
# CSE's Act on AMR Series | Compilation of Articles Contributed by Experts

## World Antimicrobial Awareness Week 2020

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Note: Photos of only the lead authors have been published

## THEME- Global and national efforts on AMR containment

## Drug-resistant infections: The silent pandemic that we must tackle now

*As the world reels from the impact of COVID-19, it would be a tragedy not to apply the lessons we are learning to the fight against drug resistance*

By Manica Balasegaram
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Drug-resistant 'superbug' infections kill an estimated 700,000 people each year, a number set to rise to 10 million per year by 2050 as drug resistance to antimicrobial agents grows and weakens our ability to treat even common infections.

A worrying number of infections are becoming harder and extremely complicated to treat due to drug resistance. The consequences of not addressing this silent pandemic now could result in a future where we will not be able to treat even common infections like pneumonia, urinary tract infections and infections in newborns.

We now have an opportunity to avert this potential catastrophe through strong leadership, collaboration and investment in measures to counteract the threat of drug resistance.

The novel coronavirus disease (COVID-19) has been our first experience of a pandemic in a generation that has been both, devastating and far-reaching. It has highlighted that governments are now willing to make substantial and long-term investments in preparedness to tackle global health crises.

With limited tools to prevent or treat COVID-19, the pandemic has disrupted health systems and global economies in ways the world has not seen before.

Despite solutions being at hand, a similar situation could be on the cards for the evolving pandemic of drug-resistant infections unless urgent action is taken to address decades of disinvestment in late-stage antibiotic research and the lack of access to antibiotic treatments.

In several countries like India, antibiotics, while not effective against viruses, are being used frequently in people with COVID-19 to prevent or treat suspected or confirmed secondary bacterial infections.

Even though key antibiotics cannot be used without prescription, the lack of enforcement can lead to significant overuse, further fuelling antibiotic resistance.

If COVID-19 has taught us one important lesson, it is that pandemic preparedness requires a global coordinated effort and no country can do it alone.

Similarly, strengthening our ability to fight drug-resistant infections requires a sustained, coordinated response, which must also ensure affordable access to solutions.

Particularly critical to tackling drug-resistant infections is the One Health concept, recognising the importance of connecting the health of people to both, the health of animals and our shared environment.

Drug-resistant infections move silently within populations and between animals, humans and environments; they do not know boundaries and neither should our responses.

COVID-19 has reinforced the concept of a global community, where our health and well-being are inextricably linked, regardless of where we live.

Solutions will therefore only be successful if they are available to everyone around the world, including those in low- and middle-income countries, and if their reality, know-how and capacity are part of a comprehensive response.

Ensuring universal research and development, equitable and affordable access to solutions needs to be a cornerstone of pandemic preparedness and response.

The evolving pandemic of drug-resistant infections has the potential to cripple the world in the same way that COVID-19 has done this year.

However, unlike with COVID-19, we know what it will take to combat drug resistance and that meaningful change can be achieved with sufficient political will and resources.

There is an opportunity now to significantly step up our response to drug-resistant infections and prepare ourselves to handle the unpredictable and silent nature of the pandemic, where the true extent of damage done remains somewhat invisible.

The fight against drug-resistant infections will rely on governments seizing this opportunity to develop a more robust, coordinated and equitable approach to pandemic preparedness and global health security.

Our success in fighting this pandemic will depend on the motivation now to secure investment and ensure access to solutions like better surveillance of resistant infections, strong infection prevention and control, healthy enforcement of antibiotic policies, tests to identify resistance and the development of novel antibiotics.

*About the author: Manica Balasegaram is the Executive Director of the Global Antibiotic Research & Development Partnership, a not-for-profit organization developing new treatments for drug-resistant infections that pose the greatest threat to health*

## Current policy developments to contain AMR not enough: South Centre expert

*Viviana Muñoz-Tellez was interviewed by Rajeshwari Sinha, CSE on the gaps and challenges in the ongoing global policy-making decisions. (Edited excerpts)*

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**Rajeshwari Sinha: What is your opinion about the sucessess, gaps and challenges in the ongoing global policy-making and governance-related efforts to combat AMR?**

Viviana Muñoz-Tellez: In the past five years, progress towards AMR response has accelerated with new commitments and awareness, but it is still far from what is needed. The United Nations Resolution, from the High Level Political Forum on AMR in 2017, as follow up to the WHO Global Strategy and Action Plan on AMR was a major achievement.

The expanded work by the World Health Organization, the Food and Agriculture Organization of the United Nations and the World Organization for Animal Health in particular to support countries' National Action Plans on AMR from a cross-sector approach is important progress.

Recognition of the importance of a 'One-Health' approach to tackle AMR is also being evidenced in country NAPs and greater collaboration across agencies.

Keeping up the sense of urgency of tackling AMR and level of political will expressed in 2017 is a major challenge. Many global commitments are the result of compromise and therefore, are broadly worded. More specific targets need to be set while allowing for policy space to adapt to specific context of countries.

The tripartite organisations are mandated to advance the development of a global stewardship and development framework, but this work has not advanced.

Importantly, implementation needs to take place in the context of countries' NAPs. Effective implementation is very challenging for many developing countries due to insufficient awareness, monitoring and data to estimate and understand the AMR burden, technical and financial resources in the context of diverse health priorities and health system weaknesses.

Moreover, gains made so far may also be reversed if efforts for AMR response are not sustainable. This points to the need for increased global collaboration and sustained solidarity to support context-specific AMR interventions in the global South.

Insufficient progress has been made at the global level in advancing a workable model for bringing about new antibiotics to target priority pathogens, which ensures access to all those need them and stewardship to conserve them.
Moving towards concrete and insufficient technical and financial support for developing countries to adopt and implement their national action plans on AMR is a major challenge.

The COVID-19 pandemic has created new challenges for AMR, but has also highlighted the importance of stronger infection prevention and control measures and improved hygiene, including low-cost effective measures such as hand washing.

**RS: What are your thoughts on the extent of representation and participation of representatives from the global South in this process?**

VMT: The global South is under-represented, in terms of AMR champions, country policy makers, civil society, practitioners, veterinarians, academia, media, etc. International bodies and funders need to scale up efforts to include the voices of the global South if we want an effective global response to AMR.

**RS: How do you view the efforts of the tripartite with respect to alignment with AMR containment needs of the low- and middle-income countries of the south?**

VMT: The tripartite is an important source of technical support for developing countries. These institutions also suffer from lack of sufficient technical and financial resources to provide the level of support needed to developing countries.

Government and philanthropic funders in the AMR space need to play a greater role in fostering greater collaboration amongst themselves, the tripartite and other relevant institutions and stakeholders, and to empower developing countries to define the priority areas and actions.

**RS: What should be the key areas / aspects that need greater focus in the future to help these countries better manage AMR?**

VMT: The main priority is to provide greater technical and financial support. It would also be valuable to foster broader sharing of needs, experiences and good practices in AMR response among developing countries, including expertise from the South.

The South Centre has been supporting 'South-South cooperation' in this regard at yearly regional conferences. A third virtual conference will be held among React Africa and South Centre in December, 2020 to discuss the status of national action plans in the African region.

**RS: What is the role of South Centre in global AMR containment efforts?**

VMT: The South Centre strongly advocates urgency in accelerating the global response to AMR, which must include action by all countries and stakeholders across sectors and support for developing countries. Developing countries suffer from a double burden.

Ultimately, AMR will affect developing countries the most for they have a disproportionately high burden of infectious diseases. Yet, currently, more people die due to lack of access to antibiotics than from antibiotic-resistant infections.

In its role as intergovernmental think tank of developing countries, the South Centre is an active participant in the global discussions on policy and measures to contain AMR. We work closely with our member countries as well as the broader membership of the Group of 77 and China.

We participate in deliberations and expert groups in multilateral institutions and support developing countries in these processes, collaborating closely with academic and civil society partners. We publish information and analysis on ongoing processes.

*About the interviewee: Viviana Munoz Tellez is a coordinator, health, intellectual property and biodiversity programme at the South Centre.*
*The South Centre is an intergovernmental organisation of developing countries that helps them combine efforts and expertise to promote their common interests in the international arena.*

## Managing antimicrobial resistance amid COVID-19 is a challenge

*Addressing the challenge of excessive use while at the same time assuring sustainable supply of essential antibiotics is key to making health systems resilient to both COVID-19 and antimicrobial resistance*

By Dusan Jasovsky , Jyotsna Singh, Leena Menghaney
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The advent of antibiotics significantly increased the chances of surviving serious bacterial infectious diseases. Moreover, antibiotic therapy enabled the development of chemotherapy, organ transplantation, surgery in general and a wide range of medical interventions over the past eight decades. Effective antibiotics are the cornerstone of modern medical practice.

However, in India, poor availability and utilisation of diagnostics, insufficient antibiotic stewardship and compromised infection control both in community and hospital settings result in over-reliance on and over-use of antimicrobials.

Illnesses usually caused by viruses such as diarrhoea and acute upper respiratory infections account for many inappropriate antimicrobial prescriptions in community settings.

With an increased focus on AMR globally and in India, the Indian Council of Medical Research and other stakeholders made important steps to introduce antimicrobial stewardship to rationalise antibiotic prescriptions in hospital settings.

However, according to experts, the novel coronavirus disease (COVID-19) threatens to undermine these efforts. COVID-19 creates conditions that lead to inappropriate use of antibiotics.

Broad-spectrum antibiotic use and overuse is common among COVID-19 patients and prescribing is often based on clinical presentation rather than laboratory markers; besides that, differentiation between bacterial and viral pneumonia can be difficult even with availability of laboratory tests, particularly for severe cases.

The World Health Organization is concerned AMR will be further fueled by the inappropriate use of antibiotics during the COVID-19 pandemic.

Only a small proportion of COVID-19 patients may need antibiotics to treat subsequent or concomitant bacterial infections and the organisation has issued guidance specifically to not provide antibiotic therapy or prophylaxis to patients with mild COVID-19 or to patients with suspected or confirmed moderate COVID-19 illness unless there is a clinical indication to do so.

The risk of acquiring healthcare-associated infections in the COVID-19 context due to long hospital stay and invasive medical procedures such as invasive ventilation and indwelling catheters expose the importance of keeping antibiotics working for the management of severe COVID-19 cases.

**Integrating stewardship into pandemic response**

It is therefore important for countries like India to introduce guidelines to define indications and conditions of antibiotic use in COVID-19 patients and encourage treatment providers follow the principles of antimicrobial stewardship.

The development, updating and dissemination of evidence-based guidelines at the country level is urgently needed to support antimicrobial stewardship interventions specific to COVID-19.

In addition, it is crucial to make available diagnostic tests to help in the identification of bacteria and their resistance patterns such as culture / Aspartate aminotransferase or equivalents and the diagnostic capacity to differentiate between simple COVID-19 infections from those including co-infections or alternative diagnosis (like imaging, procalcitonin, etc).

In low-resourced systems, laboratory infrastructure is often a challenge. With labs responding swiftly to the pandemic, shifting their limited capacities to COVID-19 and deprioritising cultures / anti-microbial susceptibility testing, not enough cultures are being sent for confirmation for the presence of secondary bacterial or fungal infections in COVID-19 patients.

Concrete measures such as systematic testing of severe COVID-19 patients with suspected bacterial co-infections are needed to better integrate antimicrobial stewardship into the pandemic response.

The increased focus on COVID-19 and the restrictions imposed by the pandemic have affected aspects of the health system response to AMR such as surveillance and training. These aspects have to be preserved and strengthened.

Through proper microbiology diagnostic capacity, it is possible not only to provide better targeted individual patient care but also conduct proper surveillance of antibiotic resistance: Health systems will be able to monitor the threat of antimicrobial resistance that lurks behind the pandemic.

In addition, monitoring of antibiotic consumption is another essential component of proper antibiotic stewardship. Some studies are reporting an increase of up to 75 per cent in antibiotic prescribing.

This is especially true for localised selection pressures in COVID-19 units where antibiotics are being reportedly over-prescribed. This further exposes the need to generate and monitor local trends to inform sound stewardship practices in COVID-19 clinical management while informing the international discussion on reviving the void currently present in the antibiotic innovation pipeline.

**Success means achieving sustainable access**

Besides the issue of excess, there is an often-overlooked access issue.

As we pointed out a year ago in our article depicting an access issue in ABR, the current pharmaceutical market in India promotes the 'increases of consumption rates of last-resort antibiotics. The pharmaceutical industry does not see profit in producing relatively inexpensive 'Access' group antibiotics, while drugs that guarantee higher pay offs (often from the Watch and Reserve group) are ensured a reliable supply.'

This is however in direct contrast with the WHO General Program of Work 2019-2023 that calls for the proportion of access antibiotics to be more than 60 per cent of overall antibiotic use.

The access crisis in 'access' group antibiotics has been further underlined by lack of sustainable suppliers of active pharmaceutical ingredients due to low profit margins over-reliance on imports and certain suppliers.

The Indian drug regulatory authority's reaction to impose export restrictions on active pharmaceutical ingredients (including antibiotics) during the COVID-19 pandemic to deal with possible shortages at the domestic level could have further threatened continuity of supply.

Managing and mitigating the risks associated with the competition for scarce resources, like essential antibiotics, during a pandemic and beyond requires international cooperation and global solidarity.

Without international mechanisms to achieve sustainable access to novel and existing antibiotics, there remain many challenges for both, low-and middle income countries and high income countries that can be efficiently addressed in a collaborative way.

These include a diversification of manufacturing capacities, improving transparency and forecasting across distribution lines, establishing collaborative pooled procurement mechanisms and initiatives that could be developed among the United Nations, global procurers and other stakeholders to mitigate stock outs and shortages and introducing international platforms with access conditionalities and stewardship measures countries could subscribe to in order to access relevant antibiotics sustainably.

