More than Just Contaminants: Frequency and Characterization of Polymicrobial Blood Cultures from a Central Clinical Microbiology Laboratory Serving a Large Healthcare System

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Guest: Dr. Kaitlin Mitchell is a laboratory leadership service fellow at the Centers for Disease Control and Prevention and recently completed an ASM CPEP fellowship at Washington University in St. Louis. Dr. Melanie Yarbrough is an assistant professor at the Washington University School of Medicine and currently serves as an assistant medical director of Clinical Microbiology Infectious Disease Serology and urinalysis testing at Barnes-Jewish Hospital in St. Louis.

Randye Kaye: Hello, and welcome to this edition of JALM Talk from the *Journal of Applied Laboratory Medicine*, a publication of the American Association for Clinical Chemistry. I'm your host, Randye Kaye.

The presence of multiple infectious organisms isolated from a patient by a blood culture is referred to as a polymicrobial blood culture. While polymicrobial bloodstream infections may occur clinically, some polymicrobial blood culture results are attributed to sample contamination from a blood draw process.

Few studies have investigated the incidents and causes of polymicrobial blood culture results. Further, diagnostic technologies for organism identification can have different performance characteristics when multiple microorganisms are present.

An article in the November 2021 issue of JALM describes a study that evaluated the frequency of polymicrobial blood cultures among multiple hospitals using different blood culture systems. That study also characterized the microbial composition of these cultures.

Today, we are joined by two authors of this article. Dr. Kaitlin Mitchell is a laboratory leadership service fellow at the Centers for Disease Control and Prevention. She recently completed an ASM CPEP fellowship at Washington University in St. Louis, where the work for this article took place.

We are also joined by Dr. Melanie Yarbrough, an assistant professor at the Washington University School of Medicine, who is board certified in both clinical microbiology and clinical chemistry. Dr. Yarbrough currently serves as an assistant medical director of Clinical Microbiology, Infectious Disease Serology, and urinalysis testing at Barnes-Jewish Hospital in St. Louis. Drs. Mitchell and Yarbrough, welcome.

First, let us start with you, Dr. Yarbrough, and we will start with some fundamentals. What are polymicrobial blood cultures and why are they clinically relevant?

Melanie Yarbrough: Well, that's a really good question. Because polymicrobial blood cultures can actually be defined in a few different ways. In our study, we looked at cultures that had more than one microorganism isolated from either bottle of a patient's blood culture set. In this case, a set consists of one aerobic and one anaerobic bottle.

So, a common misconception about polymicrobial blood cultures is that they do not frequently occur and that they simply indicate contamination and while this certainly can be the case for polymicrobial blood cultures, for example, multiple coagulase negative staph species in a culture might suggest the introduction of skin microbiota during a blood draw. But that isn't always the case.

The clinical microbiology lab does see polymicrobial blood cultures with organisms like gram-negative rods that are associated with the gut, and this should probably not be considered contaminants. Multiple studies have found that patients with polymicrobial blood cultures are more likely to have higher mortality rates. And some organisms in these cultures can even be an indicator of an underlying malignancy for the patient.

Randye Kaye: Wow. So, we should not underestimate the importance of polymicrobial blood cultures. Dr. Mitchell, how did your study examine these cultures?

Kaitlin Mitchell: Well, broadly, we really wanted to get a better understanding of how common polymicrobial blood cultures were among the different hospitals in our system. And we were also able to look at differences in epidemiology among the different patient populations. And since our centralized microbiology lab serves a large hospital system, we were able to stratify blood culture data by different hospital sites. And these included a large academic medical center, a pediatric hospital, and also three community hospitals in St. Louis and the surrounding area.

And for our study, we looked at blood culture data from over 160,000 cultures and we used data that were collected from 2017 and 2018. And so, our study has come at a good time to give an updated look at this topic. Most studies of polymicrobial blood cultures were actually conducted 10 years ago or more, and were pretty small in size. And in the past few years, the technology of automated blood culturing systems and blood culture media have dramatically improved, and these are factors that would certainly impact the rates of polymicrobial cultures.

