SHRI MUN 2024

WORLD HEALTH ORGANISATION

Agenda: Deliberating upon viable solutions to counter Antimicrobial Resistance

BACKGROUND GUIDE

Letter from the Executive Board-

Dear Delegates,

It gives us immense pleasure to welcome you to the second edition of interschool Shri MUN in 2024. We hope that you all have a wonderful MUN experience and that these three days in committee result in some fruitful debate on a very pertinent issue.

To give you a helping hand on how to prepare yourselves for this committee, we suggest familiarising yourself with the history and workings of the World Health Organization (WHO). This year's agenda focuses on deliberating upon viable solutions to counter antimicrobial resistance. Ensure you have a comprehensive understanding of the causes, consequences, and current strategies in place to combat this global health threat. Make sure that you have your facts in place and be confident while speaking. A folder with important documents and research may come in handy for this purpose. We would like to reiterate that this background guide points you in the direction of actual research. However, read up thoroughly on the issue at hand and do not restrict yourselves to this background guide.

Remember that each delegate is the representative of their respective nation and the views and strategies expressed by you should be in line with the fundamental beliefs of the nation that you represent. Any formal queries regarding Shri MUN or our committee can be directed to our official email address: shrimun@tsrs.org. Please note that any form of documentation sent prior to the beginning of committee sessions will not be entertained.

Best of luck!

Warm Regards,
Abeni Sethi

Introduction-

This year the World Health Organization committee has been brought in with the agenda – "**Deliberating upon viable solutions to counter Antimicrobial Resistance"** – which helps explore antimicrobial resistance from the perspective of different countries in multiple ways.

Antimicrobial resistance (AMR) is a pressing global health crisis that threatens the efficacy of antibiotics, which have been the cornerstone of modern medicine. The rise of drug-resistant pathogens means that common infections could become untreatable, leading to increased mortality and morbidity. AMR occurs when bacteria, viruses, fungi, and parasites change over time and no longer respond to medicines, making infections harder to treat and increasing the risk of disease spread, severe illness, and death. As delegates of the Model United Nations, it is imperative to understand the complexity of AMR, its drivers, and the multifaceted approach required to combat it, including stewardship programs, surveillance, and the development of new antimicrobials. This issue not only impacts health but also has profound implications for global economics and security.

Antimicrobial resistance (AMR) has emerged as one of the principal public health problems of the 21st century that threatens the effective prevention and treatment of an ever-increasing range of infections caused by bacteria, parasites, viruses and fungi no longer susceptible to the common medicines used to treat them. The problem of AMR is especially urgent regarding antibiotic resistance in bacteria. Over several decades, to varying degrees, bacteria causing common or severe infections have developed resistance to each new antibiotic coming to market. Faced with this reality, the need for action to avert a developing global crisis in health care is imperative.

The World Health Organization (WHO) has long recognised the need for an improved and coordinated global effort to contain AMR. In 2001, the WHO Global Strategy for Containment of Antimicrobial Resistance has provided a framework of interventions to slow the emergence and reduce the spread of antimicrobial-resistant microorganisms;[1] In 2012, WHO published The Evolving Threat of Antimicrobial Resistance – Options for Action[2] proposing a combination of interventions that include strengthening health systems and surveillance; improving use of antimicrobials in hospitals and in community; infection prevention and control; encouraging the development of appropriate new drugs and vaccines; and political commitment.

Following the indication of a primary role for surveillance, in April 2014, WHO published the first global report on surveillance of AMR collecting experiences from national and international surveillance networks. This report shows that surveillance data, where available, can be very useful for orienting treatment choices, understanding AMR trends, identifying priority areas for interventions, and monitoring the impact of interventions to contain resistance. The lack of adequate surveillance in many parts of the world leaves large gaps in existing knowledge of the distribution and extent of this phenomenon.

Our review examines the main factors contributing to the development of antibiotic resistance and the consequences for human health focussing on the impact of resistance in species commonly associated with infection (i.e. *Staphylococcus aureus, Klebsiella pneumoniae,* non-typhoidal *Salmonella*) in different settings and in the treatment of tuberculosis.

Background-

Antimicrobial resistance (AMR) is a critical global health issue that affects all countries, regardless of income levels. It's estimated that bacterial AMR was directly responsible for 1.27 million global deaths in 2019 and contributed to 4.95 million deaths. The misuse and overuse of antimicrobials in humans, animals, and plants are the main drivers of drug-resistant pathogens. AMR makes infections harder to treat and increases the risk of disease spread, severe illness, and death. The world bank estimates that AMR could cost an additional $1trillion in health expenditures by 2050. Priorities in combating AMR include disease prevention, improving diagnose and treatment, and developing vaccines and medicines.

Impact of antimicrobial resistance-

The impact of antibiotic resistance in terms of mortality and of the public health cost is quite difficult to estimate, and there are few studies addressing this issue. The US Center for Disease Control and Prevention (CDC) conservatively estimated that, in the US, more than two million people every year are affected with antibiotic-resistant infections, with at least 23 000 dying as a result of the infection.

In Europe each year, the number of infections and deaths due to the most frequent multidrug-resistant bacteria (*S. aureus*, *Escherichia coli*, *Enterococcus faecium*, *Streptococcus pneumoniae*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*) was estimated at ∼400 000 and 25 000, respectively, in 2007.

