SOUTH CENTRE

SOUTH BULLETIN

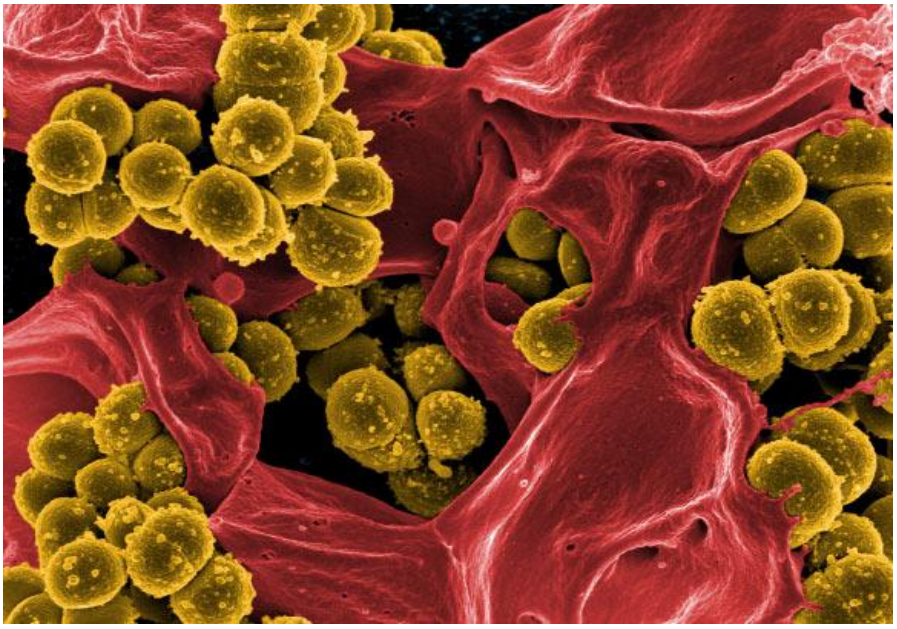
Published by the South Centre • www.southcentre.int • 18 April 2018, Issue 101

AMR: The gravest threat to global health

Antibiotic resistance—and the broader antimicrobial resistance (AMR) - is a silent but major killer. In fact it is emerging as the most serious threat to global health, with experts warning of a "post-antibiotics apocalypse".

This special issue of South Bulletin focuses on the AMR crisis, especially on how it affects developing countries—and the great challenges on fighting this threat.

• Pages 2-3



NIAID

Methicillin-Resistant Staphylococcus Aureus (MRSA) Bacteria

Superbugs are super dangerous: The biggest threat to global health

New Atlas

The UK Review on AMR estimates that superbugs could kill 10 million people a year by 2050.

By Martin Khor, Executive Director, The South Centre

There is a threat to the future of humanity so silent that few people notice it, so pervasive that many families have suffered from it and so dangerous that it may soon be the leading cause of premature deaths worldwide.

If climate change has now become more obvious and visible as the No.1 risk to our civilisation, antibiotic resistance will soon rival it as the gravest threat to human life and health.

Many friends have told me of how their relatives have contracted infections while staying in hospitals and could not be cured with a normal dose of antibiotics. Some of them have died.

For example, the mother of a close friend of mine died from MRSA (methicillin-resistant *Staphylococcus aureus*) after a visit to the hospital for an unrelated minor ailment.

MRSA is an antibiotic-resistant pathogen that causes a variety of serious infections. It is well known for being spread in hospitals, but it is also a problem elsewhere in the community.

Resistance of bacteria to many antibiotics is growing. The genes of some bacteria that survive an antibiotic attack change and adapt to better defend themselves, and tougher new generations of these bacteria have become increasingly immune to the same or other antibiotics that are stronger.

Unfortunately, in the never-ending race between stronger bacteria and stronger medicines, the bacteria are winning.

The war zone is our bodies. The bacteria that survive, widely called "superbugs", are growing and becoming more immune to antibiotics treating the same disease.

Their resistance genes can also spread to bacteria that cause other diseases, thus jumping species barriers and resulting in that resistance moving quickly to threaten our ability to treat many diseases.

In fact, there are specific genes that specialise in resisting antibiotics and jumping species barriers to enter other pathogens. These "jumping genes" are accelerating the problem.

In 2013, there were about 480,000 new cases of multidrug-resistant tuberculosis. There are high proportions of antibiotic resistance in bacteria that cause common infections like urinary tract infections, pneumonia and bloodstream infections in all regions of the world. Gonorrhoea is now almost untreatable in many countries.

The problem is not confined to antibiotics and resistant bacteria. Besides bacteria, there are other pathogens such as viruses that cause AIDS and hepatitis, and parasites which cause malaria that are treated by other antimicrobials.

These other microbes are also becoming resistant to medicines. For example, malaria is becoming more resistant to artemisinin-based therapy in some South-East Asian countries, and AIDS patients are increasingly not responding to first-line anti-AIDS medicines.

So, the problem of antibiotic resistance has now broadened to antimicrobial resistance (AMR) and the crisis now covers more people and more diseases.

At present, an estimated 700,000 people worldwide die annually from antimicrobial resistance. This number is projected to swell to 10 million deaths a year by 2050, according to a 2015 review on AMR commisioned by the British government.

The report also estimates that 300 million people will die prematurely because of drug resistance in the 35 years from 2016 to 2050 and that between now and 2050, the world could lose US$60 trillion to US$100 trillion of economic output if AMR is not tackled. Most of the deaths and economic losses will be in developing countries.

Health leaders are finally sounding the alarm bell. Britain's chief medical officer Dame Sally Davies has warned of a "catastrophe".

Before her term as head of the World Health Organization ended last year, Dr Margaret Chan spoke of the end of modern medicine in a post-antibiotics era, in which common infections such as strep throat or a child's scratched knee could once again kill.

These warnings have come very late, but it is better late than never. In the 1980s, the Consumers' Association of Penang (CAP), where I used to work,

published studies on unethical marketing by drug companies of almost 20 medicines, which led to their inappropriate use and contributed to resistance. The health authorities took action by banning or restricting the sales of most of those medicines.

CAP also published a book in the mid-1990s titled *Revenge of the Killer Germs*, warning of the looming AMR crisis and calling for urgent action.

CAP was ahead of the curve and its warnings have been vindicated.

A recent international action is the 2015 Global Action Plan on AMR adopted by the World Health Assembly, which has spurred most countries to formulate their own national plans.

Another action is the United Nations summit-level event on AMR in 2016, where heads of governments pledged to take action to address the crisis. This led to an interagency coordination group that will come up with recommended actions in 2019.

At the national level, a lot more can be done, including surveillance and data collection, infection control, better diagnosis aided by diagnostic tools, introduction of many new regulations and guidelines on drug marketing, proper prescription and dispensing, and a policy ensuring that new antibiotics are freely or cheaply available to the public.

The recognition of AMR as a crisis is only at the beginning stage. Much needs to be done. Every day of delay will allow the bugs to become superbugs and super-superbugs with dire consequences for all of us.

Martin Khor is the Executive Director of the South Centre.

Contact: director@southcentre.int

New WHO guidelines: Don't use antibiotics for growth promotion in animals

As global health leaders warn that antibiotic resistance is leading to the end of modern medicine, the World Health Organization (WHO) issued guidelines to prohibit or restrict using antibiotics to feed animals reared for their meat. Urgent coordinated actions are needed to avoid the end of modern medicine.

While an effective antibiotic kills most of the targeted germs, a few may survive and develop resistance which can spread to other bacteria that cause the same infection or different infections. The rate of resistance and its spread can increase if antibiotics are wrongly or over used, and they then become increasingly ineffective to treat bacterial infections.

A key tipping point was reached recently when it was found that some bacteria had evolved to be resistant to colistin, the antibiotic of last resort which is used on a patient when all other antibiotics are found ineffective.

In 2016, researchers in China found colistin-resistant E. coli bacteria in 20 per cent of animals, 15 per cent of raw meat and 1 per cent of hospital patients that were sampled. The colistin resistance gene (mcr-1) could easily be transferred among different bacteria.

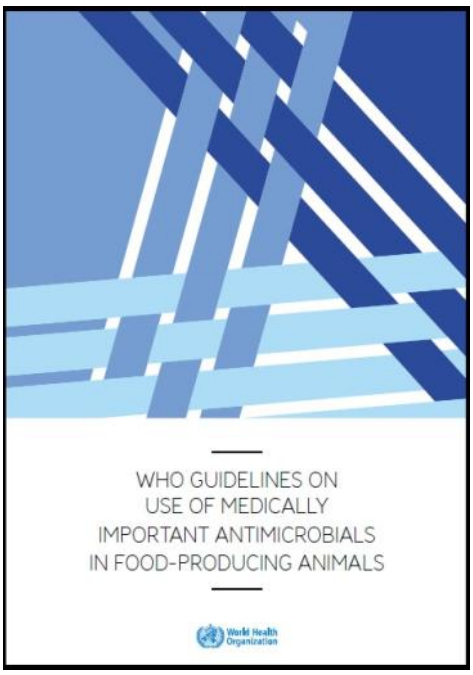
If this resistance continues to spread, colistin will become less and less effective and we will eventually lose the "antibiotic of last resort."

The colistin story also carries another lesson. It is widely thought that resistance is due to over-use of antibiotics by consumers or the spread of infections caused by resistant bacteria to patients in hospitals.

However resistance is also spread through the agriculture sector and the food chain, as

Max Whittaker/Reuters

In most large-scale livestock operations, antibiotics are mixed with water to prevent illness and encourage growth, which contributes to the breeding of drug-resistant bacteria that enter the food supply.



shown in the study on colistin in China.

In many countries, much of the antibiotics used (80 per cent in the case of the United States) are fed in farms to animals as growth promoters, to make them grow fatter and faster, as well as to prevent or treat diseases.

Resistant bacteria build up in the animals and are present in raw meat. Some of these bacteria are passed on to humans when they eat the meat.

The environment is another source of the spread of resistance. Residues and wastes containing resistant bacteria flow from farms and hospitals and contaminate soils, drainage systems, rivers and seas. Some of these bacteria find their way to humans.

The European Union banned the use of antibiotics as growth promoters in animal feed in January 2006 while the US started action to phase them out in December 2013.

In most developing countries, little action has so far been taken. Hopefully that will start to change. In November 2017, the World Health Organization issued its first ever guidelines on the use of antibiotics in food-producing animals.

"Scientific evidence demonstrates that overuse of antibiotics in animals can contribute to the emergence of antibiotic resistance," said WHO's Food Safety Director, Dr Kazuaki Miyagishima.

A WHO-sponsored study published in *The Lancet Planetary Health* in November 2017 found that interventions that restrict antibiotic use in food-producing animals reduced antibiotic-resistant bacteria in these animals by up to 39%, according to a WHO press release.

The research paper (authored by William Ghali and 10 other scientists), reviewed thousands of studies, and selected 179 relevant ones, to find if there is an association between interventions that restrict antibiotic use and reduction in the prevalence of antibiotic -resistant bacteria in animals and in humans.

The key findings are that:

• "Overall, reducing antibiotic use decreased prevalence of antibiotic-resistant bacteria in animals by about 15% and multidrug-resistant bacteria by 24-32%."

• The evidence of effect on human beings was more limited but showed similar results, "with a 24% absolute reduction in the prevalence of antibiotic-resistant bacteria in humans with interventions that reduce antibiotic use in animals."

This study influenced the development of the WHO's new guidelines, which are aimed at influencing policy makers in the agriculture and health sectors. According to a WHO press release, the guidelines include:

• An overall reduction in the use of all classes of medically important antibiotics in food-producing animals.

• Complete restriction of these antibiotics for growth promotion and for disease prevention without diagnosis.

• Healthy animals should only receive antibiotics to prevent disease if it has been diagnosed in other animals in the same flock or herd or fish population.

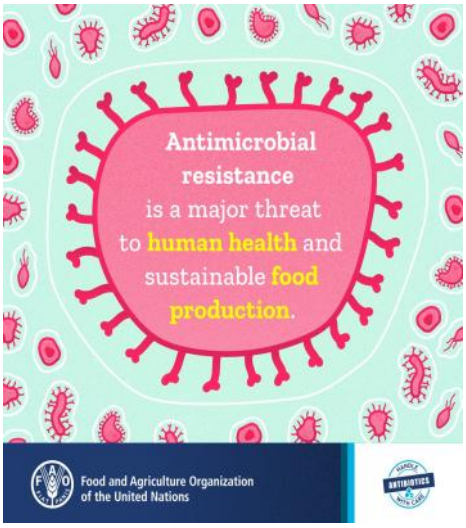
• Antibiotics used in animals should be from the WHO list as "least important" to human health and not from "highest priority critically important."

In 2015, Health Ministers attending the World Health Assembly adopted a Global Plan of Action on anti-microbial resistance, and they agreed that each country should prepare national action plans by 2017.

Since there are many sources of antibiotic resistance, the national effort must include not only the health authorities but also those responsible for agriculture and the environment.

The agriculture authorities should phase out inappropriate use of antibiotics for animals, especially for growth promotion, while the environment authorities should prevent resistant bacteria and genes from contaminating soils, drainage systems, rivers and seas.

By Martin Khor



Landmark Asian workshop on AMR organized by South Centre and TWN

Opening ceremony of the workshop: From left, Chee Yoke Ling (TWN), Adam Tregidga (hidden) (Fleming Fund), Dr Chong Chee Keong (Health Ministry, Malaysia), Martin Khor (South Centre), Dr Ying-Ru Jacqueline Lo (WHO) and Dr Katinka de Balogh (FAO).

The antimicrobial resistance (AMR) crisis is affecting many Asian countries seriously. There has been progress in the last few years in recognizing this crisis. But for most countries the battle is only at the beginning stage, much more needs to be done, and several problems of implementing national plans need to be overcome if real progress on the ground is to be made.

This picture of the situation emerged at a South-east Asian regional workshop on AMR attended by 60 participants, including policy makers from 10 countries, as well as representatives of civil society, scientists and regional AMR focal points of the World Health Organization and the Food and Agriculture Organization.

The workshop, held in Penang (Malaysia) on 26-28 March 2018, was co-organised by the South Centre and the Third World Network, with the support of the Fleming Fund. The policy makers were from Indonesia, Thailand, Malaysia, the Philippines, Myanmar, Vietnam, Cambodia, Laos, China and India. NGOs from most of these countries, as well as Australia, also attended.

It was a landmark meeting for several reasons. Firstly, high-level policy and technical experts, most of them being focal points or coordinators of their national AMR committees, took part. Secondly, the government officials were AMR experts from both the human health and animal sectors, which is quite rare as usually international AMR meetings involve officials from only one sector or the other. The workshop thus lived up to the concept of a One Health approach.

