



RCPCH The Paeds Round

The Guardians of the Antibiotics

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Sanjay: We are going to run out of antibiotics if we're not careful, because you only have to steward something if it's a finite resource.

Emma: I think the thing that holds everybody back from not prescribing is fear.

Sanjay: So many of our paradigms are being challenged.

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Emma: Good afternoon, and that's our countdown to our next episode of the Paeds Round. And it's my huge pleasure to welcome an old friend of mine, Sanjay Patel.

Sanjay, it's a pleasure to introduce you. And Sanjay is a paediatric infectious disease and immunology consultant working at Southampton's Children's Hospital in the UK. And actually, Sanjay, you are a kind of polymath. You are interested in so many different things, but particularly outpatient parental antimicrobial therapy (OPAT) and antimicrobial stewardship, which is what we're going to be talking about today. And Sanjay holds a title as the officer for stewardship and surveillance for the British Society of Antimicrobial Chemotherapy and chairs the Paediatric Network of the ESCMID study group for antimicrobial stewardship. So, I think that makes you really very well qualified to talk to us today. Welcome.

Sanjay: Thank you, Emma. It's great to be here. Lovely to see you again.

Emma: So, what we're talking about today is stewardship, and stewardship is such an interesting work because there's something about supervision, but it's also something about taking care or looking after something that's worth protecting. And I guess it's about responsible and careful use of antibiotic medications, to ensure their effective use for current and future generations. And I guess that's why in paediatrics, we find it so important, because it's children now and their future.

Tell me a bit about why you feel we should all care about antimicrobial stewardship.

Sanjay: Would you know, before I do that, I think the term stewardship, you raise this, it is an interesting word. It's really interesting, isn't it? It does rely on the fact that we are going to run out of antibiotics if we're not careful. Because you only have to steward something if it's a finite resource, you know, if it's an infinite resource, and you've got a cupboard that's got more and more and more antibiotics you can delve into, then you don't need to stewardship, steward them at all. So, we are talking about something that has beyond sanitation and access to clean water and vaccines having the greatest impact on the delivery of high-quality health care and reducing mortality out of any intervention we have. So, it's something that clearly we all love.

Christo: Thank you very much, Sanjay. So why does antimicrobial stewardship matter, particularly for us as paediatricians?

Sanjay: So, Christo it's really important for us, because we use a lot of antibiotics. And when we look at the data on children in hospitals, we see, and people will know from their own clinical experience, that about a third of children in hospital are on antibiotics. And then in addition, we have a proportion of children yo-yoing in and out of hospital, on intravenous ambulatory antibiotics. So, it's a big proportion of the children we look after.

Emma: Well, I think the one thing that we can take out for this is that antimicrobial stewardship is important. It's important for three different reasons. It's important because, actually it's thinking about your prescribing patterns, patient safety minimising side effects. Is thinking about, how do we prevent resistance? Are we thinking about this idea of protecting this resource and preserving the effectiveness of antibiotics?

Christo: And as you say, Sanjay, it's something that we use a lot of, so it's worth us taking the time to think about how we can do it properly, because it does form a big part of our working day.

Emma: So, if we take those points one at a time, let's think through the cornerstones of antimicrobial stewardship. Let's break it down into the three really important questions about antimicrobial stewardship: why, who and how we do it?

Sanjay: Yeah, I think that's right. I think that's a good way to break it down. I think the why, there are loads of reasons why, actually, first and foremost, relates to antimicrobial resistance. So, I think every clinician listening to this podcast will have noted that they're seeing more and more Rs along the microbiology results of children presenting with urinary tract infections and other infections, and that's because bacteria will naturally become resistant if exposed to antimicrobials, antibiotics, and so that's the main reason why we have to start thinking about antimicrobial stewardship.

Emma: Brilliant. I think that's such an important point that actually, when you give a child antibiotics, you might treat that infection, but you actually are just going to increase the number of bugs that are resistant to that antibiotic. So, it is an inevitable fact of using antibiotics that you get resistance.