Several fields of modern medicine depend on the availability of effective antibiotic drugs; chemotherapy for cancer treatment, organ transplantation, hip replacement surgery, intensive care for pre-term newborns and many other activities could not be performed without effective antibiotics. In fact, infections caused by multidrug-resistant bacterial strains are among the main factors influencing morbidity and mortality in patients undergoing these procedures. A report from the University of Texas, published in 2014, showed high antibiotic resistance rates in infections in cancer patients with chemotherapy-related neutropenia A recent study from the Medical University of Warsaw, on infections after orthotopic liver transplantation, showed a high proportion of isolates of antibiotic-resistant bacteria.

Common infections in neonatal intensive care are increasingly becoming extremely difficult, and sometimes impossible, to treat. *Staphylococcal* species, most notably *S. epidermidis* and *S. aureus,* cause ∼60%–70% of infections, and numerous outbreaks of methicillin-resistant *S. aureus* (MRSA) have been reported in these units.

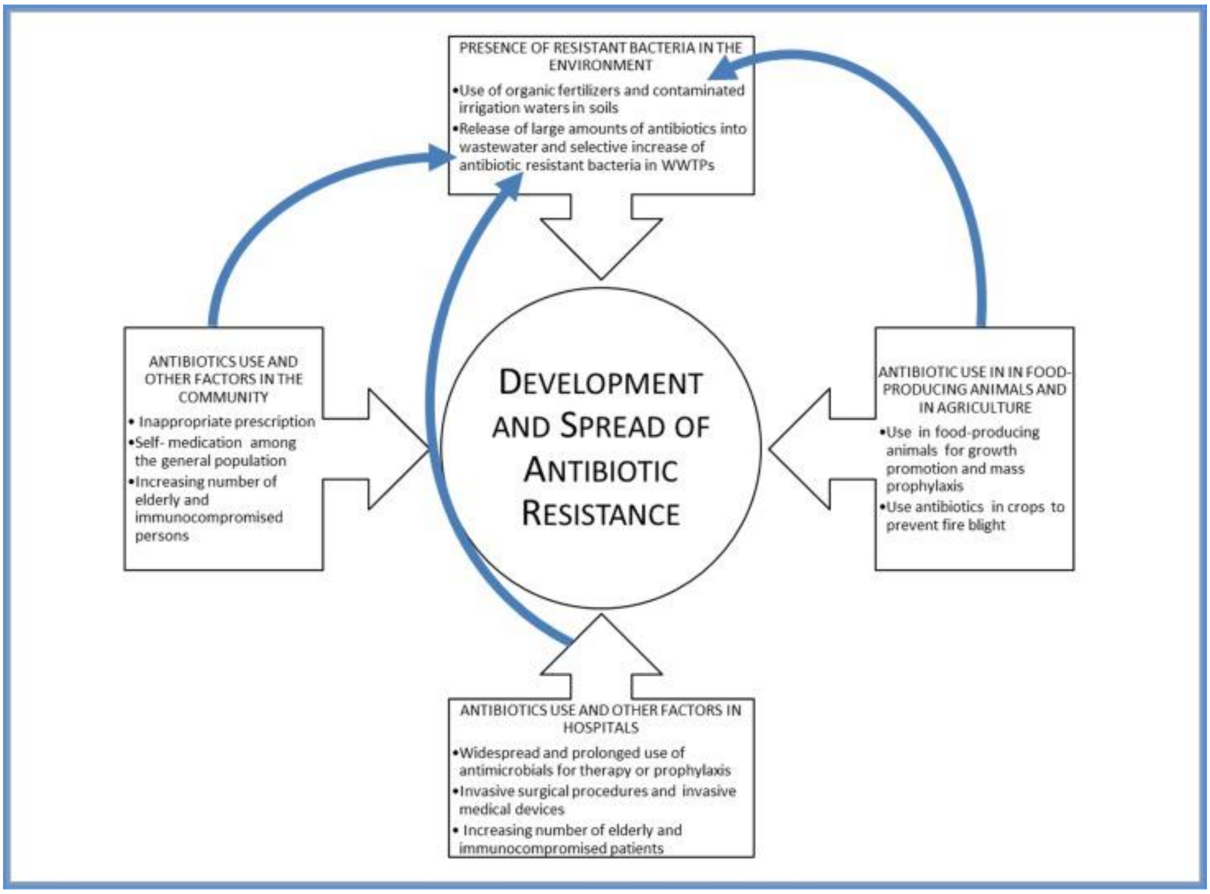
Also the economic impact of antibiotic resistance is difficult to quantify, as several types of consequences must be taken into account. Increased resistance leads to elevated costs associated with more expensive antibiotics (when infections become resistant to first-line antimicrobials, treatment has to be switched to second- or third-line drugs, which are nearly always more expensive), specialised equipment, longer hospital stay and isolation procedures for the patients. Societal costs include death and loss of productivity. In Europe, the overall crude economic burden of antibiotic resistance was estimated to be at least 1.5 billion euros with more than 900 million euros corresponding to hospital costs. Productivity loss due to absence from work or death from infection accounted for 40% of the total estimated cost.[5] However, the estimate was based on antibiotic resistance surveillance data collected in 2007 and may underestimate the present burden of antibiotic resistance, which is a constantly evolving phenomenon.