Thirdly, civil society groups involved in AMR or general health issues were also represented, enabling dialogues to take place between the governmental and non-governmental sectors. It was recognized that actions by both are crucial to generate public awareness and mobilise public support for AMR actions. Fourthly, the workshop provided the most up-to-date information on global and regional developments (provided by experts, including from the WHO, FAO and South Centre) as well as the state of policies and actions at national level.

The workshop was opened by Dato Dr Chong Chee Keong, Director of Disease Control of Malaysia's Health Ministry, who stressed the importance of Asian countries to join the global fight against AMR. Malaysia is taking the challenge seriously, as seen in the recent launch of the national action plan by the Ministers of Health and Agriculture.

Martin Khor, Executive Director of the South Centre, presented a comprehensive analysis of why developing countries are being affected the most from the AMR crisis and must join in the global effort to address it. However their interests and challenges while doing so should be recognized so that they can effectively implement their national plans.

The countries need international cooperation in funding and technical equipment to set up the institutions and coordinating mechanisms to undertake the required actions, including surveillance, diagnosis, infection control, regulation of prescription, dispensing, marketing of antimicrobials to ensure rational use of drugs, as well as actions to phase out antimicrobial use as growth promoters in animals and in aquaculture, and to keep antibiotics out of the environment. Khor said that affordable access to existing and new antibiotics, and encouraging the de-linkage models of innovation, which were highlighted in the UN General Assembly Declaration on AMR, should also be components of international cooperation.

In a session on the AMR situation in Asia, the AMR regional focal persons for WHO (Dr Socorro Escalante,

Martin Khor, The South Centre

Dr Katinka de Balogh, FAO

Beverley Snell, HAI, Asia-Pacific

Sunil Gupta, Indian Health Ministry

WHO-WPRO and Prof Tjandra Yoga Aditama, WHO-SEARO) and the AMR regional focal person for FAO (Dr Katinka de Balogh) presented on the state of the AMR problem in the human health and the animal sectors, and the roles played by their organisations. Beverley Snell (HAI, Asia-Pacific) gave a review of the AMR national action plans submitted by Asian countries and the status of implementation.

On the session on international action and processes, Dr Viviana Munoz of the South Centre gave an update on the origins and progress of the Inter-Agency Coordination Group established by the UN General Assembly. Dr Socorro presented on the WHO's global surveillance system (GLASS) and its most recent implementation report. Adam Tregidga explained the role of the Fleming Fund, an initiative of the United Kingdom's Department of Health, in supporting the developing countries' activities on AMR.

A highlight of the workshop was a session on the need for a One Health Approach to AMR. Dr Peter Collignon, Director of ACT Pathology at Canberra Hospital (Australia) spoke of the AMR situation in the human health, animal, aquaculture and environment sectors and their interconnectedness.

He also gave a presentation on the WHO Guidelines on the Use of Medically Important Antimicrobials in Food Producing Animals, which had been published in November 2017. Dr Collignon was the Chair of the Guidelines Development Group that produced the guidelines after a rigorous process. There was a lot of interest in the guidelines, as seen from the many questions and comments to Dr Collignon in this session and in the breakout groups.

In the session on actions at the national level, the lead speaker Dr Christopher Lee (National Head of Infectious Disease Service, Malaysian Health Ministry) gave a lively and frank account of the process that a country needs to initiate in order to set up a coordinating body involving all relevant Ministries (especially health and agriculture) to implement AMR policy measures.

Viviana Munoz (South Centre) explained the importance of affordable access to antibiotics, and an appropriate system to encourage innovation that produces new antibiotics. Lim Kah Poh (Malaysian Pharmaceutical Society) spoke on the marketing practices used in promoting antibiotics and the need for regulation, while Beverley Snell (HAI, Asia-Pacific) presented on obstacles that need to be overcome if rational use of antibiotics is to be achieved.

Two sessions were held on national AMR policies and experiences in the human health sector. Presentations were made by Harry Parathon (Chair of AMR Committee, Indonesia), Suraya Amir Husin (Malaysian Health Ministry), Htay Htay Tin (General Secretary, National AMR Committee, Myanmar), Li Dachuan (National Health Commission, China), Nov Vandarith (Cambodian Health Ministry), Somphone Soulaphy (Laos' Health Ministry), Nithima Sumpradit (AMR Focal Point, Thai Health Ministry), Sunil Gupta (Indian Health Ministry), Cao Hung Thai (Vietnam's Health Ministry), Nina Isabelle Tolentino (Philippine Department of Health).

This was followed by two sessions on AMR national policies in the animal and food sector. Speakers included Riana Arief (Director, CIVAS, Indonesia), Rozanah Asmah Abd Samad (Malaysian Dept. of Veterinary Services), Adela Contreras (Bureau of Animal Industry, Agriculture Department,

Dr Peter Collignon giving a presentation on the WHO guidelines on antibiotic use in animals.

Dr Christopher Lee, Malaysian Health Ministry

Martin Khor (South Centre, left) presenting a certificate of appreciation to Harry Parathon (Indonesia, right) for good practices in the livestock sector. Indonesia recently banned the use of antibiotics as growth promoters in animals.

Philippines), Sasi Jaroenpoj (AMR containment section, Dept. of Livestock Development, Thailand), Le Thi Hue (Veterinary Dept., Vietnam), Min Thein Maw (Veterinary Dept., Myanmar), Sun Jing (Peking Union Medical College, China), and Chea Rortana (National Animal Health and Production Research Institute, Cambodia).

The Experiences of Civil Society on AMR were then discussed, with speakers from national groups from Indonesia, Malaysia, India, Thailand as well as international or regional groups Third World Network, Antibiotic Resistance Coalition, ReAct-Asia and HAI-AP.

Four breakout groups were organized with participants discussing the state of AMR plans and coordination in their countries, the challenges of implementing activities and control measures, and what support is required to enable speedier progress.

From the reports of the breakout groups and from the earlier country presentations, the following main points can be drawn:

• There has been quite a lot of progress in making a start in combatting AMR, with countries already formulating their national action plans and having a national AMR committee. However, while some countries have incorporated both the health and agriculture/animal sectors in their AMR committees, others have only the health ministry.

• While the health ministries have embarked on a number of activities such as surveillance and infection control, the agriculture/livestock sector in many countries have still to catch up with regards to actions.

• One encouraging sign is that Indonesia has banned the use of antibiotics as growth promoters in livestock since January 2018, whereas Vietnam imposed a similar ban a few years ago and in Thailand there has been a ban on antibiotic use as growth promoters in chickens since 2006.

• In most countries, little work has been done on the environmental component of the spread of AMR. This is an area requiring much more work.

• While plans and guidelines have been formulated in a number of areas, implementation in most countries is still inadequate. This is because of various factors, depending on the country concerned. The factors include that there is lack of priority and lack of political interest or will; lack of financial and human resources; too few equipment needed for diagnostic work; lack of champions and of a systematic stewardship program at national or local level.

• There is still inadequate understanding of the AMR issue in the animal sector in many countries. The WHO guidelines on antibiotic use in animals is a useful and important reference as it takes a human health perspective. This should be supplemented by guidelines jointly issued by WHO, FAO and OIE, so as to involve all the relevant international organisations.

• To increase the speed of implementation and of progress, a fund or funds to help developing countries to coordinate their AMR actions and to build their technical and organisational capacity should be made available with sufficient resources.

Feedback from participants through a final session (and through evaluation forms that they filled up) was that they found the workshop very useful for enabling the sharing of experiences and best practices, and the coming together of participants from different sectors (human, animal and food; government and non-government) and countries. Many of the participants also flagged the importance of focusing attention on the animal sector including following the example of Vietnam and Indonesia in

Breakout group discussions in progress.

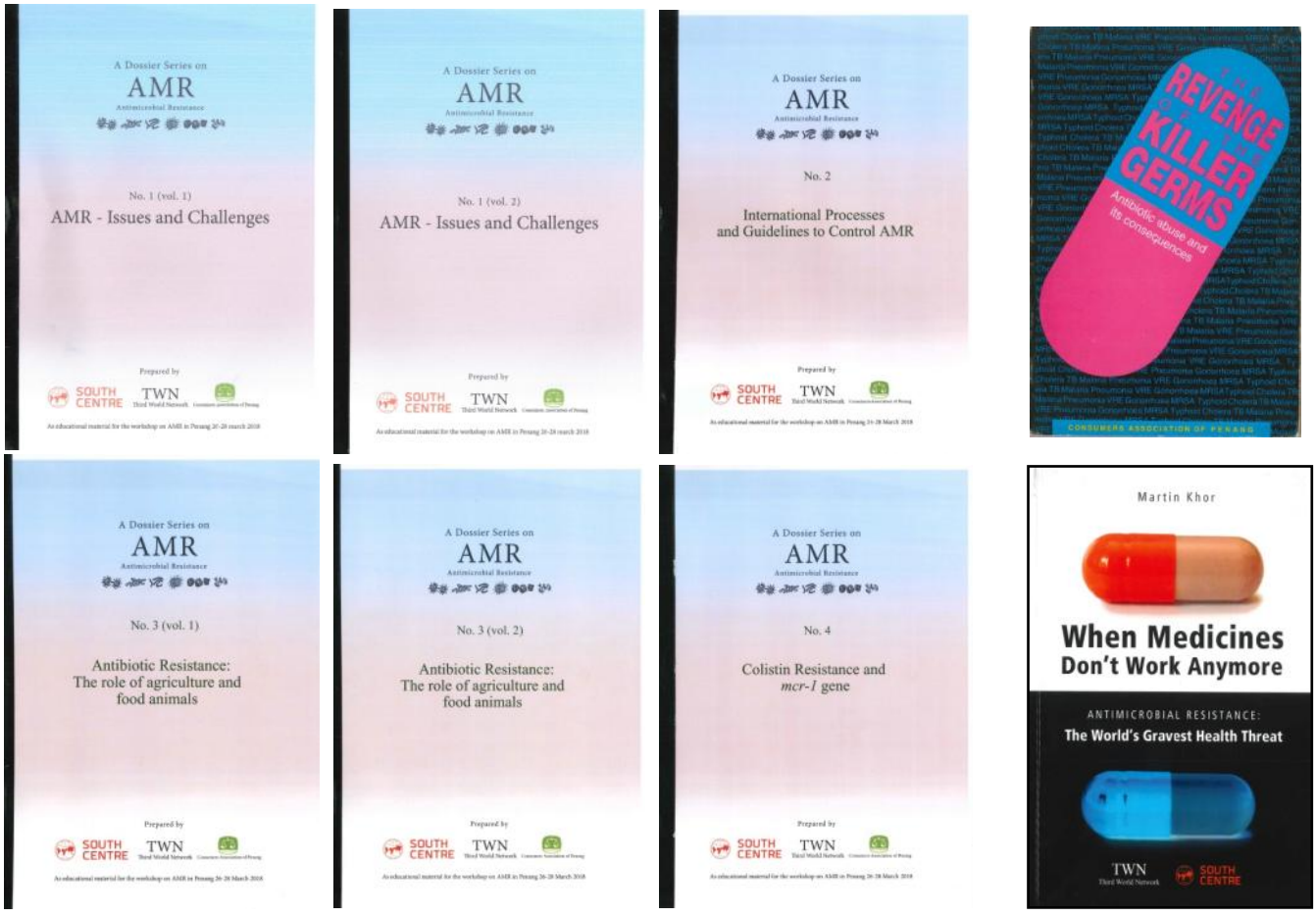
Group photo of the participants of the Regional Workshop on AMR

banning of the use of antibiotics as growth promoters for animals. Participants also would like discussions on AMR and the environment.

Among some of the follow-up actions that the participants would like from the South Centre and TWN are to organise workshops on a regular/ annual basis to take stock of countries' progress; to form a "Community of Practice" (CoP) or an Asian coalition on AMR; and to come up with an Asian Action Plan.

Educational materials were produced for the workshop. These include six dossiers (compilation of useful articles) on general AMR issues; International Processes and Guidelines to Control AMR; Antibiotic Resistance: The role of agriculture and food animals; and Colistin Resistance and mcr-1 gene. Two books were also produced: *When Medicines Don't Work Anymore* (by Martin Khor) and *Revenge of the Killer Germs* (a reprint of a CAP book first produced in 1996).

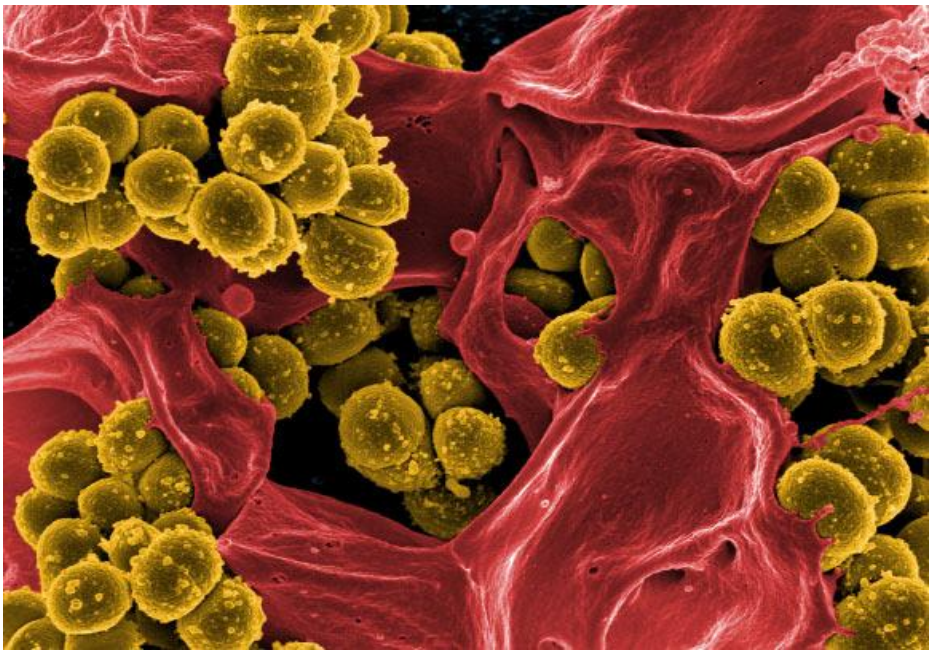
In the concluding session, South Centre director Martin Khor said the organisers were interested in publishing a book of the workshop presentations. A report of the proceedings of the workshop will be produced. Updated versions of the dossiers will also be produced. He said that a workshop on AMR in Asia will also be organized in 2019, with a focus on South Asian countries.



