Inflammatory markers in neonatal sepsis-Pediatric Grand Rounds-5-29-2026-Meeting Recording

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Calderon, Delia started transcription

Ranch, Daniel 0:13

All right. It's 730, so we'll get started. Good morning, everybody, and thank you for joining UT Health San Antonio Pediatric Grand Rounds. It's that time of the year, the end of the year, so we have another special guest speaker today, our very own Dr. Sarah Trippen. Sarah is currently a graduating
surgery fellow in the neonatal and prenatal medicine at the University of Texas Health Science Center in San Antonio. She completed her medical school degree at McGovern Medical School in Houston, Texas, and then her pediatric residency at Children's Memorial Hilmeron Hospital. She looks forward to remaining on our faculty here at University Hospital and UT Health, which is fantastic.
because they're going to need help with the five to 6,000 births they're doing each year. Otherwise, Sarah focuses on clinical care and medical education. So Sarah, the floor is yours.

Sarah Trippett 0:56

Yes.
Awesome. Thank you so much for that introduction. Just confirm that everyone can still hear me and see my screen. I'll minimize Maple 2.
There we go.
Yep.
So thank you everyone for joining me today. I appreciate this opportunity to present to the whole pediatric division. And I think today's topic is a particular interest of mine, particularly because I've always had an interest in sepsis and infectious disease. Once upon a time, there was a time where I thought I was going to be an infectious disease fellow, but if you listen to Dr. Canty, he says there's still time, but I think that's not my future. But I do still have a particular interest in ID. And in my patient population of the neonates that we work with, I think there's a lot of uncertainty in this area.

particularly when it comes to some of the ways that we diagnose and try to trend these infections, particularly with inflammatory markers. And then just trying to think about judicious use of labs and blood draws from our very small babies. And so this all kind of accumulated in my particular interest.
first and what I'm going to discuss with everyone today. So go ahead and get started. So my introduction, I will go over a lot of information that shouldn't be a surprise to most people listening. So sepsis, particularly in the neonatal population, as we all know, causes a lot of morbidity and mortality, both in the US and worldwide. So we have about a 0.3 per 1000 live birth incidents of neonatal sepsis here in the US. But then when you look at the global
scheme, it's an incredible burden. The incidence quadruples. So we have about a 20 to 170 1000 live births globally. So for those of us that are have an interest in global health, this is something that is very important because it can cause a lot of morbidity and mortality in our neonates worldwide.
And that mortality can range anywhere between 10 to 20 percent, so which is not an insignificant number. And this incidence of mortality will increase with decreasing gestational age, as we all know, our smallest, tiniest babies that we deal with in the NICU are going to be the highest risk for mortality from sepsis.
So what, how do we define neonatal sepsis? So there's a lot of different definitions in the literature of what specifically we use to define it. This was particularly the definition that is, I've seen the most often and what I would, what I defined for my particular research. So generally any infection of a previously sterile body site, so that could be blood, urine, CSF,
plus signs of clinical illness. And that's an intentionally vague term, signs of clinical illness. More or less, people generally think of that as any kind of hemodynamic change that will lead to eventual morbidity and mortality. And there's a lot of more literature about broadening this definition because as we know, just the systemic inflammatory response that's present in sepsis is what causes a lot of that morbidity and mortality in that clinical.
instability. It's the body kind of going haywire. And so there's more thought to maybe broadening that definition to include the substantial effects of just systemic inflammation. And as we most of us know, the onset or sorry, the definition of neonatal sepsis is divided basically by the onset.
So you have your early onset generally considered less than 72 hours and late onset. So for the early onset, like I said, most of the literature and what we think of in our