With weaknesses in health systems and public health capacities in many countries, addressing the challenge of excessive use while at the same time assuring sustainable supply of essential antibiotics is key to make health systems resilient to both COVID-19 and antimicrobial resistance.

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## Antimicrobial resistance: The need to tackle access-excess problem

*AMR, like every process, has its own drivers and determinants. The threat has evolved over time due to our acts of omission and commission*

By Nafis Faizi
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Antimicrobial resistance (AMR) is perhaps the greatest health threat to human beings, partly because of its direct or indirect impact on most diseases affecting human health. This, however, exists because the warning was not paid heed to.

Alexander Fleming spoke in depth about negligent use and resistance in his Nobel Prize acceptance speech in 1945. Not only was resistance to sulphonamides known before the discovery of penicillin, 38 per cent of Staphylococcus aureus strains were reported penicillin-resistant in a London hospital three years after Fleming's warning in 1948.

We are currently staring at a world where several anti-microbials have stopped working or will stop working if we do not mend our ways. One must, however, resist the temptation to consider AMR an event, as war-like metaphors about it often suggest.

AMR is a process, and like every process, it has its own drivers and determinants. The threat has evolved over time due to our acts of omission (not paying enough attention to health systems, infection prevention and other determinants) and commission (overuse / misuse of antibiotics and jeopardising access through intellectual property rights).

Here, I focus on one fundamental cause of antimicrobial resistance in the human health sector: The access-excess problem. Lack of access or excess (overuse / misuse) of antimicrobials is irrational and contributes to AMR.

The World Health Organization (WHO) defines access as "having medicines continuously available and affordable at public or private health facilities or medicine outlets that are an hour's walking distance from the home."

Poor access, including no access and delayed access to antibiotics, causes about 5.7 million deaths annually. This is far more than AMR itself, which causes about 0.7 million deaths.

This means that lack of or delayed access to antibiotics kills more people than antibiotic resistance. Poor access of antimicrobials leads to increase in resistance due to three main factors.

First, it leads to ineffective treatment and death. More than one million children die every year due to untreated pneumonia and sepsis. Only 12.5 per cent children with suspected pneumonia in India

receive antibiotic treatment. Both ineffective treatment and death leads to continuance of the infection transmission cycle as they infect others.

Second, when patients do not complete the full course of antibiotics, often after symptomatic relief, it gives the surviving micro-organisms a golden opportunity to develop resistance against the antimicrobial used.

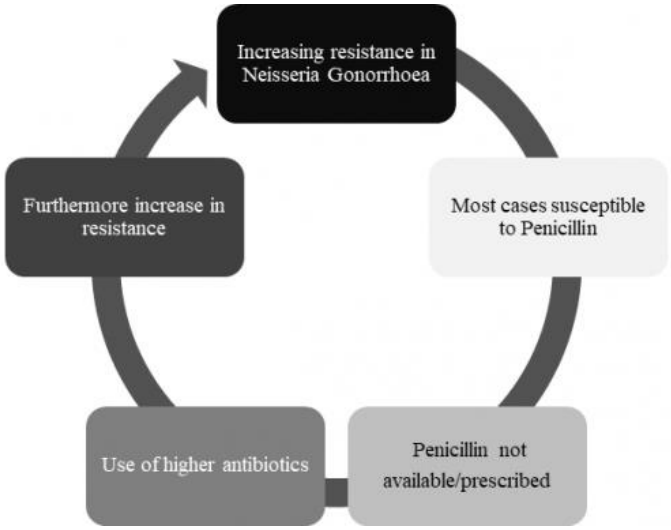
This is what Fleming warned about in his speech: 'If you use penicillin, use enough.'

Third, poor access to first-line antibiotics, leads to increased and unnecessary use of higher group of antimicrobials. Unnecessary use of higher group of antibiotics further lead to development of resistance in second line and at times, last resort antibiotics. A key example that might turn Fleming in his grave is penicillin itself. Benzathine Penicillin stockouts is a key example of poor access to first line antibiotic.

Despite its vital role in treating gonorrhoea, acute Rheumatic Fever and prevention of mother to child transmission of syphilis, Benzathine Penicillin stockouts in as many as 39 countries have been reported in the last few years.

Ironically, this increases the resistance potential of *Neisseria gonorrhoeae*, which is already a high-priority pathogen for research and development of new antibiotics.

Access barriers could be due to therapeutic (scientific / therapeutic bottlenecks in bringing new antibiotics to market), financial (unaffordability of a rational course) or structural (obstacles in delivery at the system/clinic level).




However, in case of antimicrobials, more than 95 per cent on the WHO Essential Medicines List (EML) are off patent, the bulk of the remainder being second-line antiretroviral drugs for HIV / AIDS.

Despite this fact, shortage, stock outs and unavailability is common. The lack of access is dependent on four factors: Reliable healthcare and supply systems, sustainable financing, affordable pricing and rational selection and use (WHO, 2004).

As part of the 2017 Essential Medicines List, WHO carried out a comprehensive review of antibiotics and introduced a new categorisation to guide prescriptions and treatment while monitoring consumption.

By the end of 2023, WHO aims that 60 per cent of all antibiotics by 2023 is from the access category, the narrow spectrum antimicrobials with lower resistance potential.

Penicillin belongs to the access category. While the effort is laudable, in most countries in the south including India, the data of total access antibiotic consumption is not available so far.

On the other extreme lies the overuse and misuse of antimicrobials or the 'excess' problem. Way back in 1943, Rene Dubos, widely hailed for discovering the most powerful antibiotic of his time, Gramicidin (which was later eclipsed by Streptomycin) prophetically warned students against 'the wasteful and inconsiderate use of antibiotics'.

Despite the warnings, the antibiotic use has increased by 36 per cent between 2000 and 2010 (Laxminarayan et al, 2016). Though the increase in consumption is worldwide, it is not uniform across the world.

About 75 per cent of this increase is reported from BRICS countries (Brazil, Russia, India, China, South Africa), with 23 per cent increase in retail sales volume in India alone, which has poor control against over the counter (OTC) sales (Laxminarayan et al, 2016).

As the per capita consumption of antimicrobials in India remains low, the bigger problem is misuse of higher antimicrobials. Such misuse is due to provider, regulation or user-related factors.

The provider related factors include prescribing antibiotics when it is not required and using broader spectrum antimicrobials or multiple antimicrobials as shotgun therapy. Such factors are prevalent due to poor antimicrobial stewardship knowledge among doctors, as Chennai declaration noted.

Diagnostic uncertainty, lack of quality and timely diagnostics as well as unavailability of locally relevant and regularly updated Standard Treatment Guidelines are other reasons that contribute to provider and regulation problems.

Sadly, the general public has little knowledge about antimicrobial resistance. This lack of information leads to pressure to prescribe (providers) or sell (pharmacists) from the patients / end users themselves as well.

The access-excess problems are directly related to AMR and need to be addressed if we want to avert this global catastrophe. However, this problem cannot be solved with quick-fix solutions, but a health system-centric response.

The fight against AMR needs a strong inclusive health system with a well-funded and publicly provisioned primary healthcare and a regulated private health system together with a model of continuum of care that is systematic and organised.

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## Indian public sector health facilities, workers should lead the fight against AMR

*Both are important links across sectors; they should unleash their full impact on the life of the common man for curtailment of AMR.*

By Sagar Khadanga
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It has been more than three years since the National Action Plan for Anti-microbial Resistance (NAP-AMR) was rolled out across India, in line with the Global Action Plan for Anti-microbial Resistance (GAP-AMR).

Different states of the country have been at various stages of development of the State Action Plan for Anti-microbial Resistance. Till date, only three states (Kerala, Madhya Pradesh and Delhi) have come out with their state action plan.

There have been multiple ice-breaking sessions among Health Care Workers (HCW) across the country and the result is that Anti-microbial Resistance (AMR) is no more a buzz word to us.

Once given the most important priority, healthcare facilities and HCWs have played only a limited role in the containment of AMR. Hence, the concept of 'One Health' has emerged, emphasising the role of other sectors like animal health, food, agriculture and environment in addition to human health.

Moreover, the multimillion industries which run these sectors are the fulcrum of AMR containment.

Public Sector Health Care Facilities (PSHCF) remain the most sought-after healthcare facilities for more than two-thirds of Indians. There has been a pyramid-shaped provision of primary, secondary and tertiary healthcare facilities, with the maximum number being of primary care facilities at the base.

Over the last decade or so, there has been a rapid progress in teaching tertiary care facilities. During the same time period, many apex institutes like the All India Institute of Medical Sciences (AIIMS) have come up across the country to balance the regional differences in healthcare delivery.

Each type of healthcare facility has different challenges and opportunities for the containment of AMR.

The scope of individual healthcare facilities is beyond the scope of this article. Anti-microbial stewardship practice (AMSP) has been a low-hanging target but is yet to be unleashed to fullest of its capability.

Stewardship literally means supervising or taking care. But in the context of AMR, AMSP has far more implications than initially thought.

**Diagnostic stewardship**

This emphasises the quality of the microbiology laboratory and hence the local antibiogram. There are only handpicked PSHCFs with antibiograms of their own in India. Compare that with the West, where almost all hospitals have their own antibiogram.

An up-to-date antibiogram provides confidence to clinicians while choosing an antimicrobial empirically. In absence of an antibiogram, the practice of 'hit hard' and 'hit fast' will prevail and only increase AMR.

The use of freely available WHONET to generate local antibiograms and the practice of truncated reporting of drug susceptibility is the need of the hour.

**Clinical stewardship**

Clinicians have to be trained in common principles of antimicrobial use, especially common pharmacological properties. They have to practice different sets of principles for out-patients, in-patients and those with or without sepsis-defining illness.

There are 5 'Ds' to practice: Right diagnosis, Right drug, right dose, right duration and right time to De-escalate (decrease or stop).

Regular Point Prevalence Study (PPS) of antibiotic usage, Days Of Therapy (DOT) and Defined Daily Doses (DDD) are a good way of surveillance. But in the absence of computerised platforms, this becomes hard to achieve.

Prospective feedback is an attractive yet herculean task. Formulary restriction of antimicrobials are still debated, considering the fact that most of the emergency cases are handled by relatively junior HCWs.

**Infection control stewardship**

Infection Control Practice (ICP) is one of the most neglected yet most powerful link to break the cycle of AMR. It ranges from simple hand hygiene, surface cleaning, bio medical waste segregation to complex issues of operation theatre air change, positive and negative pressured cabins to biomedical waste management.

There have been recent improvements in overall ICP measures of most of the PSHCFs under the ambit of 'Kayakalp', a Government of India initiative across the country. The concept has been apt covered during the novel coronavirus disease (COVID-19) pandemic.

**Environment and sanitation stewardship**

PSHCFs have to be role models for protecting the nearby environment. Many cases of hospital-transmitted infections are often noticed. Though a matter a debate, the proposed and contested theory of the seepage of the Wuhan virus from a laboratory and the subsequent COVID-19 pandemic it caused is still fresh in our memory.

**Stewardship in training-teaching and research**

A deep knowledge of AMR and its consequences has to be imparted to the budding HCWs graduating from tertiary PSHCFs, who will work with communities.

Investing in them will lead to rich rewards in the times to come and save many more dollars than changing their practices at a later date. Research ideas of microbes, AMR and AMSP need to be fostered and nurtured.

**Administrative & leadership stewardship**

Overall, the PSHCFs most often than not, lack leadership identity in the field of AMR. This may be because of AMR being non-rewarding, non-profiting and results in it being hard to measure.

However, the time is apt for PSHCFs to portray themselves as role models to all stakeholders. Doctors are one of the most influential people in society.

They should utilise this influence to the fullest for highlighting AMR in each and every platform, from primary education to politicians. No wonder, the role of leadership has been the only difference between the strategic points of GAP-AMR and NAP-AMR.

**Conclusion**

HCWs and PSHCFs are an important link across sectors as role models in the field of AMR. It is time that PSHCFs rise to the occasion and unleash their full impact on the life of the common man for curtailment of AMR.

*About the author: Sagar Khadanga is an Assistant Professor at the Department of Medicine, All India Institute of Medical Sciences Bhopal.*

## AMR has to be addressed not as a microbiological problem but as a social construct

*We must realise that AMR is an occurrence because of a natural instinct for survival of living beings, which has got aggravated because of multisectoral excessive use of antimicrobial agents by humans*

By Vandana Roy
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Antimicrobials are probably one the most successful group of medicines to have been discovered. The understanding of the concept of hygiene and disinfection followed by discovery of a number of classes of antimicrobial groups increased survival and human life expectancy.

Among the reasons attributed to increase in survival and life expectancy between the early 19th and 20th century, the role of antimicrobials is undoubtedly among the top.

It was opined by many that the war against infections had been won but there were others who were not sure about it, including Alexander Fleming who said:

The greatest possibility of evil in self medication is the use of too small doses so that instead of clearing up infection the microbes are educated to resist penicillin and a host of penicillin fast organisms is bred out which can be passed to other individuals and from them to others until they reach someone who gets a septicaemia or pneumonia which penicillin cannot cure (New York Times June 26, 1945)

Within a short period of four years, resistance to penicillin had spread. However, the importance of increasing resistance was not realised then as new antimicrobials were getting discovered.

The situation as we all know is different now. There is widespread resistance to a majority of antimicrobials and there are no new antimicrobial agents in sight.

Globally, 700,000 people die every year from antimicrobial resistance (AMR) and this number is expected to increase to 10 million by 2050, more deaths due to cancer and traffic deaths combined. The world's economy will lose more than seven per cent of its gross domestic product ($210 trillion) by 2050.