Educational materials distributed during the workshop.

The Global Threat of Antimicrobial Resistance and the Challenges and Needs of Developing Countries

The antimicrobial resistance crisis will affect developing countries the most. Yet they are not well prepared to tackle it. This is part of a paper used by Martin Khor when speaking at a panel at the High-Level Event on AMR at the UN General Assembly in September 2016 and updated for the Asian Workshop on AMR in March 2018.



NIAID

Methicillin-Resistant Staphylococcus Aureus (MRSA) Bacteria

By Martin Khor, South Centre

Antimicrobial resistance has become a major global health crisis

Antimicrobial resistance (AMR) is a major and serious problem. It represents possibly the greatest global crisis in public health in the world today, akin to climate change as the top environmental problem.

Antimicrobial resistance is resistance of a microorganism to an antimicrobial drug that was originally effective for treatment of infections caused by it. Resistant microorganisms (including bacteria, fungi, viruses and parasites) are able to withstand attack by antimicrobial drugs, such as antibacterial drugs (e.g. antibiotics), antifungals, antivirals, and antimalarials, so that standard treatments become ineffective and infections persist, increasing the risk of spread to others.

Resistance by bacteria and other microbes to antibiotics and other medicines may be a natural process, as the microbes causing diseases evolve through time in response to the medicines. However, the rate of resistance is accelerated and the scope of resistance is broadened by several factors: the inappropriate use of antibiotics, due to inappropriate prescribing and dispensing; inappropriate marketing methods and sales promotion; lack of awareness by patients; the inappropriate and widespread use of antibiotics in the animal husbandry and agriculture sector, which passes on resistant microbes to humans; the spread of resistance through the environment; and the existence of certain genes that specialize in accelerating and spreading resistance among bacteria, thus greatly increasing the rate and spread of resistance to many species of bacteria that cause diseases.

AMR is now a global crisis, with many pathogens becoming resistant to many antibiotics. As leading public health officials and senior scientists have warned, we are now entering a post-antibiotics world, in which it is increasingly difficult to treat simple ailments and dangerous diseases. The incidence of multi-drug resistance has risen significantly, and for a few diseases there is almost no cure left. In 2012, World Health Organization Director-General Dr. Margaret Chan warned that every anitibiotic ever developed was at risk of becoming useless. "A post-antibiotic era means in effect an end to modern medicine as we know it. Things as common as strep throat or a child's scratched knee could once again kill." The Chief Medical Officer of the United Kingdom, Dame Sally Davies, warned in 2013 of a "catastrophe" of AMR being so widespread that we would be back to a 19th century situation of a pre-antibiotic era when many diseases could not be treated.

The UN General Assembly High-Level Event and Political Declaration on AMR

A landmark development at global level is the adoption on 21 September 2016 of a Political Declaration on AMR by the heads of states and governments at a high level event on AMR. It was subsequently formally adopted by the General Assembly.

Many political leaders and Ministers spoke at the event on the need to fight the AMR crisis. The Political Declaration recognized that antibiotic resistance is the "greatest and most urgent global risk" and that "due to AMR many 20th century achievements are being gravely challenged, particularly the reduction in illness and death from infectious diseases…" This is the first ever statement by the heads of all the countries that recognize the AMR

Recent information on the extent of resistance

A good description of the extent of the AMR has been given by WHO in its Fact Sheets on AMR. The following is a summary of the WHO findings as at January 2018:

- Antimicrobial resistance threatens the effective prevention and treatment of an ever-increasing range of infections caused by bacteria, parasites, viruses and fungi.

- Patients with infections caused by drug-resistant bacteria are at increased risk of worse clinical outcomes and death than patients infected with non-resistant strains of the same bacteria. They also consume more health-care resources than patients having non-resistant strains of the same bacteria.

- There are high proportions of antibiotic resistance in bacteria that cause common infections (e.g. urinary tract infections, pneumonia, bloodstream infections) in all regions of the world.

- Resistance to Klebsiella pneumoniae (common intestinal bacteria that can cause life threatening infections) to a last resort treatment (carbapenem antibiotics) has spread to all regions. In some countries, because of resistance, carbapenem antibiotics do not work in more than half the people treated for K. pneumoniae infections. K. pneumoniae is a major cause of hospital-acquired infections such as pneumonia, bloodstream infections, and infections in newborns and intensive-care unit patients.

- Resistance in E. coli to a widely used medicine for treating urinary tract infections (fluroquinolone antibiotics) is very widespread. This treatment is now ineffective in over half of patients in countries in many parts of the world.

- A high percentage of hospital-acquired infections are caused by highly resistant bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA) or multidrug-resistant Gram-negative bacteria. People with MRSA are 64% more likely to die than those with a non-resistant form of S. aureus, which is a common cause of severe infections in the community and hospitals.

- In 2016, there were 490 000 new cases of multidrug-resistant tuberculosis (MDR-TB). Only a quarter of these were detected and reported. Extensively drug-resistant tuberculosis (XDR-TB) has been identified in 121 countries. MDR-TB requires treatment courses that are much longer and less effective than those for non-resistant TB. Among new TB cases in 2016, 4.1% were MDR-TB (19% for those previously treated for TB). About 6.2% of people with MDR-TB have XDR-TB.

- As of July 2016, resistance to first-line treatment for P. falciparum malaria (artemisinin-based combination therapies or ACTs) has been confirmed in 5 countries (Cambodia, Laos, Myanmar, Thailand, Viet Nam) of the Greater Mekong subregion. Patients with artemisinin-resistant infections recover if they are treated with an ACT containing an effective partner drug. However, along the Cambodia-Thailand border, P. Falciparum has become resistant to almost all available antimalarial medicines. The spread or emergence of multidrug resistance, including resistance to ACTs, in other regions could jeopardize important recent gains in malaria control.

- Treatment failures due to resistance to treatments of last resort for gonorrhoea (third-generation cephalosporin antibiotics) have been confirmed in at least 10 countries. The new updated WHO guidelines for gonorrhoea do not recommend quinolones (a class of antibiotic) due to widespread high levels of resistance. Gonorrhoea may soon become untreatable as no vaccines or new drugs are in development.

- In 2012, WHO reported a gradual increase in resistance to HIV drugs, albeit not reaching critical levels. Since then, further increases in resistance to first-line treatment drugs were reported. In 2010, 7% of people starting antiretroviral therapy (ART) in developing countries and 10-20% in developed countries had drug-resistant HIV. In some countries, resistance of 15% or more is reported for those starting HIV treatment, and up to 40% among those re-starting treatment. Those who have HIV resistant to first-line treatment require second and third line regimens but these are 3 and 18 times more expensive respectively than first-line drugs.

crisis and in which they pledge to take action.

The Declaration stressed the need of developing countries to obtain financial resources. It also stressed that "affordability and access to existing and new antimicrobial medicines, vaccines and diagnostics should be a global priority."

On the need for innovation, the Declaration recognised the importance of delinking the cost of investment in R&D from the price and volume of sales so as to facilitate equitable and affordable access to new medicines, diagnostic tools and vaccines.

The declaration established a task force of agencies (co-chaired by the WHO and Secretary-General's office) which would provide guidance for global action on AMR and requested the UN Secretary-General (UNSG) to report on progress of implementation of the Declaration and to make further recommendations.

In 2017, the **Interagency Coordination Group** was established by the UNSG to follow up on the Declaration. It is made up of individual experts (many drawn from health ministries) and representatives of UN and other international organisations. The IACG has a plan of action, and has held

three meetings to date. It also established six sub-groups to come up with analysis and recommendations. The report of the IACG will be submitted to the UNSG who will present his own report to the UN General Assembly in 2019. The IACG will be holding more consultations with the member states and with public interest groups. It is important for developing countries' policy makers and NGOs to engage with the IACG.

The global fight against AMR has to involve the developing countries as a top priority

It is to be expected that the developed countries will take the lead in the global fight against AMR. This is due to the greater availability of financial resources, and higher levels of scientific knowledge, research capability and technology as well as institutional and organizational capabilities including in the health care sector.

However, the developing countries will have to play a central role in the global battle against AMR, since it is in the developing countries that the majority of the world population reside, that there is the highest number (and in some cases highest incidence) of people suffering from drug-resistant diseases, and that pathogens with the genes specializing in spreading resistance have been mainly found in patients in developing countries. Moreover, in an increasingly globalised world with a high degree of travel and trade, there can be the easy spread of drug resistant bacteria and diseases.

Therefore, the special needs and interests of the developing countries have to be given the highest priority in the global fight against AMR if we are to make adequate progress.

Developing countries are becoming more aware of the AMR crisis

Political leaders and public health officials in developing countries are becoming more aware of the AMR crisis.

At the Summit meeting of the Group of 77 and China, which has around 130 members from developing countries, held in Santa Cruz (Bolivia) in May 2014, the political leaders of the Group adopted a Declaration which included the following paragraph 66:

"We are concerned about the increasing problem of antimicrobial resistance to existing drugs, including those against TB and malaria. As a result, increasing numbers of patients, especially in developing countries, face the prospect of dying from preventable and/or treatable diseases. We urge the international health authorities and organizations, especially WHO, to take urgent action and to work together upon request with developing countries that do not have adequate resources to address this problem."

However, in most developing countries, the public is still lacking knowledge and awareness of the threat of AMR, while coordinated and systematic action is also at only a beginning stage. Therefore, much more has to be done.

People in developing countries are most affected by AMR

People in developing countries will be most affected by the AMR crisis. At present AMR is estimated by the UK-sponsored Review on AMR to globally cause 700,000 deaths annually (and this is a low estimate). The annual deaths attributable to AMR is projected to rise to 10 million in 2050. Of these deaths, it is projected that 390,000 will be in Europe, 317,000 in North America, 22,000 in Oceania, 4.7 million in Asia, 4.2 million in Africa and 392,000 in Latin America.

For most diseases the majority of people affected by AMR are in developing countries. The Review on Antimicrobial Resistance (2014: p. 9) concludes that "countries that already have high malaria, HIV or TB rates are likely to particularly suffer as resistance to current treatments increases." Particular countries at risk include India, Nigeria and Indonesia (malaria) and Russia (TB) and Africa will suffer greatly as the HIV and TB co-morbidity is likely to get worse.

The Review also estimates that 300 million people are expected to die prematurely because of drug resistance over the next 35 years (i.e. 2015 to 2050) and world GDP will be 2 to 3.5% lower than it otherwise would be in 2050. Between now and 2050 the world can expect to lose US$60 to 100 trillion of economic output if AMR is not tackled. OECD countries are expected to have US$20-35 trillion in cumulative loss of output by 2050; which means that about US$40-65 trillion or two-thirds of the losses will be borne by non-OECD countries.

The case of tuberculosis is illustrative. The Review on Antimicrobial Resistance (2016) found that of "the 10 million deaths that might be associated with drug resistance each year by 2050, around a quarter will come from drug-resistant strains of TB." Most of these anticipated cases and deaths from resistant TB will be from developing countries, although TB is also affecting several developed countries.

The majority of people affected by increasing resistance to drugs treating malaria and to the first-line treatments for HIV-AIDS are also from developing

Source: Longitude Prize

countries. Pathogens that are increasingly resistant to powerful antibiotics (E coli, K. pneumonia, S. Aureus, salmonella, shigella, gonorrhoea) are prevalent in developing countries.

Policy makers and the public in developing countries should therefore recognize that the AMR crisis is mainly taking place in their countries and that they have to give the highest priority to addressing it. On the other hand, the international community has to pay special attention to the needs of developing countries and to assist them in addressing the AMR crisis.

In recent years, there has been the discovery of at least two types of genes (NDM-1 and MCR-1) that have the characteristic of being able to make bacteria highly resistant to known drugs and to also spread from one species of bacteria to other species through horizontal gene transfer. Bacteria containing these genes were first found in developing countries, and their presence is now confirmed in many other countries. The discoveries of NDM-1 and MCR-1 add urgency to the task of addressing anti-microbial resistance.

Developing countries face many challenges in addressing AMR

Developing countries face many challenges in addressing AMR. There is a lack of awareness, expertise, funds, technical equipment, personnel and political will to take the range of actions required. These are serious obstacles to the implementation of AMR action plans.

Another issue is that AMR is a problem that involves the mandate of several sectors and thus government Ministries or departments. The sources of the problem are in health, agriculture and livestock, and the environment. To educate the public, the education and information departments need to be involved. The involvement and commitment of all these departments are required in the multi-faceted fight against AMR. Obtaining the commitment and coordination of the various sectors requires great effort and the commitment of political leaders at the highest level. It is not easy to achieve this.

The developing countries also have other problems that compete with AMR for attention and resources. Although it is a very major problem, AMR is a silent killer rather than an obviously critical issue compared to other issues within and outside the health sector (such as malnutrition, infection outbreaks and epidemics; conflict and terrorism; floods, drought, water scarcity and climate change; unemployment, poverty, migration and refugees).

In the competition for scarce funds and personnel, it is difficult for AMR

Actions needed to address AMR at national level

Boosting the capacity of developing countries to take required actions is of key importance. The actions that need to be taken at national level include:

- Research in science, including analysis of bacteria mutation, gene transfer, rates and ways of the spread of resistance, and AMR in the food chain.
- Vastly improving surveillance and data collection on resistance in various pathogens to various drugs, and resistance of bacteria in food-related animals, in food, and in the environment.
- Improve and upgrade laboratory equipment especially diagnostic tools, to enable better diagnosis, to distinguish between bacteria and viruses, and between resistant and non-resistant bacteria (and pathogens) so as to enable appropriate treatment.
- Infection control in hospitals, including hygiene, upgrading of rooms and theatres, equipment, air-flow systems etc.
- Infection control through provision of safe water, proper sanitation and habitat and a clean environment.
- Formulating and implementing a national policy for rational and appropriate use of antibiotics and other anti-microbials.
- Regulation and enforcement in the sale, prescription and dispensing of anti-microbials.
- Guidelines or regulations for medical personnel, hospitals and clinics on the appropriate use of antibiotics, and on relations with industry sales representatives.
- Regulating drug companies in marketing practice to improve their role in appropriate drug use, and address effects of incentives to sales personnel and to medical and veterinary personnel that are linked to volume of antibiotic sales.
- Regulation of the agriculture and livestock sector to phase out the non-therapeutic use of antibiotics, as this inappropriate use is a major factor in the AMR crisis. As a first step, antibiotics that are used for treatment of life threatening diseases in humans should be prohibited as use in animals as growth promoters.
- Addressing the contamination of the environment by residues of antibiotics, including those emitted by drug factories and medical facilities.
- Educating the consumer and community on the appropriate use of antibiotics.
- Formulate policies enabling affordable access for the public to existing and new antibiotics and other antimicrobials.
- Establishing a national action plan on AMR and the institutional framework for implementation, including coordination within the health sector and with other Ministries including of Agriculture, Education, Information.
- Boosting the capacity of health related NGOs, the media and educational institutions to take on AMR issues as a priority.
- Mobilise domestic and external funds to enable implementation of the national AMR plan and activities.

