Transcript

CHATHAM HOUSE
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Anti-Microbial Resistance: A Global Health Security Threat

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Mike Turner

Good evening, everyone. Very nice to see such a large turnout. So, my name is Mike Turner. I'm the chairman this evening. I'm working at the Wellcome Trust. I don't have a particular background in anti-microbial resistance, but I have worked in infectious diseases for 30 years, so I've come across it in a number of contexts.

I'm delighted we've got such a varied panel. I'm looking forward to a very stimulating conversation. And I'm looking forward to all of you contributing to the stimulating conversation, as well as these guys. I think the hallmark of a good meeting such as this is when you hardly hear the chairman at all. I even think that when I'm in the audience, not just when I'm in the chair.

If I could remind people, this meeting is being held on the record and if people wish to comment via Twitter, it's using #CHevents. Please put your phones on silent, please.

Without further ado, we have a distinguished panel. First up is Professor Dame Sally Davies, who I suspect needs no introduction here, so I won't introduce you, our chief medical officer and a major advocate for moving AMR up the agenda within the UK and globally. Then Professor Kevin Outterson, who has a background in law, health law and corporate law. Really interesting, do you guys all get the biographies like I have? It's really interesting. So coming from a very different background, and then works on things like communicable disease dynamics, which for me as a former scientist sounds very un-lawlike and very scientific. I'm very much looking forward to hear your blend between law and science.

Third up, delighted we've got Manica Balasegaram, who is executive director of Médecins Sans Frontières, access campaign. It turns out we actually share a history. We've actually both worked on a relatively obscure disease called African Sleeping Sickness, he at the hard end, at epidemics, and me at the other end as in trying to understand what this curious beast is that keeps causing so many difficult problems.

Then last but by no means least, Nick Cammack, senior vice president and head of Medicines Development Campus at GSK, which is a really unusual and interesting and different industrial approach to – their contribution, if you like, to this, which I hope you're going to tell us about, Nick.

Without further ado, six minutes each. I will keep an eye on the clock. Sally, would you like to start us off, please?

Sally Davies

Thank you, Mike. I was asked to set the scene on anti-microbial resistance and I'll try not to slip into calling it AMR, as a global health security threat. Many of you who are British will know that I stumbled on understanding about this when I wrote my first annual report as chief medical officer to the government in 2013. I discovered that antibiotic resistance – there are other anti-microbial resistance issues, HIV, malaria, TB, that we could discuss but let me just pick antibiotics – is already a reality with 25,000 people

dying each year at a minimum in Europe. At least that number in the States and one child every five minutes in South East Asia.

I could go on about this data, but it is quite incredible. I've managed to excite our prime minister that this is akin to climate change. It's something we're doing to ourselves and if we don't sort this out because we have a dearth of antibiotics, then we face a really very difficult future as before antibiotics, 43 per cent of people died of infection. At the moment, it's only seven per cent across the world.

So he's asked Jim O'Neill, an economist, to do a piece of work around the market failure, and he published – Jim did – with input from RAND and KPMG an economic analysis of what would happen looking forward to 2050 if we go on in the way we are, no new antibiotics and increasing resistance.

Essentially that data suggests that we would have, and we hope it will never get to this, 10 million deaths a year across the world of anti-microbial resistance as compared with just over eight million from cancer and 1.5 million from diabetes or diarrhoea. So you can see that if we don't do something, this is going to be dreadful in terms of human suffering, but his data also suggests that actually it will cost us dear – up to 3.5 per cent of the GDP, the total GDP.

You can dispute the figures and you can say, 'Well of course we won't let it get that bad.' But that begins to show you some of the magnitude of this problem that we need to do something about.

What I'm also interested in is who's it going to hit most? His modelling, based on this work, shows that while it won't be nice for us in Europe, North America, and Oceania, it will be disastrous for Africa, China, India, Asia and Russia. This really is very bad and very worrying. They only looked at three of the seven worrying bugs that WHO worry about.

I would argue that anti-microbial resistance is one of the critical health security issues we're facing at the moment. Many people are trying to do something about it. How do we protect the antibiotics we've got, yet giving better access to poor people who haven't got the effective access that they have, I think, a human right to? How do we develop new antibiotics? How do we go forward? Actually, do we really know what's going on? Do we have the laboratories in place across the world and the networks to do the surveillance we need? Then can we act on it?

So there's a terrific amount of work to do there, but then if you look at where we are at the moment, sitting here, at what we hope is the beginning of the end of the Ebola outbreak, now I worry that if we talk about it in that way, the politicians will take their eye off the ball, the money will disappear and we won't get rid of it. I hope we're at the beginning of the end, but there is no doubt that that outbreak has shown us how we need in countries to strengthen the health systems and the public health systems.