Sanjay: Absolutely and clearly with everything, there's a risk benefit ratio. So, if you know that the child is going to benefit from antibiotics, and that benefit has to be a quantitative benefit, either in terms of mortality or the length of their symptoms or morbidity. So if we have evidence based approaches to knowing which cohort of children benefit from antibiotics, so if you've got a child with invasive group A strep or meningococcal disease, there is no way we're saying, don't give them antibiotics, but we are saying that for a child with mild pharyngitis or a lower respiratory tract infection that's likely to be a viral etiology, the harms for both the patient and the population outweigh the benefits

Emma: Absolutely.

Christo: So, apart from trying to prevent our patient in front of us getting colonised with resistant bacteria, are there any other benefits that we can think of for that patient rather than just thinking about the population?

Sanjay: Really good question, and you're right, this whole concept of population resistance is so abstract that I struggle with it, and I think all of us do to some extent. We look after individual patients as frontline clinicians. And those benefits are also that when children are starting on antibiotics, and probably if we're honest with ourselves, we know that they're invariably going to be intravenous antibiotics when they're first started. And that's what all the evidence shows when we look at UK prescribing in hospital. Then those children are more likely to stay in hospital than if they'd been started on oral antibiotics or had an early switch. So, it impacts on their length of stay, which we know that that's so costly for so many families. I think that that tangible benefit or impact financially and, on the wellbeing, and happiness of that family is massive having children in hospital unnecessarily.

Emma: Sanjay, that's a brilliant point. You're absolutely correct. It is really expensive being in hospital for families, not just financially, but also lost work and finding childcare for other siblings who may remain at home. And so many families are now on zero hours contracts, so that has a huge impact. So, trying to keep children at home is really vital.

Going back to other points, I think this is a really growing area of knowledge and something that we didn't used to think about. But what is the impact of antibiotics on a child's normal microbiome? Because we know even from pregnancy, antibiotics affects children's microbiome.

Sanjay: Yeah, I think you're right. We don't totally know, but there are enough signals to suggest that we are having a long-term impact, in many ways, on children. And personally, I think the earlier they're exposed to antibiotics, the bigger that impact perhaps is. And so, I think this really speaks to that neonatal prescribing bit. So many neonates are getting antibiotics unnecessarily. You look at the rates of early and late onset sepsis, especially early onset sepsis, it's now down at one in 1000 less than that, nought point three in 1000 and yet, in some hospitals, 10 to 15% of all babies born in that hospital are starting from antibiotics. So, the answer is a big impact. We don't know all of the impact but definitely focus on neonates and try and reduce unnecessary exposure to antibiotics, because it is having an impact on their microbiome.

Emma: So, I guess that brings me round to if you are sitting there wanting to prescribe, do you have any tools or resources to help decide when to prescribe and when not to prescribe?

Sanjay: Yes. So, you raise a good point. I mean we need firstly, that decision point of when a child presents, what's their diagnosis, and it's always diagnosis, diagnosis, diagnosis. It's like when you're buying a house, it's location, location, location. And this is the same, if you start off with the wrong diagnosis, you end up on the wrong decision tree, treatment pathway, and harm will befall the child, which may be unnecessary exposure to antibiotics from another misdiagnosis. So, let's assume you've made a correct infection diagnosis.

Emma: I love that. I think you're so right. It's about diagnosis, diagnosis, diagnosis, and I guess the question then is, what we really need is better tests and better quick bedside or point of care tests?

