Antimicrobial Resistance
Structuring the problem and containing it

Online Media Workshop
Antimicrobial Resistance in Africa: A Growing Scourge
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What is Antimicrobial Resistance?

- **Antimicrobial resistance** happens when microorganisms (such as bacteria, fungi, viruses, and parasites) change when they are exposed to antimicrobial drugs (such as antibiotics, antifungals, antivirals, antimalarials, and anthelmintics) (WHO)

- **Antibiotic resistance** happens when germs like bacteria develop the ability to defeat the drugs designed to kill them. That means the germs are not killed and continue to grow. (CDC)

- How does AMR develop?
  - Occurs **naturally over time**; accelerates by misuse and overuse of antimicrobials
  - Antibiotic use exerts **greater selection pressure** on bacteria, causing resistant ones to survive
  - At a cellular level, resistance is acquired through **transfer of genetic material** from one bacteria to another
TRANSFORMATION
Bacterial plasmids
Bacteria acquire new genetic material from the environment

CONJUGATION
Protein tube
It is the process of direct transfer of DNA from one bacterium to another through a protein tube

TRANSUDCTION
Bacteriophage
Bacteriophage, viruses that infect bacteria pick up genetic material in the process and pass it on to other bacteria

1. Lots of germs. A few are drug resistant.
2. Antibiotics kill bacteria causing the illness, as well as good bacteria protecting the body from infection.
3. The drug-resistant bacteria are now allowed to grow and take over.
4. Some bacteria give their drug-resistance to other bacteria, causing more problems.

Figure source: Down to Earth

Figure source: CDC
Scale and impact of the AMR problem is huge

- **Multiple microorganisms** (bacteria, virus, fungi, parasite)
- **Different types of a bacteria** (e.g. Gram positive bacteria, Gram-negative bacteria)
- **Infections of multiple organ systems/body tissues** (gut, respiratory, urinary, blood etc.)
- **Different sources of infection** (community-acquired, hospital-acquired, food-borne)
- **Impacts outcome of infectious diseases, non-communicable diseases** (e.g. chemotherapy in cancer, diabetic foot), **post-surgical infections** (e.g. hip transplant, cardiac surgery)
- **Resistance against almost all antibiotics** (old antibiotics like tetracycline, penicillin; new antibiotics like 3rd, 4th, 5th generation cephalosporins; last resort like colistin)
- **Prevalent across globe, all age groups**

Antibiotics becoming ineffective leading to untreatable infections, longer hospital stays, expensive treatments, more morbidity and deaths; Economy, livelihood, food security and safety, attainment of several SDGs can be severely impacted
AMR is cross cutting; has strong multi-sectoral linkages w.r.t. both cause and effect

**Animal health and production**
- Poultry, fisheries, dairy, swine
- Intensive production systems
- Routine antibiotic use for growth promotion, disease prevention
- Use of critically important antibiotics (CIA) for humans

**Human health**
- Self medication
- Over prescription
- Over-the-counter sale
- Access vs excess issue

**Waste and Environment**
- Point and non-point sources
- Hotspots include waste from farms, factories, healthcare settings and sewage/water treatment plants
- Non-point sources include rivers etc.

**Plants**
- Routine use of antibiotics as fungicides in crops to prevent diseases;
- Use of streptomycin, a CIA used in certain Tuberculosis cases such as in India
High annual deaths due to AMR leading to huge cumulative damage vis-à-vis viral pandemics of the 21st century (which are acute crisis of a limited duration)

- **700,000** deaths globally every year estimated due to AMR (Review on AMR, 2016)
- **2,30,000** deaths globally in 2017 due to multidrug-resistant (MDR) or rifampicin-resistant TB (WHO, 2018)
- **45% of deaths** in both Africa and South-East Asia to MDR bacteria (WHO GLASS Report 2014)
- **USD 100 trillion** – cumulative cost to global economic output by 2050
- **3.8% expected loss in annual GDP** globally by 2050 in a high AMR-impact scenario (World Bank, 2017)

<table>
<thead>
<tr>
<th>Pandemic</th>
<th>Causative organism</th>
<th>Worldwide deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spanish Flu (1918-19)</td>
<td>Influenza A (H1N1) virus</td>
<td>20-50 million</td>
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<tr>
<td>Asian Flu (1957-58)</td>
<td>Influenza A (H2N2) virus</td>
<td>1.1 million</td>
</tr>
<tr>
<td>Hong Kong Flu (1968)</td>
<td>Influenza A (H3N2) virus</td>
<td>1 million</td>
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**After 2000**

