The Smallest Victims of Drug Resistance

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SPEAKERS
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Maggie Fox 00:01
Hello and welcome to One World, One Health where we take a look at some of the biggest problems facing our world. I'm Maggie Fox. This podcast is brought to you by the One Health Trust with bite-sized insights into ways to help address challenges, such as infectious diseases, climate change, and pollution. We take a One Health approach that recognizes that everything on this planet — the animals, plants and people, and the climate and environment — are all linked.

Newborn babies are the most vulnerable of us all. They can't do anything for themselves, and their bodies are not fully developed on the outside or on the inside. They're uniquely susceptible to infections, including the most serious of all infections, sepsis. Infections that affect the entire body, known as systemic infections, kill more than 2 million newborns a year. These systemic infections can lead to a more serious complication known as sepsis. And sepsis affects an estimated 3 million newborn babies a year, more than half a million of these babies die — many because the right antibiotics aren't available to treat them.

This problem is made worse by the rise of drug resistant infections. These are a problem for everyone, but especially for tiny newborns.

Professor Mike Sharland specializes in pediatric infectious diseases at St. George's University of London. He's been studying this problem and says more testing is needed to find out which antibiotics work safely in newborns. He says it's especially important to come up with clear global guidelines so that health care professionals racing to save these infants don't have to experiment on the fly. And he's speaking about this with us today.

Mike, thanks so much for joining us.

Mike Sharland 01:48
Thank you much indeed, my pleasure, Maggie.

Maggie Fox 01:50
Sepsis is a big problem for newborns around the world. But how big of a problem is it?

Mike Sharland 01:54
It's a big problem, Maggie. So, there's around 100 million babies born each year in the world. And many of those over 2 million die each year of infections. And infections are one of the top three leading causes of death in babies still, unfortunately right across the world.

Maggie Fox 02:13
Sepsis is one of those conditions that people don't really understand. Is there a difference between sepsis in adults and sepsis in newborns?

Mike Sharland 02:22
There is! So, in adults sepsis just really means infection, bloodstream poisoning, like bugs in your bloodstream. And in adults, that's usually secondary to just infection, or a urine infection or another type of infection, (but in) babies it's different — Infections from one part of the organ can just spread really quick to through the body. So, sepsis, unfortunately, in babies, usually a severe and life-threatening bloodstream infection very quickly indeed. And that's what we mean by sepsis or septicemia, or bloodstream infection.

Maggie Fox 02:53
And how does a little baby get this infection?

Mike Sharland 03:15
So, babies are unfortunately very vulnerable to infection. They have a very weak immune system, and they can pick up infections very quickly. And that can be through their skin. (A) baby's skin is very fragile, very thin, they can obviously get coughs and colds, like other people, and they can also acquire infections in the environment, (whether) it's on cots or anywhere else as well. So, babies are very vulnerable to infection and (can) pick up infections very easily.

Maggie Fox 03:23
Unfortunately, cesarean sections or C sections are very popular in some countries. Does that affect a baby's sepsis risk?

Mike Sharland 03:30
They do. And they do impact I mean, there's a doubles edge here. That's because obviously, some classic infections Group B strep, for example, which is a vaginal pathogen and then acquired as a baby goes through the birth canal is rates are reduced if the baby's born by cesarean section rather than vaginal delivery. Some of them the, for the great majority of certain multi drug resistant infections, Klebsiella and elsewhere, it's still a little bit tricky to work out how much of this is in a mother to child transmission, through vaginal transmission.

And how much of this is related to just being in (the) hospitals and therefore requiring infection in hospital because the mother has a cesarean section? The baby is often in (the) hospital longer, and the big risk of acquiring (a) multidrug resistant infection is being in (the) hospital. A newborn baby has basically (a) 20 percent per day risk of acquiring a multi drug resistant infection. So, if you stay in (the) hospital for more days, the more chance (of) you picking up something bad. But the best thing that you can possibly do is to not take your baby anywhere near a hospital unless you have to.