Under a WHO instrument, it's a treaty, isn't it? Treaty, the international health regulations, every country has a duty over the next couple of years to have the basics in place and to report internationally to the WHO outbreaks. Yet when we have the Middle

East respiratory coronavirus, MERS-CoV, there was some delay in reporting the first cases from the Middle East.

How are we going to strengthen countries so they can deliver on their international health regulations and work to reduce anti-microbial resistance? Our prime ministers, very exercised by global health security – we work not only with the World Health Organization but with the US-led Global Health Security Agenda that is bringing many countries together to work on that. We're looking particularly at surveillance, but as well, at the drugs pipeline and the support services.

So I'm going to finish early actually. I could have talked for longer, but I'm not going to. We need to move forward. Developing countries, health systems, public health systems and their international health regulation strengthening but to make it work, we've got to have WHO reform. The Ebola outbreak has shown us that the WHO is not where we need it to be.

We had a special session of the WHO on both Ebola and reform 10 days ago, on the Sunday in Geneva, of the executive board. I'm on that. I was the only person who sat there and said that we as an international community are ashamed by how we responded to Ebola. As it happens, once Britain got going, we were asked to, I'm very proud of what our people and our government has done in Guinea. I think other countries have risen to the challenge.

Some countries, Mali today was declared Ebola free, have done it with support but essentially they have done it. But we need WHO reform. We need to look at the skillsets at country level, at regional office level, and how do they get elected as regional directors. We need them to have a rapid response force, but we probably need other rapid response forces and Germany and the EU are leading a discussion of white helmets, but it's a very medical force. I think we need both medical and public health.

And we need an emergency global contingency fund. So our government, through me, put on the table 10 days ago up to $10 million as a country as a first offer for the emergency global contingency fund for another emergency, assuming that everyone else contributes and we can set it up with proper governance.

Clearly, we're only going to get this right if we get in place the diagnostics, the treatments, be they new antibiotics or treatments for Ebola. Of course, some of these things, we need vaccines and we need to think about what happened in Ebola. Since 1976, we've had 18 small outbreaks, yet in this outbreak, more than 20,000 cases and 8,000 deaths. At least three vaccines, but none had gone into humans. The first ones in a clinical trial phase 3, it's the GSK one that started yesterday or the day before.

We can't let this happen again. So I'm going to leave it to the rest of you to pick up from there, once I've just re-emphasized that AMR and global health security is a global issue and we all have a duty to get this right. Thank you.

Mike Turner

Thank you, Sally. Are there any specific, very specific questions? Or should we move onto the talk? Okay, we'll have the discussion with everyone involved at the end. Without further ado, Kevin.

Kevin Outterson

The lawyer is here because to design a system, a global system that works, that does require law and requires understanding how the companies will make money and how we regulate and control this valuable resource of anti-microbial susceptibility. The fact that these drugs work, we want to keep that. We don't want to waste it.

So we have two twin problems here. One is the one that Dame Sally just described. 25,000 people at a minimum dying each year in Europe, equivalent or even larger numbers in the United States, if you count Clostridium difficile, a horrible way to die. So it's a significant problem around the world.

Simultaneously, we have an access problem. If we're worried about the post-antibiotic era, what would our hospitals look like if antibiotics didn't work? They'd be very different places. Billions of people on the planet live today almost in a pre-antibiotic era. We have hundreds of thousands of deaths every year of children who are dying from susceptible bacterial infections. A normal antibiotic that we have today is not reaching them, so there's an access crisis on top of our overuse sort of crisis.

These twin problems are difficult to solve. So when you react to resistance, you might say, 'Well, let's prevent the companies from overselling and overmarketing.' Hospitals in the United States, hospitals in every developed country have programmes to try and restrict the unnecessary use of antibiotics. We do this in the community too. We educate people, 'Don't take antibiotics for a virus. You're wasting your money. You're harming yourself. You're harming society by doing so.'

But from a company perspective, what just happened with an excellent and thoughtful and totally necessary medical response was to restrict the unnecessary use of these drugs is that the market just got smaller. It would be like if you looked at your phone, your Android phone or your Apple phone, as if Apple was not allowed to sell the iPhone 6 until every iPhone 3, 4 and 5 on the planet was worthless. It would ruin their business model.