There's also new diagnostic assays that have been introduced that can identify organisms and perform susceptibility testing directly from positive blood culture broths. Now, the accuracy of these assays could be greatly affected if more than one microorganism was present in the broth. So, their utility might be lower in patient populations where polymicrobial cultures are a bit more common.

Randye Kaye: So, Dr. Yarbrough, what were the main findings of your study?

Melanie Yarbrough: Well, first, we found that polymicrobial blood cultures actually weren't all that uncommon. Across the five hospitals in our study, about 1 in 10 positive blood cultures had more than one organism isolated. Most of these cultures did have two organisms, but a few had as many as six different organisms in the blood culture.

Looking closely at the epidemiology of these polymicrobial blood cultures, we found that more than half of these cultures included organisms that would likely be clinically significant including organisms like E. Coli or staphylococcus aureus that should not be ignored in a positive blood culture.

We also found that like really did come with like. So, organisms that typically originated from a certain ecological niche (like the GI tract or the skin) were typically found together in these polymicrobial blood cultures. Interestingly, no single hospital or unit was associated with higher rates of polymicrobial cultures. Although the types of microbiotas that were represented between the different hospital sites did vary widely.

One thing we did look at more closely was the proportion of cultures with microbiota from the GI tract like E. Coli or enterococcus, and of all of the polymicrobial blood cultures with GI microbiota in our study, the majority originated from an adult academic medical center compared to our community or pediatric settings that we included.

And within that academic medical center, the units with the highest rates of GI microbiota were the intensive care units and the bone marrow transplant units. These has significantly higher rates than the emergency department, for example. This is probably due to the high numbers of neutropenic patients in these units, where the patient populations have been shown to have more degradation of their gut mucosal integrity and this could often lead to GI tract bacteria being introduced into the bloodstream.

Randye Kaye: Very interesting, and important work. So, finally, let's just come back to the laboratory. Dr. Mitchell, what can you tell

me about the impact of polymicrobial cultures on the microbiology laboratories' blood culture workflow?

Kaitlin Mitchell: Well, there's a few different ways it can impact the lab. So, first, polymicrobial cultures can complicate the initial gram stain evaluation from a blood culture. And this can affect initial patient management and potentially cause delays in the downstream organism identification and antimicrobial susceptibility testing.

So, we were curious about the actual scope of this. So, we did further analysis of a subset of polymicrobial cultures from our study. We checked if the initial gram stain report could have been used to reliably predict the organisms that ultimately grew out of that culture.

However, the gram stain report matched the final organisms only about 48% of the time. This was sometimes due to overlooking one of the organism morphologies the first time around, but more often, it was because all organisms had the same morphology. For instance, cultures with two different staph species. Or sometimes the appropriate morphology was not found on gram stain due to low organism burden and another factor, as we touched on earlier, is that polymicrobial cultures can impact diagnostic assays that rely on direct testing of positive blood culture broths.

While these technologies can have a really positive impact on patient outcomes, their performance with polymicrobial cultures not very well understood yet. So, if you look at the package inserts for these assays, they state that the most abundant organism will be reported for some polymicrobial cultures, but for other cultures the result will just come back as no call.

And most clinical investigations of these assays do not strongly address the issue of polymicrobial cultures, either because they had low enrollment of these types of cultures, or they simply excluded them totally from their analysis.

And so, with our results suggesting that polymicrobial blood cultures are more common than was once thought, and we're also seeing that they occur more frequently in critically ill patient populations. So, all together, we are considering that these organisms isolated in many of these cultures are not just contaminants and it's critically important that future studies address and include polymicrobial blood culture results and their analyses. And this will give us a better understanding of utility of rapid blood culture diagnostics for treating these infections.

Randye Kaye: Very interesting and important work. Thank you so much for joining us today.

Kaitlin Mitchell: Thank you very much.

Melanie Yarbrough: Thank you.

Randye Kaye: That was Drs. Kaitlin Mitchell and Melanie Yarbrough from Washington University in St. Louis describing the JALM article "More than Just Contaminants: Frequency and Characterization of Polymicrobial Blood Cultures from a Central Clinical Microbiology Laboratory Serving a Large Healthcare System." Thanks for tuning in to this episode of JALM Talk, see you next time and don't forget to submit something for us to talk about.