Making resources available for developing countries

In order to implement the necessary actions, the developing countries require international cooperation for the following:

- Obtaining adequate financial resources for addressing AMR. Developing countries will have to mobilise domestic resources to carry out activities to address AMR. However some of them, especially lower income countries, will require international funding to augment the domestic resources, due to the high cost involved and the competing issues that also require financing. Countries should prepare their comprehensive AMR action plans together with cost estimates and a budget with estimates of the resources that can be mobilized nationally and resources that are sought from international cooperation.
- Obtaining Equipment and Technology needed to address AMR. This would include equipment for diagnosis, for making hospitals and clinics AMR-proof, scientific research, and innovation.
- Upgrading hospital facilities to improve infection control, surveillance and diagnosis, the ward and surgery environment, to minimise the spread of infections (especially resistant infections) within the hospitals and to provide an appropriate environment for patients with resistant infections.
- Obtaining antibiotics and other anti-microbials to treat patients including those with ailments caused by drug-resistant pathogens.
- Costs of phasing out the non-therapeutic use of antibiotics in the animal husbandry sector.
- Costs of addressing the environmental aspects of AMR.
- The recruitment and training of adequate numbers of personnel including for management and coordination of the AMR action plan, surveillance, administration and enforcement of guidelines and regulations.
- Boosting the capacity of communities, civil society organisations, educational institutions and the media to raise public awareness and take other actions relating to AMR.

An international fund, or a number of funds, should be established to assist developing countries to meet the above costs of addressing AMR.

Part of the fund should be used for making available technical equipment that may be required for surveillance, diagnosis and treatment.

to obtain the resources and attention it deserves.

Developing countries also need affordable access to existing and new antibiotics and other microbials

Another major issue of concern to developing countries is their need for affordable access to antimicrobials, including existing and future ones. Even when the medicines are not patented and there is competition from generics, many poor patients cannot afford treatment. If the antimicrobials are patented, the prices escalate and pose a big barrier to access. As resistance builds, 2nd and 3rd line drugs are needed to treat existing diseases; these new drugs are likely to be patented and expensive.

There are several examples of the high cost of new anti-microbials that is a barrier to access.

- Two new drugs for treating drug-resistant TB which have been recommended by WHO have been on the market for four years, but only 4,800 people with DR-TB in 2016 were treated with them, according to Médecins Sans Frontières (MSF). Only 469 people received delamanid and just over 4,300 received bedaquiline. Thus, fewer than 5% of people needing the drugs received them while others continued to be treated with older and more toxic regimens that cure only 50% of people treated and cause severe side effects. More than half a million people were infected with DR-TB in 2015. In an earlier statement in 2016, MSF said the price of a single course of delamanid in developing countries was $1,700 per person, and it called for a 98% price reduction. Delamanid has to be taken with several other drugs to effectively treat DR-TB, and the regimens, without delamanid, already cost $1000-4500 per treatment course at lowest prices available in developing countries, which is unaffordable for governments. MSF is advocating a target price of $500 per treatment course for DR-TB.

- The prices of second and third line HIV medicines are much higher than first-line medicines. Patients who no longer respond to first-line treatment (due to resistance) have to switch to the newer medicines but face cost and access problems. According to MSF, in 2015 the lowest available price of a first-line one-pill-a-day combination (tenofovir+emtricitabine+efavirenz) was $100 per person per year. But the lowest price of newer drugs (or 'salvage' treatments) needed by people who have run out of other treatment options was $1,859 per person per year (raltegravir+darunavir+etravitine). This is 18 times the price of first-line therapy and over six times the price of second-line combination. The MSF report finds that "prices of older HIV drugs continue to decline while newer drugs remain largely priced out of reach. This is in large part because pharmaceutical corporations maintain monopolies that block price-lowering generic competition."

- The new drug for Hepatitis C, sofosbuvir, was introduced in the US market at US$80,000 for a course of treatment. In middle-income developing countries that were not offered a voluntary license by the drug company (Gilead), the price varied from about $10,000 to $40,000. Sofosbuvir, usually taken in combination with another drug, has an efficacy rate of 95% and less side effects, compared to a much lower rate with more side effects of older regimens. But the price of sofosbuvir is out of reach to most people and governments in developing countries (and developed countries too). The high prices could be maintained due to

a patent owned by Gilead. Malaysia in 2017 issued a compulsory license for sofosbuvir. A local firm is now importing generic sofosbuvir from Egypt. The lowest price offered by Gilead to the government for sofosbuvir was RM50,000, according to the Health Minister. The government has now negotiated to obtain a generic version of sofosbuvir at RM 1,000 (US$250) a patient. The government is now offering the combination of sofosbuvir and daclastavir at government hospitals free; it will bear the cost of treating patients. Previously, some patients had to pay RM300,000 for a treatment course. Malaysia has 400,000 people with Hepatitis C. According to the news report, 23,000 patients in the Health Ministry's list will be treated in stages, with 2,000 treated in 2018.

These three examples illustrate that access to new antimicrobials being developed will be a major issue. With regard to antibiotics, the new antibiotics should be considered international public goods accessible to people especially in developing countries which do not otherwise have financial resources to afford them if they are sold at monopoly prices.

Developing countries also need affordable access to vaccines as well as laboratory and diagnostic equipment.

Affordable and reliable access is required not only for new antimicrobials but also for existing ones. Many people in developing countries still do not have access to the existing medicines, either because they are not available in the market or the public hospitals, or they are unable to afford to buy them. According to presenting key stakeholder groups including ReAct, GARDP and the European Society of Clinical Microbiology and Infectious Diseases, in a Commentary in the Lancet Infectious Diseases journal, unsustainable production and supply of old antibiotics is becoming a serious global problem that further limits the treatment options for common bacterial infections and this is adding to the worldwide crisis of antimicrobial resistance. "Shortages and sudden price increases of antibiotics have been reported, indicating a fragile supply system. Consequences might include worse clinical outcome, accelerated resistance development and increased costs for the individual and society at large," according to one of the authors, Thomas Tangden, Medical Director at ReAct.

When patents become a barrier to access, countries have the policy option of making use of the flexibilities in the WTO's TRIPS Agreement, such as establishing patent criteria that improve the quality of patents by awarding patents only for genuine inventions; and issuing compulsory licenses or government use orders to increase market competition by enabling the production and importation of generics. However, countries that exercise their right to make use of these flexibilities often find strong opposition from originator companies and their governments. The legitimate use of flexibilities should not be opposed.

It is important that the principle of access is given priority when evaluating and developing the models for research and development of new antimicrobials.

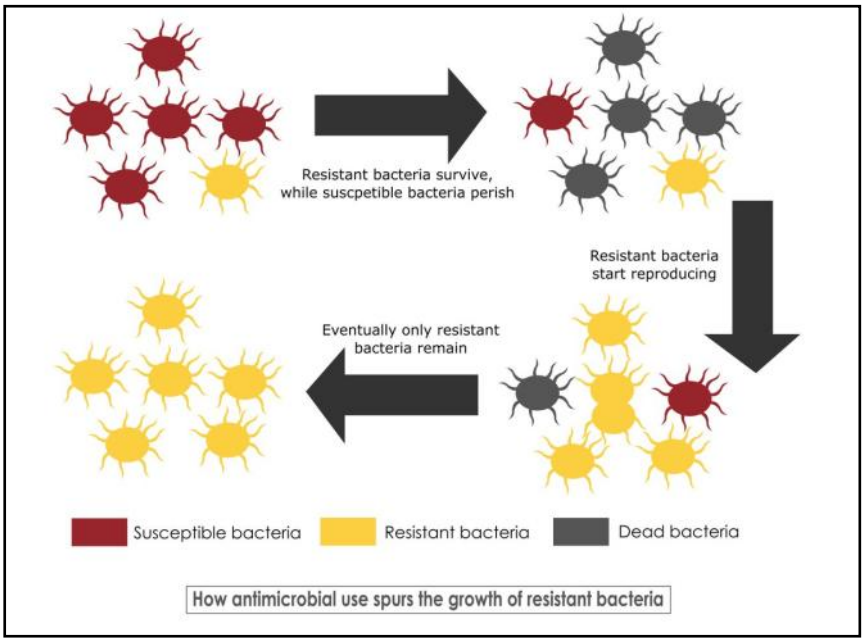
The Political Declaration on AMR places great emphasis on access. In many parts, the Declaration mentions affordable access to existing and new antimicrobials as an important principle and objective.

The issue of financing and of access was prominent in the Political Declaration of the UNGA

The Political Declaration of the UNGA on AMR is very strong on capacity building, access to medicines, technology transfer and financial support to developing countries. It says (in Para. 10.d) that the heads of state and government "underline further that affordability and access to existing and new antimicrobial medicines, vaccines and diagnostics should be a global priority." Para. 10.f says the heads of state and government want to "enhance capacity building, technology transfer on mutually agreed terms and technical assistance and cooperation for controlling and preventing antimicrobial resistance, as well as international cooperation and funding to support the development and implementation of national action plans, including surveillance and monitoring, the strengthening of health systems and research and regulatory capacity, without jeopardizing, in particular in the case of low- and middle-income countries, health or posing barriers for access to care."

At the WHA in May 2017, several developing countries, including Brazil and India, stressed the need to place access to affordable existing and new antibiotics and diagnostic tools as priority issues, as it was not enough to take action on the control and distribution of antibiotics. They also highlighted the need to use innovation models based on the "delinkage" principle, to ensure affordable medicines. These two issues of access and delinkage were prominent in the UNGA Political Declaration, but were not given due recognition in the Development and Stewardship Framework document, complained Brazil.

The need for an innovation model consistent with access



Source: ReAct

to new antibiotics

It is imperative to develop new antimicrobial medicines, diagnostic tools, vaccines and other products, as a major part of addressing the AMR crisis. There are deep-rooted problems with R and D in relation to antibiotics. One is that there have been few or no new categories of antibiotics discovered in the past two to three decades, and there are few promising new products in the present pipeline. A reason for this may be that there is less profit to be made from antibiotics compared to drugs for diseases which require long-term treatment.

Second is that the dominant R&D model links medicine prices to the cost of R&D, with patents for the company, which results in high prices for new drugs which are unaffordable to most people in developing countries. There is thus a need for a R&D model that is compatible with access to medicines, one which delinks the cost of innovation from the price of new medicines as well as from sales volume. This is often referred to as innovation models based on the de-linkage principle.

There are at least two main strands of thinking on what kind of R and D model to encourage. The first is to continue with the dominant model but increase the incentives to companies by providing more R and D grants to them and allowing an extended patent term for new antibiotics in the hope that this will provide more incentives to the major drug companies and result in new products. The downside is that this increases the period of monopoly and high prices, and worsens the problem of access.

The second is to establish public funding by governments and donations by charities, so that the cost of innovation is not borne by the companies. The proprietary rights to the new products would belong to the public fund or charity, which has the option of providing licenses freely to companies or institutions, at least to those from developing countries; or licenses granted to companies would be linked to conditions that favour access. This would delink the cost of innovation from the prices of the new products, which can be set at affordable levels. The WHO has been exploring options for new partnerships for open collaborative models of R and D. It is partnering with the Drugs for Neglected Diseases initiative to set up a non-profit partnership, the Global Antibiotic Research and Development Facility to develop new affordable antibiotics that will also be subjected to a conservation scheme.

The Political Declaration on AMR adopted by political leaders at the UN is clearly in favour of R and D activities that are closely linked to access to medicines and that are in line with the "delinkage" model. It has a lengthy paragraph (10.c) dealing with R and D. It states that heads of states and governments "underline also that all research and development efforts should be needs-driven, evidence-based and guided by the principles of affordability, effectiveness and efficiency and equity, and should be considered a shared responsibility: in this regard we acknowledge the importance of delinking the cost of investment in research and development on antimicrobial resistance from the price and volume of sales so as to facilitate equitable and affordable access to new medicines, diagnostic tools, vaccines and other results to be gained from research and development."

The UN Secretary General's High-Level Panel on Access to Medicines states that its report "emphasizes that market-based models of innovation for AMR are unsustainable. Funding for R&D to address AMR and related challenges must be operationalized through delinkage models. Indeed, the challenge of AMR represents an important and incontestable context in which the viability of delinkage innovation models can be fully explored."

Summary of key points on meeting the needs of developing countries

Programmes dealing with implementing actions on AMR should include the following points:

- Fully take into account the challenges and needs of developing countries.

- Strong international cooperation for building capacity of developing countries to address AMR.

- Mobilising of financial resources to support capacity building and implementation of AMR action plans in developing countries.

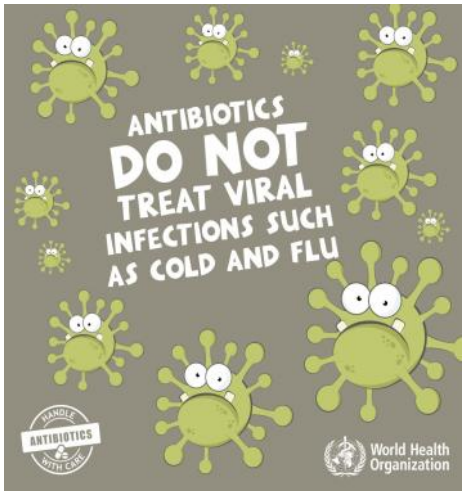
- Establish a global fund for capacity building in developing countries on AMR issues, to be based in the UN, and linked to implementing the Global Action Plan on AMR. Meanwhile, governments should be encouraged to establish their own funds or allocate part of their ODA to assist developing countries to address AMR.

- Technology transfer and the provision of technical equipment including diagnostics and know how to developing countries on grant or concessional terms.

- Ensuring affordable access to existing and new antimicrobials, vaccines and diagnostics, especially to people in developing countries.

- Developing and encouraging R&D models which delink the price of antimicrobials and other products from the cost of R&D; including where the innovation costs are financed through public funds and charities, and the license to produce the new products is available cheaply or at low cost, at least to companies and institutions in developing countries.

- Support to developing countries for capacity building and financing of the comprehensive range of activities in addressing AMR at national level, including prevention of infections, appropriate use of antibiotics, new regulations including on marketing, prescription and dispensing of drugs and their enforcement, reform of antibiotic use in agriculture, improvement of practices in hospitals and clinics, educating the public, etc.