In the US, the CDC estimated the cost of AMR as $55 billion per year overall: $20 billion in excess for direct healthcare costs, with additional society costs for lost productivity as high as $35 billion a year.

Factors contributing to the emergence of antibiotic resistance

Antibiotic resistance is a natural phenomenon that occurs when microorganisms are exposed to antibiotic drugs. Under the selective pressure of antibiotics, susceptible bacteria are killed or inhibited, while bacteria that are naturally (or intrinsically) resistant or that have acquired antibiotic-resistant traits have a greater chance to survive and multiply. Not only the overuse of antibiotics but also the inappropriate use (inappropriate choices, inadequate dosing, poor adherence to treatment guidelines) contribute to the increase of antibiotic resistance.

The following figure shows a schematic representation of factors involved in the emergence and spread of antibiotic resistance. We identified four main sectors involved in the development of antibiotic resistance: human medicine in community and in hospital, animal production and agriculture, and the environmental compartment.



Factors involved in the spread of antibiotic resistance, in the sectors: human medicine in the community and in the hospital, animal production and agriculture, and the environment. These sectors are also connected among them: misuse of antibiotics in human beings, animals and agriculture is the main responsible for the presence of resistant bacteria in the environment.

Antimicrobial resistance in human medicine-

In the community of affluent countries, the excessive prescription by general practitioners, even in the absence of appropriate indications, plays an important role in the inappropriate use of antibiotics. Diagnostic uncertainty often fosters over-prescription especially when the clinical picture of viral or bacterial aetiology is similar. Self-medication (see below) also plays an important part.

In many developing countries, excessive use is due to the easy availability of antimicrobial drugs that can be purchased without prescription of a physician or other qualified health professional. In both situations, there is the perception that antibiotics are the "wonder drugs" that can rapidly cure any kind of ailments.

In the hospital setting, the intensive and prolonged use of antimicrobial drugs is probably the main contributor to the emergence and spread of highly antibiotic-resistant nosocomial infections; but other factors can play an important role: presence of highly susceptible immunosuppressed patients (e.g. AIDS patients, cancer patients, or transplant recipients) and fragile elderly patients, invasive surgical procedures and intensity of clinical therapy, lengthy of stay in hospital, failure to control infections spread from patient to patient.

- Antibiotic consumption in the community and in hospital settings

The annual report of the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) reported that in Europe during 2012 the consumption in the community of antibacterials for systemic use [Anatomical Therapeutic Chemical (ATC) group J01], ranged from 11.3 (the Netherlands) to 31.9 (Greece) defined daily doses (DDD) per 1000 inhabitants per day. In all ESAC-Net reports, a geographic gradient in the amount of antibiotics used can be noted, with higher DDD in the South of Europe. In 2012, the beta-lactams/penicillins group (ATC J01C) accounted for 50% of the consumption of antibacterials for systemic use and amoxicillin, alone or in combination with clavulanic acid, was the antibacterial agent most often used in almost all countries, with the exception of Norway and Sweden where the most used agent was phenoxymethylpenicillin.

In the hospital sector ESAC-Net estimated that in 2012, the population-weighted EU/EEA mean consumption for systemic use of antibacterials was 2.0 DDD per 1000 inhabitants, ranging from 1.0 DDD per 1000 inhabitants per day in the Netherlands, to 2.8 in Finland. Also in the hospital setting, the beta-lactams/penicillins group was most often used, accounting for 29.3% of all the consumption of antibacterials for systemic use.

According to a recent point prevalence survey on healthcare associated infections in Europe, 35.0% of the hospitalised patients in 2011 were receiving antibiotics.

In the US, healthcare providers prescribed 258.0 million courses of antibiotics (833 prescriptions per 1000 persons) in 2010. Penicillins (23%) and macrolides (22%) were the most common categories prescribed. The most frequently prescribed antibiotic agents were azithromycin and amoxicillin.

Large-scale assessments of antimicrobial use in hospitals in the USA are derived from studies conducted in groups of acute care hospitals. According to one of these studies, a mean of

59.3% of all patients received at least one dose of an antimicrobial agent during their hospital stay.

• Incorrect knowledge about antibiotics in the population and self-medication

Many studies indicate lack of knowledge about antibiotics in the general population, specifically incorrect knowledge about the activity of antibiotics on bacteria and viruses, insufficient awareness about antibiotic resistance and about the adverse effects of antibiotics.

A survey, carried out in 2009, on the use and on the knowledge of antibiotics among European citizens, revealed that 20% of the people interviewed admitted they had taken antibiotics to treat flu-like symptoms, although they knew that antibiotics do not act against viruses. In addition, 14% also said that they had taken antibiotics to treat a common cold.

A survey among adults in the United Kingdom showed that 38% of respondents did not know that antibiotics do not work against most coughs or colds. On the contrary, in Sweden, the knowledge about antibiotics as well as the risk of antibiotic resistance is fairly good and homogeneous. Only one-fifth of respondents was convinced that antibiotics cure common colds more quickly.