neonatal population in the NICU is going to be less than 72 hours of life. However, for those of you who are in the outpatient setting or seeing these babies in the ER or the urgent care, some
thoughts are extending that period of time to seven days for infants that were initially well and then went home and still have a lot of those associated risk factors for the common bugs that we see in early onset.
Most of the time, early onset is associated with the perinatal period, maternal risk factors, labor and delivery. So things like chorioamnitis, long rupture membranes, and then the ever popular GBS colonization are all risk factors for the development of early onset sepsis. And so because of that, our causative organisms are going to be associated with either the vaginal canal or maternal fecal flora.
The most common, as we all know, is GBS, group B strep. And thankfully, because of the work of our OB colleagues, the incidence of GBS has decreased substantially over the years because of the very set criteria for antibiotic prophylaxis while in labor. However, I do believe we are probably going to start seeing more of the GBS as we see more mothers declining this
antibiotic prophylaxis while in labor, we will probably start to see more GBS than we currently do. E. coli is going to give you your highest mortality. Again, this kind of makes sense to most people. And then you have your strep, listeria, and enterobacter as well.
And then late onset, so everything else past that point. And really, this is the meat and potatoes of what I am interested in and what I will be discussing in terms of diagnosing and predicting late onset sepsis. And we see it typically in our hospitalized neonates because it's associated with things that sort of we do to them or exposure that they have while they're in the hospital.
But this still can occur in infants in the outpatient setting that come into the ER with forward sepsis. So the risk factors are associated mostly with length of stay, indwelling devices. So we think of our catheter associated infections, you know, urinary catheters, PICC lines, and then any kind of medication exposure.
that can adjust the, you know, microbiota of the gut and all these things that can lead to increased risk of sepsis. And then our causative organs are a much more broad range. The bacteria we think of as coagulase negative staph or staph aureus itself, particularly MRSA as a burden while in the hospital. And then your gram negative bacteria. Gram negatives tend to be what we see
which causes the most morbidity mortality. There can be very nasty bugs, especially

in our tiniest babies. And so we are very hypervigilant about these particular microbes. And then you think of your viruses, HSV, herpes, simplex is the big scary one that we think about because that can also cause a lot of morbidity mortality in our neonates and typically does present in the late onset period. So around 7 to 10 days of life. But then even CMV, RSV, as we all know, just from outside exposures. And then for our micro preemies, Candida from Lyme infections and things like that can also be a cause of sepsis in the late onset period.

So how do we diagnose it? The gold standard, as we all know, is always going to be in a culture of the affected body site that reveals the organisms. But the culture has a lot of downsides, particularly with just collecting the sample. And I don't think any of us that have been through a pediatric residency have ever not failed an LP attempt. And so, you know, we all know how difficult it can be to get CSF in particularly dehydrated neonates, but neonates in general. And then for us in the NICU with our 500, 600 gram babies, getting that urinary catheter sample in them is next to impossible at times, even with the most skilled NICU nurses. So there's a lot of difficulty with collections and there's a lot of difficult, there's a lot of different definitions of what's considered a positive versus negative culture.

Particularly as I'll reveal with my own research in urinary tract infections, the definition of what's considered a positive versus negative urinary culture is very broad in the literature, anywhere from less than 10,000 CFU to greater than 100,000. And so no one can really quite exactly pinpoint what is considered a true infection or not. And then as we all know,

Cultures take time to grow and result. And so that can, in that period of time that you're waiting on a bug or a sample, the baby could be clinically decompensating. And so you need to know what to do in the interim while you're waiting for that result. And then for particularly for blood cultures, there's still not a lot of agreement on what's considered an adequate amount of sample to be able to grow an organism. So the classic adage is that we need about 1 mL for blood cultures to result positive, but there's still a result, there's still a risk of false negatives if not enough sample is sent for the culture. So then the question becomes, okay, well, can we clinically or have clinical criteria to define sepsis like they do in adults. You know, you think of your classic search criteria. But search criteria in the definitions in terms of the temperatures and the heart rate and blood pressure, that can just be different in so many different neonates and so many different neonatal conditions just based off of their innate propensity to have certain