Tackling Antimicrobial Resistance: Challenges for Developing Countries

The following article is based on a South Centre Policy Brief on AMR that focuses on problems and issues facing developing countries in confronting the AMR crisis.

Ian Cuming – Getty Images/Ikon Images

E.coli bacteria. An antibiotic-resistant strain of E. Coli was found which is resistant to colistin.

By Mirza Alas and Viviana Muñoz Tellez

Introduction

There is a need to escalate the global public health response to the growing threat of antimicrobial resistance (AMR).

Antimicrobials – including antibiotics – are used to treat infections caused by bacteria, as well as by other microbes, such as viruses, parasites and fungi. Globally, millions of people are infected with antibiotic-resistant bacteria each year; hundreds of thousands lose their lives. More and more strains of bacteria are resistant to an ever-rising number of antibiotics, and pathogenic species that have become resistant cause infections that can no longer be treated with antibiotics. This seriously jeopardizes not only our ability to treat common infections but also to perform complex medical procedures such as organ transplants and cancer treatments.

Although resistance is a natural process, the inappropriate use of antibiotics causes it to accelerate. The extensive misuse and overuse of antimicrobials both in humans and animals have accelerated the emergence and spread of resistance. Without a radical change in the current medical practices to reduce infection and rates of inappropriate antibiotic usage, antimicrobial resistance will become one of the greatest threats to humankind; to public health and to the global economy.

This is aggravated by the fact that no new classes of antibiotics have been developed since 1987. There are very few effective, safe options to switch to once resistance develops to existing antibiotics, as the antibiotic development pipeline is nearly dry, particularly for gram negative pathogens. In 1990, 18 pharmaceutical corporations had active programs to address antimicrobial resistance. By 2010, only four remained in this space. There is some progress being made but not significantly or rapidly enough. A new antibiotic substance was found in the human nose, which could potentially be used to treat antibiotic resistant pathogens such as methicillin-resistant *S. aureus* (MRSA). However, for this new antibiotic substance to be ready for human use, many more tests and clinical trials will need to take place to prove it is safe and effective to use. There is also hope for effective alternative treatment for bacterial infections, such as the use of peptide polymers to kill superbugs without antibiotics. We are still years away from new antibiotics and alternative treatments.

The lack of effective antibiotics against resistant infections can affect us all – patients and doctors, farmers and consumers, humans and animals – without regard for international borders.

Recognizing the dire need for action, a broad global commitment was made among countries on a new global plan to combat AMR. The World Health Assembly of the 194 Members of the WHO in May 2015 adopted the Global Action Plan on Antimicrobial Resistance. The plan outlines the following five objectives that are meant to support the actions needed to address antimicrobial resistance:

- Improve awareness and understanding of antimicrobial resistance through effective communication, education and training;
- Strengthen the knowledge and evidence base through surveillance and research;
- Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures;
- Optimize the use of antimicrobial agents in human and animal health;
- Develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions.

Now it is a question of implementation. In September 2016 at the sides of the United Nations General Assembly there will be a High Level Meeting on AMR that will deliver a political declaration and hopefully pave the way for coordinated actions on AMR with a higher political commitment.

There is enough evidence to demonstrate that AMR is already causing untreatable infections all over the world and for developing countries, it is both a public health challenge and a development challenge. Tackling AMR in developing countries requires deep understanding of the particular context and needs of the rural and urban populations. In this note, we examine four critical issues for developing countries to design an effective public heath response to AMR, and for which international support is needed, in the form of public financing, investment and policy space for implementation.

1. Access

For developing countries the challenges that AMR pose add to already existing ones, particularly when it comes to access to medicines, vaccines and diagnostics. A 2012 report by UNICEF found that diarrhea and pneumonia are the leading causes of child death globally and that "less than a third of children with suspected pneumonia received antibiotics in developing countries, with South Asia averaging 18 per cent." These figures resonate with a Lancet study from early 2016 which found that more than a million children worldwide die each year because of untreated infections such as pneumonia and sepsis.

The case of pneumonia provides an important example of the current challenges on access since pneumonia infections can be prevented with the pneumococcal conjugate vaccine (PCV). Countries that are able to provide immunization for children have seen important decreases of infection and therefore there is less need to use antibiotics. However, today the price of such a vaccine is out of reach for many children in developing countries, prompting Médecins Sans Frontières (MSF) to launch a campaign directed at Pfizer and GlaxoSmithKline (GSK) for the reduction of prices. According to MSF data, PCV alone accounts for about 45 per cent of the total cost to vaccinate a child in the poorest countries. Moreover, even at the lowest subsidized GAVI prices, the cost of fully vaccinating a child increased 68-fold from 2001 to 2014 and many middle income countries are paying higher prices. If we are to tackle resistance it is important that we make sure preventive measures such as vaccines are affordable, without which the challenge is an even bigger one for developing countries.

Another example is the rapid increase of resistance in tuberculosis (TB) and the low access to treatment. Today there are more and more cases of extensively drug-resistant TB (XDR-TB) and the majority of these cases are in developing countries. The increase in resistance is threatening the possibility to provide adequate treatment for this infection and even estimates by the Review on Antimicrobial Resistance emphasized that from "the 10 million deaths that might be associated with drug resistance each year by 2050, around a quarter will come from drug-resistant strains of TB." This means that efforts to step up adequate treatment for TB need to take into account the particular needs of developing countries. The prices of new drugs, where they do exist as well as delays in their registration in developing countries are also creating barriers in dealing with AMR. The pricing and availability of new TB drugs such as bedaquiline and delamanid, remain a huge challenge in high TB burden countries. MSF estimates that two years after these two drugs have come to the market, less than 2 per cent of those who need these treatments can access them, and at current prices they are out of reach for most governments and patients.

The access challenges also include the need for laboratory and diagnostic capacity that is necessary for detecting pathogens that will help health workers to determine the best course of treatment. For developing countries access to vaccines and diagnostics are key tools to prevent infections but this alone is not enough. It is also necessary to step up important public health improvements in sanitation, hygiene and safe water initiatives. Access to current and new antibiotics will be necessary to ensure not only the health of the population but to design strategies that will allow countries to improve the use of existing antibiotics and the conservation of new ones. Thus, access to affordable antibiotics, vaccines and diagnostics tools constitutes an urgent priority for developing countries and it is important that price is not used as an incentive to curb misuse, especially in resource-poor settings.

2. Research and Development

One of the aggravating factors for the rise in AMR is that there are few prospects of **new** medical products such as vaccines, medicines and diagnostics. In the face of drug-resistant bacteria, the dry pipeline for new antibiotics is particularly troubling. The lack of innovation on TB is also particularly concerning for developing countries as about 95 per cent of the cases of tuberculosis infection occur in low and middle-income countries, where cases of multidrug-resistant tuberculosis are on the rise.

Accelerating research and development efforts to bring about new products must be a priority. These efforts must ensure that new medical products are able to adequately meet health needs and they must be accessible and affordable to all who need them. If new products are developed but they are not affordable or accessible in countries and areas where the diseases burden is high, these will be out of reach for people who need them.

There is substantial evidence that the current incentive model for research and development (R&D) fails to drive private pharmaceutical firms to produce new medical products to treat a number of diseases that do not offer profitable commercial returns. Private firms will bring to market the products that are more profitable. Thus, increasing R&D to meet health needs, which are a global need and integral to the public health goal, is not necessarily in line with the private sector goal of profit and sales maximization. For many diseases that lack private R&D efforts, such as neglected diseases, it is due to the low purchasing power of the countries and populations most affected. Antimicrobials are of more general use across populations and low purchasing power is not the major factor deterring private investment efforts. There are many other factors that reduce prospects of revenues for private firms in new antimicrobials. These include the fact that companies cannot rely on high level of sales to recover profits and investments due to short dosing regimen of patient intake in their lifetime and government policies discouraging unnecessary use of antibiotics.

Considerations of access, affordability and stewardship must be at the centre of any initiative to increase R&D

efforts for new antimicrobials. This is particularly pertinent as discussions are ongoing with regard to the global pooling of resources towards R&D.

Two policy perspectives can be taken to address the gap in R&D efforts for new antimicrobial products. One way is to focus on mobilizing private sector R&D. Countries can make efforts to address the mismatch of incentives for the private sector to invest in R&D. The big challenge here is designing incentives that will create R&D while at the same time ensure affordability, access to new products, and ensuring the cost-effectiveness of governments' limited resources. In this area, a consortium of large pharmaceutical firms has declared interest in increasing investment in R&D in antibiotics but call on governments to help create a "sustainable business model." Governments are requested to allocate more funds – the magnitude is unclear due to lack of transparency in industry costs of R&D – to "create a sustainable and predictable market" for new antibiotics, diagnostics and vaccines. No one knows with certainty how much funds are required. The report of Lord Jim O'Neill estimates that such costs would entail about USD 0.8 to 1.3 billion in the form of upfront large payments called "market entry rewards" for antibiotics, and proposes the establishment of a Global Innovation Fund for AMR, endowed with USD 2 billion over five years. There is also a call for additional incentives, such as facilitating regulatory approvals or extending time during which the product is not subject to any competition.

The assumption is that if there are significant funds available to ensure profitable compensation for R&D, private firms will populate the antimicrobial pipeline. However, it would be misguided to assume that if the cost of R&D is largely met by public funds, high prices and enforcement of patents and other legal monopoly rights against potential competitors and other competition reducing strategies would not be practiced by private firms. Evidence to date shows that this is not the case. Public funding support for basic and translational research is already substantial and this has not deterred regular industry profit-maximizing strategies, to the detriment of access to affordable medicines and treatment.

Another approach to promote R&D and innovation is to consider complementary models to the industry-led R&D model. Various innovative approaches to R&D have been tried and identified. To some extent private sector firms are engaged in some efforts such as public-private partnerships for the development of products for neglected diseases for which commercial markets are non-existent. One new related initiative, the Global Antibiotic Research and Development Partnership (GARDP), has surfaced for R&D in antibiotics, building on the experience of the product development partnership, Drugs for Neglected Diseases Initiative (DNDi). Other approaches include open collaborative R&D models and prizes. In such an approach, the R&D process is undertaken by a public-interest organization; the financing of R&D is mainly through public-sector or donor funds, alternative incentive models are used to delink cost of R&D from volume-based sales and prices of antibiotics – which support conservation of and access to new antibiotics – and to ensure that products will be accessible through prices that are as low as possible. This requires measures such as removing barriers to follow on innovation and competition, including patents and other forms of intellectual property protection.

A set of principles can assist in prioritizing the type of initiatives or mechanisms that developing countries may choose to support for promoting R&D in antimicrobials, at the national level or as part of a regional or global initiative. These have been developed under the WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPOA) and the Consultative Expert Working Group on Research and Development: Financing and Coordination (CEWG). Mechanisms should delink (separate) the cost of R&D from the price of medical products and sales to ensure that these will be available and affordable in a sustainable manner to the populations that need them. Any measure that can promote R&D but that can have the effect of limiting access or allowing for high prices and inappropriate promotion/sales is not an effective mechanism for the purposes of public health.

Moreover, special considerations should be given to mechanisms that build on open knowledge approaches to allow knowledge to be shared and to ensure that access to R&D outputs is not restricted, including access and sharing of information from clinical trials. Developing countries should also consider mechanisms that can contribute to strengthen the R&D capacity of and/or technology transfer to these countries. Pooling funds and collaborative R&D are means to support cost-effective and collaborative interventions. Public sector support for R&D is necessary and commitments should be relative to the financial capacity of the country concerned, while ensuring a public return in terms of affordability and priority setting on this public investment.

Any global initiative that developing countries support should effectively promote de-linkage of the costs of

FAO/Giulio Napolitano

A poultry operation in Egypt. Good hygiene on farms can help stem the rise of Antimicrobial resistance (AMR) due to over-reliance on antimicrobials.

R&D from prices and sales volumes, be needs-driven and evidence-based, guided by agreed priorities set by governments and by principles of shared responsibility, affordability, effectiveness, efficiency and equity.

3. Regulation on Use of Antimicrobials

Use in animals

One of the many drivers of the overuse of antibiotics and its contribution to resistance is the use of antibiotics for animal husbandry and aquaculture. While many of these treatments are necessary, the problem is intensified by the use of antibiotics as growth promoters and other non-therapeutic uses in animals.

Improving regulation of antibiotics in animal husbandry, including limiting and eventually phasing out their use for growth promotion, is an important measure to reduce rates of antibiotic resistance in humans. Because a lot of the same drugs that are used to treat infections in humans are also used for animals, selection of the resistant bacteria has resulted from either type of usage.

An increasing number of studies indicate that a major proportion of resistant *E. coli* that cause extra-bowel infections in humans may have originated in food animals. Another example is Campylobacter infections that have markedly increased in both developed and developing countries and more antibiotic resistance strains suggest that the use of fluoroquinolones as growth promoters is accelerating this trend. The 2014 WHO surveillance report points out that "the classes of antibiotics used in food-producing animals and in human drugs are mostly the same, thereby increasing the risk of emergence and spread of resistant bacteria, including those capable of causing infections in both animals and humans." There is little separation of the types of antibiotics that are being used in human beings and animals, and the vast amount of antibiotics that is being used at the moment in animals is a contributing factor of resistance, and must be addressed in order to help curb resistance spreading further.

To add to the existing evidence of resistance, the case of colistin is an important example. This antibiotic has been used to treat gastrointestinal infections in livestock and was rarely used in humans because of the toxicity to the nervous system and kidneys but with the emergence of resistance to all other antimicrobials, colistin has begun to be used as a last resort. Even though colistin had hardly been used to treat infections in humans, scientists have found the gene MCR-1, that is resistant to colistin, and that today has spread to a number of countries around the world which means that even this last resort antibiotic will no longer be effective.

Thus there is more and more scientific evidence that shows that resistant bacteria can be transferred to humans from animals and one of the ways in which this occurs is through the food chain. The discovery of the resistance to colistin has prompted the Pan-American Health Organization (PAHO) to issue an epidemiological alert urging its Member States to take measures leading to prohibiting the use of colistin for prophylaxis and as a growth promoter in animals. The call for a ban on a particular class of antibiotics or for growth promotion purposes is not new; in fact the WHO in the Global Action Plan on Antimicrobial Resistance has called for "phasing out of use of antibiotics for animal growth promotion and crop protection … and reduction in nontherapeutic use of antimicrobial medicines in animal health."

Moreover, new data is emerging that points to the disproportionately high amount of antibiotic use in animals, particularly in the industrial production of food animals, which is generating resistant genes, such as the MCR-1. This situation is reducing options for treating infections in humans. Accordingly, antibiotics should only be used for treating animals when indicated by a genuine therapeutic need and based on antibiotic therapeutic guidelines.