The WHO (World Health Organization) clinical trials are all predicated on making sure that many babies as possible are treated in the community for sepsis and actually not treated in the hospital sepsis. They don't say a hospital is a dangerous place, but you look at the trial design, you go this is all about hospitals being dangerous places. So, the indirect effects probably of the baby being in hospital because the mother had a cesarean section are probably more important than the direct effects of a transmission. At the rate of acquisition of multidrug resistant infection on neonatal units in India and Africa and elsewhere, I look at the data and I just go like, oh my God, my God, you know, these babies are roaring with multi resistant pathogens, from day one, day two, day three!

They are absolutely everywhere on the phone, they're on the desk, they are all over, everywhere. So, it's a real challenge to think about.

Maggie Fox 05:31
And some of the research you've done indicates that these infections might be becoming more common. Why is that? What's changing in society that's making that happen?

Mike Sharland 05:41
I think there's a lot of reasons why things are changing with infections. And this is really what we have to think about: infections in high-income countries, in richer countries where infections are actually still relatively low so now. There are some threats, but they're most commonly a threat to very premature babies, very little babies born in intensive care units with very limited immune systems as well. And there are more premature babies being born so therefore, there are more infections in babies in high-income countries.

In poorer countries, there are also infections transmitted from the mum's bodily fluids, or indeed, in hospitals as well. There's a big change in the world, and that's all about globalization. In cities, more and more people are living, and more and more people are being born. WHO estimates, by around 2050, there'll be another couple of billion people living in cities, and young people live in cities. They have their babies in hospitals, therefore in cities rather than at home.

Maggie Fox 06:44
And that's a little counterintuitive, because one might think, wow, cities, civilization, hospitals, cleaner, why would living in cities make this a more common problem?

Mike Sharland 07:52
Yeah, it is. So, it's become an ever more common problem. And the difficulty is that infections are therefore becoming more frequent. Also then, because of antibiotic resistance, are getting (more and more) harder to treat.

Maggie Fox 07:05
And let's talk about that, how many of these infections are drug resistant?

Mike Sharland 07:10
Now, sadly, a lot still remain sensitive to antibiotics, or a few. There's an infection called Group B strep, the teaser infection that mothers can pass on, unfortunately, sadly to their babies. And still, after all these years, it's still absolutely sensitive to penicillin, nearly 100% sensitive to penicillin. So, it's not all infections that are resistant, but unfortunately, many of them are increasingly drug-resistant now, and they are resistant.

These are more, one called gram-negative gut infections. And those are some very, very serious pathogen, some serious bacteria, Klebsiella and other ones, and now resistant to most of the usual antibiotics that you were treating infections for first one.

Maggie Fox 07:55
And how can one expect a physician to know which infection this little baby has?

Mike Sharland 08:01
You can't! So, you just see a baby who's sick, unfortunately, babies look really pale, they don't move, they start

floppy, they don't feed, but that doesn't tell you what it is that's causing the infection. Now you can do a blood culture, you can do a test for that and have a look at the blood culture and sendoff (a) bit of the blood to the lab that may take a couple of days to grow, two or three days to grow. And then it goes, you get the results back to you. And that's not so easy in many sites, many other countries, many other hospitals that have very limited facilities or lab facilities, you can't take any tests at all.

Maggie Fox 08:34
And on top of this, I think there's a problem because there aren't as many antibiotics approved for use in newborns as there are for adults, right?

Mike Sharland 08:45
Wow, you couldn't be more clear than that. There are virtually no new antibiotics approved in newborns rather than adults. So, we've had only a couple of new antibiotics approved recently. For newborns it takes time. Adult trials are usually done first. Obviously, that's perfectly right and appropriate, but the children's studies are often delayed quite significantly till the adult trials are completed. And then the baby studies, the newborn baby studies are done, if they're done at all, many years after that as well. So, it's not at all uncommon that you won't get a license for those, for a dose in the baby for maybe 10 years after the drug has been approved in adults.

Maggie Fox 09:22
This is starting to sound like almost an impossible problem. You've got doctors who don't have time to test these babies to find out what they have. Even if they know what they have, there is a very limited number of drugs they can use to treat them.

