomial organisms. Yeah, in fact, all three of those are very valid choices in that category.

The other reason why I struggle a little bit among those three is because a lot of times people are sick in the ICU or something and you want to get pseudomonal coverage, but let's say these people have also had isolated MSSA.

Or *Enterobacter*.

Yeah. Which one is the best choice with regard to treating both Gram-positives and Gram-negatives, if you want to cover everything and be elegant?

I guess I would choose—if a patient is critically ill and has not had prolonged hospitalization and prolonged exposure to other antibiotics, I would go with cefepime or piperacillin-tazobactam, if only from the antibiotic stewardship perspective that you want to save the carbapenems because after carbapenems, there's really not much else behind that. But someone who has been hospitalized a long time, someone who's been, say, at a long-term care facility, receiving intermittent courses of oral antibiotics, and then back and forth from the hospital, I think that's the setting where meropenem is really the drug to use.

Okay.

Did you think about using ceftolozane/tazobactam or ceftazidime/avibactam in this draft? That would be sort of next level.

No.

Yeah. I didn't either. Those antibiotics are still very, very, narrow use.

Yeah.

Alright. My next choice is—it may be a little controversial—trimethoprim-sulfamethoxazole. What do you think?

I love it.

Let's just start with the name. It's a real mouthful, and I know that when I am rounding on the medical service and we're using that drug, the medical residents would rather I not say trimethoprim- sulfamethoxazole every time. They're in a hurry. They have a lot of work to do. And they would rather I just use Bactrim, which is interesting because there are some antibiotics where the generic name is kind of gone. If you ask a typical smart medical resident what exactly is in Bactrim, they might have no idea. They might know that there is a "t" and an "s," but to tell you exactly what's in it and exactly the dose, they're not going to know. They're not going to know that a double strength has a 160 mg of trimethoprim, and 800 of sulfamethoxazole, but we know it. That's one of the things that makes ID special—that we know that stuff. Alright. What do you think about Bactrim versus Septra versus Cotrim?

Well, I went to medical school on the West Coast and we definitely called it Septra.

Where did you go to…

It's an exclusive medical school on the West Coast in California. It's one of our main competitors.

I see. In the Bay Area maybe?

The Bay Area.

Yeah. I've heard of that medical school. It's got an excellent reputation.

It certainly does.

I'm sure you got a good education.

Extremely.

Okay. So the reason I choose trimethoprim-sulfa is that it's an incredibly useful antibacterial, it covers Gram-negatives in the genitourinary tract. It covers skin and soft tissue infections, especially in the MRSA era. It has some really wacky antibacterial coverage; for example, you just mentioned meropenem, all of those weird Gram-negatives that are resistant to meropenem like *Stenotrophomonas* and *Burkholderia*, they're often susceptible to trimethoprim-sulfa. Then, as a bonus, it's a treatment for two very important AIDS-related complications. One of them is *Pneumocystis* pneumonia, which is antifungal, and also toxoplasmosis, which is an anti-parasitic. So boy I think trimethoprim-sulfa has a lot of uses so I'm picking it very proudly as number four. The only problem with it—guess the problem.

Adverse reactions.

Oh my goodness yes. If you ask a bunch of experienced primary care doctors or general internists or hospitalists whether they've ever seen someone hospitalized or in the emergency room with a severe antibiotic allergy, this is probably the one that they would bring up the most. It can be really, really scary. People with high fevers, terrible total body rashes, hepatitis, Stevens-Johnson syndrome. That is a problem.

I saw a woman who had pneumonitis, hepatitis, and nephritis.

It can be really bad.

It can be really bad. On the plus side though, because I want to support the choice because it was also on my list a little bit further down, because your point about Gram-negative rods that are difficult to treat is a good one because it has a different mechanism. You get down to a few classes that are active against some Gram-negative rods and you can use Bactrim, which also has excellent bioavailability, which is a big seller with me.

Anything to avoid a PICC line.

Anything to avoid a PICC line.

That's right. We are anti-PICC line in this podcast. Okay.

So my last choice is ceftaroline.

Ceftaroline. Interesting. Wow. I never expected that to be number five.

Paul, we've known each other a long time, and you've been my clinical mentor for many, many years. Now when you question my choices, it makes me question them too, but anyway I'm going to defend it.

Defend it.