<table>
<thead>
<tr>
<th>Pandemic</th>
<th>Causative organism</th>
<th>Worldwide deaths</th>
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</thead>
<tbody>
<tr>
<td>Swine Flu (2009)</td>
<td>Influenza A (H1N1) virus</td>
<td>0.15-0.57 million (during first year)</td>
</tr>
<tr>
<td>MERS (2012)</td>
<td>MERS-CoV virus</td>
<td>858 (since Sept 2012)</td>
</tr>
<tr>
<td>Covid19 (2019-20 ongoing)</td>
<td>SARS-CoV2 virus</td>
<td>&gt;0.8 million (as on August 27, 2020)</td>
</tr>
</tbody>
</table>

Source: WHO and CDC
10 million lives a year estimated to be at risk by 2050, if AMR not contained; About 90 per cent to be in Asia and Africa

Deaths attributable to AMR every year by 2050

Source- AMR: Tackling a crisis for the health and wealth of nations
CSE’s work to help contain AMR in animal and environmental sectors

- 2010 (Honey)
- 2014 (Poultry)
- 2016 (Fish)
- 2017 (Poultry farms)
- 2017 (Fast food)
- 2019 (Crops)
- 2019 (Unused drug disposal)
- 2020 (Feed)
- 2020 (Fast food)
- 2020 (Dairy)
CSE’s work to support NAP implementation in developing countries including African countries

- Pan-Africa Workshops to help support implementation of National Action Plans (NAP) on AMR
- Collaboration with Zambia to help implementation of Multisectoral NAP-AMR
- Beginning collaborations in Zimbabwe to support implementation of One-Health AMR NAP
Antibiotic use in food systems

Intensive food-animal farming

Poultry

Dairy

Pigs

Fish
More food is now grown in intensive settings; the very nature of such industrial production can create crisis

- In **high income countries**, most of food from animals is grown in intensive settings
- In **low and middle income countries** intensification is growing due to **animal protein demand**

But the very nature of such production systems can create crisis

- **Large-scale units** with **high stocking density** of animals/birds/fish
- **Genetically selected breeds** for productivity (not disease resilience)
- Confined conditions; **limited focus on animal husbandry**
- Dependence on **commercial feed**, inputs (also known as animal feeding operations, factory farms)
- Often **geographically concentrated**; vertically integrated by large players; involves contract farming
- Industrial systems but considered agriculture; do not get **required regulatory attention**

**High use of chemicals and drugs** (easy/economical substitute)

Intensive food production is also linked to several pandemics
Antibiotic use in livestock

Non-therapeutic antibiotic use

- **Routine** antibiotic use to promote faster growth and prevent diseases despite no clinical sign
- Use of medically important antibiotics including critically important and last-resort

Source: Review on AMR-Antimicrobials in agriculture and the environment: reducing unnecessary use and waste
Only collective action on both growth promotion and disease prevention would solve the purpose

- **Antibiotic use in animals>> humans;** ~70% of medically important antibiotics for human health sold in the US and >50% percent in most countries are used in livestock

- **Non-therapeutic use** a big contributor

- **Focus so far on restricting growth promotion**

- **No fine line** – segregating where one role stops and other begins

- **Need for collective action**
  - EU banned all growth promoter use in food-animals in 2006, rise in antimicrobial use for disease prevention
  - Based on its learnings, EU will enforce ban on preventive mass medication in animals from 2022

*WHO Guidelines on Use of Medically Important Antimicrobials in Food-Producing Animals (2017); IACG Report “No Time to Wait” (2019)*
Countries need to regulate the way food is grown; re-think the relationship – how it is produced and its overall impact

- Ban antibiotic use for growth promotion; regulate feed well – antibiotics not to be allowed
- Restrict mass disease prevention (i.e. group preventative use); regulate over-the-counter sale of antibiotics
- Limit use of critically important antibiotics; preserve those with highest priority for human use (quinolones, macrolides, 3rd, 4th, 5th gen cephalosporins, polymyxins, glycopeptides)
- Reduce need for chemicals by focusing on animal husbandry, bio-security, alternatives, diagnostics, and veterinary extension systems
- Reduce dependence on intensive systems; grow more food in other settings