Taking cognizance, the World Health Organization took the lead and the World Health Assembly (WHA) adopted the Global Action Plan (GAP) on AMR in 2015. This was subsequently endorsed by

the Food and Agriculture Organization of the United Nations and the World Health Organization for Animal Health (OIE).

Realising the multisectoral nature of the problem involved in the process — humans, animals, birds, fish, plant health, food production, water, sewage, sanitation and environment — a One Health Approach has been adopted.

**National and state plans**

India was a signatory to the above and adopted the National Antimicrobial Action Plan (NAP) with six priorities in 2017, with the Union Ministry of Health and Family Welfare (MoHFW) as the nodal ministry and the National Centre for Communicable Disease Control as the key surveillance body.

Guidelines for the State Action Plans (SAP) have been developed. Till date, three states — Kerala, Madhya Pradesh Pradesh and Delhi — have prepared SAP. In addition, FAO has facilitated the establishment of the Indian Network for Fishery & Animals Antimicrobial Resistance in 2017.

The MoHFW banned the use of colistin in the fish and livestock industries in 2019. The Food Safety and Standards Authority of India introduced maximum permissible antibiotic residue limits for meat, fish and milk in 2018.

The Central Standards Control Organization has made a separate schedule H1 for antimicrobials which require a prescription, the record of which has to be kept by the pharmacist.

The Red Line campaign began in 2016, to draw attention to the safe use of antimicrobials, with a red line drawn on antimicrobial packaging. The most recent step taken by the Union Ministry of Environment, Forest and Climate Change, has been the publishing of draft standards for antibiotic residues in pharmaceutical effluents under the proposed Environmental (Protection) Amendment Rules 2019.

The strategies broadly defined in the NAP are:

- Increasing knowledge, awareness, communication
- Increasing databases and evidence
- Preventing infection
- Improving rational use
- Looking for alternative strategies
- Establishing a collaborative leadership role for the country in AMR.

While India is moving steadily ahead in its plan, some points for consideration are being put forward.

The problem of antimicrobial resistance has to be looked at from an evolutionary perspective. There is enough evidence that genes conferring resistance to several classes of antibiotics in nature were present well before the antibiotic era.

Structure-based phylogeny of serine and metallo β lactamases established that these ancient enzymes originated more than two billion years ago. It has been realised that the diversity of these enzymes is not the result of recent but ancient evolution.

So far, a bullet target approach has been used to explain the mechanisms of AMR. But recent works suggest another mechanism for AMR — "the kin selection concept" — according to which, a few highly resistant mutants improve the survival of the population's less resistant constituents, at some cost to themselves.

They do so in part by producing indole, a signalling molecule generated by actively growing unstressed cells. The indole serves to turn on drug efflux and oxidative stress productive mechanism, thus boosting the survival capacity of the whole population.

The above observations highlight that Charles Darwin's theory of survival of the fittest for living beings holds true for microorganisms also. Like all living creatures, microorganisms will evolve to survive.

This adaptation is instinctive and destined by nature. Discovering newer antimicrobials would be a short term measure at a great cost, since resistance to them would also develop, due to anthropocene forces. So this has rightly been put as Strategy 5 in the action plans.

**A social issue**

Having a NAP and SAP is good as it helps put things down on paper. A multi-sectoral approach with all stakeholders working together is another positive step.

But as far as human health is concerned, what we must look at are the reasons why antimicrobials are being prescribed, sold and used by people. Why simply telling doctors not to prescribe for some infections or fevers may not work. Why having a H1 schedule and a Red Line on packaging may also not be a deterrent to sell or buy. And why patients will ask for antimicrobials for fevers.

A doctor often prescribes antibiotics because the patient is asking for it, sometimes unconsciously through suggestions and queries. The doctor knows that if it is not prescribed, the patient will get it from somewhere else.

The same thinking holds true for a pharmacist. The forces at play here are market forces. Nearly 80 per cent of outpatient healthcare is by the private sector. And the private sector is governed by market forces first.

Keeping the customer happy is a priority. While training of doctors, pharmacists and others involved in healthcare is of paramount importance, the demand by the public has to be decreased by increasing awareness and educating the masses.

In the absence of infection control environments in health facilities and practices, doctors having patients come from communities where sanitation is poor and water quality doubtful, would practise defensive medicine.

Telling them more about science may not be the best policy. What may help change practices could be treatment guidelines for common infections. These must be based on evidence as regards local sensitivity patterns and they must be brought out by experts with no conflict of interests.

These guidelines must have government support. They must also be of such a standard that they can withstand judicial queries if at all patients go to consumer courts, claiming negligence in treatment if no antimicrobial agent is prescribed.

An infection-controlled environment would also go a long way in decreasing prophylactic prescribing of antimicrobial agents in public health facilities. Clean environment, good sanitation practices, clean drinking water, clean food, hand hygiene would affect occurrence of infections, decrease breeding of pathogens.

The government has to beyond the Swachh Bharat Abhiyan and Smart City concept for this. “A clean, safe environment for all” has to be made a mantra and has to be handled on a war footing. This would be the first step in prevention.

So far, the emphasis in most deliberations on AMR in India has been on surveillance and diagnosis. Most conferences and meetings on AMR spend most of the time discussing data from microbiology laboratories, focusing on the nature, mechanism and genes involved in the resistance present in the microorganisms.

The maximum representation in all these deliberations is also of microbiologists. It is as if AMR is a microbiological problem. Very little or no time is spent on looking at reasons for why it is happening and how to tackle that.

Probably because it’s easier to do surveillance, present data and more difficult to actually address the problem. Currently, we are doing what can be done and not what actually needs to be done to correct the problem.

The team looking at AMR needs to involve social scientists. Sociologists, anthropologists, psychologists should be a part of the team that is planning strategy on how to decrease use of antimicrobials not only in humans but also in other sectors.

It has to be realised that the problem of AMR is part of an evolutionary social construct. How the different parts are related and how they influence the use of antimicrobials by people has to be understood. Only then can it be addressed.

The action plan needs to permeate all levels of society. GAP has translated into NAP. It is moving at a snail’s pace into SAP. The plan needs to evolve into district action plan, town / city action plan,

village action plan, healthcare facility action plan and lastly, human action plan that an individual person must take.

It must be realised that AMR is an occurrence because of a natural instinct for survival of living beings, which has got aggravated because of multisectoral excessive use of antimicrobial agents in most cases indiscriminately and irrationally by humans.

The problem has to be addressed not as a microbiological one but as a social construct. According to the kin selection concept, if a small microscopic living cell can evolve to protect its weaker brethren, I am sure the human race can collectively rise above narrow sectarian interests to protect antimicrobials so precious for patients in need.

*About the author: Vandana Roy is the Director, Professor & Head at the Department of Pharmacology, Maulana Azad Medical College, New Delhi.*

## AMR action plan in MP a satisfying, progressive endeavor: Experts

*Only three states in India — Kerala, Madhya Pradesh and Delhi — action plans to deal with AMR*

Pankaj Shukla and Sagar Khandaga were interviewed by Rajeshwari Sinha, CSE
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**Rajeshwari Sinha: How did you ensure the role and involvement of multiple sectors during the process of drafting the Madhya Pradesh State Action Plan for Containment of Antimicrobial Resistance (MP-SAPCAR)?**

**Pankaj Shukla and Sagar Khandaga:** To be honest, this part was the most difficult part to execute. It was challenging to bring departments like the animal husbandry, fishery, farmer welfare and agriculture development, labour, medical education and public work and environment as well as the Department Health and Family welfare on board.

Once the administrative machinery was convinced about the importance of the state action plan, the job was half done. We organised multiple meetings with technocrats of these stakeholder departments for sensitising them on their roles and responsibilities.

We tried to identify their bottlenecks and discussed feasible solutions, thus winning their confidence.

We identified the technical committee members among these sectors and launched the MP-SAPCAR on July 26, 2019. Looking back, it was the most difficult yet the most satisfying endeavour.

**RS: How far have you moved on implementation after the release of MP-SAPCAR?**

**PS and SK:** The state has progressed quite a bit post the MP-SAPCAR release. State Quality Cell has facilitated human resource development over the last one year.

With the help of All India Institute of Medical Sciences Bhopal and support of Antimicrobial Resistance Surveillance and Research Network, the Indian Council of Medical Research, we have trained about 2,000 healthcare workers across the state on multiple platforms.

Madhya Pradesh is one of the few states with a state antibiotic policy and we are in final stage of its revision. We have made Standard Treatment Guidelines (STG) available to all district hospitals. Systems are in place to identify its practice at the grass root.

Nealry 70 per cent of public sector healthcare delivery facilities have been *KAYAKALP*-accredited, demonstrating progress in infection control practices (ICP) by leaps and bounds. We have taken on board, important stake holders like private nursing home association and association of pharmacists.

We have arranged successful meetings of the technocrats of animal husbandry, fishery, farmer welfare and agriculture development with the team of Kerala to share each other's experience.

We have identified the district nodal officers from the Department of Animal Husbandry to move forward. State veterinary department supports in providing veterinary laboratories in 22 districts for culture and sensitivity assessment for animal health.

Having travelled so far, it becomes more and more challenging to achieve new highs in this field.

**RS: What is the effort being made by stakeholders belonging to different departments (animal husbandry, food, drug, environment, agriculture)?**
**PS and SK:** The state drug store association for human health has supported in restricting the over-the-counter (OTC) sell of schedule H drugs. We are working on a proposal to add more antibiotics to this list.

State pollution control board has almost brought all health care facilities under its radar and the remaining facilities will be covered soon. We will be facilitating the laboratory culture and sensitivity for animal health in 22 districts for uniform quality.

This ambitious pilot project is aimed at the development of state antibiotic policy for Department of Animal Husbandry, which will be of first of its kind in the country. We are working on the process of testing the animal foods for illegal antibiotic residues so that culprits van be penalised.

We are also aiming to improve the animal health care facilities in line with its human health counterpart 'KAYA KALP'.

**RS: What are some of the key gains or successes that you have achieved so far with respect to MP-SAPCAR implementation?**
**PS and SK:** Madhya Pradesh is only the second state in the country to formulate a state action plan for AMR containment. The 'Bhopal declaration' was signed by the state ministers of five departments, showing the trans-sectorial commitment for MP-SAPCAR.

We have more trained human resources than ever, for anti-microbial stewardship practice (AMSP) at primary and secondary care healthcare delivery centers. We have our own state antibiotic policy and STG to be emulated.

All India Institute of Medical Sciences Bhopal, Antimicrobial Resistance Surveillance and Research Network, the Indian Council of Medical Research and WHO have done the necessary hand holding all throughout.

Human health prescription audit is ongoing with support of Atal Bihari Institute of Good Governance, Bhopal to identify the gain in AMSP.

Hand holding of about 100 human resources from the Department of Animal Husbandry and Fishery was provided by the team from Kerala.

The district nodal officers from the department have been identified and we are almost ready to formulate state antibiotic policy for animal health.

**RS: Please share what are some of the challenges you are seeing in MP-SAPCAR implementation efforts? What do you think needs to be done to address these issues?**
**PS and SK:** The most important challenge has been identifying the leaders across the sectors. Once identified, their commitment to the cause is the sole reason of success. It becomes challenging to collaborate and coordinate with so many diverse sectors along the path.

Once the minimum feasible time bound targets are identified, budgetary allocation across the sectors is a challenge. Even with allocated fund, time seems to be the most common limiting factor with so much additional commitments.

Quality check in data collection is of utmost importance and we are yet to make progress in applying WHONET, even in all human microbiology laboratories for uniform antibiogram from primary care setting.

The novel coronavirus disease (COVID-19) pandemic has almost brought to a standstill our efforts for the last couple of months. But we are all geared up to continue with more vigor than ever before.

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## Combating AMR: How Delhi's campaign design for school kids helped

*Schools, as institutions for people in their formative years, are strategic settings for advancing health promotion skills, practices and community links*

By Sangeeta Sharma, Renu Gupta, Ravindra Aggarwal, Anuj Sharma, Arti Bahl
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Antibiotics are important life-saving medicines and their inappropriate use is a major driver for antimicrobial resistance (AMR). Emerging antibiotic resistance is an important global public health challenge, which is threatening our ability to treat infectious diseases.

About 80 per cent of antibiotics used in the community are either prescribed by healthcare providers or purchased directly over the counter by consumers / caregivers without prescription for trivial illnesses.

Approximately half of community use of antibiotics is inappropriate (unnecessary use, inadequate dosage and combination therapy) and adds to the already existing burden of antibiotic resistance.

Tackling the global spread of AMR is both a priority and a challenge for the World Health Organization (WHO). India developed the National Action Plan on combating AMR (NAP-AMR) in 2017 — based on the Global Action Plan on AMR — as a national priority for the same.

Following NAP-AMR, national capital Delhi developed its State Action Plan to Combat Antimicrobial Resistance (SAPCAR-D) in alignment with the six strategic objectives outlined in NAP-AMR after Kerala and Madhya Pradesh.

Among six strategic priorities, the first was to improve awareness and understanding of AMR through effective communication, education and training. This strategy envisioned that educating prescribers and raising awareness among consumers had immense potential for behaviour modification with subsequent reduction in misuse of antibiotics.

World Antibiotic Awareness Week (WAAW) aims to raise awareness of antibiotic resistance and encourage best practices among the general public, health workers and policy makers to avoid further emergence and spread of antibiotic resistance.

Schools, as institutions for people in their formative years, are strategic settings for advancing health promotion skills, practices and community links. Raising awareness about judicious use of antibiotics, hazards of antimicrobial resistance and promoting behavioral change through school children is critical to tackle this issue.

Engaging school students can promote a better understanding and awareness about the problem from an early age. Children strongly influence parental behavior as well as that of their family and community.

When children step into the role of the educator, they are inspired to solve problems such as self-medication, sharing and using left over antibiotics, etc.