Because I think that ceftaroline—it covers MRSA and it also covers many Gram-negative rods. And just like the things I've been saying about, for example, meropenem, piperacillin-tazobactam, and cefepime, if you want broad coverage, but you're looking for MRSA rather than MSSA coverage, I think that this is a good choice. I'm not going to right now recommend it as something that should be pushed in the emergency room, but I think that once the dust settles and you know what this person has and you know that the organisms are susceptible to ceftaroline, because not all of them will be, then it's a good consolidative therapy.

Yeah. I think it's an interesting choice. I don't say it's wrong. I just was surprised you chose it. I would say that this is like picking for your team three years from now because you know we're going to start seeing some more data on ceftaroline outside of FDA-approved invitations. Right now it's really just approved for skin and soft tissue infections and pneumonia, but we'll start seeing studies and observations for treatment of bacteremia. In fact, there will be a paper soon in OFID on that topic, and there will be actual clinical trials, and if those clinical trials are successful, then I think ceftaroline could be a real game changer, to use a cliché commonly used in business world and in sports. It does actually combine two of my choices in some ways: vancomycin and ceftriaxone. Ceftaroline, right? It's that simple equation. I think that is a little easier to understand than the analogy between levofloxacin and ceftriaxone.

I still stand by that.

Okay. My fifth and final choice—I'm going to go a little more mundane than ceftaroline. I'm going to go with cefazolin. I think cefazolin is kind of the tortoise in the tortoise in the hare race. We've had cefazolin now for a long time and we didn't really appreciate it. There were all of these fancy antibiotics out there getting all this attention, and along comes slow and pokey cefazolin, and lo and behold. What would you say is the treatment of choice for severe MSSA infections in 2017? It very well could be cefazolin, and I don't have to tell you, ID expert, that there is a lot of serious MSSA out there, and boy I think the data are looking better for cefazolin over nafcillin and oxacillin all the time. It wouldn't surprise me if in the next iteration of various guidelines they actually say, "We recommend cefazolin over oxacillin and nafcillin because it's just as effective and it's safer. I'm going to go with cefazolin, and that's my fifth and final choice.

I think it's a great choice. I do want to bring up the issue of MSSA because you're backing up from advanced treatment of MSSA, right? I think that it's a common misconception that people do better on anti-staphylococcal penicillin such as oxacillin and nafcillin. If it's penicillin-sensitive actually, it'd be great to be able to use penicillin. Now I understand that the last endocarditis guidelines, they don't recommend use of penicillin at all because they don't trust the laboratory results.

Exactly. I wasn't aware of this. I was expecting them to mention that if it's a penicillin-sensitive *Staph aureus* that you should use penicillin for endocarditis, but they didn't. That is because I guess some of the labs cannot correctly identify penicillin susceptibility. I've never worked in one of those labs so I didn't realize that's a phenomenon, but getting back to my choice cefazolin, I think it's defensible to use it in almost all cases of severe MSSA infection, with the exception of course of meningitis, because it doesn't penetrate well into the central nervous system.

I also want to give it a final plug—we commonly see people on hemodialysis with a line infection for MSSA, and it can be dosed just after dialysis. That's a great thing to have in your back pocket if you're trying to send someone out and you don't want to put another line in them when they just came in with a line infection—cefazolin postdialysis.

As I just mentioned we are a pair of people opposed to PICC lines unless absolutely necessary. We have a couple more minutes, what are some of the ones that you considered but didn't get to choose, or some of that you already knew that you weren't going to choose at all?

Well, the other things on my list I didn't get to say were trimethoprim-sulfamethoxazole, metronidazole, ceftriaxone, and the only one that wasn't on your list but was my number ten choice is linezolid.

That would have been very controversial. I think that's… We'd probably have a different podcast about linezolid just all on its own because it's such a weird drug. I think it's interesting that neither you nor I choose azithromycin. Azithromycin, which is perhaps the most widely used oral antibiotic in the world, certainly in the United States right now, but it's a crappy drug. There is so much resistance, it doesn't really work that well. The people who get better on it probably had a virus anyway. I didn't even consider it. Did you?

I didn't even consider it. I can't remember when I've ever prescribed it.

Yeah. If you look at ways in which ID doctors are different from non-ID doctors, I would say we don't like azithromycin, right?

Yeah.

Rebeca, thank you so much, this has been fun. We have several other topics that we're going to do in the future. This is just the first of them. It's been a draft where we're talking about choosing antibiotics with Dr. Rebeca Plank.

Thanks so much, Paul.

Bye.