vital sign changes. So obviously a micro preview is going to have a very different definition of what's considered an abnormal blood pressure than a full term neonate or a child. So this makes it a lot trickier to really nail down a diagnosis based off of just your kind of classic search criteria. And there was an interesting study that was published a couple of years ago that was actually looking at neonate
and trying to see what was the sensitivity and specificity of your classic search criteria in this population. And it's, as you would expect, not very good. The sensitivity is only about 42%, specificity at 74%. So this is not really a useful tool. There's more and more literature coming out about getting more focused clinical criteria for neonates. So
There's sort of this FIRS or fetal inflammatory response syndrome, as well as the SOFA scores, which I think a lot of our PICU colleagues will use.
NSOFA score, neonatal SOFA score, which are helpful, but still have not gotten us to the point where we can feel confident that we are adequately diagnosing based solely on clinical criteria. So this leads to our whole conundrum that I'm going to discuss.
So ideally, you would have a biomarker or some lab test that you could send right away that results quickly that you could use to adjust your clinical management of these babies while you're waiting for the gold standard culture to result. And so this particular table is just sort of discussing what would make the
ideal biomarker. And it's divided into clinical properties and laboratory properties. So biomarkers in general should have a well-defined cutoff value, a sensitivity and negative predictive value approaching 100%. So we could potentially rule out late onset sepsis, but still have that high specificity and positive predictive value. We want it to detect infection early, again, so that we are kind of ahead of the curve and can make clinical decisions rapidly.
and then be able to identify either a specific pathogen or category of pathogens to be able to monitor the disease progress and be able to guide antimicrobial treatment. And this is really important in the era of antimicrobial stewardship. And then potentially even be able to predict the disease severity so you can really stay on top of these babies that are at highest risk and then eventually predict the prognosis. And then in terms of just basic lab
properties, you know, you want to be able to have a stable compound that allows for an adequate time for specimen collection within, I love this, normal working hours, as we all know, these things always happen at 3 o'clock in the morning, and then be

able to easily store it without it decomposing or affecting the results.
to be able to have a quantitative determination and then automatic and easy method of measurement with quick turnaround time. That's going to be the biggest thing is that we're able to get this in, get this resulted and get it back so that we can make clinical decisions based off of it. And that it has a small volume because as we know, even our smallest babies, that
or 1 mL is actually a good percentage of the blood volume. So we're trying to minimize the amount of blood that we're taking from them to reduce risk of anemia that has on these babies. And that it's also low cost. And that's a big thing too, is thinking about the cost effectiveness of all these lab tests, you know, are we doing the best for our healthcare system as well as for our babies?
So I'm going to kind of look at the different biomarkers, the different tests that we typically see or we typically use in this patient population. And I'm going to start with the complete blood cell count because not a lot of people think of this as quote unquote a biomarker, but it tells us a lot of information. And this was the particular test that I was the most interested in because I feel like it's the most ubiquitous. Everybody knows what a CBC is. Everybody sends it in all of our different units, and it tells us so much information, but how useful is it in potentially diagnosing or guiding our clinical management in the setting of sepsis? So it's one of the oldest, most used tests. But as we all know, there's a lot of differences based off gestational age, chronological age, associated medications can affect these results, et cetera, et cetera.
And so, you know, various parts of the CBC have been looked at pretty extensively in the literature, and the results are very variable and kind of controversial. And so they don't really have any studies that really kind of slam dunk this is the best thing to look at when you're worried about sepsis. There was a large study that was out of the pediatrics database

Arandes, Michelle 14:25
Okay.

ST **Sarah Trippett** 14:25
back in 2012 that was looking at different combinations of CBC values for prediction of land onset sepsis. So large group of infants, about 38,000 with over 70,000

cultures. So this is blood, CSF, and urine. And they looked at various, you know, the bodies themselves, the white blood cell count, the platelet count.

Arandes, Michelle 14:31
One of the Nikki phones that saw her utility stuff in.

ST **Sarah Trippett** 14:45
And then sort of those differential ratios, you know, how many neutrophils were there, the I to T, all of this stuff. And even with all of that data, the best, you know, ROC test with area under the curve was only 0.686. So it's still, it gives us some information, but it is not as useful as I think a lot of people wish it was.
wish it would be. And so this was the main question that I wanted to look at for my particular research. So because of this, in our NICU, it's pretty common practice that anytime we have a concern for late onset sepsis in our babies, we're sending blood, urine, blood and urine cultures and a CBC. That's just kind of our standard of practice. So we have a lot of that data to look at because
It's just so common for us to do this. So I was particularly looking at CBCs in association with urine cultures because there's not a lot of data about UTIs. There's more data about CBCs in the setting of bacteremia, but I wanted to look specifically at UTIs. So we hypothesis that we would see an association between abnormal CBC values and positive and negative urine cultures.
So I took retrospective data from our EMR. I looked at about a three year period of cultures taken in our unit. So all the urine cultures that were sent from all the babies in our NICU for three years. And then I divided them into cases and controls. So cases I defined as any infant that was older than three days, because I was specifically looking at late onset sepsis.
So that was my cutoff was at 72 hours. And then my cutoff for what I considered a positive culture, again, this varies in the literature, but what I did was greater than 10,000 CFU of a single pathogen on a urine culture, I considered a positive. And then I looked at controls, which I was able to match based off of sex, gestational age, and birth weight to try and mitigate some of those confounding variables.
So in terms of the breakdown that I was able to get, I started out with 540 cultures, which I think is a pretty robust data set, given how many we do send. And then I excluded for the various things I've already mentioned, particularly looking at ones that just didn't have CBC value, CBC data taken at the time of the culture.