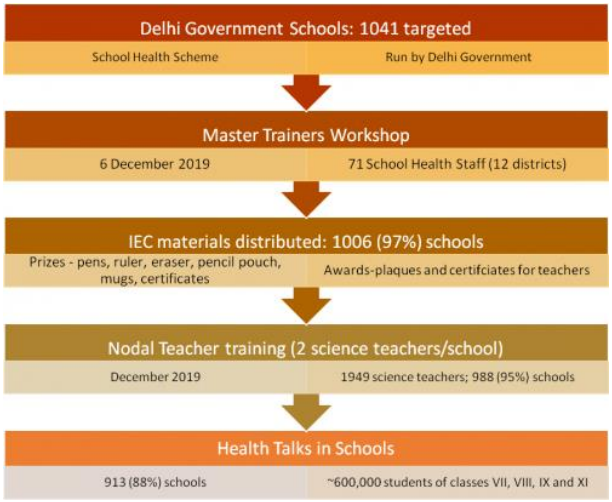
Aligned with WAAW theme for 2019, a school health campaign was organised by Delhi Society for Rational Use of Drugs (DSPRUD) in collaboration with WHO, National Centre for Disease Control and Government of Delhi with the objective to raise awareness among school children about antibiotics and antimicrobial resistance.

**Campaign design**

Delhi has 12 districts with 71 school health staff members and 1,228 schools (1,041 government schools and 187 government-aided schools) under School Heath Scheme (SHS), Department of Health and Family Welfare, Government of Delhi.

Only 1,041 government schools were targeted for the campaign. All SHS staff members were trained as master trainers by experienced faculty. The training schedule and contents comprising presentations and quiz was developed in joint consultation with SHS staff.

Information, education and communication (IEC) resources, power point presentations, key messages and quiz were based on 2020's theme of WAAW, focusing on the problem of antibiotic misuse and common practices that promote development of resistance to antibiotics and spread of infection.




(Campaign design employed to reach school)

Multiple pedagogical, participatory and physical techniques such as display of posters, standees, health talks, quiz, prize articles inscribed with messages, certificates for the students and the teacher, plaque for the school principal to acknowledge their active participation etc., were used for dissemination of messages.

To utilise the power of social media, a WhatsApp group of the SHS team was also employed for coordination and resource sharing. To understand the usefulness of the campaign, school teachers were asked to respond to a questionnaire about the contents of the messages, IEC materials. This kindled an interest among students.

At least 71 SHS staff members were trained to be master trainers. Information education and communication material was distributed in 1,006 schools (97 per cent).

Master trainers trained two nodal teachers per school in 30 training sessions; a total of 1,949 science teachers were trained from 988 schools (accounting for 95 per cent coverage).

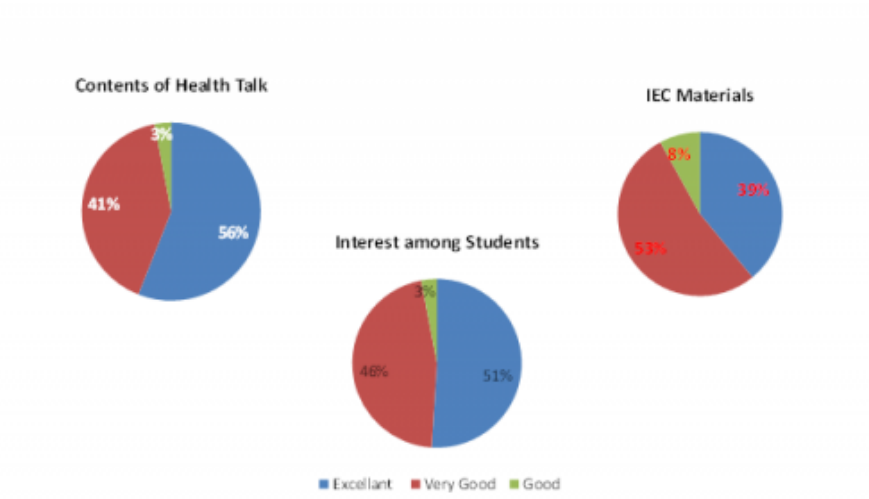
These nodal teachers organised quiz and health talks in their respective schools over a period of 30 days. A total of 913 Delhi government schools with approximately six lakh students between 12 and 17 years were part of the campaign.

The engagement was ensured through prizes distribution to around 30,000 students.

The commitment of schools and teachers were acknowledged by distributing certificates (of antibiotic champion and antibiotic guardian) and plaques to all nodal teachers and school principals respectively.

School teachers were highly enthusiastic and gave important inputs and suggestions for future campaigns.

The topic of the campaign was well-appreciated. There were, however, suggestions to hold these sessions regularly and for a longer duration. Further to increase the reach, health talks could be held on days when parents are also present (sports day or annual days).




(The feedback for future campaigns)

They also suggested that rewards / prizes be given to as many students and teachers as possible for broader engagement and greater motivation.

This campaign not only targeted school students but also educated, motivated and empowered large number of science teachers about judicious use of antibiotics and need to save antibiotics for future. The short duration of campaign proved to be a useful strategy in keeping the enthusiasm of teachers high with wide dissemination of messages.

The clear, precise, relevant, high impact messages for appropriate antibiotic use may serve as a powerful tool to boost explicit memory among students. School-based health education about

antibiotics has immense potential for greater involvement as through right education students can help build up a better society by helping their parents, family and community about optimum use of antibiotics.

It is well known that informed, empowered patients and caregivers can lead to safer patient care with possibility of reducing self medication with antibiotics.

Huge success of this campaign motivated us to make it a continuous feature. However, due to limitations imposed due to COVID-19 pandemic an online campaign has been designed created which was inaugurated on November 24. 2020. More than 3400 Delhi schools are participating. Another unique feature of the campaign 2020 is IDEAthon, an online competition for the school children based on the theme 'United to preserve antimicrobials'

"There is only one way under high heaven to get anybody to do anything. And that is by making the other person want to do it" – Dale Carnegie

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## Combating AMR: How Kerala reduced antibiotic misuse in animals

*Kerala has operationalised AMR protection plan in animal health by conceptualisating a 'one-health' response*

By Robin Paul
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The importance of antibiotics in human and animal health cannot be understated, which is why antimicrobial resistance (AMR) is such a global threat.

As bacteria develop resistance to antibiotics, we risk returning to a time when animals and people fell ill and died from simple, treatable infections. So, antibiotics are a cornerstone of modern medicine and public health.

Antibiotics are the tools to manage animal disease in animal health as well. Reducing antibiotic use without first tackling disease rates would mean sick animals go untreated, causing unnecessary suffering and mortality while increasing risk of transfer to other animals and people.

By better protecting animals from the threat of disease, identifying health issues earlier and treating them quickly and responsibly, we can decrease disease levels and the need for antibiotics.

This requires exploiting the long-term and preventative health benefits of tools such as vaccination, nutrition, biosecurity, disease surveillance, diagnostics, husbandry including housing and other animal health technologies. But antibiotics are the only way to treat a bacterial disease and there is currently no alternative.

In addressing issues such as AMR, it must recognised that such complex issues can only be resolved through intersectoral National Action Plans, which are cornerstone for action by any state.

Such action plans are the starting point for implementation of control strategies. They help identify relevant stakeholders, followed by mapping of available infrastructure and capabilities of stakeholders to arrive at a 'One Health' action plan for control.

Health is a state subject in India and individual states can formulate decisive actions. Only a very few states have developed a strategic action plan based on a national action plan. Kerala was the first state to ramp up efforts to control AMR, which was guided by WHO.

AMR can only be addressed by working across disciplines. The state, therefore, launched such a plan called Kerala AMR Strategic Action Plan (KARSAP) for the same.

Kerala has operationalised the plan in animal health by the conceptualisation in-KARSAP: A 'One-Health' response to AMR containment. It took action on each of the six strategic priorities as detailed below:

**Strategic priority 1: Awareness & Understanding**

The extension and training wing of the animal husbandry department is the livestock management training centers (LMTCs) located across various districts of Kerala. Each centre trains around 200 farmers every month.

A one-day training programme was conducted for veterinarians of LMTCs titled Train the trainers on AMR so that this message could be given to farmers. Kerala State Veterinary Council, the statutory registration body controlling veterinary practice, is now conducting Continuing Veterinary Education (CVE) programme for veterinarians on AMR.

The Veterinary University has AMR in its curriculum, with an aim to improve the understanding on AMR and promote prudent use of antibiotics.

**Strategic priority 2: Knowledge & evidence**

Laboratories: ISO 17025: NABL accreditation for Labs as well as that of all four apex labs of the Veterinary Department to the International Standard has been completed. Staff training to the lab personnel of microbiology divisions on WHO-NET has also been completed. These trainings were conducted by Govt Medical College, Trivandrum, the State nodal Centre for AMR.
Surveillance: Residue monitoring for antibiotics in broiler chicken by govt of Kerala to cover farms from various districts of Kerala.

AMR in food and food animals: An integrated veterinary surveillance programme for Kerala (meat, milk, poultry) and molecular identification and resistance study of bacterial isolates from animal products
Detection of common antibiotic residues of oxytetracycline & penicillins in milk in select pilot districts including study of AMR patterns for staphylococcus in milk and MRSA isolation
AST for bacterial avian diseases is an ongoing activity.

**Strategic priority 3: Infection prevention & control**

To optimise the use of antibiotics, the AMR working group has developed a standard operating procedure (SOP) for IPC in veterinary hospitals and plans to distribute it initially among district vet hospitals in Kerala.

An SOP for biosecurity for livestock and poultry farms has been developed by the AMR working group and the same would be given to departmental farms in the first phase.

**Strategic priority 4: Optimise use of antibiotics**

Regulations: Kerala Livestock and Poultry feed (Regulation of manufacture and sale Act 2018) is now in draft stage and the work is underway.
Surveillance of antimicrobial use: Restricting veterinary antibiotic use by making them prescription only medicines by RVP and conducted a survey on prescription practice with respect to antimicrobials among veterinary doctors in select districts.

**Strategic priority 5: Research & innovations**

The state livelihood mission's "Kerala Chicken" tested for antibiotic residues distribution of field level rapid antibiotic sensitivity kits to veterinary institutions throughout Kerala

Mapping and geo tagging of all animal farms in Kerala along with individual animal identification for disease control and animal traceability (BHUMIKA app)

**Strategic priority 6: Collaborations**

ReAct Asia Pacific conducted a one-day workshop at Ernakulam on biosecurity and antibiotic issues in poultry industry and on antibiotic smart communities
Training programme for veterinarians on AMR are being organised by Indian Veterinary Association, Kerala
Training programme for government veterinarians from other states and sharing of Kerala model on AMR action plans facilitated by the think-tank Centre for Science and Environment, New Delhi, was held at Thiruvanthapuram. Nine different states participated.

**Disease control programmes**
The department of animal husbandry had two major diseases control programmes for control of major diseases in animals and poultry. Better animal health management is very important as healthy animals and birds, just like healthy humans do not require any antibiotics.

As with the human health, the animal health aspect of AMR is a complex issue that requires concerted, coordinated action.

The lack of detailed antimicrobial usage (AMU), epidemiological, molecular data (antibiotic resistant genes) impacts our ability to interpret prevalence / surveillance data on AMR and to design efficient interventions. Therefore, monitoring systems on use and residue monitoring in animal products is essential to fill this knowledge gap.

Finally, the ecology of AMR should be addressed with a holistic, one-health approach combining expertise from different disciplines, such as medical doctors, veterinary clinicians, fisheries professionals, public health scientists, microbiologists, wildlife specialists, environmental scientists (ecologists) and epidemiologists.
The KARSAP for AMR is a first such endeavour for Kerala.

*About the author: Robin Paul is working as a Quality Manager at the State Laboratory for Livestock, Marine and Agri Products which is under the Department of Animal Husbandry, Kerala*

# THEME- AMR in Food Systems and Environment

## Why prudent, responsible use is needed to avert AMR crisis in Nigeria

*The problem of AMR cuts across human, animal and environmental sectors and requires a multi-disciplinary and inter-sectoral approach*

By Dooshima Kwange
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Antimicrobial (AM) agents are essential for protecting human and animal health and hence, their use is a public good. Antimicrobial resistance (AMR) emanates from abuse and misuse of antibiotics or the use of poor quality / counterfeit antimicrobials.

In agriculture, the consequences of AMR include increases in the cost of production in livestock farming, morbidities and mortalities, transmission of resistant pathogens and low-grade AM as residues to humans and the environment.

Over the years, there has been a deviation in the use of antimicrobials from therapeutic purposes to prophylaxis and growth promotion.

The use of low-grade level AMs in feed is a risk factor in the development of AMR as well as environment contamination. There is also lack of adherence to withdrawal periods, which leads to residues in animal products.

The problem of AMR cuts across human, animal and environmental sectors and requires a multi-disciplinary and inter-sectoral approach.

Antimicrobial resistance in animals affects humans through direct contact with antibiotic-resistant bacteria from a sick animal or through ingestion of food contaminated with resistant organisms as well as AM residues in animal products.

**Situation in Nigeria**

Intensive agriculture is a factor in the increased use of AMs in animal production. It is estimated that Nigeria's population will reach 400 million by 2050, which will put added pressure on livestock production, culminating in increased AMU in food-producing animals.

It is common for farmers to add antimicrobials in feed and water for prophylaxis. A study carried out in 2015 to access the use of growth promoters showed that some feed mill operators do not adhere to codex recommendations in the production of medicated feed. This results in an unintentional carryover of AM in animal feed.

Sub-standard and falsified drugs circulate in the market and all classes of antimicrobials can be purchased over the counter.