So we have these twin problems. The companies want to make something out of it. We don't want them to overmarket. We want to rationally restrict them, and we have this third issue of many people on the planet not having access to the drugs. Fixing any of those problems in isolation makes the others worse. If we just say, 'Let's give free drugs to the world!' and push them out there, we just generate a resistance.

So access without something else is no good. If we say, 'Let's just make innovation happen,' billions of dollars for new drugs, that will just pop all these new drugs, what will we do with them? The same thing we did with the drugs in the 1940s and 1950s and 1960s. We'll waste them. We'll use them inappropriately.

If we just conserve the drugs and constrain them, it might make them last longer. It won't ultimately stop resistance and it will constrain access to people who need them, people who will die without them, both in developed countries and in poor countries around the world

All these three things have to be done simultaneously, which is a really hard lift and it's a really difficult task. But I think it's doable. I think that we're capable of doing this as a global society. It's similar in some ways to climate change. It's a global collective action problem. We all have to do this together. Britain, you can't solve climate change by yourself. Everyone has to get into this together. Similarly with antibiotic resistance.

The best country with perfect infection control still can't prevent resistant bacteria from coming in. There are some horrible studies of watching tourists leave the Netherlands and go off to Thailand and testing them before and after, and people just on normal vacation, not doing anything unseemly, come back with a bacteria that have resistance genes in them. So even the perfect country in terms of doing this right, unless you prevent travel and trade, which we can't. You can't wall yourself off.

So how do we solve these things simultaneously? I think it's a little bit easier than climate change for a couple of reasons. The first is that there's a strong scientific consensus on what we need to do. The scientists understand what needs to be done in terms of research priorities, in terms of conserving the drugs we have, and getting access to the people who need them.

There's also the situation that it's very different from climate change in that if in climate change you might worry about what do the fossil fuel companies think about this model? Here the drug companies, Glaxo being one of them, but many of them are in the leadership saying, 'We understand the business model is broken. Something has to happen differently in this area.' They're not the opponents than they may be in some other situations.

And you have this amazing political mobilization right now, which governments in many countries are focusing on this in ways that we haven't seen before, so in the last – President Obama's budget request that came out just a week ago, a tremendous amount of money, $1.6 billion being proposed. That's the right order of magnitude for the United States per year to try to address this issue. It's not made it through Congress yet. Our Congress has some problems. But it is showing that leadership in many countries understands this is a critical idea, a critical problem.

I'm hopeful and optimistic that we can do something to solve that. A final thing is that Chatham House, back in 2013, became interested in this issue. We've had meetings that went back over the last year and a half and specifically a working group trying to figure out how would this system work, specifically how do the rewards work? How do we incentivize conservation as well as new drugs? How do we finance it?

These sorts of questions have been part of a working group that, within the next month or two, the final report will come out. It feeds into other processes, like the prime minister's commission from Jim O'Neill, a European Union led effort called DRIVE-AB, and a

project in the United States government called CARB, Combatting Antibiotic-Resistant Bacteria.

All these things are showing efforts of different governments to look at the data and where they need more data to generate it, to do the studies, then to come up with a policy solution that works, not just in one country, but in all countries.

Manica Balasegaram

I've been asked to talk about the global implications of anti-microbial resistance. I'll probably start by saying, Dame Sally has given some of the figures that come out of the O'Neill report. But we also see it in a daily reality of the places that we work. I work for a medical organization that works in over 70 countries and we've already seen for some time the impact of anti-microbial resistance. Whether it's in a therapeutic feeding centre in Sub-Saharan Africa in countries like Niger, to surgical units treating Syrian refugees in Jordan, to our health programmes in India.

This is a very troubling reality. What it does really show for us is that it is an international problem. It is a global problem. But there are very specific problems that we see in developing countries. First of all, while recognizing there is a problem, we lack understanding about the problem. We do not know what is the depth or scale of the problem and what are the drivers of the problem. That's a real issue, because when you try to think about the solutions, sometimes you feel you're just lost in a vast ocean of multiple complex issues to deal with. You really don't know where to start.

There's also lack of access to life saving drugs. This is still the reality as Kevin mentioned. Infectious diseases are the number one killers in many developing countries, particularly in the under five age group. Many, many children die simply because they can't get treatment to treatable infections.

Then there's another problem, which as a clinician who has worked in different countries, is a real problem. We have a total and utter inability at times to identify and appropriately manage common infectious diseases. You have a child coming in with a fever, you often have no clue what is the real driver of this problem. Why is the child sick? Often the child has multiple infections, not just malaria, which you can diagnose easily and treat.