Sanjay: Yes, it still comes down to clinical acumen as well. You know, I think some of this is people making the right diagnosis, your right tests and fancy novel tests will help, but they're not here now and we have patients in front of us now. So, there are courses people can attend, there's reading people can do, there are seniors that people can consult with. But diagnosis is important, once you've made the right diagnosis, my advice would be to look at the BSAC common infection pathways. We and in my role within BSAC, with lots of colleagues around the country, have developed some really straightforward pathways that you can follow that make you think about the differentials and walk you through investigations, assessing severity, management and treatment, and that you'd find online if you type in BSAC paediatric pathways into Google or any search engine, you'll come across the 12 or more that we've developed.

Emma: Thank you. Yeah, I think that's really important, because there's something about having consistency, getting everybody to do the same thing, making a diagnosis, and especially if you choose to make a diagnosis and not treat, is something that sits with us badly. We all want to do things. So sometimes it's about holding back about that risk, about waiting to see what will happen. And I think if you have a pathway to follow, a

paediatric pathway that takes you through and weighs up all the evidence, that's really helpful. So, the British Society of Antimicrobial Chemotherapy, as you say, their paediatric network has a series of paediatric pathways. We also have regional pathways on Healthier Together which would work for your region. So professional pathways agreed within a local area between an ICB. So, I think that is a really helpful way to look at thinking about the diagnosis and deciding what is the evidence you really need to give antibiotics.

I think the thing that holds everybody back from not prescribing is fear, and it's always the fear of missing sepsis and serious bacterial infections. But actually, we know these are rare events, so serious bacterial infections, if you look at paediatric emergency departments, that's only 10 to 30% of children presenting with fever, and sepsis in that scenario is about 1%, so what do you think about fear, sepsis and antibiotics?

Sanjay: I think a lot about this because, as you say, the commonest reason children are started on broad spectrum IV antibiotics is that they're labelled with a diagnosis of sepsis when they walk in the front door, because they're either tachycardic or tachypnoeic. And our current kind of screening tools for sepsis, and even that term is a complicated term of very poor specificity, so a lot of false positives more importantly.

I think this goes back to the diagnosis, diagnosis, diagnosis discussion. I think that if one can make a diagnosis and have the time to make a diagnosis of the site of the infection, you go down an appropriate pathway, and we have more and more evidence for many conditions, including osteoarticular infections and pyelonephritis, that starting a child on oral antibiotics is just as effective as starting on IV antibiotics. However, to do that, you need some time, and so the approach taken by the Academy of Medical Royal Colleges is a permissive approach to sepsis, where, clearly, if you have overwhelming sepsis, you get antibiotics within 30 minutes. If you've got a suspicion of sepsis, there's no evidence to say that withholding antibiotics for two to three hours befalls any harm to the patient. Do that, do your investigations and work out if they have an invasive bacterial infection and where it is, and then follow the appropriate BSAC common infection pathway.

Emma: So, if we just think about that really important point, if a child is really unwell, low blood pressure, and they clearly have sepsis, yes, absolutely you need antibiotics within a short time frame, 30 to 60 minutes. But for the other children who you're just suspecting sepsis, you have time to do tests. You have time to think about what's wrong. You can give them antibiotics, but think, do they really need IVs? Do they need orals? The point of having them in hospital is you have them in a safe place where you can observe them and take time to make the right decision and not necessarily treat everybody with broad spectrum ceftriaxone.

Christo: Thanks, Andrew, that's clearly really important, and in terms of picking the right antibiotic when you think that you've got a child in front of you where you are seriously worried about sepsis. How do you go about that? What resources are there to help?

Sanjay: So, there are two approaches. One is what you do empirically when you don't have microbiological results, and the second is, what do you do once you get those microbiology results back. And so, to make a good choice about empirical antibiotics requires a lot of you know, a lot of knowledge, actually, about patient related factors, bug related factors and antibiotic related factors. And to make that process easier, we should be using guidance and guidelines, and we have excellent national guidance produced by an organization called UK PAS, which is the UK Paediatric Antimicrobial Stewardship Network. And under the guidance of Paddy McMaster and our colleagues in St George's, there are really good evidence based, expert supported guidance on all common infection phenotypes. So, I'd just look up UK PAS, or on EOLAS App. If you go into the space or organisation called UK PAS, you'll find that you'll have access to that guidance, and that reflects the sort of resistance patterns of organisms in the UK, etc.