And then the early onset sepsis, as well as if there was any repeat cultures just to kind of mitigate the effects of, you know, test of cure cultures that were done within a seven day period. And that left me about 421, which I divided into 355 negatives, 66 positive, which gave me an overall prevalence of about 15%.
And then this is a very busy slide and a very busy table, but the long and short of it is that I looked at just the basic characteristics, looking at associated maternal characteristics, birth, you know, birth statistics, and then associated treatments. So things like postnatal and antenatal steroids, which can affect white blood cell count and neutrophils.
looking at NSAIDs, which can affect platelet counts, and then looking at kind of the associated signs of illness, whether they were mechanical ventilation, they had lines present, they were requiring fluconazole prophylaxis, which we do in our less than 750 gram babies, et cetera. And then I looked at how old they were at the time, as well as what other infections were being investigated for at the same time. And in terms of the two groups, they were overall very similar.
The only thing that was of note was that the positive group did have a higher prominence of males, which you can see here at 80% compared to 60%. And there were some differences in, you know, who got which associated cultures with a little bit more of
the negative group actually having more other infections, so CSF infections in the tracheal, and then having more, it's a little bit cut off at the bottom, I apologize, but for respiratory viral panels, the positive group actually had more positive RVPs.
And then what I essentially did was I matched my two groups, and then I performed a conditional logistic regression to see was there any association with various parts of the CBC. And I looked at just discrete values, so your white blood cell count, your hematocrit, and your platelet. And then I looked at these three ratios. So we are, a lot of us are very familiar with that I to T ratio, the immature to total neutrophil count. But its usefulness is kind of debated. And so there's actually other parts of the differential, these other ratios that more and more literature is starting to look at to see, is there any association that we can find? So the neutrophil lymphocyte, and the long and short of it is that no, I was not able to find any association between any of these ratios or any of the values in the CBCs.
Between the two groups, so they were not associated in when you're looking at the odds ratios and the associated P-values.
So I'm going to kind of, so that was essentially the long and short of my particular

research. So now I'm going to kind of transfer over to other markers that we see commonly in clinical practice. So the next one I'm going to talk about is the CRP. So the C-reactive protein, which is an acute phase reactant. It's part of the Pentrexin superfamily.
which is just another part of the immune system. Excuse me. And it's about a 200 amino acid contraction domain at the C-terminal end, which is why it's called C-CRP. And it's primarily produced in the liver, and it responds to inflammatory signaling by IL-6. It also can activate the complement cascade by binding to C1, so it has a pretty significant role in
just the overall immune response in the human body. And what we know is that there's actually an association with normally mildly elevated levels when babies are first born. So having a little bit of a bump in the CRP, 1 to 1.6 until babies are a couple of days old is actually pretty common. And CRP is a little bit more of a slow responder when you look at the overall
overall responsiveness to the immune system that all of the different inflammatory markers we'll discuss has. So it typically will respond within 12 to 24 hours. And it usually peaks at about 10 to 12 hours after infection and has a half life of 24 to 48 hours. So it's not as useful as we would like it to be because we would like something that's very reactive, responds well, peaks well,
and we can catch it early, but CRP does take a little bit of time to kind of show a response.
And this graph sort of depicts that CRP and then comparing it with some of the other inflammatory markers that are looked at as sort of biomarkers for infection. So the CRP is the red line. And as you can see again, starts to respond about 10 to 12 hours, peaks later on. And then this is comparing to so the procalcitonin, which is what I'm going to discuss next, has an earlier peak.
than CRP. So that is why that is starting to becoming more popular than the CRP in the literature because it's responds a little bit faster than CRP does.
So looking at it as a diagnostic marker in late onset sepsis, there's been a lot of literature about this. This particular systemic review I thought was very nice and sort of did a good job of compiling everything. So this was published in 2020 and it compiled a total of 22 studies which covered about a little over 2,000 infants.
And the nice thing about this one for me and my publishing in the NICU is that most of these babies were premature and small. So very helpful in helping us with our determination of late onset sepsis. And so they basically just looked at kind of the