The inappropriate use of antibiotics is also associated with other common behaviour patterns, such as failure to complete the recommended treatment or self-medication. Self-medication with antimicrobials almost always involves unnecessary, inadequate, and ill-timed dosing, creating an ideal environment for microbes to adapt rather than be eliminated. Self-medication with antimicrobials is common in many areas of world, particularly in developing countries with loose regulatory systems where antibiotics are sold over the counter drugs, but also in some affluent countries. A higher prevalence of self-medication with antibiotics was reported in South Europe (19%) in comparison with northern Europe (3%) and central Europe (6%). In some countries of Africa, 100% of antimicrobial use is without prescription and in Asia it reaches 58%.

The environment and the spread of resistance-

During the last years, the importance of the environment in the spread of antibiotic resistance has been widely recognised.

The soil is regarded as a reservoir of antibiotic resistance genes, since most antibiotics are derived from soil microorganisms that are intrinsically resistant to the antibiotics produced. In addition, water potentially contaminated with faecal microorganisms and organic fertilisers used on food crops may disseminate drug-resistant bacteria in the soil.

Water is a major way of dissemination of bacteria between different environmental compartments. Large amounts of antibiotics are released into municipal wastewater due to incomplete metabolism in human beings or due to disposal of unused antibiotics. Some available data show that antibiotic-resistant bacteria and antibiotic-resistant genes can be detected in wastewater samples and that the conditions in wastewater treatment plants (WWTPs) are favourable for the proliferation of resistant bacteria. In the last decade, several studies have reported high concentrations of tetracycline and sulphonamide-resistant bacteria and sulphonamide-resistant genes in WWTPs.

The emergence of resistance in some bacterial species commonly cause of human infections-

An increasing number of pathogenic organisms are resistant to one or more antimicrobial drugs. As a consequence, some common infections have become extremely difficult and in some cases nearly impossible to treat. Pneumonia, which was readily treatable after the introduction of penicillin, now more often requires second- and third-line antibiotics. Cystitis, one of the most common bacterial infections in women, which was easily treatable using oral medication, now needs quite always more complex antibiotic treatments that impose additional costs on the patients and the health system.

We describe below three bacterial species, which exemplify antibiotic-resistant pathogens causing infections in different settings: *S. aureus*, common in hospital and in the community; non-typhoidal *Salmonella* (NTS), a major cause of foodborne diseases; and *K. pneumoniae*, causing healthcare-associated infections. In addition, a paragraph will be devoted to drug-resistant tuberculosis.

The following table shows the extent of resistance in *S. aureus*, NTS and *K. pneumoniae* to antibiotics commonly used to treat infections caused by these pathogens, summarised by WHO region. We have considered only national data (based on at least 30 tested isolates) and not single studies, to limit the heterogeneity of the information. Unfortunately, in few countries only, national official sources are available and therefore the table provides insight into the existing surveillance gaps in ABR surveillance.

Resistance to key antibiotics of *S. aureus*, *K. pneumoniae* and NTS in the six World Health Organization (WHO) world regions. The data are derived from WHO:

WHO regions		***S. aureus* resistance to methicillin (MRSA)**	***NTS* resistance to fluoroquinolones**	***K. pneumoniae* resistance to third-generation cephalosporins**	***K. pneumoniae* resistance to carbapenems**
Africa region (47 countries)	Countries with national data	9 (19.1%)	9 (19.1%)	13 (27.6%)	4 (8.5%)
	Range (%)	0–100	0–35	8–77	0–4
	Country with lowest/highest	Lesotho/Guinea-Bissau	Central African Republic/Mauritania	Namibia/South Africa	Central African Republic/South Africa

WHO regions		*S. aureus* resistance to methicillin (MRSA)	*NTS* resistance to fluoroquinolones	*K. pneumoniae* resistance to third-generation cephalosporins	*K. pneumoniae* resistance to carbapenems
	proportion				
Region of the Americas (47 countries)	Countries with national data	15 (31.9%)	13 (27.6%)	17 (36%)	17 (36.2%)
	Range (%)	21–90	0–96	4–71	0–11
	Country with lowest/highest proportion	Canada/Chile	Several countries[a]/Peru	Canada/Peru	Canada-Dominican Republic/United States of America
Eastern Mediterranean region (23 countries)	Countries with national data	4 (17.4%)	4 (17.4%)	4 (17.4%)	4 (17.4%)
	Range (%)	10–53	2–49	22–50	0–54
	Country with lowest/highest proportion	Bahrain/Iran	Oman/Jordan	Oman/Bahrain	Oman/Iran
European region	Countries with	36 (67.9%)	29 (50.9%)	33 (62.3%)	31 (58.5%)