The increase in resistance due to the use of antibiotics in animals represents a bigger challenge for developing countries. In many settings there is little surveillance and the use of antibiotics follows established animal production practices that will require very costly investments to move away from. The economic impact that changing current animal husbandry practices will have might not be so significant in high-income industrialized countries but estimates from the OECD point out that "countries with less optimized production systems could observe larger productivity and economic effects."

The investment needed for transition to alternative production methods that would not require the extensive use of antimicrobials, will be of high cost and will definitely have an impact for producers in developing countries and small farmers. In order for these countries to make the necessary transitions to more sustainable production practices, resources, technology, and technical assistance will need to be mobilized for this transition to be possible in the developing world.

Promotion of antibiotics

Another issue that will need to be addressed is the promotion and advertising of antibiotics, including the marketing of inappropriate uses or incentivizing medical and veterinary personnel to overuse or inappropriately prescribe antibiotics. In many countries healthcare professionals are influenced by profit gains when prescribing certain antibiotics. Economic incentives that encourage inappropriate use as well as marketing and promotion for non-therapeutic use in animals should be prohibited.

Prescriptions

In many places around the world antibiotics are sold without prescription and there has been considerable debate on how this situation increases resistance since there is little control over what medicines are sold, and whether people are taking antibiotics in the most appropriate manner. Even though this is a very important and serious concern, it is equally important to look at the fact that if a "prescription only" status is enforced, poor and rural populations will not be able to access lifesaving treatments and this in turn would increase existing health inequities. Such regulations cannot take place without acknowledging the different levels of development and the context of each country. It is therefore necessary that these regulations are examined at the national level and that countries have enough policy space to adequately decide on the best course of action. Also, strategies need to be crafted that will improve prescription by using surveillance data that will guide health-care professionals into providing more ade-

World Antibiotic Awareness Week activity in Kenya

quate treatments.

4. Human and Infrastructure Capacity

The World Health Organization has highlighted that countries with weak and poorly resourced health systems will have the greatest problems in managing drug resistance. Key policies that need to be pursued include strengthening overall health systems, enhancing infection prevention and control, and strengthening surveillance and laboratory capacity. International resources need to be deployed to support national implementation in developing countries.

Developing countries bear the greatest burden of infectious diseases and in many settings access to adequate sanitation and safe water is a challenge that increases the risk of transmission of infections. Moreover, many countries face shortage of health care personnel, which in turn affects the adequate supply of health care needs. Furthermore, the medical costs of health treatments are also a significant challenge and patients who have to pay medical costs out-of-pocket are less likely to seek appropriate care and therefore might delay getting medical care or just directly buy medicines. Poor patients may not have the resources to pay for a full prescription of antibiotics and may just consume partial amounts that may be sold at a cheaper price than a full course.

Infection and control protocols are key in reducing infections but in order to effectively establish them in health care settings, it is necessary to have enough health personnel who can be trained and to assist in the control of infections. However, this might not be the case in many settings. Other risk factors that increase the likelihood of acquiring drug resistant infections in hospital settings, particularly in developing countries, include poor hand washing practices and isolation facilities, patient overcrowding and frequent patient and staff transfers.

Strengthening laboratory and human resources capacity is particularly important to carry out surveillance that will help inform decision makers and health-care professionals on the best courses of treatment. The 2015 report from WHO on the country situation analysis found that: "countries cited a lack of laboratories with sufficient competent technical staff, weak infrastructure, poor data management and lack of standards as impediments to effective laboratory surveillance". The lack of proper laboratory infrastructure not only impacts on proper surveillance systems, it also affects the possibility to provide accurate diagnosis and in many cases infections are diagnosed empirically due to the lack of laboratory capacity and affordable and efficient diagnostic tests. Therefore there is a clear need for investment in laboratory capacity and also in diagnostic tests that are suitable for resource-poor settings.

5. Policy Recommendations

♦Development and implementation of National Action Plans to address AMR, in which affordable and timely access to new and old antibiotics, vaccines and diagnostics is at the forefront of the strategy for the containment of AMR.

♦Financial and technical assistance for developing countries to formulate and implement National Action Plans to address AMR.

♦Regulations for drug companies on ethical promotion and marketing of their medical products and prohibition of sales promotion that target doctors or veterinarians.

♦Strengthen investment for surveillance systems.

♦Strategies for prescriptions of antibiotics that take into account the national context and realities.

♦Phase out of antibiotics that are not used for therapeutic purposes or ban the use of particular classes of antibiotics in animals.

♦Financial and technical assistance for developing countries to make the transition into more sustainable animal husbandry models and practices.

♦Support initiatives to promote R&D in new antimicrobials that fully delink R&D costs from price and volume; and ensure access, affordability and stewardship; and do not rely on intellectual property rights as an incentive mechanism.

♦Educate the public and health workers on using/prescription of antibiotics properly, including when they should not be used.

Mirza Alas is a Research Associate and Viviana Muñoz Tellez is the Coordinator of the Development, Innovation and Intellectual Property (DIIP) Programme of the South Centre.

This article is based on South Centre Policy Brief No. 29, available from https://www.southcentre.int/policy-brief-29-september-2016/.

Note: The inputs and contributions of the Third World Network are acknowledged and appreciated.

Civil society and South Centre call for urgent actions to tackle AMR and ensure access and new innovation models

At the side-lines of the 70th World Health Assembly session in May 2017, the South Centre supported and chaired a multi-stakeholder dialogue between civil society and governments, with the speakers calling for urgent global action to tackle anti-microbial resistance.

The side event "Responding to the Challenge of Antimicrobial Resistance (AMR): Perspectives of Civil Society, Intergovernmental Organizations and Developing Countries" was held on 22 May 2017 at the Palais des Nations in Geneva. The event was sponsored by Médecins Sans Frontières (MSF), Drugs for Neglected Diseases initiative (DNDi), Health Action International (HAI), and Medicus Mundi International Network (MMI), and was supported by the South Centre and ReAct Action on Antibiotic Resistance. Viviana Munoz of the South Centre chaired the event. The Centre played a key role in organizing the meeting.

Below is a report of the event.

The side event on antimicrobial resistance taking place in a packed hall of the Palais des Nations at the World Health Assembly. Dr. Viviana Munoz of the South Centre chaired the event.

By Mirza Alas

Civil society is becoming increasingly active in advocating for more effective and coordinated actions to tackle the crisis of antimicrobial resistance (AMR). Senior representatives of leading global CSOs spoke in a side event at a packed hall (with many participants having only standing room) at the World Health Assembly, and stressed the need not only for urgent action to control the misuse of antibiotics, but also that the new antimicrobials must be made affordable and accessible to all.

CSO leaders from Médecins Sans Frontières (MSF), Drugs for Neglected Diseases initiative (DNDi), ReACT and Medicus Mundi International Network stressed that the poor and the low and middle income countries (LMICs) suffered the most from AMR. It is imperative that as more funds are poured into research and development (R&D), the outcome or new antibiotics, other antimicrobials, vaccines and diagnostic tools must be affordable to LMICs, especially their poor. The Chair of the event, Viviana Munoz of the South Centre, also shared these points in her opening and concluding remarks. Representatives of the Health Ministries of India and Thailand also made presentations of their countries' plans to combat AMR; they brought up issues of implementing the plans and called for more assistance from WHO.

DNDi, ReACT and MSF emphasized that R&D efforts to counter AMR should adhere to internationally agreed principles including affordability, effectiveness, efficiency and equity and de-linkage. Several speakers stressed the importance of adhering to the principle of de-linkage – the prices and sales volumes of antibiotics are not linked to the cost of investment in R&D –, and that therefore new innovation models based on de-linkage should be put into practice.

The problems of access to medicines and innovation models that are consistent with access were the main highlights of the CSO presentations, which said these models were to ensure benefits arising from better stewardship of new and existing antibiotics.

Viviana Munoz, South Centre, welcomed participants to the event and noted that the outstanding tournout was an expression of the broad support for coordinated global action to tackle AMR. She noted that AMR is a multifaceted problem. For example,

AMR is linked to misuse and excessive use, but there is also the problem of access to antimicrobials. Moreover, AMR is linked to human use, use in animals and impact on the environment.

On the positive side, AMR is now firmly placed on the global agenda, and increasingly on national health agendas. There is recognition of the need for a holistic approach to the problem that involves multiple sectors and actors. With this, she noted great pleasure to moderate a panel composed of CSOs and people that are working hard to make a difference and whose engagement on the AMR agenda is essential, as they have an extraordinary capacity to inspire and mobilize collective action, and a deep understanding of the root causes of the problems relating to AMR. She highlighted that the South Centre is convinced that there is a need to give more voice to civil society to engage in and help shape the AMR agenda, if we really want change.

Anthony D. So, Director, IDEA (Innovation+Design Enabling Access) Initiative at the John Hopkins Bloomberg School of Public Health and Director, ReAct - Action on Antibiotic Resistance Strategic Policy Program, suggested that the problem of AMR should be approached from a systems perspective, considering the inter-related elements of (1) innovation, (2) access and (3) stewardship.

Dr. So highlighted the need to curb the non-therapeutic use of antibiotics and phase out the use of certain antibiotics in food animal production such as colistin, which is a last-line treatment in human medicine. He noted that a larger volume of antibiotics is not used in humans but in agriculture and aquaculture.

Dr. So further elaborated on issues around prices of antibiotics. He noted that the idea of rationing antibiotics through higher drug prices is not an effective way to ensure rational use. Infectious diseases do not skip the poor and fall more heavily on those who cannot afford antibiotics. He also noted that if courses of new antibiotics could cost thousands of dollars, we should begin to wonder how we will ensure access and stewardship from such an innovation pipeline.

Dr. So also talked about how push incentives for new antibiotic drugs (e.g., CARB-X, the European Union's Innovative Medicines Initiative, NIH, BARDA and the U.S. biodefense program) address the key scientific bottleneck in the R&D pipeline, but existing efforts are insufficient and must better address de-linkage as well as conditions for access and stewardship. However, he explained that CARB-X has only $350 million dollars in commitments, but the needed expenditure in incentives is billions of dollars.

In his opinion, the overemphasis on pull incentives (e.g., priority review vouchers, transferable intellectual property rights, and late stage market entry rewards) is misplaced. The evidence shows that first-in-class antibiotics can command first-in-class returns on investment. He added: "Linezolid and daptomycin are prime examples, two first-in-class antibiotics, each with sales that place them among the top 50 drugs in the U.S. These drugs came to market before new incentives like the GAIN Act that extended the period of monopoly protections."

He underscored the need to focus the incentives and that when policymakers and industry call for billion dollar market entry rewards "it may be too much, too late" since those market entry rewards may focus the public's resources on the wrong part of the pipeline.

There is a need to delink the return on investment from both prices and quantities of sales of antibiotics, he said. He thus concluded that fair returns on public investment in R&D should be ensured and that it is not just innovation, but affordable access and stewardship that are needed, stressing that "stewardship should not be an afterthought at the end of the pharmaceutical value chain."

On the animal health sector Dr. So talked about the importance of phasing out non-therapeutic use of antimicrobials, and to invest in developing alternative sustainable agricultural practices that help transition farmers and food production away from the intensive use of antibiotics. He also mentioned the need to change retail and institutional procurement practices and the need to engage consumers in demanding products without routine use of antibiotics. In his concluding remarks Dr. So emphasized the need for an "AMR Watch" of civil society organizations that could contribute with monitoring governments' development and implementation of the National Action Plans as well as the intergovernmental organizations and other key actors, and making them more accountable.

Michelle Childs, Head of Policy Advocacy, Drugs for Neglected Diseases initiative – Latin America, highlighted the need to implement and adhere to internationally agreed R&D Principles to guide innovation and access for AMR. These include the principle of de-linkage of prices and sales volume of antibiotics from the cost of R&D.

Ms. Childs spoke on the role of guiding principles on research and development (R&D) and stressed that any initiative should focus on the public health priorities with an emphasis on global needs. Ms. Childs emphasized the need to ensure the implementation of globally agreed key norms and principles to ensure innovation and sustainable access such as: affordability, effectiveness, efficiency and equity as well as the importance of de-linkage – investments in R&D not linked to returns from sales volumes or prices.

Ms. Childs also pointed out the importance to ensuring sustainable financing at the national, regional and global level. She stressed the need to continue exploring new incentives for innovation such as push and pull mechanisms based on agreed priorities, principle of delinkage and conditions to ensure sustainable access. Other important elements she mentioned were the need to identify R&D needs and gaps, to have a clear priority setting mechanism, coordination, sustainable funding and the core principles of: affordability, effectiveness, efficiency, equity.

Ms. Childs also mentioned the recently created Global Antibiotic Research and Development Partnership (GARDP) which is a not-for-profit R&D organization that will develop new treatments for bacterial infections. GARDP is a joint initiative of the World Health Organization (WHO) and the Drugs for Neglected Diseases initiative (DNDi).

Els Torreele, Executive Director of Médecins Sans Frontières (MSF)'s Access Campaign, spoke on how MSF, as

one of the largest non-government providers of humanitarian medical care, is now witnessing the growing burden of AMR. "We see AMR in trauma patients in Jordan, newborns in Pakistan, malnourished children in Mali and burn victims in Iraq. We see people with infections that can only be treated with the last lines of antibiotics, after first, second and even third line no longer work."

She stressed the importance of an urgent, comprehensive, global and public health-driven response to this growing problem and to ensure that the needs of patients and health care providers are at the center of any response. Ms. Torreele also referred to the challenges caused by drug resistance in patients with TB, malaria, HIV/AIDS and other infectious diseases. She described how MSF in 2015 treated more than 20,000 patients with TB, of which 2,000 had MDR-TB. This could just be the tip of the iceberg of an estimated 580,000 people with DR-TB worldwide since most who are infected are undiagnosed and untreated.

Ms. Torreele added that one of the biggest challenges for the medical teams is the lack of appropriate diagnostics. Thus there is a need to equip doctors and nurses with the right diagnostics and treatment tools to help them determine types of infection and whether the standard drugs still work.

She mentioned other key issues in the AMR response which include: health system strengthening, improving medical practice and the need to increase access to vaccines such as the Pneumococcal Conjugate Vaccine (PCV) and rotavirus vaccines. "Increasing coverage of these vaccines could dramatically reduce the use of antibiotics. But high vaccine prices are a key barrier today to increasing vaccination, especially in middle-income countries," she remarked.