compiled median sensitivity and specificity from all of these different studies and found that the CRP only had a median sensitivity of 0.62 with a specificity of 0.74. So not
as helpful as we would like it to be.
So then moving on to the procalcitonin, as I've already kind of alluded to. So procalcitonin is a prohormone of calcitonin, hence the name, and it is also derived from the hepatocytes. And its particular job is mostly in the invoking the cytokine response. Similar to similarly to CRP, it also has kind of expected rise after birth. So Both of these inflammatory markers aren't going to be very helpful in that early onset group, again, that less than 72 hours because they're expected to be a little bit elevated just in the setting of birth itself. And as I've already mentioned, ProCal does respond quicker to infection than the CRP does about two to four hours and then peaks earlier. So it's getting more popular in literature.
And that's what this review was looking at, was comparing the two. So looking at procalcitonin versus CRP. This was also a systemic review published back in 2019. This looked at 39 studies, only four of which had VLBWs, but still a good patient population. However, the problem with this review was that there was a lot of heterogeneity
as there is in this particular area of research of what's constituted early onset, late onset, and how you define cultures, et cetera. So they did their best to kind of compile what they could, knowing that there was a lot of heterogeneity with all these studies, and then looking at the two markers against each other, both in early and late onset sepsis.
And so essentially, they kind of made the conclusion that they both have their pros, but compared to the two, compared to each other, they don't really have a big difference. So ProCal has a slightly higher mean sensitivity. When you look at the numbers, again, kind of what we've been talking about, that 74 to 80% or so.
okay, but not as good as we'd like it to be. But then CRP had a slightly higher mean specificity. So again, comparing the two, they each have their own roles, ProCo has better sensitivity, CRP has better specificity, but the numbers still aren't where we'd like them to be.
So I've already kind of talked about ProCal CRP in the setting of late onset sepsis for babies, say in the NICU or a premature babies. So, but as we, you know, this is the pediatric grand rounds, there's a lot of pediatricians on the call. And so what I always thought going into fellowship, having done my pediatric residency training,

was the idea of that well-appearing febrile infant that comes into the ED, what do you do? And the management has changed drastically, I think, over the last few years because of this particular clinical practice guideline, which I'll touch on a little bit because it involves the CRP and ProCal so closely in the management. And so I kind of wanted to compare, you know, the
evidence that I've shown so far about how it's maybe not as useful in our late onset neonatal NICU population, but can we have a use for it in the outpatient population for our overall full term well-appearing babies that maybe that spike a fever when they're 21 days old. So I'm going to kind of break this down a little bit to see what does the AP
say for these inflammatory markers in the use of our management in this particular situation.
So as for anyone who's looked at this algorithm and this clinical practice guideline, it breaks it up into, because it's from 8 to 60 days old, so it breaks it up into a couple different of time points. So this first one is that 8 to 21 days old, less than three week old baby, well appearing, no obvious source of infection, and they come into the ER or the urgent care with a fever. And so what do you do? So starting out kind of
So at the top, you have your basic things that, you know, we do for our babies too. We get a UA, we get a blood culture. And then in this particular group, we would recommend, the AP recommends performing an NLP. And then it has this comment about may it pay inflammatory markers. And then based off of that information, you go through the rest of the algorithm and decide what to do with the baby, whether to hospitalize, whether to treat, et cetera.
And so I brought the sort of bottom part where it kind of has all the references and everything and what the AP considers an abnormal inflammatory marker. Oops, sorry. And so they define it as ProCal greater than.5 and CRP greater than 20. And then they also make this comment about the ANC. So again, a lot of times we're getting CBCs with these babies.
to look at ANC and things like that. So ANC greater than 4,000 to 5,200, they would consider an abnormal inflammatory marker in this situation.
But then you move to the 22 to 28 day old period, which the management kind of shifts. And I remember this was a big deal because this clinical practice guideline came out pretty much right when I was doing my ER rotation as a resident. And so this was the game changer, right? So before any baby less than 30 days, they'd come in, they'd get the full workup, they would get admitted, IV antibiotics, the whole