However, every clinician has to also manage the child in front of them, and so if they've come from an area of high incidence and resistance, say they've come from a hospital in India, then you have to think, are they appropriate for following the guidelines? Or if you've got microbiology results about what they're colonised with, or what they have at the time, then the empirical guidance may not be appropriate.

Emma: Brilliant, so vital. It's really important, when you have a child in front of you, to take a history, to think about where they've been, to think about the site of the infection, source of the infection, and to read any old medical notes and look up all the old results to see if they're already colonised by a resistant bug.

I have to tell you, I'm a huge UK PAS. That's the UK Paediatric Antimicrobial Stewardship guidelines fan. I send everyone there because it's really clear and it's beautifully evidence based, like you just look at it, there's all the evidence. It gives you an antibiotic choice. It gives you a choice if you know that they have a penicillin allergy. It puts all the information in one place, and it gives you some idea about duration and dose, and I guess that brings me to thinking about appropriate doses and shortest duration.

Sanjay: So, we're lucky in this country because we've got the BNFC. And actually, the BNFC is our kind of Bible for prescribing in terms of dosing, not all antibiotics, especially some of our novel antibiotics, which aren't necessarily licensed in children are in there, which is why we have to work very closely with our pharmacy colleagues and within our networks, our regional networks or national networks. And that's where an organisation like UK PAS could be really helpful. In terms of duration, I think UK PAS guidance is excellent, because it tries to summarise and take account of the evidence that we have currently in terms of shortening antimicrobial courses. And many of you will remember a few years ago, 10 years ago, for a gram-negative bacteraemia you treat for 14 days, we now have excellent evidence from adult studies, which are now applied to children, that seven days of antibiotics is absolutely appropriate for those children.

The other big shift has been in IV to oral switches. So, we now recognise that oral antibiotics are just as good as IV, except if you have overwhelming sepsis where your gut doesn't really work and you don't absorb antibiotics well. If you don't have a gut or a working GI system, or if you've got a CNS infection, and that last one, you know, watch this space. That may change too. But for those three reasons we give IVs, I struggle to think of many other indications for IVs, and that includes neonates.

Emma: Thank you, Sanjay, that's absolutely brilliant. We need to be clear that actually the times when you need IV or intravenous antibiotics are when you have sepsis, where you need high levels of antibiotics in your blood quickly, you need IV antibiotics if you've got gut failure and you might not absorb and we've also thought about it in CNS, Central Nervous System infections, and I think that your point about all these guidelines are on UK PAS and they're also on EOLAS, this is a platform that holds hospital guidelines. So, you may have guidelines that are local to your area, and we keep all our guidelines on EOLAS for paediatrics, but also for other specialties. So, it's really great resource as well.

So, thinking about the children that do need IV antibiotics, when can you switch them from IV to oral? Because we really need to think about how quickly can we get them out of hospital? How quickly can we get them off IVs?

Sanjay: So, for most children, you can switch very quickly, actually. So, for most children, once they are clinically improving, once they're inflammatory markers, if you decide to recheck them are improving, then if they don't have one of those three categories, or if they don't have gut failure or meningitis, you can do an early switch to oral antibiotics.

I would be a little bit more careful with very young children under a month of age. But that said, there are some lovely data coming out of out of Holland and out of Denmark, showing that neonates treated with all antibiotics with confirmed early or later onset sepsis have outcomes that are identical to those treated with IV after initial periods of IV antibiotics. So, many of our paradigms are being challenged. There are obviously some children that need to be treated with prolonged courses of IV antibiotics. And I think if you need to do that, you need to do that within the safety of a well-managed, well clinically governed system and OPAT service, I'd call it, and that stands for outpatient parental antimicrobial therapy. And we've developed national guidance on the approaches and the systems you need in place to deliver high quality care to those children.