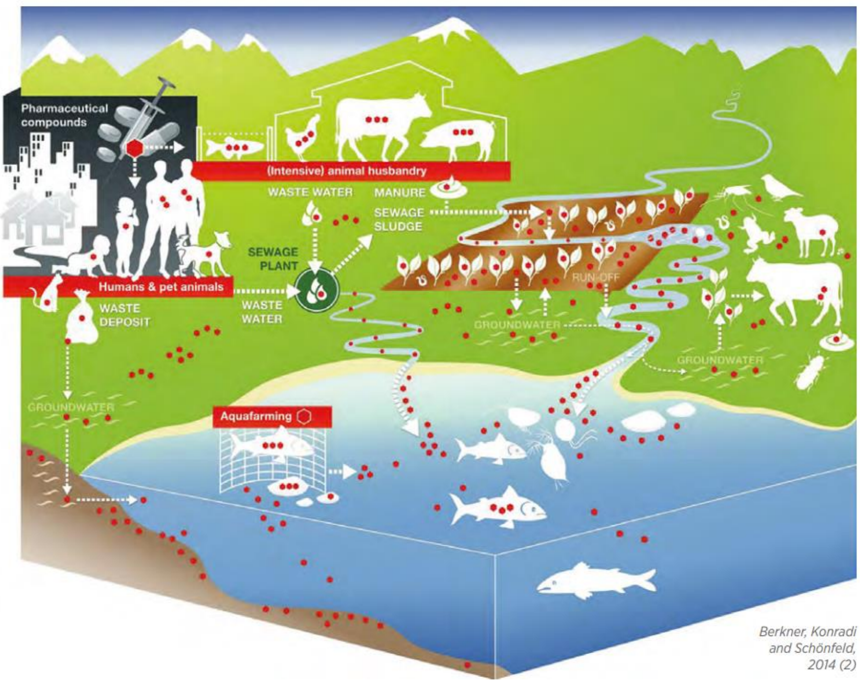
WHO regions		*S. aureus* resistance to methicillin (MRSA)	*NTS* resistance to fluoroquinolones	*K. pneumoniae* resistance to third-generation cephalosporins	*K. pneumoniae* resistance to carbapenems
(53 countries)	national data				
	Range (%)	0.3–55	0–21	2–82	0–68
	Country with lowest/highest proportion	Norway/Portugal	Several countries[a]/Finland	Sweden/Georgia	Several countries[a]/Greece
South-east Asia region (11 countries)	Countries with national data	3 (27.3%)	2 (18.1%)	4 (36.4%)	4 (36.4%)
	Range (%)	10–26	0.2–4	34–81	0–8
	Country with lowest/highest proportion	Bhutan/Myanmar	Thailand/Nepal	Bhutan/Sri Lanka	Bhutan/Myanmar
Western Pacific region (37 countries)	Countries with national data	16 (43.2%)	9 (24.3%)	12 (32.4%)	9 (24.3%)
	Range (%)	4–70	0–14	1–71	0–8

WHO regions		***S. aureus*** **resistance to methicillin (MRSA)**	***NTS*** **resistance to fluoroquinolones**	***K. pneumoniae*** **resistance to third-generation cephalosporins**	***K. pneumoniae*** **resistance to carbapenems**
	Country with lowest/highest proportion	Micronesia/Republic of Korea	Brunei Darussalam/Philippines	Kiribati/Micronesia	New Zeland/China

<u>How does antimicrobial resistance impact the SDGs-</u>

Addressing antimicrobial resistance is integral to achieving the Sustainable Development Goals (SDGs). Progress in many of the goals (e.g. improved access to clean water and sanitation, sustainable consumption and production such as more sustainable food production, and appropriate use of antimicrobials in humans and animals) will help to address antimicrobial resistance. However, at the same time, rising levels of antimicrobial resistance will make it more difficult to achieve the goals for health, poverty reduction, food security and economic growth. There is increasing recognition of the relationships between human health, animal health, plant production, food safety and environmental sectors, in both the evolution of the antimicrobial resistance problem and solutions to that problem. To adequately address antimicrobial resistance, it is therefore necessary to take a “One Health” approach, with integrated actions across all sectors, as shown in Fig. 1.

FIG. 1. A ONE HEALTH APPROACH TO AMR



Berkner, Konradi and Schönfeld, 2014 (2)