In 2017, Nigeria developed the National Action Plans for AMR that is being currently implemented. The Fleming Fund has a country grant and assists Nigeria to strengthen the 'One Health' governance framework for AMR and AMU surveillance.

The 2019 World Organisation for Animal Health (OIE) follow-up mission for Nigeria scored two in AMR and AMU critical competency, with a recommendation to build AMR diagnostic capacity of the national lab and improve awareness among stakeholders.

Residue testing, monitoring and management received the same score, with a recommendation to introduce residue monitoring in large commercial establishments producing animal products for local and external trade.

Development partners (Food and Agrigulture Organization of the United Nations, OIE) have assisted in building capacity of veterinary service (VS) to combat AMR in animals.

The FAO Reference Center for AMR, United Kingdom, also supported Nigeria in the development of a National Residue Surveillance Plan.
As a fallout from the 2019 OIE PVS Evaluation mission, the Nigerian Veterinary Services Strategic Plan 2021-2025 was developed. It aims to implement AMR activities to mitigate the AMR scourge.

The National Agency for Foods and Drugs Administration and Control (NAFDAC) has prohibited the use of 12 antimicrobials for use in food-producing animals in line with Codex recommendations.

There is 'One Health' collaboration between the VS and other ministries, departments and agencies such as the National Veterinary Research Institute (NVRI), NAFDAC, Nigeria Centre for Disease Control and Veterinary Council of Nigeria (VCN).

Nigeria has been submitting AMU data to the OIE global database for antimicrobial agents intended for use in animals since 2015. The data (2014-2019) indicates that tetracycline is the most widely used AM in animal health.

There are awareness creation activities that target veterinarians and veterinary para-professional through the VCN continuing education programmes, the annual Nigerian Veterinary Medical Association conferences, livestock and aquaculture producers, policymakers, journalists, school children, etc, during the annual antibiotics awareness week.

The thrust is on responsible and prudent use of AMs, biosecurity, use of alternatives to AMs, adherence to withdrawal periods and consumption of antibiotics-free animal products among other messages.

The veterinary services are in the process of updating the Animal Diseases Control law, wherein a new section on AMR has been added.

**Challenges**

Nigeria operates a three-tier system of government: Federal, State and local government. Currently, most activities in AMR governance are at the federal level, which need to be stepped down to the lower levels.

AMR in agriculture is multi-disciplinary and covers animal and plant health and food safety. This has a bearing on trade and livelihoods as well as the human and environment interface. But we do not understand the ramification of these issues much, especially in regard to plant health.

There is a very low-risk perception of the threat of AMR by stakeholders in most low- and middle-income countries, including Nigeria. This is especially so because AMR is not strictly a disease and data on the causal relationship of AMR and death / transmission from animals to humans is lacking.

In rural communities, there is an infrastructure deficit in the provision of laboratory services required for disease diagnosis. Transportation of samples to laboratories in urban areas is also challenging. This is compounded by the lack of national treatment guidelines.

There is a gap in appropriate AMR messaging that elicits positive action to the extent that some fear impending loss of their investments, reduction in income from sale of AMs and their administration.

Updating laws and regulations is a slow process. AMR as a global threat is novel, but the laws often skit it. Even where requisite regulation is available, enforcement is mostly lacking.

In animal health, there is a need to have cost-benefit analysis studies on the economic losses that accrue to AMR for evidence-based information that can attract the attention of policymakers.

A recurring challenge is the low funding for AMR activities in agriculture generally and animal health specifically.

Adherence to responsible and prudent use of antimicrobials, development and updation of requisite laws and legislation to guide the use of antimicrobials, especially in food-producing animals as well as the institution of biosecurity is the need of the hour.

Use of alternatives to AMs and good animal husbandry practices will help achieve production of safe food products of animal origin, reduce the emergence of AMR, facilitate the trade of animals and animal products and preserve critical antimicrobials for use in human and animal health.

*About the author: Dooshima Kwange is the CEO of Tesedona Foundation for Animal Health, a not for profit organisation with the vision of promoting animal health for improved livelihoods and protection of public health*

## Vietnam is focusing on veterinary drug shops to tackle antimicrobial resistance

*This is critical as the owners of such shops are often the first point of contact for Vietnamese farmers when their herds experience disease*

By Juan Carrique-Mas
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A recent study estimated that in Vietnam, a country located in southeast Asia with a population of 96.7 million in 2019, a total of 3,838 tonnes of antimicrobial active ingredients (AAIs) were used. Of those, 72 per cent correspond to animal use.

In Vietnam, veterinary drug shops are key gatekeepers of antimicrobial use (AMU), since they often are the first point of contact to farmers when their flocks / herds experience disease and have considerable influence over farmers' AMU behaviour.

We estimate that in the Mekong Delta, >70 per cent antimicrobials are purchased in veterinary drug shops, with the remainder corresponding to antimicrobials procured directly by integrated companies in large and industrial-scale farming settings.

Therefore, engaging veterinary pharmacists is critical to achieve sustainable, measurable, large-scale reductions in AMU in small-scale farming systems. Furthermore, reaching out to veterinary drug shops is more feasible (and cost-effective) than reaching out to a large number of small-scale farms.

**On-site training veterinary pharmacists through 'roadshows'**

A current project aims to improve the knowledge base about prescription of antimicrobials intended for terrestrial animals among all 330 veterinary drug shops registered in the Mekong Delta province of Vietnam.

Owners and staff of these shops (~600 participants) have been invited to attend a series of training workshops delivered as 'roadshows' in a location close to them.

These roadshows are delivered by a team of trainers and facilitators that include microbiologists, veterinarians, medical doctors and researchers. The aim is to train and engage veterinary pharmacists on the issue of AMU / AMR.

Travelling to multiple sites across the province in order to enable attendance of such a large number of people is logistically complex and requires the use of pre-recorded material (in the form of video webcasts).

The training materials are currently being developed by Oxford University Clinical Research Unit (OUCRU) in collaboration with the Food and Agriculture Organization of the United Nations (FAO) as well as the University of Can Tho and some industry partners.

Each 'roadshow' is delivered in a maximum of two hours. The first roadshow was delivered in August 2020 and it included presentations on:

- Legislation about antimicrobials and AMR as well as the Vietnamese National Action Plan to control Antimicrobial Resistance for Vietnam (with the input of FAO)
- The problem of excessive AMU; impact of AMR in humans and animals (with the input of medical experts
- Introduction to the World Health Organization list of critically important antimicrobials (CIA)
- Practical measures to control diseases and reduce AMU on pig and poultry farms (with participation of poultry and pig health experts)
- Use of alternatives to antimicrobials to improve productivity and enhance immunity of herds and flocks

Each topic is typically delivered over 10 minutes, followed by 5 minutes' discussion. The first roadshow was also an opportunity to get feedback from the vet drug shop owners / staff in order to plan contents for the second and third roadshows (scheduled for December 2020 and March 2021).

In addition, attendants of the first training session were invited to participate in a study involving collecting a rectal swab to be investigated for phenotypic resistance in commensal Escherichia coli.

Results are to be presented aggregated and anonymised in order to increase the pharmacists' awareness about excessive AMU and AMR.

For the second and third rounds of training, we plan to include specific workshops about postmortem and diagnosis of pig and poultry diseases, as well as developing adequate training materials (including leaflets and videos on biosecurity, cleaning and disinfection and flock / herd management).

**Providing evidence of changes in AMU / AMR**

Levels of AMU / AMR in humans and in animal production will be measured before and after the implementation of the training intervention described above. A random sample of 400 representative farms will be drawn from the farm census before and after the training intervention.

Data on AMU in each animal species raised (chickens, ducks, pigs) and humans will be collected. From each farm species raised, one pooled faecal sample is to be collected.

In addition, humans (2-3 from each household) will be invited to consent to provide a rectal swab. From each sample, two commensal *E. coli* strains will be isolated.

It is therefore expected that a total of 1,600 animal and 1,600 human *E. coli* strains will be isolated at each step (baseline and post-intervention) and these will be investigated for their antimicrobial susceptibility against a panel of 16 antimicrobials commonly used in humans and in animal production in the area.

The main outcome of this project will be a comparison in levels of AMU as well as phenotypic levels of AMR in each of the species.

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## ‘One Health’ key in Zimbabwe’s fight against antimicrobial resistance

*Since AMR is a complex problem involving several sectors, Zimbabwe is using the best possible strategy to fight it*

By Canaan Tinashe Hodobo
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Antibiotic misuse is a serious threat to human and animal life and biodiversity. Zimbabwe is observing a week set aside by the United Nations (UN) to understand the threat of antimicrobial resistance (AMR).

This has been the case since the country launched its National Action Plan (NAP) on AMR in September 2017. The NAP was developed in line with the World Health Organization Global Action Plan (WHO-GAP).

In 2015, WHO designed the GAP combat AMR. The plan was a brainchild of the tripartite that includes WHO, Food and Agriculture Organization of the UN and World Organisation for Animal Health (OIE).

They resolved to fight AMR using a ‘One Health’ approach. UN Environment is also an important partner since the environment harbours resistant micro-organisms and can assist their spread.

The OIE is the standard setting body for the World Trade Organization on issues to do with animal health with respect to land and water animals. Its standards assist members to consistently improve animal health.

In Zimbabwe, the animal health sector’s efforts to fight the misuse of antibiotics have been made through a number of methods.

These include education and awareness, collaboration with farmers and farmer organisations, legislative review, One Health collaboration with veterinary drug manufacturers, wholesalers and retailers and antimicrobial use (AMU) / AMR behaviour change Knowledge, Attitudes and Practices (KAP) studies among other initiatives using a One Health approach involving partners in the human and environmental sectors.

**Education and awareness**

Use of electronic, audio visual and print media including writing articles as a way to reach out to a wider audience of Zimbabweans to raise awareness on the topic of AMR and AMU has been a common method.

The AMU animals are key for food security, public health and trade. Awareness targets key stakeholders including veterinary doctors, veterinary students, farmers, pharmaceutical products manufacturers, pharmaceutical products wholesalers and retailers and stock feed manufactures since in some cases, there is use of medicated feeds.

**Farmers as key stake holders**

Farmers are advised on the correct directions of use of the medicine and that they must be strictly followed. They are strongly advised to adhere to the recommended withdrawal periods for each antimicrobial they use.

In food-producing animals, advice is given to farmers to respect the withdrawal periods of drugs since drug residues remain in the meat and animal products are consumed by humans.
There are serious health implications when humans consume drug residues, in food, beyond the certain benchmark values.

**Legislative review**

Careful examination of the existing legislation on antimicrobial use was done. The aim of this legislative review was to appreciate the existing laws on the use of drugs and identify possible gaps. A report was written that explained the findings and gave recommendations for amendments of the law on use.

**Collaboration with veterinary drugs industry**

Pharmaceuticals wholesalers and retailers are key players in the use of antimicrobials and play a critical role in AMU since they are the gateway to access of drugs for animal use by professionals and farmers.

Prescription medication has been recommended never to be sold over the counter and retailers of pharmaceuticals are being encouraged to always request a doctor's prescription from the farmer before medication can be dispensed.

Free access to prescription drugs can result in irrational use by poorly informed users. As the old saying goes, prevention is better than cure.

There is a need to uphold principles of infection prevention and control, biosecurity and hygiene. Preventive medicine through the use of vaccines reduces incidences of infections and hence cancels the need to use antimicrobials.

If there is no infection, there is no need to use antimicrobials, hence averting the dangers of AMR. Rational use of antimicrobials under the guidance of experts is a must.

Antimicrobial resistance can have devastating impact on human and animal health and negative impact on livestock productivity and the economy.

In the crop sector, use of antimicrobials is kept in check in line with the Zimbabwe NAP. Use of antibiotics as growth promoters is a practice that is being discouraged.

All supply chain stakeholders are advised to seek implementation of alternatives to the use of antimicrobials.

The dealers in veterinary medicine are key stakeholders in the prudent use of antimicrobials and within the national AMR governance structure, some key veterinary drug dealers are members of the Technical Working Group on AM prudent use and stewardship.

**AMU / AMR Behaviour change studies**

Pilot KAP studies have been conducted in selected districts of the country focusing on the poultry value chain. The aim was to understand the major drivers of AMU.

The bottom line is that disease pressure is a key driver for the use of AMs. However, in some cases some pharmaceutical retailers encouraged farmers to use tetracyclines in apparently healthy day-old chicks.

From the KAP study findings, interventions centred on good husbandry practices were encouraged as a means to reduce disease pressure and hence the use of AMs.

The use of AMs in animals that are not sick was discouraged and awareness raised about the dangers of misuse of the AMs.

**Challenges**

Efforts to deal with misuse of antibiotics have met with challenges. Lack of knowledge and understanding of the dangers of misuse of AMs is a key challenge.

Limitation of material resources has hampered awareness efforts since some stakeholders cannot be reached due to limited availability of enabling resources.

Enforcement of legislation on AMU cannot be fully realised due to the limited numbers of inspectors from the medical authority and lack of coverage of veterinary professionals in some localities.

Illegal importation of AMs from neighboring countries has also led to unauthorised use of AMs. The price of certain medicines is beyond the reach for others so some people resort to use of cheap drugs, which in most cases, can be counterfeit or expired drugs.

On-farm biosecurity measures, general hygiene and best practices in animal husbandry and preventive vaccination among are the initiatives that are being promoted among the farmers.

The sectors of human and animal health, food and agriculture, environment and civic society too are collaborating in the fight against AMR.

A One Health approach involving multi-sectoral partners has been the means which Zimbabwe has been using to combat AMR in a concerted fashion since AMR is a complex problem involving several sectors.