Mike Sharland 09:35
It's a really serious problem. And the other part of that of course, is you've got to get on and treat with your best guess antibiotics, straightaway. So, you know, (for) sepsis, it's a medical emergency (that) needs to be treated with antibiotics straightaway. And (in case of) babies, you really want to get them on treatment and make sure that you start antibiotics straightaway. That's true all over the world when people see it – a baby is septic.

And it's not uncommon that the healthcare workers usually make the diagnosis, and they understand that they need to give treatment, there is WHO guidelines, for penicillin or (the) old antibiotic gentamicin, and they are usually started straightaway, whether those are in inverted commas, the right antibiotic is (something) you can't tell and that's empirical. That is your first best guess if you're like antibiotic treatment, and you've got to get on with that quickly.

Maggie Fox 10:26
Can you tell us a little bit about how newborns are different even from other children and how they respond to and process antibiotics?

Mike Sharland 10:34
So, the baby's metabolism, the way in which they break down medicines, and (their) kidney excretion, how they do that is generally much less mature than adults or even older children. So, a baby's kidney function, if you've had a baby, then you know that the first couple of days your baby doesn't urinate much.
And the reason for that is because breastfeeding takes time to settle and takes time to get going. So, babies are designed to not urinate much from the first few days, so their kidney function is really not good in the first few days of life. It takes time to kick in.

Baby's liver function also is not so great. And that also takes time to mature as well. You have to be very careful how for babies antibiotics are dosed, and then as well in newborn babies.

Maggie Fox 11:19
So, that brings us to this question, do antibiotics need to be tested differently in newborns?

Mike Sharland 11:24
Certainly, you have to! The studies or clinical trials in newborns that are taken forward by either anybody who's doing research in this area need to carefully look for safety effects and monitor those carefully as well, to make sure those sorts of new drugs coming into babies are done safely.

Equally, it has to be said that the majority of antibiotics that are looked at in children and babies have fairly well-known side effects. And it's very unusual to find different side effects in a baby than you'd expect related to the drug in adults. So, I think they're generally predictable. You need to do good studies, you need to get good research to make sure they're safe. But antibiotics are usually, in fact, surprisingly safe in babies, they're dosed and given correctly.

Maggie Fox 12:12
Your team is doing some of these tests, though. Can you tell us a little bit about the studies you've got going or planned?

Mike Sharland 12:18
So, I mean, we've had an interest in for quite a while now in terms of thinking through how - the right drug at the right dose for the right duration to try and treat new sepsis. We are very focused on the fact that multidrug-resistant. These multidrug resistant infections are now a very serious threat to newborn health. We are working in collaboration with the Global Antibiotic Research & Development Partnership (GARDP) and a range of other groups, including the Medical Research Council Clinical Trials Unit at University College London (MRC) and other investigators globally.

Our group has been working to think through what are the commonest causes of infection in babies globally across Asia and in Africa, South America and China? And then we're thinking through what the better treatments or novel treatments or new treatments that we can think of? New antibiotics - how they're placed? For sure, but there are very few coming through with those. We've been particularly focused on the other older antibiotics that have been around since the '70s, '80s, '90s, and can we go back to those which are generally cheaper antibiotics and start to use new combinations of those?

Maggie Fox 13:25
You mentioned the MRC, that's Britain's Medical Research Council funding. Some of these sounds like you've got a lot of nonprofit funding, (but) the drug companies aren't jumping on this.

Mike Sharland 13:34
You are correct. And you know, and to be fair, in the nicest possible way, it is a small market.

I mean, obviously, there is a very little market for new antibiotics anyway. And that's in adults, and there's even a smaller market in babies. So, I think it is appropriate that the not-for-profits and others (help as) this is a public health problem. And so therefore, it's correct that public health funding should come into this area.

Maggie Fox 14:01

Mike, thank you so much for joining us and talking about this.

Mike Sharland 14:05
No problem. Happy to do so.

Maggie Fox 12:55
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