shebang.
And so now we have this sort of in between group, the 22 to 28 day olds, again, well appearing, no source of infection and a temperature. And our inflammatory markers actually help us sort of decide how much of A workup are we going to do on this baby. So it's very different than the previous algorithm, which is like, eh, you can send them if you want to, but it's not really going to affect your management. Whereas this really does. And so when you look at it at the start, you know, you change your labs and then you potentially decide on whether it's sending a catheter specimen based off your UA. But then it has this tree right here talking about the abnormal inflammatory markers. And again, they define it the same way, protocol greater than 0.5, CRP greater than 20. And that determines whether or not you're going to perform an LP.
and whether or not you're going to eventually treat. And so this, I think, is a pretty big, you know, way of managing the clinical scenario. That's what we're trying to find with these biomarkers is that can we use them to guide our clinical management? And based off of this situation, the AP says yes. So what's the evidence behind that? And so when you look at their sort of graded recommendations,
further on in the practice guideline if you read all the pages. And so this one is talking about that 8 to 21 days group. But if you notice here, they say this quote unquote may assess inflammatory markers. They call it a week recommendation, probably not helpful in that age group. But then when you move to that sort of three to four week age group,
It's a strong recommendation because they're using it to adjust your clinical management, which I think is very interesting because it's not something that we do very routinely in our practice, but our situation of babies that are most of the time, especially if they're at that age in the NICU, they're probably former preemies, you know, they have a lot of issues going on.
They've been hospitalized. And so we have other ways of managing this clinical scenario. And they're already hospitalized too. So versus this practice guideline, which is discussing should we even hospitalize a well-appearing baby that otherwise doesn't have issues that, you know, might have gotten a cold and spiked a fever. So I think it's very interesting just kind of the juxtaposition of the two clinical scenarios.
And then moving on to just kind of your other biomarkers that you see. So there's tons of them in the literature. And, you know, everybody's trying to find the one magic number that will sort of solve all these issues and make it super clear. And

unfortunately, we haven't quite got there yet, but there's over 200 plus that have been studied in literature. Some of the other ones that come up pretty commonly, IL-6, as I mentioned, this is
Part of what CRP is involved with, IL-6 kind of triggers CRP, so they're related. It's also pro-inflammatory, made in the liver as well, peaks again a little bit later at 24 hours. And then the results, there's been quite a few studies that have looked at this, but it performs as you would expect pretty similarly to CRP and ProCal.
And then there's other cytokines, TNF, IL-8, there's various CD markers, serum amyloid A. So everyone's trying to find the gold mine of what would be the perfect biomarker, and we haven't quite gotten there yet.
So now where do we go from here? Trying to predict and diagnose sepsis is going to be an endless, you know, investigation. We're always going to have sick babies. And so how do we move forward with the information that we have so far? And one of the things that I think was really interesting was this particular
machine and sort of clinical guidance monitor. And was recently at PS, if anyone else was there, and you know, the exhibition hall, there were quite a few companies that were sort of selling this particular type of product. And what this is, is it sort of compiles data in real time. So you hook it up to your standard, like,
NICU vital sign monitor and it gathers all the data from heart rate, blood pressure, all these things.
and compiles it into a score. And that score adjusts what they believe is the probability of developing infection in the next, you know, 24 hours. So it's called the HERO score, Heart Rate Characteristic Index. Like I said, it compiles ongoing heart monitor data with alerts for various validated cutoffs to alert conditions to possible developing sepsis. So again, calculates
full increased risk of a sepsis-like illness in the next 24 hours. And how this kind of manifests, and I've talked to other people that are in other units that use this type of scoring system, and it's like they kind of have it like a green light system. So your baby that's doing fine, that's not having a lot of issues, not having events, you know, they're green. And then you have a preemie that's starting to have events or drops in their heart rate, drops in their blood pressure, but it's intermittent, they're otherwise doing okay.
maybe a yellow. And then you have your baby that's really tanking, that's going to be a red. And so it's sort of a way to sort of, you know, as you're just walking around your unit, can you spot these babies from afar to try and intervene as soon as