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## How antimicrobial resistance and zoonoses are linked

*AMR and its relationship to human and animal morbidity is one of the biggest challenges facing modern medicine*

By Jaspreet Mahindroo, Neelam Taneja
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The problem of antimicrobial resistance (AMR) is massive. As many as 700,000 deaths have been reported due to resistant infections worldwide.

Excessive antibiotic usage in the human, agricultural and livestock sectors remains the key driving factor for sweeping expansion of resistance.

There is a considerable overlap of antibiotic classes used in the human and veterinary sectors.

Antibiotics such as prophylactics for disease prevention, metaphylactics for infection control and growth promoters, are extensively used in commercial poultry farms, piggeries and aquaculture.

Antibiotics are estimated to increase body weight by five-six per cent and feed efficiency by 3-4 per cent.

They are, hence, convenient options for farmers, especially in countries where antibiotics are easily available without any restrictions.

The estimates on global antibiotic consumption in agriculture vary substantially across countries. In low- and middle-income countries (LMIC) like India, these estimates are more of guesses than actual data due to lack of active surveillance. Van Boeckel et al (2015) estimated global antibiotic consumption in agriculture would rise by 67 per cent from 2010 to 2030.

British economist Jim O' Neil found that 72 per cent studies demonstrated direct links of AMR in humans, with antibiotic consumption in animals.

Prolonged exposure to antimicrobials generates perfect conditions for cultivation of drug resistance and increases the population of antibiotic-resistant bacteria, significantly causing an imbalance of gut microbiota.

This is also the cause of antibiotic pollution in the environment, where 75-90 per cent of antibiotics are excreted in unmetabolised form that then spreads in the environment.

These antibiotics, due to their high water solubility and extensive half-life, do not get easily degraded. Instead, they persist in the environment for a long time. So animal waste is not only the source of resistant bacteria, but also contains active residues of antibiotics which further spread to water and soil.

The manure, if used as fertiliser for crops, can disseminate the resistance in plants. Fat soluble antibiotics, like tetracycline and sulphonamides, get accumulated in animal tissues over a period of time.

There are several examples of zoonotic transmission of antibiotic resistant food-borne pathogens like *Campylobacter jejuni, Salmonella enterica, Typhimurium* DT104, *E. coli* O157:H7 etc. Some of these examples include emergence of ciprofloxacin-resistant Campylobacter after introduction of fluoroquinolones, particularly ciprofloxacin in poultry production since 1995.

Other notable examples are antibiotic avoparcin that promoted vancomycin resistance, as well as vinginicmycin that has a similar effect with streptogramin. Cross-resistance (when a particular drug influences bacterial resistance and susceptibility to other antibiotics) occurs regularly between antibiotics of the same class.

An example being presence of extended spectrum β-lactamases (ESBLs) causing cross-resistance to the antimicrobials in classes of penicillins and cephalosporins. ESBL producing *Enterobacteriaceae* are a major challenge to treat.

Extensive use of ceftiofur and cefquinome, which are third- and fourth-generation cephalosporin, as veterinary medicines for treating mastitis caused by *Staphylococcus aureus* has resulted in the emergence of ESBL- *E. coli.* Ceftiofur is also used prophylactically in piglets to prevent arthritis, meningitis, septicaemia, and diarrhoea.

ESBL enzymes are present on self-transmissible plasmids compounding the transmission of these organisms across human, animal and environmental sectors. Resistance has developed to absolutely last resort drugs like carbapenems against which colistin is used.

Colistin is not a new drug. In fact, its human use was banned in the 1970s due to its nephrotoxicity. However, it remained in use as a prophylactic and a growth promoter in pigs. Resistance to colistin has now emerged in *Klebsiella pneumoniae*, an important human pathogen that causes hospital-acquired and community acquired infections.

Resistance genes are often present in clusters on mobile genetic elements like transposons, plasmids and integrons. Resistance genes against heavy metals and biocides are more common in nature and they may co-select for resistance genes.

The resistance genes may disseminate through a wide variety of bacterial species of different taxonomy. One of the recent examples is the emergence of high-level of resistance to fluoroquinolone antibiotic ciprofloxacin in non-typhoidal *Salmonella enterica* serovar Kentucky belonging to sequence type 198 (ST198).

Through whole genome sequencing, S Kentucky ST198 was found to be widely present in Indian poultry samples and displayed considerable genetic relatedness with Indian and international human isolates.

Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) found that voluntary removal of ceftiofur antibiotic use in hatcheries correlated with decrease in ceftriaxone resistant *Salmonella* and *E coli* infections in humans. To reduce the proliferation of AMR, the European Union (EU) banned the agricultural use of antibiotics as growth promoters in 2006.

Scandinavian countries like Denmark, Norway, Sweden and the Netherlands have set an example for the world by completely banning antimicrobial use in the animal sector for prophylactic and growth promotion purposes.

Since bacteria will always be present and there is no germ-free natural meat, they tested another new strategy called 'test and freeze' in Iceland, Norway and Denmark. In this, poultry is tested before slaughter and the ones that tested positive for *Campylobacter* are frozen after slaughter to reduce the microbial load.

AMR and its relationship to human and animal morbidity is one of the biggest challenges facing modern medicine. Zoonotic transmission of disease presents an area that may allow for some improvement or reduction in the rate of emerging resistant species.

An integrated 'One Health' approach is required to study the zoonotic linkages of AMR and its transmission, using state-of-the-art sequencing technologies.

Our world is rapidly changing. It is more interconnected than before due to extensive travels, imports and exports of meat. So what is present on the other side of the world can be in our homes, on our plate in a few days. It is time to innovate new methods to curb the spread of AMR.

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## Antibiotic misuse in India's livestock sector can be reduced

*Awareness of farmers, legislation for clean sanitary practices in animal farms and its strict implementation can do the trick*

By Amit Kumar
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India is being designated as the 'epicentre' of the global drug resistance crisis. This is due to a combination of factors that is being described as a 'perfect storm' and has led to the spread of superbugs. These factors need to be addressed urgently.

One of them is the misuse of antibiotics in India's livestock sector. The use of antibiotics in animal husbandry has increased significantly in recent times.

One major concern is that the use of antibiotics as growth promoters in animal feed has led to their continuous exposure to gut microbiota. This, in turn, has led to the development of resistance even in commensal pathogens that can then be transferred to other pathogenic bacteria.

In animal husbandry, poultry is the most rapidly growing sector. A study conducted to estimate the demand for egg and poultry meat predicted significant growth of both egg and poultry meat in rural as well as urban communities in the coming two decades.

It is a good source of income. Income from rearing poultry is set to triple by 2020. To fulfil the demand for eggs and meat from poultry, farmers are being forced to use antibiotics as growth promoters.

This is because a majority of deadly diseases affecting poultry are either of viral or bacterial origin. These include viral diseases like Marek disease, infectious bronchitis, gumboro disease, infectious laryngotracheitis, litchi diseases and pox. They also include bacterial diseases like salmonellosis, collibacillosis, campylobacteriosis, mycoplasmosis, etc.

Good quality vaccines are available against almost all viral diseases. The vice versa is true about bacterial diseases. Good quality, cost-effective and safe vaccines are required for the prevention of such diseases.

This leads to the use of antibiotics to prevent these bacterial infections to avoid any mortality or morbidity.

So how do we address the misuse of antibiotics in tackling bacterial disease among livestock in India. Here are some approaches:

1. Creating awareness among farmers and end users about drug residue and its after-effects

2. Restriction on the unregulated sale of antibiotics for use in animals
3. A complete ban on the use of those antibiotics that are classified by the World Health Organization as being “critically important to human medicines”
4. Development of disease diagnosis facilities accessible to farmers at nominal costs, for recommendation of drugs of choice
5. Trainings and awareness campaigns to educate farmers on good managemental practices to avoid the exposure of livestock to pathogens and ultimately, the need for therapeutics
6. Availability and guidelines for the proper disposal of waste. Strict regulations need to be imposed to avoid drainage of untreated waste into rivers and water bodies
7. Legislation for the implementation of good sanitary practices in and around animal and poultry farms and other related units
8. Continuous monitoring of drug resistance bacterial pathogens like *E. coli, Staphylococcus* spp, *Pseudomonas* spp and *Klebsiella* spp in particular.
9. A national level antimicrobial monitoring plan in collaboration with all associated agencies including Food Safety and Standards Authority of India, Department of Biotechnology, Department of Science and Technology, Indian Council of Medical Research, Indian Council of Agricultural Research, Department of Animal Husbandry and Dairying, Union Ministry of Ayurveda, Unani, Siddha and Homeopathy and Drugs Controller General of India is need of the hour

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## Handle with care: The dictum for using antibiotics in livestock

*Using natural additives in animal feed, educating farmers, timely vaccination, ethnoveterinary practices and strict implementation of rules can reduce antibiotic use in farm animals*

By P Anand Kumar
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The use of antibiotics in veterinary medicine is fundamentally to treat the microbial infections and diseases in livestock, poultry, pet animals and game animals.

The development of antimicrobial resistance (AMR) in microorganisms of veterinary importance not only has a significant impact on animal health but also on public health due to the increased consumption of foods of animal origin in developing countries.

The consumption of animal protein is expected increase further in the coming years. Therefore, mitigation strategies for containment of AMR in the animal sector assumes paramount importance.

Subtherapeutic concentrations of antibiotics as growth promoters (AGP) were widely used in animal feed in countries where beef cattle and swine farms were maintained on commercially intensive farming lines.

This was done without realising the potential impact of AGP use in feed on the development of AMR in microorganisms. In India, as cattle and buffaloes are maintained primarily for dairying and intensive swine farming is also not common, the issue of AGP in feeds didn't arise much.

Sheep and goats are maintained by shepherds with grazing practices in the open fields. However, research findings about the detection of genes conferring AMR in certain bacterial species isolated from chickens raised concern about food safety.

Like other sectors, attention should be paid to misuse of antibiotics in the veterinary sector. Bacterial infection of udders (mastitis) is very common in dairy animals where the misuse of antibiotics is mostly observed.

A qualified veterinarian always prescribes specific antibiotics to treat the bacterial infection. S/he also advises the farmer about the waiting period for milking to avoid the issue of antibiotic residues in milk.

But at the field level, the involvement of quacks for unauthorised prescription of antibiotics and the purchase of antibiotics over the counter are not uncommon, though legally forbidden.

The presence of antibiotic residues in milk and meat is a serious issue, one that must be brought to public attention. The possibility of development of AMR in microbes due to antibiotic residues in animal foods is being widely investigated and debated.

The Food Safety and Standards Authority of India (FSSAI) has fixed 'tolerance limits' for veterinary drug residues, including antibiotics, in animal foods like milk, meat, eggs, etc. Therefore, emphasis should be laid on the responsible use of antibiotics.

Intensive farming practices in poultry helped India to not only increase the production of eggs and meat but also provided much needed animal protein in human nutrition to prevent malnutrition.

But intensive poultry farming also gave opportunity to certain people for unscrupulous practices such as using antibiotics as feed additives in the guise of growth promoters. Certain poultry farmers who use such feed are even not aware about what they are using.

Therefore, educating farmers about the consequences of using feeds laced with antibiotic additives and its impact on public health is the need the hour.

**What should be done?**

Livestock and poultry farmers must be trained in economical 'biosecurity' practices to be implemented in their farms. These will minimise the incidence of common microbial infections.

This will also automatically reduce the need of antibiotics in the animal sector.

Further, the use of prebiotics, probiotics, organic acids, enzymes, essential oils and phytogenic feed additives (PFA) rich with flavonoids in livestock and poultry feed has to be extensively encouraged with incentives.

Many of these natural additives have evidence-based antimicrobial and immunomodulatory properties.

It is highly rare for microbes to develop resistance against natural products. Also the immune system of animals is boosted and keeps them immunocompetent.

Time-bound vaccination practices are crucial to prevent infectious diseases in livestock and poultry, which will further reduce the use of antibiotics in the veterinary sector.

Ethnoveterinary practices with credible evidence too should be encouraged. A road map for reducing the need of antibiotics for animal use should be prepared by involving all stakeholders.

Antibiotics are indispensable tools to fight microbial infections and diseases in human and veterinary medicine. It is inevitable for veterinarians to prescribe antibiotics to protect animal health and to alleviate animals' pain and suffering.

Total avoidance of antibiotics including certain critically important ones for therapeutic use in animal sector is practically not plausible. That is because many small and marginal farmers depend on livestock and poultry farming for their livelihoods.

Since foods of animal origin occupy an important share in human nutrition, the misuse of antibiotics in the animal sector should be curtailed by government regulations, and responsible use of antibiotics should be promoted.

**A complex phenomenon**

AMR can't be addressed just by focusing on antibiotics use / misuse in food animals. Certain research reports indicate no perceptible change in the AMR pattern in bacteria even if certain classes of antibiotics were withdrawn for veterinary use.

AMR is a complex phenomenon and needs a multi-pronged strategy to address it. Untreated / improperly treated effluents from certain pharma industries and discharges of hospital wastes directly into drainage causes antibiotics residues to enter the environment.

There is every chance that these effluents and discharges contaminate drinking water resources like tanks and ponds. Use of biocides, antiseptics and disinfectants also have an impact on AMR in microbes, due to the cross resistance phenomenon.

Therefore, the 'One Health' approach is the best way to address AMR since resistance against antimicrobials is operated among human, animal and environmental sectors.

Lack of authentic information on AMR and antimicrobial use (AMU) in the veterinary sector is a major limitation. Extrapolation of data on AMR from different splinter research groups may not present a correct picture on the resistance pattern of microbes to antibiotics.

To address this issue, the Indian Council of Agriculture Research has initiated a national programme called the Indian Network for Fisheries and Animals Antimicrobial Resistance in coordination with the Food and Agriculture Organization that will provide pan-India AMR data in the coming years.