Emma: That's great advice. So, I think remember thinking about that IV to oral switch. Are they clinically improving? Have their inflammatory markers like CRP or Procalcitonin reduced? Are they older than a month of age? Those are the easy ones where we know they can switch. And have you got a definitive diagnosis? So, do you know which bugs that you're actually trying to treat?

And I think it's really important to remember that just because you're changing them to oral antibiotics, it doesn't mean that you're not taking great care of them and watching them carefully, watching their observations, their temperature, their improvement, as you say, that can be done as an outpatient.

So really, really fascinating. And I think the other thing is, is the savings are not just in bed days. These are in real financial savings. So, we know that IV antibiotics are more expensive. They take more resources, because you've got cannulas, you've got pain, you've got drawing up the drugs, all the other things that that takes and the nursing time. But even on another level, if you are prescribing antibiotics, you can prescribe the cheapest, best antibiotics. So often those are as pills. So, if we take the example of trimethoprim or Nitrofurantoin, really common drug, you can give the right number of days as pills. But if you use syrups in a bottle, you're often wasting the end of the bottle, because you'll use five doses and then the other five are just sitting in the bottle. Those wasted doses sometimes sit on the shelves to be used again or get tipped down the sink that pollutes our water course, or very rarely get returned to pharmacy. So, I think this idea about the financial impact of antibiotics when they're prescribed and used, as well as the environmental impact, is really, really important.

Sanjay: Yeah, do you know, Emma, there's another big impact, which is the ecological impact on the child and on the environment. Invariably, in this country, in the UK, when we prescribe IV antibiotics, we prescribe ceftriaxone, and when we benchmarked ourselves against a number of other European countries recently in the PERFORM study, we've shown that we love ceftriaxone, other countries, when they use IVs in children, they may go to narrow spectrum, but we love the convenience of a once a day antibiotic. If you prescribe all antibiotics, you will almost always be on a narrower spectrum antibiotic than ceftriaxone. And so, for the child, it reduces the evolution of resistant organisms in that child, but also when they pee and when antibiotics go into the surrounding ecosystem, there is a greater impact of patients on broad spectrum antibiotics around hospitals than if there are narrow spectrum orals. So that's from a resistance perspective. It also makes sense. It's better for the child, it's better for the environment. It's better from a green agenda perspective, which we're all taking very seriously, and it's cheaper.

Emma: Fantastic. Completely agree. I couldn't agree more, and the carbon footprint of antibiotics is huge. So, it's not about saving the cardboard and the glass of the bottle, the actual antibiotic footprint of the active drug is like 96% of everything. So, if you can save a dose, then you're saving resistance, you're saving the environment. You're saving the carbon footprint, you're saving money. So, it all goes back to your idea about think hard. Do you really need to prescribe this drug today? This time?

Christo: Clearly there are a whole host of benefits that come with embracing antimicrobial stewardship in day-to-day practice. But I just wondered if you have some tips on how we can actually do that in our normal working days?

Sanjay: Yeah, so many of the listeners to this podcast don't work in tertiary children's hospitals. I have colleagues within my team. I work with specialist nurses and antimicrobial pharmacists. But clearly that isn't the case in your average DGH in England or any of the devolved nations. And so we, and this is in my NHS England role as national political advisor for antimicrobial stewardship, we've been thinking about models we can use to try and improve how antimicrobials are used in hospitals up and down the country in DGHs, and that model has to use staff that are currently in place, so those staff are general paediatricians. They are pharmacists. They are nurses, often nurses that work in hospital, at home or ambulatory services. They are sometimes trust antimicrobial pharmacists who, in theory, cover all ages, but generally dedicate their time to adults and our microbiology colleagues, and so what we have successfully negotiated is for funding for four pilot sites, and this is going to start off in Bristol, Southampton, Evalina London and Sheffield, where we are going to empower infection teams across our regions. So, in my region, there are about 12 DGHs, include the Channel Islands and include the Isle of Wight. And we have identified a paediatrician, a microbiologist, pharmacist plus or minus, nurse plus or minus trust antimicrobial pharmacist to be involved in an education program so that we can share learning across all of us, and to benchmark prescribing, both in terms of the process of how antimicrobial stewardship is viewed within the hospital, and also how prescribing, how you benchmark against your similar hospitals in your region.