possible? So I think it's interesting. They did a pretty large RCT back in 2011 that looked at over 3,000
and they did show a reduction in mortality, particularly in your ELBWs. So could this be the future? We'll have to see because there's a lot of questions about its use and its efficacy and so we have to do bigger trials as always. But this is interesting and this is starting to get more and more popular and especially because
just an industry trying to kind of sell this as like a, can you pick it up just from visual inspection? And then obviously the old adage, AI is coming, we all know it. Can we use AI or machine learning to predict late onset sepsis? So this particular article was published
back, I think, either 2024, 2025, pretty recently, looking at machine learning model to predict particularly necrotizing enterocolitis. And so they compiled clinical data. Again, not the best numbers, so only a 69% sensitivity for mild late onset sepsis cases.
better with the severe ones, which makes sense to me, 81%. They did find it reduced time to diagnosis by about 10 hours compared to your standard evaluation. And this is important, right? Because this is, again, this is the whole adage that we're discussing. We want to try and find something that will tell us if a baby is sick as soon as possible so we can intervene as soon as possible. Because as we all know, the earlier you get antibiotics and the earlier you get the appropriate treatment in,
the better the baby does. And so there is some gumption to this, but it is still, again, not the magical gold mine that we would like it to be. And this is kind of where I leave everybody. And I know I haven't really answered a lot of questions and have probably brought up more, but I do think it's an interesting area of research. I have a lot of interest in it because
just looking at, again, not even just, you know, antimicrobial stewardship, doing the right infections or doing the right treatment for the right babies, but even just cost effectiveness, not sending a ton of labs that we don't need to, reducing lab draws in our itty bitties, not putting them through invasive procedures with LPEs and urinary catheterizations that can cause
further issues, all of this goes together. And so I think there are, you know, pros and cons to the various ones that we have so far. I think there's utility in certain situations, like I mentioned, you know, maybe the CRP and program aren't as helpful for us in the NICU, but they can be on for the well-appearing infant in the ER.
And so I think it's an interesting area of discussion. I'm curious to hear if anyone has

any other questions or thoughts about any of this. And if anyone knows me, oh, not this one. Oops. I was like, I always, I always include a little picture of my dog, but he's there in spirit. But if anyone has any other questions, I will be happy to answer. Thank you very much.

Ranch, Daniel 34:57

Sarah, thank you very much for that wonderful review and sharing your work. We'll open up for questions. You go ahead and unmute yourself and ask your question, or you can raise your hand or put it in the chat.

Brooks, Edward G 35:13

This is Dr. Brooks of question.

Can you hear me? Okay. Historically, one of the best markers of sepsis in these types of studies has been a pediatrician's exam.

Sarah Trippett 35:17

Yes, hi, yes, yes.

Yeah.

Brooks, Edward G 35:28

How do you AI that?

Sarah Trippett 35:28

Yes, very true.

Very, very true.

Brooks, Edward G 35:31

How do you anybody working on that? That's the most sensitive marker.

Sarah Trippett 35:37

Yeah, I wish, I mean, I think I think that that you bring up an excellent point is that sometimes just laying eyes on the baby, doing your exam, getting your assessment can be so much more helpful than all of these other, you know, machine models and, you know, monitor complete monitors that compile data, you know, how do we how do we

compile all this data that we're getting, we can just put eyes on the baby. I completely agree. I think that's an excellent point.

cynthia blanco 36:07
This is Cynthia Blanco. Excellent job, Sarah. I believe there is an AI tool that I saw that they're utilizing a PAS as like, you know, a pilot with cameras and the cameras recording the patient in the NICU and in the

Sarah Trippett 36:17
Mhm.
Mm-hmm.
Mhm.

cynthia blanco 36:26
you know, in the pediatric area, but more in the NICU. So then they can utilize that as part of the physical exam, but it will not be, of course, a physical exam. It'll be just a view of the patient. So I agree with Ed that we're not going to be able to

Sarah Trippett 36:39
Yes.

cynthia blanco 36:46
replace a full physical exam that easy.