TABLE 2. AMR AND THE SDGS

CORE SDGs	HOW AMR IMPEDES PROGRESS ON THE SDG	HOW PROGRESS ON THE SDG HELPS TO ADDRESS AMR
1 NO POVERTY	• People living in poverty are more prone to infectious diseases, and resistant infections are more likely to spread in poor living conditions. The poor are less able to access effective treatment. Substandard care and partial treatment can drive infection. • High costs of treatment and chronic infections will impoverish millions. An additional 28.3 million people could be pushed into extreme poverty by 2050 because of AMR, most of them living in LMIC *(1)*.	• Financial and social protection strategies will allow poor people to access quality services and decrease the impact of AMR.
2 ZERO HUNGER	• AMR in animals increases costs of animal health, infections become untreatable, production decreases and working animals cannot carry out their tasks, affecting the livelihood of farmers and food security. • Livestock production in low-income countries would decline the most, with a possible 11% loss by 2050 in the high-AMR impact scenario *(1)*.	• Developing sustainable food production systems with less reliance on antimicrobials and with the phasing out of antibiotic use in livestock for growth promotion will be essential for long-term AMR control. • Increased professional advice and vaccination of food animals can reduce the emergence and spread of drug-resistant infections.
3 GOOD HEALTH AND WELL-BEING	• Globally, drug-resistant diseases currently cause at least 700 000 deaths a year *(3)*. • AMR will increase treatment costs, making effective care unaffordable for many, and UHC unattainable. • Emerging and increasing resistance to drugs to treat HIV, TB and malaria is one of the key barriers to eliminating these diseases. Multi-drug resistant TB alone is estimated to cause 230 000 deaths annually *(3)*. • Reducing child and infant mortality relies on effective antibiotics. Currently, 200 000 neonates die each year from drug-resistant infections, such as pneumonia or resistant bloodstream infections *(4)*.	• Strategies to reduce the risks of AMR must be linked to improving care and ensuring access to effective care when needed. • Central to addressing AMR is ensuring that health systems are accessible and have a trained workforce providing evidence-based high-quality care in a hygienic setting *(5)*. • Increased vaccine coverage reduces the incidence of disease from resistant pathogens and limits the need for antibiotics; in turn, this prevents the development of AMR *(6)*. • Falsified and poor-quality antibiotics contribute to AMR. Hence, improving access to high-quality antimicrobials and preventing falsified and substandard medicines reaching the market will help to reduce AMR. • Reliance on out-of-pocket payment for health care correlates with AMR in LMIC *(7)*.
6 CLEAN WATER AND SANITATION	• Globally, 1 in 4 health care facilities have no access to basic water services, 1 in 10 have no sanitation services available, 1 in 3 do not have adequate facilities to clean hands at the point of care, and 1 in 3 do not segregate waste safely. Lack of the availability of basic WASH services is greatest in least developed countries, where 50% of health care facilities lack access to water services and 60% have no sanitation services at all *(8)*. • Lack of access to adequate WASH services is giving rise to the spread of infectious diseases; in turn, this increases antibiotic use and thus drives the emergence and spread of AMR.	• Each year, hundreds of millions of cases of diarrhoea in humans are treated with antimicrobials. Universal access to WASH could reduce such cases by 60% *(9)*. • Improved WASH services are critical to reducing the spread of infection.
8 DECENT WORK AND ECONOMIC GROWTH	• By 2030, increased mortality and morbidity due to AMR and thus reduced labour supply could cause a decrease in the global economic output of 1–3%, with estimated losses as high as US$ 3.4 trillion *(1)*.	
12 RESPONSIBLE CONSUMPTION AND PRODUCTION	• Antimicrobial compounds and their metabolites can be found in the wastewaters from manufacturing sites for medicines and APIs. In extreme cases, antimicrobial compounds have been found in water downstream from manufacturing sites in concentrations higher than those found in the blood of patients taking medicines *(9)*.	• Effective pollution controls on pharmaceutical production, health facilities and agricultural production will substantially decrease the risk of AMR emergence and spread in the environment.
17 PARTNERSHIPS FOR THE GOALS	• To effectively tackle AMR, collaboration and partnerships are needed across all relevant sectors (human, animal, plants and the environment) and at all levels (national, regional and global).	• Working in partnership means taking up the One Health approach to addressing AMR.

What action is the UN taking-

The Global Action Plan on antimicrobial resistance was adopted by the World Health Assembly in 2015, and subsequently endorsed by the Food and Agriculture Organization of the United Nations (FAO) and World Organisation for Animal Health (OIE) (10). The plan calls for all countries to develop and implement multisectoral national action plans (NAPs) on antimicrobial resistance. World Health Organization (WHO) and FAO country offices and the OIE regional and subregional representations play a key role in helping countries to realize these commitments, but it is important to involve United Nations (UN) country teams (representing resident and non-resident UN development entities). At the 2016 UN High-level Meeting on antimicrobial resistance (11), global leaders committed to tackling antimicrobial resistance and called upon the Tripartite1 (FAO, OIE and WHO) to scale up support through a One Health approach (12). The UN Secretary-General convened the ad hoc Interagency Coordination Group on antimicrobial resistance (IACG) in May 2017, in consultation with the Tripartite organizations. On receiving the IACG report in 2019 (3), the UN Secretary-General called upon Member States for urgent support and investment to scale up antimicrobial resistance responses at national, regional and global levels. He recommended that one component of this should be the inclusion of antimicrobial resistance in the UN Sustainable Development Cooperation Framework (Cooperation Framework). The IACG report recommended the urgent establishment of three global governance structures to strengthen overall governance, accountability and cross-sector collaboration in efforts to tackle antimicrobial resistance. In response, the Global Leaders Group on antimicrobial resistance was established in 2020. The Independent Panel on Evidence for Action against antimicrobial resistance and a Partnership Platform, involving multilateral organizations, civil society, governments, academia and the private sector, will also be established. Actions to address antimicrobial resistance at country level will be strengthened by the Tripartite and the UN Environment Programme (UNEP), but other agencies and organizations also have a role to play, including the UN Development Programme (UNDP), the UN Children's Fund (UNICEF), the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund), the World Bank and other development banks, bilateral agencies and foundations.