Ms. Torreelle stressed MSF's mandate to save lives and treat infections and therefore it took seriously the need to have affordable access to diagnostics and treatment tools, new and old and future ones. She said that "medical innovation is only relevant if the resulting products are available and accessible for those in need." TB was mentioned as an example of one disease where new drugs have recently become available but less than 5% of patients that could benefit from these new drugs currently have access.

A view of the panel during the AMR side event.

She remarked that the public health challenges caused by AMR are not exceptional but linked to the global health challenges caused by a society that relies on high prices and monopolies to pay for innovation, which causes both a lack of access to existing health technologies as well as lack of patient-driven innovation. She also mentioned the importance of the recommendations and findings in the recent UN High Level Panel on Access to Medicines report and the need to use them.

Garance Upham of Medicus Mundi International Network and Vice-President of "WAAAR": World Alliance Against Antibiotic Resistance, stressed that AMR infections spread like epidemics do. This partly occurs because of the lack of adequate infection, prevention and control (IPC) systems. She mentioned that more than 20 countries in Europe do not have good IPC systems and therefore this is not an issue that only affects low or middle income countries.

She pointed out that IPC systems would be beneficial in the animal sector since it would help prevent sick animals from infecting others animals. Also, hygiene practices in farms are an effective method to prevent disease in animals more than using metaprophylaxis antibiotics. She also observed that untreated or badly treated wastes from the pharmaceutical industry, fruits and vegetables industry, hospitals and health care centers are dumped into the environment releasing antibiotics and exacerbating resistance. She emphasized the need to invest in clean water, sanitation systems and proper waste treatment as preventive measures that would reduce the need to use antibiotics in the first place.

The side event also heard from two discussants: Mr. Lav Agarwal of the Ministry of Health and Family Welfare in India and Dr. Nihima Sumpradic of the Ministry of Public Health in Thailand. They presented on their countries efforts' in addressing the AMR problem, and the challenges that remain particularly on implementation of the national plans. They called on WHO to provide further assistance to developing countries.

Marc Sprenger from the WHO AMR Secretariat noted that civil society would be invited for dialogue and interaction with the members of the UN-level Interagency Coordination Group (IACG) that was established in March 2017.

In the open dialogue, other CSOs made interventions, including International TB Union, TB Alliance, HAI, Oxfam, Health Care without Harm, Save the Children and KEI.

This article was edited by Viviana Munoz and Martin Khor.

State of discussion on AMR action, two years after the WHA Global Plan

Two years after the World Health Assembly adopted the Global Action Plan on Antimicrobial Resistance, there is significant but uneven progress with many countries still preparing their national plans. Developing countries also face problems of implementation, while stressing the need to hear their concerns about access to antibiotics and the need for a "delinkage" innovation model. The report below summarises the discussions on AMR held at the World Health Assembly.

A view of the 70th World Health Assembly held in Geneva on 22-31 May 2017.

By Mirza Alas

Two years after the World Health Assembly adopted the Global Action Plan (GAP) on Antimicrobial Resistance, many countries are grappling with the challenges of formulating and implementing national action plans based on the GAP framework.

The national plans on antimicrobial resistance (AMR) were supposed to be ready by May 2017, or two years after the GAP's adoption in May 2015, but almost half the countries have yet to submit them.

A report on the progress of the global and national action plans was given by the WHO Secretariat at the World Health Assembly on 22-31 May in Geneva.

No new decision was taken on AMR issues at the WHA. But there was a session in the WHA agenda during which many countries gave their views on various AMR issues. Among these were progress and challenges regarding the national action plans, the Development and Stewardship Framework on AMR that the WHA is scheduled to adopt to complement the GAP, and the Inter-agency Coordination Group (IACG) on AMR set up by the UN General Assembly and which has started functioning.

Several developing countries, including Brazil and India, stressed the need to place access to affordable existing and new antibiotics and diagnostic tools as priority issues, as it was not enough to take action on the control and distribution of antibiotics. They also highlighted the need to use innovation models based on the "delinkage" principle, to ensure affordable medicines. These two issues of access and delinkage were prominent in the UNGA Declaration on AMR (adopted in September 2016) but were not given recognition in the Development and Stewardship Framework document, complained Brazil (see details below).

The WHO's progress report on the Global Action Plan two years after its adoption showed there is uneven progress at national level, as 67 countries had completed their National Action Plans (NAPs) and 62 were in the process of doing so.

During the discussion at the AMR session, it became clear that there is a need to assess the designs of NAPs and prospects for implementation. It was clear from the interventions made by Member States that implementation of and operationalizing the NAPs is the biggest challenge. This is especially so for many developing countries that need technical and financial assistance.

Discussion also took place on the Development and Stewardship Framework which is still being drawn up. WHO presented a report on several initiatives that have taken place and a road map, and asked for further guidance from countries. It was agreed that consultations would take place in the second part of 2017 to advance this framework. The third item that was discussed was the setting up of the Inter-agency Coordination Group (IACG) with many countries welcoming this step and looking forward to its work in the coming months.

Regarding the Stewardship and Development Framework, Brazil emphasized the need to have intergovernmental consultations. It said the current draft does not provide enough attention to the elements emphasized in the UNGA Political Declaration on AMR, adopted in September 2016. Brazil mentioned in particular the need to address two issues -- access and affordability of existing and new antibiotics and diagnostic tools, and the need to develop innovation models based on the principle of delinkage, both of which were prominent in the UNGA Declaration.

India supported Brazil's statement, adding that AMR has emerged as a major public health challenge and is rightly receiving increasing attention global-

ly. India stressed that there should not be any imbalance in a Stewardship Framework that focuses only on controlling the production, distribution and sale of antibiotics. The framework also should focus on the equally important and interrelated issues of affordable access to new and existing antibiotics and diagnostics and research and development (based on models that enable access).

India gave its support to all the three interconnected issues of antibiotic stewardship namely, R&D in new antibiotics, access to new and existing antibiotics and stewardship. It stressed this should be reflected in a balanced manner in any eventual global framework on AMR. The delineation of such a framework should be done through an intergovernmental process and not left to experts alone.

India also noted that it has amended its drugs law and rules to better regulate the sale of antimicrobials and promote rational use of drugs. India also proposed to ensure the primacy of the WHO, FAO and OIE tripartite in any initiative, with WHO in the coordinator role. India also proposed to increase the Global Antimicrobial Resistance Surveillance System (GLASS) to include animal health, agriculture and environment besides monitoring of human health.

India reiterated that adequate attention shall be given to the development and equity related aspects of AMR. There should be a clear focus on supporting member states in proper implementation of such plans through adequate technical support and mobilization of resources.

Thailand noted that in the last two years there has been good progress made by the tripartite (WHO, FAO and OIE), development partners and Member States in addressing AMR. Thailand also welcomed the establishment of the IACG to strategically and effectively coordinate and move the UNGA Political Declaration on AMR forward. The Philippines also welcomed the IACG and noted that it will be pushing for AMR to be part of the ASEAN declaration and for the alignment of action between the ASEAN region and WHO efforts.

Bahrain, on behalf of countries of the Eastern Mediterranean region, observed the need for a multi-sectoral response and need for more alignment. Bahrain called for working groups on AMR at national level. It called for the IACG to provide practical advice and coordinate the mobilizing of resources for NAPs.

WHO

The WHO headquarters in Geneva.

Algeria, on behalf of the African region, highlighted the urgency for a response to AMR and emphasized the critical needs of developing countries including access to high quality health products, vaccines, and diagnostic tools. Congo pointed out the heavy burden that AMR represents on hospital budgets, its limited resources to address this burden and how this impacts on its ability to implement national action plans.

Kenya mentioned its commitment to mobilizing resources and working to increase awareness among public and health professionals as well as for collaboration with the veterinary sector. Kenya also called on WHO to support states technically and financially in development of and operationalizing the national plans.

Ecuador highlighted the need to strengthen the health system and create healthy environments. It also emphasized the need for capacity building of human resources and to receive financial and technical assistance. Ecuador also pointed out that AMR is not only about medicines but that there is a need to work on the prevention and the factors that are causing the resistance.

South Africa remarked that there is unequal access to antibiotics among countries and regions and that WHO should ensure equitable access to new vaccines and diagnostic tools. South Africa also noted that the implementation of the One Health approach faces challenges due to many conflicts of interest and this should be a factor to consider.

Malta, on behalf of the European Union, stressed WHO's role as the leader for the implementation of the national action plans. Malta welcomed the draft road map for the framework. Malta noted the importance of the IACG to provide guidance across the UN system for AMR issues. Malta asked for greater clarity in how the WHO Secretariat would engage with the IACG and mentioned the need for greater cooperation in research and development. It noted current EU programs on push and pull mechanisms for developing new antibiotics, the need for prudent and reasonable use of antibiotics and the importance to strengthen health systems with infection prevention and control efforts. Norway called for IACG to work closely with other UN agencies particularly on the environmental aspects of AMR.

The USA noted the report of progress and emphasized the need to maintain prioritization of gram-negative bacteria. It supported the development of the stewardship framework and asked how it would be operationalized. The USA also called on WHO to develop guidelines of AMR in animal foods and increase surveillance and data collection.

FAO Antimicrobial Resistance (AMR) activity in Bangladesh: A One Health Approach

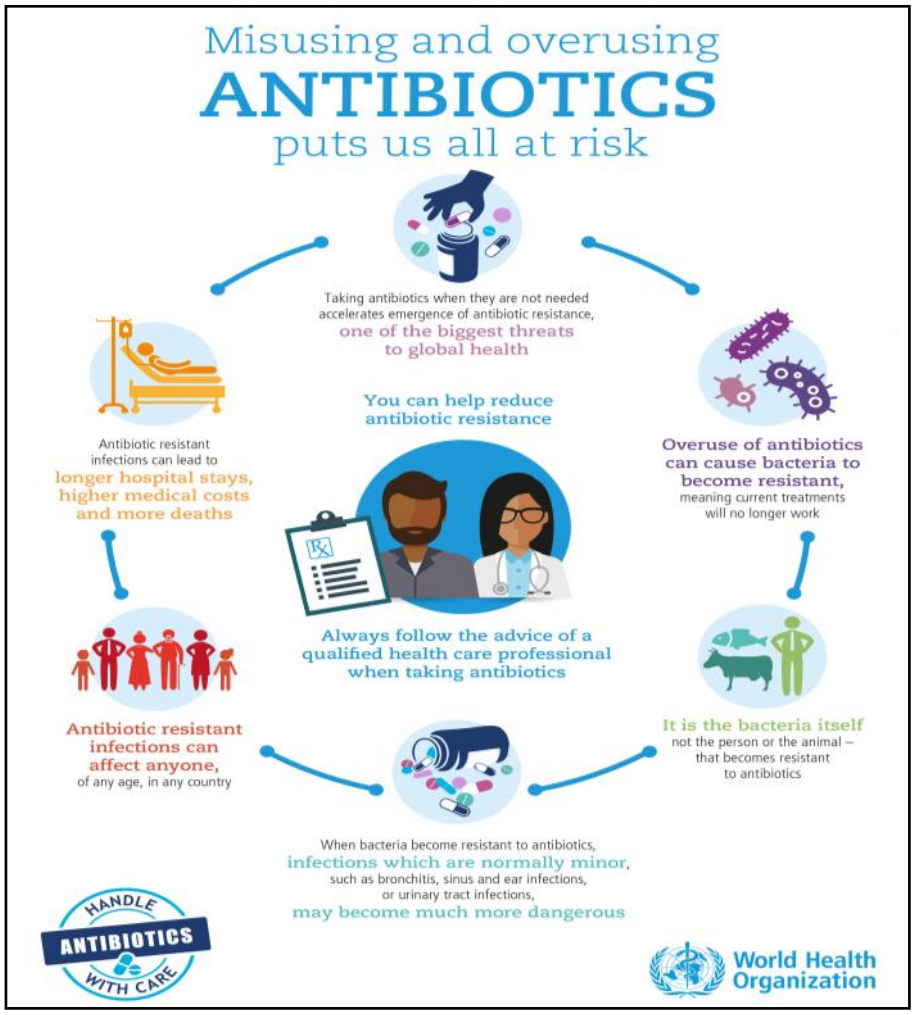
The United Kingdom spoke of the need to make the stewardship framework effective and efficient. The UK also noted that national action plans should drive the efforts of people on the ground.

The Netherlands pointed out the tremendous progress in raising the political profile of AMR but it noted that many countries have not yet developed NAPs and that some countries have picked and chosen some elements and only focused on the easy sectors and not addressing others. Examples of the difficult issues were the use of antimicrobials as growth promoters in animals, waste management issues and prescription practices; the Netherlands said neglecting these issues should not happen. There was need to think about what would be presented in 2018, the need to work together and to ensure that AMR continues to be a priority.

Germany pointed out its 2.2 million euros contribution to WHO and its support of the Global Antibiotic Research and Development Partnership (GARDP) and encouraged other countries to also step up support. It said AMR is a priority of its G20 presidency and emphasized also the need to ensure implementation of NAPs. Germany also mentioned key elements of the Berlin declaration such as: awareness, infection prevention and control, the sharing of data, need for new antibiotics, vaccines and diagnostics. Germany also pointed out the importance of affordable access to all patients in need and the criticality of addressing the environmental aspect of AMR. Germany welcomed the draft road map of the Development and Stewardship Framework, supported its approach and observed that it was essential that the framework address all areas and that member states should be involved closely in the development of the framework.

In response to the country statements, Dr. Hajime Inoue, Senior Advisor to the WHO Director-General and Special Representative for Antimicrobial Resistance, recognized the strong commitments expressed by countries and the recognition about the substantial progress made. About the joint external evaluation, he assured countries that it would be a voluntary process and it will not be mandatory for the countries that do not wish to go through that process. He further commented that for countries that do not yet have a NAP, and countries that are behind schedule, that there is a need to support them. Dr. Inoue pointed out that countries that are still preparing their national plans will be invited to a workshop to support them in finishing their plans and that WHO is planning to announce a global training practice in collaboration with the Centers for Disease Control and Prevention (US).

Dr. Inoue added that engagement with health care professionals is important and that they have been invited to consultations. Regarding guidelines for animal health, OIE and FAO have been fully involved and will continue to be. He also noted that WHO is working to make information available on prices and availability of antibiotics. The World Health Assembly took note of the Secretariat progress reports on AMR.



G77 and China Statement at the UN General Assembly's High-Level Meeting on Antimicrobial Resistance

Statement on behalf of the Group of 77 and China delivered by His Excellency General Prayut Chan-o-cha (Ret.), Prime Minister of the Kingdom of Thailand, at the plenary of the High-Level Meeting on Antimicrobial Resistance (New York, 21 September 2016).

UN

The UN General Assembly High-Level Meeting on Antimicrobial Resistance was held in New York on 21 September 2016.