Sarah Trippett 36:47
Mhm.
Yes, yes, don't worry. I truly believe doctors will not be replaced by AI. I think AI can be helpful, but there will always be a role for the human. And so, yes, I agree, Dr. Blanca. There was a lot of people at PS that were, you know, specifically with these types of like hero monitors and all this stuff. I stopped at a few.
a few booths. This is very much a booming area right now that everyone's trying to use, you know, whether it's a camera system, a heart rate system. What I think was interesting about the hero monitors is that to me in my brain, it almost works like like intrapartum fetal monitoring because they describe, you know,
You're looking at variables, you're looking at decelerations, and it's almost similar to

that, but it's for the neonate. And so I think it's interesting, and we'll we're gonna be seeing a lot more of a lot more of these types of devices in the future, for sure.

Ranch, Daniel 37:47
Waiting to see if more questions come up. You brought up early on in your talk, talking about your protocol for CBC blood culture and urine culture. But does that include a urine analysis too? And had you guys thought about looking at your urine parameters and any possible link between

Sarah Trippett 37:58
Mhm.

Ranch, Daniel 38:05
Your findings?

Sarah Trippett 38:07
That's an excellent question. And yes, the shortened answer to that is yes. We don't always send a UA with all of our urinary casts, just because, especially with the tinies, you know, we take what we can get. And so we save as much volume as we can for the actual culture. But we do have quite a bit of urinalysis data.
And so that's kind of our next step is to look, we have compiled for most of that, you know, most of those 540 cultures that I started with, one of our former medical students actually compiled a lot of that urinalysis data. And so I think you can perform the same type of analysis that I did.
with UAs, looking at is there an association with various UA data, and then looking at, you know, anything else that you can use as a potential marker. Again, as I've discussed, you know, we don't have, we don't use a whole lot of CRPs and protocols in our unit just because of the utility of it, but other units across the country do. So I've,
In my experience sort of presenting my research at various conferences, I've had a lot of people approach me about that, like, oh, have you considered doing this with a ProCal, with a CRP? I'm really curious what it looks like. And so that would be kind of the next step. But yes, to answer your question, we do have some of that UA data. So I would be curious as well to see what the association is, if any.

Ranch, Daniel 39:26
Thanks. And since urine volume is an issue in these situations, maybe something you can ask the lab, how much volume is needed for the flow cytometry part of the urinalysis? You know, traditionally our microscopic, which is not microscopic anymore, unfortunately, for better or for worse, but maybe, you know,

Sarah Trippett 39:43
Mhm.

Ranch, Daniel 39:45
Less sample would be needed for that and still gives information on what cells are there and so forth.

Sarah Trippett 39:51
Yes, yeah, I agree. I think it kind of goes up to the same question of like, how much blood do you need for a blood culture to predict the appropriate thing? I think you could also ask the same question for the urine as well.

Ranch, Daniel 40:03
There is a question in chat. What are your thoughts on culture negative sepsis in neonates? And do you think there's a higher instance of this in neonates?

Sarah Trippett 40:09
Ooh.
Very controversial topic. A lot of part of the reason why I didn't include that is because of it is very controversial. And so part of, you know, what I started out with, like, this is how we define sepsis in our patient population, because the idea of culture negative sepsis is getting more
evaluating literature, because again, there are plenty of babies that we have that don't end up growing anything that are clinically very ill. And so how do we kind of parse that out? And I don't have a great answer at this point, considering the research is very kind of, the research is all over the place with it. It's the long and short of it. And so
I think if we have more consensus and have a better definition of what we would

consider culture negative sepsis, I think we could evaluate it more, but it is very controversial. So it's kind of hard to really gauge anything from it.

Ranch, Daniel 41:15

Any other questions from the audience?

Well, if not, Sarah, thank you very much again for your presentation. I'm excited to be working alongside you in the very near future. For everyone, thank you again for joining UT Health San Antonio Pediatric Grand Rounds. If you hadn't noticed already, the link

for CME credit is in the chat. And otherwise, have a great weekend. Thank you very much.

Sarah Trippett 41:50

Thank you, everybody.

Calderon, Delia stopped transcription