As we observe World Antimicrobial Awareness Week 2020, all of us should strive towards responsible use of antibiotics in all sectors according to the slogan given by World Health Organization: Antimicrobials: Handle with care.

Creating awareness among the public about the AMR threat on the lines of the novel coronavirus disease awareness campaign will be highly useful.

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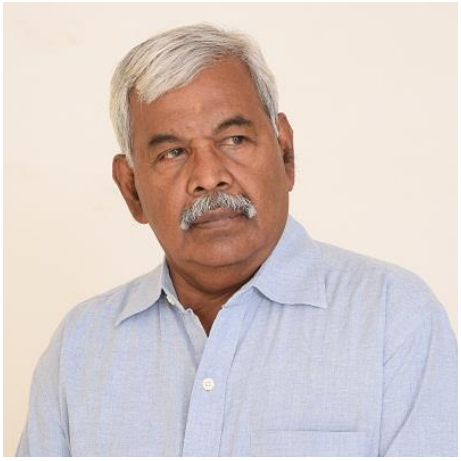
## Ethno-veterinary Practices: A game changer in reducing antibiotic misuse in livestock



*Farmers can help reduce the scourge of antibiotic residues in livestock, especially dairy animals by adopting such practices*

By M N Balakrishnan Nair, N Punniamurthy, SK Kumar
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Antibiotic resistance (AMR) is a worldwide problem created due to the excessive and indiscriminate use of antibiotics in human, animal and plant health.

About 90 per cent of the antibiotics used end up in the environment, affecting the quality of water, soils, and biodiversity. AMR makes it harder to eliminate infections from the body as existing drugs become ineffective.

In India, the annual rate of antibiotics use in the past five years has risen by 6-7 per cent. *Tackling a Crisis for the Health and Wealth of Nations* was published on the request of the UK Prime Minister to address the growing global problem of drug-resistant infections.

It states that drug-resistant infections will kill an extra 10 million people a year worldwide and that the total world Gross Domestic Product cost of antimicrobial resistance will be $100 trillion.

One of the immediate challenges regarding AMR is to reduce the use of antibiotics both for human and animal health care.

As antibiotics find their way through the food chain, there is an urgent need to focus on reducing the use of antibiotics in veterinary practice by working with veterinarians, farmers and dairy cooperatives.

We have worked with various stakeholders and established that ethnoveterinary practices (EVPs) are efficacious and safe in preventing and curing certain clinical conditions in dairy animals and thereby reducing antibiotic residues in milk.

The University of Trans-disciplinary health sciences and Technology, along with Tamil Nadu Veterinary and Animal Sciences University has documented EVPs from 24 locations in 10 states and rapidly assessed them using Ayurveda.

It has established that 353 formulations out of 441 are safe and efficacious. *In-vitro* antimicrobial activity of the extracts of the herbal formulation against mastitis had inhibitory activity against *Escherichia coli* and *Streptococus aureus.*

Clinical study using traditional formulation for mastitis showed that somatic cell counts, electrical conductivity and pH of the milk became normal within six days, indicating cure of mastitis.

We used the *in silico* approach to find the effect of the herbal preparation against the infection. The bioactive compounds were tested for their effect against the target proteins of *S aureus* using molecular docking studies.

It has been shown that traditional medicine can be used during dry periods to reduce the incidence of mastitis and reduce the retention of placenta.

We have trained 1,750 veterinarians from various organisations like the National Diary Development Board (NDDB), Amul, Karnataka Milk Federation, 30 milk unions from 14 states in India, veterinarians from the government of Sikkim, the Lala Lajpat Rai University of Veterinary & Animal Sciences, Abbott India Ltd and BAIF Development Research Foundation to use EVPs for 19 clinical conditions in cattle.

We also trained 30,000 farmers and 560 village resource persons to use EVPs for preventing and curing 19 clinical conditions without using antibiotics or any other chemical veterinary drugs.

The first table shows the per cent cure of each condition treated with EVP.

An intervention impact study undertaken with support from the Department of Science and Technology, Government of India encompassing 220 farmers from 11 milk societies in Karnataka, Kerala and Tamil Nadu indicates that milk from 123 (87.86 per cent) farmers out of 140 was without any detectable antibiotic residue.

There is a reduction in the incidence of mastitis, enteritis, repeat breeding and cowpox from 2016 to 2018 and 2019 when herbal alternatives were used.

A microbiome study of the mastitis udder before and after treatment with EVPs indicates that there is a substantial reduction of the abundance of the mastitis causing microbes after six days of treatment, comparable to that of a normal cow's milk

Adopting EVPs to combat infectious and other clinical conditions in livestock has been identified and tested as a key game changer in reducing the use of antibiotic and other veterinary drugs in veterinary practices.

It has also been shown that EVP was extremely helpful for the farmers during the novel coronavirus lockdown period as these formulations could be prepared and used by farmers themselves for the well-being of their cattle.

**Feedback from various milk societies through NDDB through ENAP on the efficacy of EVPs for 19 clinical conditions in cattle**

| Sr. No | Clinical condition | Number of Animal treated | % cure |
|---|---|---|---|
| 1 | Mastitis | 38305 | 93.27 |
| 2 | Indigestion | 9212 | 90.68 |
| 3 | Foot & Mouth (FMD) | 11669 | 93 |
| 4 | Foot lesion | 4388 | 92 |
| 5 | Fever | 51691 | 92.5 |
| 6 | Diarrhea | 50015 | 96.72 |
| 7 | Joint swelling | 500 | 90 |
| 8 | Bloat | 1830 | 86.75 |
| 9 | Udder edema | 1982 | 95.49 |
| 10 | Repeat breeding | 4637 | 84.37 |
| 11 | Deworming | 5906 | 95.77 |
| 12 | Wound | 1335 | 83 |
| 13 | Uterus prolapse | 429 | 76 |
| 14 | Retention of Placenta (ROP) | 1128 | 74 |
| 15 | Downer | 999 | 76 |
| 16 | Udder pox, warts | 658 | 67.6 |
| 17 | Teat obstruction | 1134 | 75.5 |
| 18 | Ectoparasites /Ticks | 1401 | 93.57 |
| 19 | Haemogalactia | 1336 | 95.5 |

**Feedback from ABBOTT Private Ltd - From Feb 2019 to August 2020**

| Sr. No. | Diseases | n | % cure |
|---|---|---|---|
| 1 | Mastitis | 1165 | 93.34 |
| 2 | Teat Obstruction | 458 | 90.74 |
| 3 | Pox/ Warts/ Cracks | 342 | 82.24 |
| 4 | Fever | 67 | 100.00 |
| 5 | FMD Mouth Lesions | 159 | 100.00 |
| 6 | FMD Foot Lesions/Wound | 277 | 100.00 |
| 7 | Bloat & Indigestion | 186 | 93.95 |
| 8 | Tick/ Ectoparasite | 556 | 94.37 |
| 9 | Worms | 1402 | 97.23 |
| 10 | Diarrhoea | 823 | 95.37 |
| 11 | Repeat Breeding | 107 | 58.00 |
| 12 | Metritis | 4 | 100.00 |
| 13 | Retention of Placenta (ROP) | 47 | 73.08 |
| 14 | Udder Edema | 285 | 97.5 |
| 15 | Blood in Milk | 105 | 98.21 |
| 16 | Lamness/ Bursitis | | 75.00 |

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## AMR: Balancing sustainability and food security in intensified agriculture is the solution

*Ensuring intensification of livestock farming is scientifically sound and sustainable could be key to tackling AMR*

By Philip Mathew
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Food security globally has two major components — provision for adequate dietary energy and intake of sufficient high-quality protein.

In the last century or so, the countries of the global south have been consuming a carbohydrate- rich diet, that may provide adequate energy but not enough amounts of good quality protein.

But the improvement in incomes and the greater purchasing power which comes along with it, is rapidly increasing the demand for proteins in these regions of the world and people are looking at relatively high-quality animal sources for satisfying the demand.

The consumption of animal products has sky-rocketed in most of the Low-Middle Income Countries (LMIC), as the demand for proteins are being fulfilled by various kinds of meat.

Globally, the price of many meat products has been relatively stable as compared to other commodities; and this has made these foods financially accessible to a larger section of the population.

Most of the increased production and price stability has come through intensified farming systems, which focus on improving efficiency and economies of scale.

The intensification process in food animal production and aquaculture has been traditionally associated with greater stocking density (more animals per standard area), higher use of commercial feeds and wide-spread use of antibiotics.

The irrational use of antibiotics in the farm sector is a significant driver of antibiotic resistance (ABR), a problem that is now threatening to offset several healthcare achievements of the 20th century.

If we consider the LMIC perspective, the availability of ‘cheap food’ has been the cornerstone for achieving food security even in the face of rapid population growth and intensified agricultural systems have played a significant role.

But there is greater realisation now that food produced by intensified agricultural systems are ‘cheap’ because we do not factor in the sustainability costs, which are essentially transferred to the next generation.

Considering these facts, there is a need to balance the need for food security in poorer regions of the world and at the same time ensures that food production does not rob our future generations of a healthy life.

Therefore, it is not possible to completely do away with the intensification process. Rather, we need to introduce a sustainability lens to the whole exercise and make it as scientific as possible.

The proportion of household income spent on food in LMICs is much more than High Income Countries (HICs) and any increase in this expenditure can have a cascading effect on several other domains.

Hence, calibrating food security requirements and sustainability needs is a vital process in ensuring greater buy-in from all the stakeholder groups.

Moreover, one other argument in favor of 'sustainable intensification' is that conversion of new land for agriculture (extensification or free-range breeding) may result in catastrophic and irreversible damage to the environment.

It is estimated that more than 60 per cent of farmers follow non-intensive forms of agriculture production, if we look at developing countries of south Asia and sub-Saharan Africa.

Most of them are small / marginal farmers, with low incomes and sub-optimal access to social security.

When there are pressures on land use, the only option available to them to increase production may be to shift to a more intensive form of agriculture.

Most of the time, that shift is based on unsustainable practices which is driven by poor knowledge / competence and lack of investment.

If we look at absolute numbers, millions of farmers from LMICs will shift to intensive farming over the next two decades or so.

Therefore, if the process of shifting to intensive agriculture is optimised and made more sustainable, the level of adoption of biosecurity measures (which can prevent infection) may be high and antibiotic use may be low.

Another strategy which is considered for improving the sustainability of food animal farming is localised production.

Backyard and marginal farms, which supply products only to the local markets, may not be as efficient as the 'factory farms', but they play a remarkable role in ensuring food security in the developing world.

There is a fair degree of evidence to show that antibiotic use is much lower in backyard farms, as compared to larger commercial farms.

Such farms tend to be more accountable to the local community and this is reflected in low use of growth stimulants and better hygiene measures.

Two of the biggest bottlenecks which prevent a move to sustainable intensification is the farmers' lack of access to finances and sub-optimal understanding / competence.

The latter is more serious and it can negatively influence the farmers' attitude towards sustainability measures in farms.

There are several misconceptions about the feasibility and costs involved in measures to improve quality and sustainability of the intensification process and this is resulting in active resistance from farmers' groups.

ReAct, an international science-based network on ABR, has been trying to plug this gap in the Asia-Pacific region.

Apart from regular situation analysis reports on the use of antibiotics in food systems in several countries in the region, ReAct has been working to map out the perception of farmers regarding various measures to reduce use of antibiotics.

ReAct has been working to produce toolkits for engaging farmers and increase their competencies in adopting biosecurity measures with minimal investment.

These multimedia toolkits are now being produced for small scale broiler and shrimp farmers and more such groups will be targeted in the future.

The toolkits can be used by any group or agency that wants to engage farmers in the LMIC settings and the contents have been prepared with a culture-neutral approach.

It can potentially ensure that the small farmers adopt intensification process in a scientifically sound manner and that they are able to apply a sustainability lens within their limited contexts.

An overall reduction in meat consumption may be the solution for many food systems issues, but that does not seem like a feasible option in the short / medium term.

Therefore, what we can hope for is that the farms are made more sustainable while ensuring robust production quantities for global food security.

*About the author: Philip Mathew is a public health researcher and a consultant to ReAct Asia Pacific.*

## Why we need smart regulation to contain antimicrobial resistance

*Smart regulation is a useful way to regulate complex areas that involve multiple stakeholders with converging and diverging interests*

By Anita Kotwani, Jyoti Joshi
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Misuse and overuse of antimicrobials has led to a steep rise in antimicrobial resistance (AMR), impacting planetary health, global economies and stalling sustainable development.

AMR is the resistance of a microorganism (bacteria, parasites, viruses or fungi) to an antimicrobial drug that was originally effective for treatment of infections caused by it is a public health crisis.

Within AMR, antibacterial (antibiotic) resistance is the biggest threat because common infections (respiratory, skin wound, etc.) could become untreatable.

Antibiotics are casually popped for a sore throat, common cold or fever, without knowing whether they are needed.

In fact, antibiotics are also given to healthy food animals (for growth promotion in intensive agriculture), sprayed on crops and through anthropogenic activities (hospitals, farms effluent from pharmaceutical manufacture) enter into the environment. Isolated measures addressing antibiotic misuse in humans, animals or environment will not be able to contain AMR.

Effective regulation to enforce optimum use of antibiotics is one such approach, but will only be effective if it encompasses the One Health approach. One Health includes human, animal and environmental health.

It has been suggested by the World Health Organization's (WHO) 2015 Global Action Plan on Antimicrobial Resistance (GAP) as well as AMR National Action Plans (NAP) of countries.

Objective four of the NAP-AMR aims to ensure optimum use of antibiotics in all sectors. In the areas of poultry, aquaculture, livestock and environmental protection, clear regulations with respect to antibiotic use and effluent discharge are minimal or absent.

Even though the existing regulations are fairly clear as in case of over-the-counter sales of antibiotics at retail pharmacies for both human and animal use, compliance is often poor and enforcement is patchy.