Often there's an approach of taking a blunderbuss treatment approach because you don't really know what to do, you have to send this child home and this child may die depending on the decisions you make and this child may have very difficult access to healthcare services. So sometimes you think you do what's best but you're also understanding that you are creating a problem.

Then there's the issue around irrational use and uncontrolled sales, mentioned by Kevin but it's - you just have to walk out, go to a pharmacy down the road and see how people prescribe antibiotics like Smarties. It happens in many, many places. It's happening in human health, but increasingly we are seeing this issue in animal health in developing countries. That is a very important issue that needs to be addressed.

Another issue that we commonly see – poor quality products, poor quality antibiotics. What is the impact of this? Well, it has a direct impact on people who need treatment for life threatening diseases. Imagine if you have poor quality drugs. What is the impact of that? That also is a driver, potential driver of antimicrobial resistance.

Then of course again, it has been mentioned, a lack of needs-driven innovation. There are multiple reasons why this has happened, but clearly we need a business model that incentivizes people to do research into what is clearly a major public health problem. We have to ask ourselves, what is wrong with us in a society that we cannot incentivize things that are clearly important and beneficial to society?

Amidst all these problems, what can we do? Well, it does require a holistic and multi-sectoral approach. When you hear that, you normally say, 'Uh oh,' because it's complicated. I think it is a complex problem, but I think it's within our grasp to solve it.

One of the things that I think needs to be born in mind is that the needs of developing countries are very, very important. They need to be addressed. We cannot side line them. We cannot simply say, 'Let's start with a coalition of the willing,' keep going and then forget their needs. I think the concept of solidarity is key. We need to think about this in a positive way. This is an important way of driving solidarity between countries and peoples.

Number two, prevention. Please, we should not forget prevention because there are so many things we can do. Infection control in hospitals and healthcare centres, health promotion in the populations, vaccination, prevention of infection is key. We shouldn't have to use antibiotics if we can prevent infections, particularly in children.

Legislation and improved regulation. That's easy to say, because actually you need strong health systems and governance and good governance in countries for this to happen. But it is an important facet.

Surveillance. Dame Sally mentioned this. Well, we have to start from somewhere and I think one of the simple things we can do is to support and build on existing networks, because there are networks that exist for surveillance. This is something that needs to be happening as widely as possible. Countries, particularly countries that don't have the capacity, need to be supported in building up their surveillance systems.

There's an additional component that this all plugs into a wider discussion around health system strengthening and universal health coverage. I think it's important that we join the dots here, because ultimately, this is an important debate. How can we promote access but not excess? The answer is to have functional health systems and universal health coverage. The question on how we get there is another issue, but I'll leave it at that.

Innovation. A couple of plugs that I would make is, please don't forget diagnostics. Bearing in mind what I said, having simple tools that can help us better understand where we need to use antibiotics and where we don't is key, but also telling us when we've got a problem with the antibiotics that we use. So I think there needs to be a lot more investment in the field of diagnostics and also in the field of vaccines.

We also need to have business models that promote and incentivize the research and development, but also promote conservation. There are some policy ideas out there. Some of us have our own different favourite flavours, but I think the good news is that there are a range of options. We need to consider, I think, this different range of options and hope to fit that into the different contexts that we're working in.

Lastly, I will say funding because I'm the ultimate cynic when it comes to this. I've never not been disappointed by countries' ability to say things and do something different. I would say, it's great having all of these ideas, well WTO is coming up with a great global action plan to combat this and we're talking about needs-driven innovation. Where's the money? Because the money needs to come from somewhere. It needs to be sustainable. It needs to be long term. It needs to be sufficient, whether it's to support innovation, whether it's to support building surveillance, whether it's to support strengthening health systems, and so on.

I think we need to have a serious look at how we are supporting these different aspects in the field of anti-microbial resistance, but even health security in general. I'm waiting to see how many countries, as Dame Sally mentioned, about Ebola resolution made at WHO, we want to do much more. We want to have emergency capacity. Great. How many countries have committed money to that? The United Kingdom. Bravo. I'm very proud of being British that we have done something, but other countries need to follow.

I think this needs to be done across the board and we need to move away from a model where there are just a few countries working on a donor based system. We need something different. We need a true solidarity mechanism with the capacity of countries depending on what they can afford and what they can't pay, but everyone I think doing their part to deal with this problem.

I will just finish by saying that Ebola was mentioned but in my 15 years working in international health, I have dealt with different outbreaks and been in a recurrent situation where you are trying to deal with a problem with very limited tools. It's not a new problem for me. It's not a new experience for me. For some of you, living in a country like the United Kingdom, it's unthinkable that anyone can be in the situation.