What actions are other countries taking-

Since the launch of the Global Action Plan on antimicrobial resistance in 2015, countries have substantially stepped up their response to antimicrobial resistance. As of May 2021, 144 countries had a multisectoral NAP (13) in place and most of the remaining countries are in the process of developing such a NAP. Since 2016, countries have also been reporting their progress in addressing antimicrobial resistance via the Tripartite antimicrobial resistance Country Self-Assessment Survey (TrACSS) (14). A total of 136 countries – representing over 90% of the world's population – participated in the 2019–2020 TrACSS (15). Findings reveal increased national focus on ANTIMICROBIAL RESISTANCE and growing recognition of the importance of a One Health approach in effectively tackling the issue: 76 countries reported having a functional multisectoral working group on antimicrobial resistance in place. Overall, 92% of countries (125) reported having in place regulations on the prescription and sale of antimicrobials for human use. Likewise, 77% of countries (103) introduced regulations on prescriptions and sale of antimicrobials for animal use, although implementing these regulations can be difficult. In addition, 71.8% of countries reported having policies to optimize the use of antimicrobials in human health, such as guidelines for treatment and practices to assure appropriate antimicrobial use. Some 56% of countries reported having policies to optimize the use of antimicrobials in animal health, and 63% reported having laws prohibiting the use of antibiotics for growth promotion. Overall, 60% of countries (81) reported the inclusion of the environment sector in their plans, including water, sanitation and hygiene (WASH). However, few countries reflect antimicrobial resistance issues and data in environmental plans or strategies. As of April 2021, 107 countries or territories are also enrolled in the Global Antimicrobial Resistance and Use Surveillance System (GLASS). Set up in 2015, GLASS promotes and supports a standardized approach to the collection, analysis and sharing of antimicrobial resistance data at a global level. It encourages and supports countries to set up national antimicrobial resistance surveillance systems that can monitor antimicrobial resistance trends and produce reliable and comparable data. In 2020, 160 countries reported the use of antimicrobials in animals to OIE's Global Database on Antimicrobial Agents Intended for Use in Animals (16). The number of countries reporting information has grown over time, from 130 OIE members for the first report in 2016 to 160 in the fifth report in 2020. Since 2019, nine countries have assessed the implementation of their national action plans on ANTIMICROBIAL RESISTANCE in their food and agriculture sectors, using the FAO Progressive Management Pathway for antimicrobial resistance (FAO-PMP-ANTIMICROBIAL RESISTANCE) (17). The aim of the FAO-PMP-antimicrobial resistance is to develop a road map that advances One Health responses to antimicrobial resistance at the country level. In addition, since 2016, more than 120 antimicrobial resistance laboratories in 28 countries have assessed antimicrobial resistance surveillance system with the support of the FAO Assessment Tool for Laboratories and antimicrobial resistance Surveillance Systems (FAOATLASS) (18). The FAO-ATLASS helps countries to generate quality data from their food and agriculture sectors.

<u>What are the key challenges and barriers to tackle antimicrobial resistance affectively-</u>

Antimicrobial resistance is one of many challenges that countries face. Many people are unaware that they or their livestock might have a resistant infection, and often those who are treating them are also unaware. This means that the problem is largely unrecognized and undocumented. The lack of representative data on antimicrobial resistance, especially in LMICs, continues to be a challenge. Because the real scale of the problem and potential impact remain unclear, it is difficult to build a strong national antimicrobial resistance narrative to increase political engagement, financial commitments or public awareness. Most countries have now developed antimicrobial resistance NAPs; however, there are major challenges in implementing, scaling up and sustaining programmatic and effective interventions. Coordinating ministries and involving other relevant stakeholders present logistical challenges, which are exacerbated by a lack of human and financial resources. In general, systems to manage antimicrobial resistance are better established in high-income countries, which have been implementing antimicrobial resistance programmes and activities for a longer time. Compared with countries with functional systems to address antimicrobial resistance, additional investment is required in countries that lack basic infrastructure; have weak human and animal health systems and food production systems; have a high burden of infectious diseases; lack or have deficient water treatment and waste management systems; or have weak environmental regulations. With the use of antimicrobials rapidly increasing in many middle-income countries, those that have large, unregulated private and informal sectors are particularly vulnerable to antimicrobial resistance. In many countries, substandard and falsified medicines and lack of access to essential health technologies (including diagnostics and vaccines) present a significant problem to human and animal health. This can contribute to rising levels of antimicrobial resistance. Phasing out the use of antimicrobial agents for growth promotion in animals and introducing mechanisms to control pollution may require changes in agricultural practices, waste and wastewater management, and pharmaceutical production systems. Controlling ecosystem-based approaches to minimize the use of antimicrobials in plant production is fundamental for human health and the environment. These measures are a necessary investment to protect human, animal, plant and planetary health. Countries will therefore need a blend of incentives, education, training and regulation to make these changes happen.