And so that's due to start in the coming couple of months, and I would love that sort of model to be rolled out across the country. And when we finish the evaluation and we show that it's reduced length of stay, it's reduced use of IV antibiotics, it's reduced cost, I have no doubt we'll be able to roll it out to every single region using the hub and spoke model.

Emma: Fantastic. I think that encapsulates all we want, we want antimicrobial stewardship champions. We want people to be thinking about this and about their prescribing habits. And really, my one ask to people is to collect data to see what you're doing now, so that Sanjay, when your fantastic model rolls out, you'll know what you're doing now, and then you'll be able to see, like, day by day, week by week, how to improve.

Sanjay, it's been absolutely brilliant talking to you. And like, there's so many pearls of wisdom, literally, and they're all rolling around at my feet now. And I just want to think which are the best bits. So, Christo, since you're my trusty sidekick, you've been listening to all of this. Which are the three best bits that you took out of it? What are the three learning points that you didn't think about that you've come away with today?

Christo: Firstly, Emma, I think it's really important that we get the right diagnosis. And Sanjay's point about diagnosis, diagnosis, diagnosis. And that leads on to the second thing that I've taken away from this, which is, once you have an idea as to what's going on, use

the right resources to help you make decisions. So, looking at BSAC, looking at UKPAS, looking at local guidance, if it's different. And thirdly, it's been really helpful to focus on the situations where actually IV antibiotics do need to be used, so gut failure, sepsis, CNS infections, to help focus us on making a decision about when to when it's safe to switch to oral antibiotics as soon as possible to get kids out of hospital sooner.

Emma: And that only leaves me to say, Sanjay, thank you very much. It's been absolutely amazing talking to you. We've had a really great time, and I've learned so much. So as your last parting gift, what are your three top tips to our listeners?

Sanjay: My first top tip is to challenge paradigms. You know, I think we as paediatrician have loved IV antibiotics for a long time, and we need to reflect on that love and maybe use that love elsewhere. Because oral antibiotics are absolutely brilliant. And in fact, they have so many benefits for our patients that we've seen that with all the data, everything we believe that benefited from IV antibiotics, every RCT we've done has shown that orals are just as good if used, you know, the right dose, and it's palatable. So firstly, that's it, it is orals. Think about when you can use orals.

My second bit would be to not make antimicrobial resistance and stewardship a nebulous population thing. Bring it back to your patient. That's what we do. We look after individual patients and think about the benefits for your patient in terms of their microbiome, their side effects and getting them out of hospital, and also resistance in that child, especially if they've got complex comorbidities, which is increasingly the cohort of children we all look after.

And thirdly, make this a team effort. So, the team is your microbiology colleagues, especially your pharmacy colleagues. So, empower them with the UK HSA IV to oral switch tool. They should be challenging us. Our nurses should be challenging us, because they're the ones that have to give the IVs. They've got to spend half an hour drawing them up. We don't have enough nurses on the wards, you know make their lives a little bit nicer, and they're more likely to stay in their posts. Work with them, and they will support the work we're doing with antimicrobial stewardship.

Emma: Fabulous. Oral antibiotics are best, personal care for patients and teamwork, making nurses, pharmacists, resident doctors, everybody around you think about antimicrobial stewardship. So that's thank you very much to the whole team, to you, Sanjay, and please look at our resources below. You

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