But it's not. The reality is there and I can tell you, it is a very depressing reality and soul destroying reality to be in. I really hope that we don't get into this for anti-microbial resistance. Thank you.

Nick Cammack

I think it may be left to the last speaker to provide the good news, the ray of hope, I hope. But maybe not entirely good news. I think the pharmaceutical industry clearly has a significant role to play in tackling anti-microbial resistance, but not alone. That's my message. We can't do this alone in the future.

In the few minutes that I have, I want to touch on three areas. There's science, so again there's back to the science, the clinical evaluation of new medicines and partnership approaches to finding those new medicines. As you've heard from the other speakers, imagine years back the availability of antibiotics from different companies, many and

varied. It meant that there was an increasingly fragmented market from a business perspective and so companies started to lose interest and fewer and fewer were involved in anti-microbial drug discovery and development.

But then as you've again heard from the other speakers, the rise in anti-microbial resistance started and where we are today is it's the problem we are hearing about and there are, the pipeline of new drugs is at best very limited and at worst some might say dry. For me as a pharmaceutical company scientist, knowing how long it takes to find new drugs and develop them and bring them out to the market, this is extremely worrying because we're a long way from having new medicines that will tackle the resistance issue.

So let me just come to the science and to the anti-microbial drug discovery. The few companies that stayed in the field after others pulled out have found that notoriously difficult. For many years, companies have been trying to find alternative approaches to the antibiotics that were originally discovered decades ago, with little success. I think there are a number of different reasons, but I'll pick out just three confounding factors.

Back in the 1980s and 1990s, companies were in this mode of find your target that you know belongs, in this case, to the bacteria. Screen your millions of compounds against it and there you have your lead chemical to take through preclinical development and into the clinic.

What was found there, that you can find these molecules, they inhibited the target but then when you got to the level of the actual organism, these organisms are very clever. They find ways of either preventing the molecule getting into the bacteria, or if it gets in, spitting it back out. These are sort of evolutionary mechanisms to protect it in its environment.

That sort of approach did not work. I think a second piece is that particularly organisms like E. coli, salmonella, have very, I would describe it as a thick coat and in fact molecules can't penetrate. So again, you find something that inhibits the target but it never gets into the organism. The other thing is, in this disease area, these disease areas, you need to have high therapeutic levels of your drug in the body to make sure you kill off all the bugs. That's not the case necessarily with other diseases which you can treat with medicines.

So all these together meant that the pharmaceutical industry found that even if they brought lead chemicals forward into preclinical development, with the doses that they knew they needed to achieve in man, toxicity became a big issue and I think this distinguishes this area from many others that attrition in terms of toxicity of molecules heading into clinical development has been a huge, huge problem.

I think the other thing is, and it's very easy in retrospect, we all followed the same approach over many years and never ventured out of the small molecule sort of space to find medicines. I'll just give you one example from GSK. We have in GSK stayed in this discovery space for many years. In one programme that started in 1998, there were three molecules. One, then another, then another, from this programme.

This was around the bacteria topoisomerase. Three molecules got close to the clinic and then failed for toxicity reasons, and it's the fourth one that is now in clinical trials. So

that's 1998. That's 17 years ago, so when I'm talking about the time it takes, hopefully not that long in the future, but this presents a real problem for bringing new medicines forward.

I think just briefly on the clinical evaluation, I think there's been great progress by the regulators. The European Medicines Agency now have a sort of adaptive licensing approach of looking at maybe small populations. Manica was talking about identifying who's really got the disease and infection you want to treat. FDA as well, with programmes now to allow you to focus on specific populations with significant medical needs.

In the regulatory space, there's a lot of improvement. Another good use of diagnostics is of course identifying the patients that you put into these studies to really show an effect or not of your new medicine. I do stress that. I think again, for that reason as well, diagnostics are hugely important going forward.

Then just finally, partnerships. I mentioned that I think for the pharmaceutical industry, they can't do this alone because I think whilst we are good at what we do, the sort of preclinical discovery piece and into the clinic, we're not the experts in the biology. The academic community are the experts in the biology.

I think we all need to work in partnership to bring the new discoveries forward. I think we need to open out the research agenda from just the same old traditional small molecules to maybe antibodies, maybe other ways of delivery, investigating how to disrupt biofilms which are these conglomerations of bacteria that are very hard to tackle, really break into this sort of new research space in antibacterials. For that, I think we need partnerships of academia and industry and public funding bodies to really drive that forward and provide the medicines that we can then use to treat anti-microbial resistance. Thanks.