Traditionally, regulation refers to the top-down command-and-control model of regulation that imposes fines and sanctions in case of non-compliance with the standards. However, it is difficult to enforce and monitor such regulations when there are numerous stakeholders.

Such regulations often do not allow space for meaningful engagement between regulator and regulated entity or with the range of other actors who directly or indirectly influence or are affected by regulation.

To overcome the inefficiencies of traditional regulation and the pitfall of deregulation, a concept of 'smart regulation' was coined.

Smart regulation is defined as a form of regulatory pluralism that embraces more flexible, imaginative and innovative forms of social control than conventional regulation. Smart regulation is a useful way to regulate complex areas that involve multiple stakeholders with converging and diverging interests.

Designing smart regulation involves two stages. First, there is a need to identify the desired policy goal(s), such as reduction antibiotic misuse, unique characteristics of the problem, range of potential actors and instruments and opportunities for consultation and public participation.

Then, by applying enabling 'core' regulatory design principles sequentially, an effort is made to arrive at a range of solution(s). Smart regulation approach has been successfully used to tackle complex and multi-stakeholder issues like climate change in Australia and across a range of policy domains in the European Union.

Considering the complexity and diverse range of stakeholders in both public and private sectors, including the population at large, the concept of smart regulation is a way forward to begin with and supplements the traditional legal framework for containment of AMR.

As part of the Newton-Bhabha collaboration, the Department of Biotechnology, Government of India, is funding our research work to develop innovative, flexible, soft regulations by applying the concept of smart regulation. Taking a One Health approach, we have chosen four case studies involving all the three sectors:

- Over-the-counter (OTC) antibiotic sales at pharmacies without valid prescription
- Poultry farmers using antibiotics (including as a growth factor)
- Hospital AMR containment
- Pharmaceutical industry effluents and AMR in two states (Haryana and Telangana) of India

The first step in developing innovative, plural and softer approaches is to map the stakeholder for a particular issue. Using an innovative methodology (Net-Map) for stakeholder mapping we plotted the stakeholder universe, identified stakeholder characteristics, their linkages to one another, their power and influence, interest and proximity to the issue.

This is a critical step in the design process of smart regulation. After developing this stakeholder map, we approached the central actors (stakeholders) for in-depth interviews to gauge their perspectives and practices regarding antibiotic misuse and understanding of the AMR as a public health problem.

We gauged their willingness to work together with other stakeholders, especially the regulatory authorities and suggestions for potential regulatory innovations to tackle AMR in India.

We will be conducting workshops for each case study with all stakeholders to finalise the innovative suggestions recommended during in-depth interviews with various stakeholders.

We have found the regulators, regulated entity, consumers and civil society who are eager to collaborate. Stakeholders welcomed the opportunity to work (in many cases for the first-time) and found innovative regulatory solutions. These solutions could be more than one for one particular issue.

As an example, for OTC sale of antibiotics, this could be a step-wise approach starting with voluntary agreement by pharmacists to stop the practice of OTC antibiotics, written directives or posters, advisory and dedicated workshops by state pharmacy council or an advisory by the pharmacists associations to its members (peer pressure) to checks by the licensing authority to deter antibiotic misuse.

There are many more options and they will be finalised after the workshops with the stakeholders as the project progresses. 'Smart regulation', thus, can supplement and strengthen traditional forms of 'command-and- control' regulation i.e. legal sanctions or fines.

It could take the form of economic instruments, industry self-regulation, non-binding agreements between regulators and companies or forms of information strategies that would apply pressure to non-compliant organisations, for instance proactive public disclosure or product certification.

Involving the entire chain of stakeholders from the beginning and taking all partners for developing smart regulation can give the stakeholders ownership to these regulations and be a win-win situation for all.

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## AMR driven by manufacturing our next big challenge

*Antibiotics production is an important yet often forgotten driver of antimicrobial resistance; an alliance of pioneers has decided to pave the way for more sustainably produced medicine*

By Nicolai Schaaf
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Pharmaceutical residues can be found in the environment and waters in almost every corner of the world, with potentially harmful effects on humans and ecosystems. The substances can alter the behavior of organisms, bio-accumulate, and cause antibiotic resistance.

Initially, residues were primarily associated with the consumption of medication, but a growing body of research also points to the role of manufacturing. Researchers have found high concentrations of pharmaceutical substances in surface and groundwater systems near production facilities.

There is a strong case for an immediate shift to safer manufacturing practices: It would save lives in global pharmaceuticals hubs such as Hyderabad; and it would slow the spread of antimicrobial resistance (AMR), one of humanity's greatest health threats. Not to mention that the producers of antibiotics would be able to ensure that their products remain effective in the future as well.

Despite this convincing logic, it has been difficult to achieve meaningful and large-scale change. The incentives simply are not there.

Even consumers who regularly opt for fair-trade food and organic cotton have rarely given a thought to how the medication they consume is produced. And if consumers never ask for such information, companies lack the motivation to shift to costlier production practices than their competitors.

In addition, the individual patient is normally prescribed a specific medication by a physician and hence lacks both information and the ability to effectively choose between different products.

But change may finally be around the corner. In February 2020, we launched the Responsible Antibiotics Manufacturing Platform (RAMP), a global collaboration. RAMP is special because it brings together pioneers among procurers, regulators, and companies to co-create the business-case for sustainably produced antibiotics.

RAMP builds on experiences we at, Stockholm International Water Institute, SIWI, have accumulated over many years of work, encouraging safer drug manufacturing. Interest is steadily growing, and it should be noted that there are voluntary standards for responsible manufacturing developed by the AMR Industry Alliance.

It is also encouraging that the government of India has started to talk about setting the world's first national targets for emissions of pharmaceutical residues. And both individual countries and the United Nations Development Programme UNDP have formulated environmental criteria for procuring medicine.

Even investors show a growing interest in addressing the hidden risks in antibiotics supply chains.

But for these scattered initiatives to move to the center stage and fundamentally transform the pharma business, something more is needed. We do believe that the RAMP platform can be this decisive force that makes sustainable manufacturing the norm for the whole antibiotics industry.

The more companies, procurers, and regulators that join us, the faster and smoother the transition will be. We therefore welcome all interested stakeholders to be part of this growing movement to ensure that we will have access to safe antibiotics also tomorrow.

*About the author: Nicolai Schaaf is programme manager, Stockholm International Water Institute (SIWI)*

## Agronomic recommendations: How are antibiotics being used on crops?

*A few antibiotics considered critically important for human medicine are being recommended for use on over 100 crops, an analysis has found*

By Philip Taylor, Rob Reeder
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The health of the human population has benefited greatly from the discovery and use of antibiotics to treat bacterial infections. What were once life-threatening infections are now often of minor significance due to these incredible drugs.

Veterinary uses quickly followed the medics lead; then, in the 1950s, plant biologists showed that antibiotics kill bacterial plant pathogens just as well as those infecting humans or animals.

Despite their efficacy, antibiotics were promoted as plant protection products in a few places, the most well-documented one being the control of fire blight on top fruit in North America. Until recently, it was widely believed that this was the only significant use of antibiotics in crop production.

Tracking and documenting the use of antibiotics is important. Regulation is required to prevent the spread of resistance.

However, it is not possible to regulate antibiotic use if one is unaware of where and when it is being used. Until recently, no one had any information on the extent to which antibiotics were being used on crop plants. But that has now changed owing to a recent analysis of the Plantwise POMS data.

Plantwise is a donor-funded development programme that provides support and training to plant-based agricultural extension services in 33 countries in Africa, Asia and the Americas.

Plantwise works with state-run extension services and helps train extension workers to provide advice to farmers through a network of local plant clinics. These are the places where farmers can bring diseased or infested crop samples and obtain a diagnosis and a recommendation on how to manage the problem.

The information is provided to the farmer, but also uploaded into the international database known as the Plantwise Online Management System (POMS).

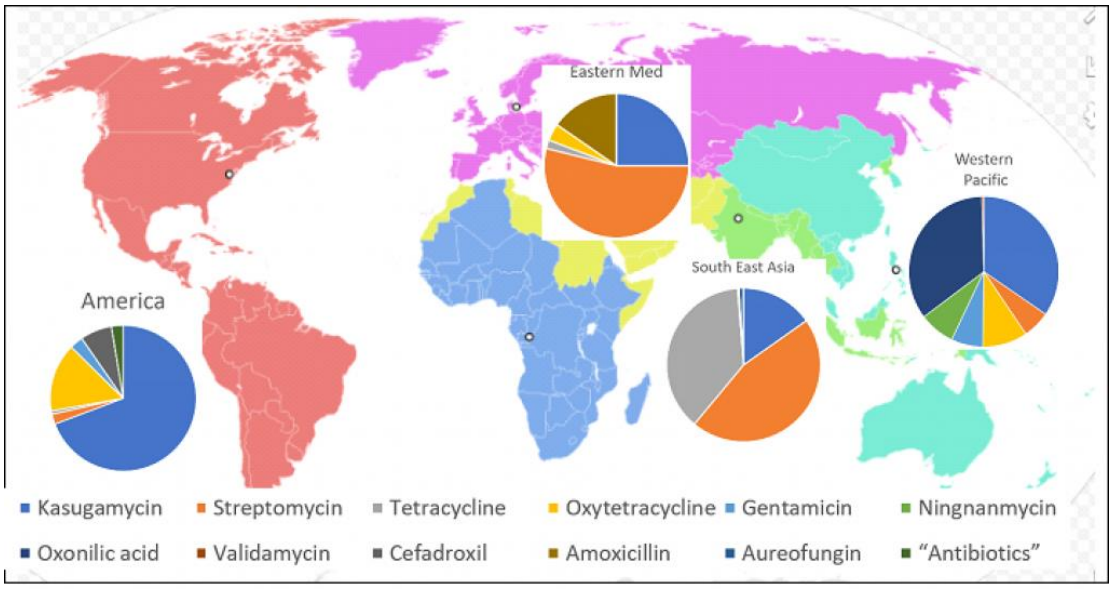
It is this large repository of information that was investigated and has revealed the extent of antibiotic use (based on the recommendations), the results of which have been recently published in CABI Agriculture and Bioscience.

The research comprised an analysis of more than 436,000 records from the countries in which Plantwise is operational. This was a total of 32 countries spread over five World Health Organization regions of the world between 2012 and 2018.

In absolute terms, the numbers of records recommending an antibiotic is low (1,659). It is, however, significant because of the threat of resistance.

In total, 11 antibiotics (often blended) were recommended on crops. Not only did the amount of antibiotics being recommended varied hugely between the regions, the type of antibiotic, the crop to which they were applied and what they were being recommended against varied as well.

The types of antibiotics recommended for use on crop plants in five regions of the world. "Antibiotics" relates to recommendation where no specific product was suggested. There were no records recommending an antibiotic from any African country.




*The types of antibiotics recommended for use on crop plants in five regions of the world. "Antibiotics" relates to recommendation where no specific product was suggested. There were no records recommending an antibiotic from any African* country

The proportion of recommendations containing an antibiotic by region was: South East Asia (2.4 per cent); Western Pacific (1.9 per cent); America (1.6 per cent); Eastern Mediterranean (0.03 per cent), there were no recommendations containing antibiotics from Africa.

Analysis revealed that those antibiotics used exclusively on crop plants (Kasugamycin and Oxonilic acid) were recommended more widely than thought, but more worryingly, some antibiotics considered critically important for human medicine were being recommended for use on over 100 crops.

It is estimated that annually, 63 tonnes of streptomycin and seven tonnes of tetracycline (both critically important antibiotics in human medicine) are sprayed on the rice crop in South East Asia alone.

In some years and some regions, nearly 10 per cent of rice recommendations featured an antibiotic. While the data revealed rice had the greatest proportion of antibiotic containing recommendations, anecdotally we are told that in some parts of the world, the horticulturalists growing crops to be used as religious offerings are the greatest users of antibiotics.

It is very interesting that there are no records from Africa. Price does not appear to be the reason as low-grade antibiotics (suitable for crop use) are astonishingly cheap in international markets, with streptomycin a cheap as $1 per kilogramme. There are as yet unknown reasons why antibiotics are not used on crops in Africa.

The data contains “checkbox data” where the agricultural advisor indicated (by ticking a box) the nature of the problem the advice was intended to overcome. While antibiotics are predominantly recommended against bacterial diseases, there is an alarming proportion of recommendations containing antibiotics against other crop problems where the antibiotic will have no effect, including fungi, insects and even weeds.

The data suggested that many advisors were either unaware that antibiotics would have no impact on insect pests and other problems, or they are recommending antibiotics as part of a cocktail of preventative measures.

While it is commonplace for antibiotics to be taken for viral conditions in humans (against which they will have no effect), that does not seem to be the case in crop cultivation. Fewer records related to treating viral conditions with antibiotics.

Although the global quantities of antibiotics being recommended for use on crops were comparatively small relative to medical and veterinary use, this niche did provide some unique avenues through which resistance could develop in human pathogens.

It has been shown that when antibiotics are mixed with other agro chemicals, bacteria can develop resistance to the antibiotic up to 100,000 times faster. This, coupled with the consumption of raw food, may provide an avenue for the development of resistant bacteria.

Studies have demonstrated that antibiotic resistance gene can be transferred to gut bacteria through a process known as horizontal gene transfer (HGT).

It is, therefore, not difficult to imagine that bacterial plant pathogen populations that have become resistant to antibiotics could pass on these resistance genes when ingested on salad vegetables; potentially generating antibiotic resistant pathogens.

Given the looming problem of antibiotic resistance and the many ways in which antibiotics are being used in medicine and agriculture, it is proposed that plant health is included in any “one health” coordinated regulation of antibiotic use.

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