What plan of action should we follow in the future-

To effectively address antimicrobial resistance, countries need robust systems to prevent and manage infections in humans and animals, and support the prudent and responsible use of antimicrobials. Health facilities and food production need to be clean and safe. Sustainable procurement of antimicrobials needs to be promoted. Animal and human health workers need to be able to diagnose and treat infections properly; and access and use the right antimicrobial drugs of assured quality, for the right duration and dose, and only when indicated. Take-back systems, and solid and wastewater treatments need to be set up. These are development priorities, particularly in the time of COVID-19, but antimicrobial resistance provides another urgent imperative to take these actions sustainably to scale. Much of what needs to be done to tackle antimicrobial resistance is part of overall good human, animal and ecosystem health through a One Health approach. Various activities will have substantial benefits beyond tackling antimicrobial resistance; such activities include strengthening WASH provisions and pollution controls, biosecurity measures in animal production and along the food chain, sound chemicals and waste management and the supply of first-line medicines among others. In the wake of COVID-19, countries should be strengthening their integrated surveillance systems, pandemic preparedness plans and One Health collaboration to address international health threats, such as antimicrobial resistance. The Global Action Plan on antimicrobial resistance (10) and countries' own NAPs provide a comprehensive set of objectives and activities. Nevertheless, there is still much work to be done to see full and robust implementation of these plans. There must be more awareness and greater capacity to decrease inappropriate use of antimicrobials in all sectors, while ensuring access to appropriate antimicrobial drugs of an acceptable quality where necessary. Many countries are scaling up domestic production of antibiotics; such production should be part of the sustainable consumption and production agenda, with associated actions to prevent the risks of environmental contamination and to ensure quality. ANTIMICROBIAL RESISTANCE-specific efforts, where focused action on antimicrobial resistance is required, include, but are not limited to, those shown in Box 1. In many cases, antimicrobial resistance can offer an additional, compelling reason to enhance the quantity and quality of existing activities. Adapting basic projects and programmes to reinforce simple antimicrobial resistance-related messages can be cost effective and impactful. Addressing antimicrobial resistance is an important component of UHC, primary health care, global health security, One Health and pandemic preparedness, and can be included within outcomes in these areas. In light of COVID-19, many countries will be strengthening laboratory and surveillance systems and IPC. Similarly, addressing antimicrobial resistance fits within the food security debate on how to sustainably feed 11 billion people by the end of the century. It is essential that antimicrobial resistance responses are tailored to specific country contexts and capacities, including in environments that are resource constrained, conflict affected and challenging to operate in. People in such environments are still more likely to die because they cannot access antimicrobials when they need them, rather than because of a growing burden of antimicrobial resistance. The most important and pragmatic entry points may be strengthening systems to prevent and treat infections; for example, by expanding immunization coverage, applying integrated water resource management including WASH provision, promoting sustainable procurement and improving access to antibiotics for those in need.

Conclusion-

Antimicrobial resistance is now recognized by the scientific community, the society at large and most policy-makers as an important problem to confront.

The WHO global report on surveillance of AMR, providing for the first time a global picture of the magnitude of AMR, also reveals the lack of adequate surveillance in many parts of the world and large gaps in information on microbes of major public health importance that preclude an accurate analysis of the real situation and of trends over time.

It is critical to strengthen and harmonise the AMR surveillance through the development of agreed epidemiological and microbiological methods, the adoption of common definitions to enhance the ability to share and compare resistance information, and to attain a better coordination of the surveillance networks.

With this aim, the WHO regional office for Europe (EURO) supports a new project (CAESAR-Central Asian and Eastern European Surveillance of Antimicrobial Resistance) to develop a network of national surveillance systems in the countries of the region that are not part of the EU and do not participate to EARS-Net, facilitating comparison of data throughout the entire European region.

Different but coordinated strategies against AMR should be implemented, considering the type of pathogen (human or zoonotic), the setting in which it spreads (hospital or the community) and possible other specific factors contributing to the emergence of resistance. A special case is represented by the strategy against the development of MDR-TB, for which the only prevention is the improvement of treatment compliance in patients with susceptible TB.

In the hospital setting, infection control measures and antimicrobial stewardship programmes – administered by multidisciplinary teams of experts such as infectious diseases physicians, clinical pharmacists, clinical microbiologists, etc. – are very important to prevent emergence and transmission of antimicrobial-resistant microorganisms and ensuring the efficacy of available antimicrobials.

Antimicrobial stewardship needs to be extended also to family doctors in the community, where there is a great consumption of antibiotics. The actions needed to reduce antibiotic misuse and inappropriate antibiotic prescriptions should consider: information campaigns for the consumers, information and training for the healthcare professionals, improved diagnostics for treatment decisions, treatment guidelines, and prescription audits.

In veterinary medicine, the urgent need to take action for monitoring the antimicrobials use in food animals was stressed during the 2011 World Health Day. The interventions required consist in enforcing regulations governing the use of antimicrobials in food-producing animals, strengthening surveillance and monitoring, and reducing the need for antimicrobials through better animal husbandry.

In January 2015, European Centre for Disease Prevention and Control (ECDC), European Food Safety Authority (EFSA) and European Medicines Agency (EMA) published for the first time a joint report on the integrated analysis of the consumption of antimicrobials and AMR in bacteria from human beings and food-producing animals. This is a very important signal for a coordinated surveillance, although several limitations in carrying out this type of analysis have been identified.

In addition, innovative approaches are needed for the development of new antibiotics and other products to limit AMR. There is a shortage of new antibiotics in the pipeline and few incentives for industry to invest in research and development in this field. Only two novel classes of antibiotics have been marketed over the past 30 years (oxazolidinones and cyclic lipopeptides) but both these molecules target Gram-positive pathogens. There are very few effective drugs to treat multidrug-resistant infections due to Gram-negative bacteria that represent the main threat at present. The introduction of new vaccines may reduce the prevalence of infectious diseases and thereby reduce the need for antibiotics. For example, the introduction of the pneumococcal conjugate vaccines has led to the reduction in resistant *Streptococcus pneumoniae* not only in the vaccinated population but also in the population as a whole. The development of rapid point-of-care diagnostic tools may be of use to reduce clinical uncertainty, to save unnecessary antibiotic treatments, and to select effective antibiotics where resistance has rendered first-line treatment ineffective. The recent discovery of a new antibiotic called teixobactin, with excellent activity against Gram-positive pathogens, including drug-resistant strains, represents a hope for the future and an example for new researches.

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