President of the General Assembly,

Secretary-General of the United Nations,

Director-General of the World Health Organization,

Director-General of the Food and Agriculture Organiation, and

Director-General of the World Organization for Animal Health (OIE),

I have the honour to deliver this statement on behalf of the Group of 77 and China.

Excellencies,

Ladies and Gentlemen,

This High-level Meeting on Antimicrobial Resistance is an historic and important landmark. It is an opportunity to raise awareness on the issue of AMR worldwide. We must also galvanise political will at the highest levels to support urgent efforts to address AMR, consistent with the WHO Global Action Plan on AMR and its five strategic objectives. These efforts must support a government and public-health driven, whole of society, multi-sectoral response based on a One-Health approach.

AMR is a universal challenge for all humankind. It affects people indiscriminately. However, the capacity of countries to deal with AMR varies drastically, from a country's level of development to the varying capacities of their health systems. The ramifications of not addressing AMR effectively, therefore, can be particularly pronounced in developing countries.

The Group of 77 and China underline that all of this must be taken into account. In the final equation, implementing policies to address AMR must not in any way further hinder affordable and equitable access to existing and new antimicrobials, vaccines and diagnostic tools.

From the vantage point of the Group of 77 and China, addressing AMR must support a number of overarching goals. First, we must encourage appropriate use of antimicrobials in animal and human health and agriculture and raise awareness on AMR. Second, we must continue to strengthen our ability to prevent infections, including by ensuring access to clean water, hygiene and sanitation, immunization, and infection control. Third, we must strengthen health systems and promote Universal Health Coverage.

Fourth, we must support, as a matter of urgency, research and development of antimicrobials, especially new antibiotics, vaccines, diagnostic tools and innovation, including in traditional and herbal medicine. This must be done while ensuring that R&D efforts are needs-driven, evidence-based, and a shared responsibility. These efforts must be guided by the core principles of affordability, effectiveness, efficiency, and equity through delinking research and development costs from prices and sales volume. The Group of 77 and China is pleased to see this delinkage principle underlined in the Political Declaration.

Fifth, we must ensure affordability and access to existing and new antimicrobials, vaccines, diagnostics and other medical tools. In this regard, we welcome the launch of the much anticipated report of the High-Level Panel on Access to Medicines convened by the Secretary-General.

Sixth, we must enhance capacity building, technology transfer, technical assistance, international cooperation and funding to support the development and implementation of national action plans, which includes developing and strengthening surveillance on antimicrobial resistance and use of antimicrobials. We must also support health systems research, and R&D in both appropriate use of antimicrobials and on how to further protect and ensure access to medicines in this regard.

Through the Political Declaration, we have reaffirmed the WHO Global Action Plan on AMR. We have committed to international cooperation, to mobilising human and financial resources, technical and other support to develop and implement National Action Plans. We have committed ourselves to action.

We have also underlined the public-health dimension of all of our coordinated efforts and that our collaboration must critically result in sustainable public health outcomes for our generation and for our children's generation. In this regard, the Group of 77 and China looks forward to receiving the report as called for in the Political Declaration for our continued consideration and work in this area.

Political Declaration of the high-level meeting of the General Assembly on antimicrobial resistance

The one-day high-level event of the UN General Assembly on Antimicrobial Resistance held in New York on 21 September 2016 was the first time that heads of states and governments addressed the AMR crisis. Below is the Political Declaration issued at the meeting.

UN

President of the 71st session of the UN General Assembly, H.E. Peter Thomson, delivers his statement at the opening session of the High-Level Meeting on AMR.

We, Heads of State and Government and representatives of States and Governments, meeting at United Nations Headquarters in New York on 21 September 2016, in accordance with General Assembly resolution 70/183, in which the Assembly decided to hold a high-level meeting in 2016 on antimicrobial resistance:

1. Reaffirm that the blueprint for tackling antimicrobial resistance is the World Health Organization global action plan on antimicrobial resistance and its five overarching strategic objectives developed by the World Health Organization in collaboration with, and subsequently adopted by, the Food and Agriculture Organization of the United Nations and the World Organization for Animal Health;

2. Also reaffirm that the 2030 Agenda for Sustainable Development offers a framework to ensure healthy lives, and recall commitments to fight malaria, HIV/AIDS, tuberculosis, hepatitis, the Ebola virus disease and other communicable diseases and epidemics, including by addressing growing antimicrobial resistance and neglected diseases affecting developing countries in particular, while reiterating that antimicrobial resistance challenges the sustainability and effectiveness of the public health response to these and other diseases as well as gains in health and development and the attainment of the 2030 Agenda;

3. Acknowledge that the resistance of bacterial, viral, parasitic and fungal microorganisms to antimicrobial medicines that were previously effective for treatment of infections is mainly due to: the inappropriate use of antimicrobial medicines in the public health, animal, food, agriculture and aquaculture sectors; lack of access to health services, including to diagnostics and laboratory capacity; and antimicrobial residues into soil, crops and water: within the broader context of antimicrobial resistance, resistance to antibiotics, which are not like other medicines, including medicines for the treatment of tuberculosis, is the greatest and most urgent global risk, requiring increased attention and coherence at the international, national and regional levels;

4. Also acknowledge that, due to antimicrobial resistance, many achievements of the twentieth century are being gravely challenged, in particular: the reduction in illness and death from infectious diseases achieved through social and economic development; access to health services and to quality, safe, efficacious and affordable medicines; hygiene, safe water and sanitation; disease prevention in community and health-care settings, including immunization; nutrition and healthy food; improvements in human and veterinary medicine; and the introduction of new antimicrobial and other medicines;

5. Recognize that the above achievements are now gravely challenged by antimicrobial resistance, including: the development of resilient health systems and progress towards the goal of universal health coverage; treatment options for HIV and sexually transmitted infections, tuberculosis and malaria, as well as other infections acquired in community and health-care settings; gains in infection prevention and control in community and health-care settings; advances in agriculture and animal husbandry that help to ensure that the quality of food is preserved; and prevention and treatment options for infectious diseases in veterinary medicine;

6. Also recognize that, due to antimicrobial resistance, there will be fewer options for the protection of people most vulnerable to serious life-threatening infections, especially women giving birth, newborns, patients with certain chronic diseases or those undergoing chemotherapy or surgery;

7. Note with concern that the fulfilment of the right to the enjoyment of the highest attainable standard of physical and mental health, as well as access for millions of people to health services and to quality, safe,

efficacious and affordable antimicrobial medicines, food, clean water and a healthy environment, remain a distant goal, especially in developing countries;

8. Also note with concern that while the current lack of access to health services and access to antimicrobial medicines in developing countries contributes to more deaths than antimicrobial resistance, without an effective One Health approach and other multisectoral cooperation and actions, antimicrobial resistance is projected to cause millions of deaths worldwide, with massive social, economic and global public health repercussions;

9. Recognize that the keys to tackling antimicrobial resistance are: the prevention and control of infections in humans and animals, including immunization, monitoring and surveillance of antimicrobial resistance; sanitation, safe and clean water and healthy environments; investing in strong health systems capable of providing universal health coverage; promoting access to existing and new quality safe, efficacious and affordable antimicrobial medicines based, where available, on diagnostic tests; sustained research and development for new antimicrobial and alternative medicines; rapid diagnostic tests, vaccines and other important technologies, interventions and therapies; promoting affordable and accessible health care; and resolving the lack of investment in research and development, including through the provision of incentives to innovate and improve public health outcomes, particularly in the field of antibiotics;

10. Also recognize that the overarching principle for addressing antimicrobial resistance is the promotion and protection of human health within the framework of a One Health approach, emphasize that this requires coherent, comprehensive and integrated multisectoral action, as human, animal and environmental health are interconnected, and in this regard:

(a) Recognize further that effective antimicrobial medicines and their prudent use represent a global public benefit and, for addressing antimicrobial resistance, it is essential to allow people to have access to efficient and resilient health systems; as well as to quality, safe, efficacious and affordable antimicrobial medicines and other technologies, when they are needed; and healthy food and environments;

(b) Underline that basic and applied innovative research and development, including in areas such as microbiology, epidemiology, traditional and herbal medicine and social and behavioural sciences, as appropriate, are needed in order to better understand antimicrobial resistance and to support research and development on quality, safe, efficacious and affordable antimicrobial medicines, especially new antibiotics and alternative therapies, vaccines and diagnostics;

(c) Underline also that all research and development efforts should be needs-driven, evidence-based and guided by the principles of affordability, effectiveness and efficiency and equity, and should be considered as a shared responsibility: in this regard, we acknowledge the importance of delinking the cost of investment in research and development on antimicrobial resistance from the price and volume of sales so as to facilitate equitable and affordable access to new medicines, diagnostic tools, vaccines and other results to be gained through research and development, and welcome innovation and research and development models that deliver effective solutions to the challenges presented by antimicrobial resistance, including those promoting investment in research and development; all relevant stakeholders, including Governments, industry, non-governmental organizations and academics, should continue to explore ways to support innovation models that address the unique set of challenges presented by antimicrobial resistance, including the importance of the appropriate and rational use of antimicrobial medicines, while promoting access to affordable medicines;

(d) Underline further that affordability and access to existing and new antimicrobial medicines, vaccines and diagnostics should be a global priority and should take into account the needs of all countries, in line with the World Health Organization global strategy and plan of action on public health, innovation and intellectual property, and taking into consideration its internationally agreed follow-up processes;

(e) Improve surveillance and monitoring of antimicrobial resistance and the use of antimicrobials to inform policies and work with stakeholders from industry, agriculture and aquaculture, local authorities and hospitals to reduce antimicrobial residues in soil, crops and water;

(f) Enhance capacity-building, technology transfer on mutually agreed terms and technical assistance and cooperation for controlling and preventing antimicrobial resistance, as well as international cooperation and funding to support the development and implementation of national action plans, including surveillance and monitoring, the strengthening of health systems and research and regulatory capacity, without jeopardizing, in particular in the case of low- and middle-income countries, health or posing barriers for access to care;

(g) Acknowledge that increasing awareness and knowledge on antimicrobial resistance and all of its implications requires the sharing of good practices and findings, collaboration with the media and national and multisectoral actors and the provision of sufficient financing for these activities across sectors;

11. Recognize that national conditions and priorities should be taken into account at all levels, and that relevant sectors of government should be engaged in the development and implementation of multisectoral national action plans, policies, regulations and regional initiatives, taking into account the national context, legislation and jurisdictional responsibilities;

12. We therefore commit to work at national, regional and global levels to:

(a) Develop, in line with World Health Assembly resolution 68.7, multisectoral national action plans, programmes and policy initiatives, in line with a One Health approach and the global action plan on antimicrobial resistance, including its five over-

arching strategic objectives, with a view to implementing national measures for strengthening appropriate antibiotic use in humans and animals: to support the implementation of such plans, national and international collaboration is needed to assess resource needs and to provide sustained technical and financial investment in shared research, laboratories and regulatory capacities, as well as professional education and training, with a view to safeguarding human health, animal health and welfare and the environment;

(b) Mobilize adequate, predictable and sustained funding and human and financial resources and investment through national, bilateral and multilateral channels to support the development and implementation of national action plans, research and development on existing and new antimicrobial medicines, diagnostics, vaccines and other technologies and to strengthen related infrastructure, including through engagement with multilateral development banks and traditional and voluntary innovative financing and investment mechanisms, based on priorities and local needs set by governments, and ensuring public return on investment;

(c) Take steps to ensure that national action plans include the development and strengthening, as appropriate, of effective surveillance, monitoring and regulatory frameworks on the preservation, use and sale of antimicrobial medicines for humans and animals that are enforced according to national contexts and consistent with international commitments;

(d) Initiate, increase and sustain awareness and knowledge-raising activities on antimicrobial resistance in order to engage and encourage behavioural change in different audiences; promote evidence-based prevention, infection control and sanitation programmes; the optimal use of antimicrobial medicines in humans and animals and appropriate prescriptions by health professionals; the active engagement of patients, consumers and the general public, as well as professionals, in human and animal health; and professional education, training and certification among health, veterinary and agricultural practitioners; and consider, as appropriate, innovative approaches to increase consumer awareness, giving attention to local conditions and needs;

(e) Support a multisectoral One Health approach to address antimicrobial resistance, including through public health-driven capacity-building activities and innovative public-private partnerships and incentives and funding initiatives, together with relevant stakeholders in civil society, industry, small- and medium-sized enterprises, research institutes and academia, to promote access to quality, safe, efficacious and affordable new medicines and vaccines, especially antibiotics, as well as alternative therapies and medicines to treatment with antimicrobials, and other combined therapies, vaccines and diagnostic tests;

13. Call upon the World Health Organization, together with the Food and Agriculture Organization of the United Nations and the World Organization for Animal Health, to finalize a global development and stewardship framework, as requested by the World Health Assembly in its resolution 68.7, to support the development, control, distribution and appropriate use of new antimicrobial medicines, diagnostic tools, vaccines and other interventions, while preserving existing antimicrobial medicines, and to promote affordable access to existing and new antimicrobial medicines and diagnostic tools, taking into account the needs of all countries and in line with the global action plan on antimicrobial resistance;

14. Call upon the World Health Organization, in collaboration with the Food and Agriculture Organization of the United Nations, the World Organization for Animal Health, regional and multilateral development banks, including the World Bank, relevant United Nations agencies and other intergovernmental organizations, as well as civil society and relevant multisectoral stakeholders, as appropriate, to support the development and implementation of national action plans and antimicrobial resistance activities at the national, regional and global levels;

15. Request the Secretary-General to establish, in consultation with the World Health Organization, the Food and Agriculture Organization of the United Nations and the World Organization for Animal Health, an ad hoc inter-agency coordination group, co-chaired by the Executive Office of the Secretary-General and the World Health Organization, drawing, where necessary, on expertise from relevant stakeholders, to provide practical guidance for approaches needed to ensure sustained effective global action to address antimicrobial resistance, and also request the Secretary-General to submit a report for consideration by Member States by the seventy-third session of the General Assembly on the implementation of the present declaration and on further developments and recommendations emanating from the ad hoc inter-agency group, including on options to improve coordination, taking into account the global action plan on antimicrobial resistance.

SOUTH BULLETIN

EDITORIAL COMMITTEE

Chief Editor: Martin Khor

Managing Editor: Vice Yu

Assistants: Anna Bernardo, Adriano José Timossi

The South Bulletin is published by the South Centre, an intergovernmental think-tank of developing countries.

South Centre website:
(in English, French and Spanish)
www.SouthCentre.int

South Centre
Tel: +41 22 791 8050
Email: south@southcentre.int