Necessary policies, surveillance, awareness, capacity building and budgets must go hand-in-hand with the above
Antibiotic use in crops is a common practice

In many geographies, antibiotics are registered as fungicides (e.g., India)

Use for treatment and prevention of diseases such as blight, canker

Unapproved use on other crops; use in higher doses and frequency

Streptomycin is commonly used

Antibiotic use is made in combination with other fungicides

A recent analysis from 32 countries also indicated similar wider practices

Source: Too much too often (Down to Earth)
Antibiotic use in food systems

Crops

Areas for action

• Regulate the misuse of antibiotic use in crops

• Re-categorize antibiotics from fungic和平s to antibacterials/bactericides

• Limit the use of CIAs in crops

• Monitor the amounts of antibiotics used in crops

• Surveillance of plant-derived food produce for residual antibiotics
### Structuring the environment sector w.r.t AMR

<table>
<thead>
<tr>
<th>Point Sources</th>
<th>Healthcare Settings</th>
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<tbody>
<tr>
<td><strong>Farms</strong></td>
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<tr>
<td>Waste from:</td>
<td></td>
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<tr>
<td>• Animal farms – poultry, dairy, pig, fish etc.</td>
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<tr>
<td>• Agriculture farms</td>
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<tr>
<td><strong>Factories</strong></td>
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<tr>
<td>Effluents from:</td>
<td></td>
</tr>
<tr>
<td>• Pharma manufacturing</td>
<td></td>
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<tr>
<td>• Feed mills</td>
<td></td>
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<tr>
<td>• Slaughter houses</td>
<td></td>
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<tr>
<td>• Processing units (meat, dairy)</td>
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<tr>
<td>• Effluent treatment plants</td>
<td></td>
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<tr>
<td><strong>Households/Community</strong></td>
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<tr>
<td>Effluents from:</td>
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<tr>
<td>• Sewage treatment plants</td>
<td></td>
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<tr>
<td>• Disposal of unused, expired drugs</td>
<td></td>
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<tr>
<td><strong>Healthcare Settings</strong></td>
<td></td>
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<tr>
<td>• Hospital sewage</td>
<td></td>
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<tr>
<td>• Waste from veterinary care settings</td>
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</table>

<table>
<thead>
<tr>
<th>Non-point Sources</th>
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<tbody>
<tr>
<td>Rivers, Reservoirs</td>
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<tr>
<td>Groundwater</td>
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<tr>
<td>Agricultural soil</td>
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Three AMR determinants that travel across the systems, sectors: Antibiotic resistant bacteria, Antibiotic resistance genes, Antibiotic residues

**AMR in the environment is a cross cutting issue. Continuous and perhaps ever-lasting interplay among AMR determinants sets the ground for resistance growing like a chain reaction**
AMR in environment has been a neglected agenda

- Focus has been on ‘what is going in’ and not on ‘what is coming out’. Missing the complete picture

- AMR containment in the waste and environment sector has largely been a neglected agenda
  - Global deliberations now include environment, but no specific guidance yet
  - Environment is not the key mandate of WHO-FAO-OIE tripartite; UNEP only recently included
  - Country level National Action Plans have outlined approaches to address the environmental AMR routes, but there is still inadequate action on the ground
  - Limited awareness and buy-in of policymakers and environmental regulators on the issue; limited expertise on microbiology related aspects
  - No environmental standards w.r.t. residual antibiotics or resistant bacteria

- Mixed scientific opinion due to complexity of the issue

It is time we re-think, re-prioritize and put the environment first; at par with human and animal sectors
A comprehensive approach is required to address this complex issue. A precautionary principle should be considered

- Antibiotics in the environment could be considered as a hazardous chemical; AMR centric waste management approaches should be adopted

- Standards for residual antibiotics in environment and waste management guidelines should be developed

- Surveillance of waste/effluents, litter, manure for AMR determinants, particularly from hotspots, should be carried out

- Policies that help keep a check on land application of farm litter should be developed

- Policies for drug take-back under Extended producer Responsibility for unused and expired medicines from human, animal sector should be developed and implemented

- Guidelines on siting, biosecurity, sanitation and hygiene for different point sources should be developed

- Ongoing research should continue to inform future policy and plans
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