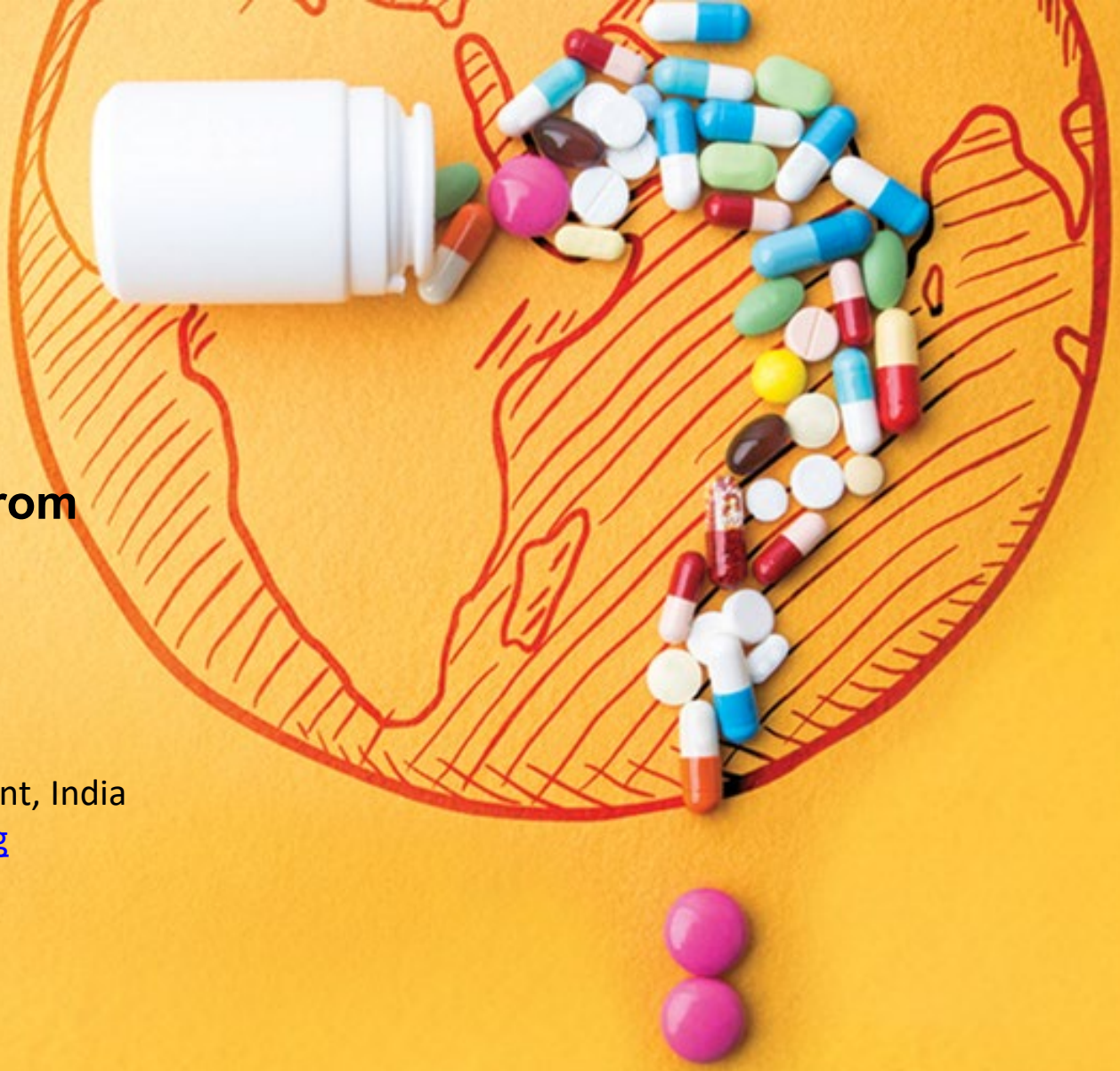


Antibiotic Pollution from Food Production

Dr. Rajeshwari Sinha
Programme Manager
Sustainable Food Systems
Centre for Science and Environment, India
s_rajeshwari@cseindia.org

Workshop on Understanding the Environmental Dimensions of Antimicrobial Resistance
March 28-29, 2023

UNEP report recognizes 'Agriculture and Food' as one of the Key economic-sector value chains affecting AMR in the environment

- 'Several points in the agriculture value chain serve as entry points for antimicrobials and antimicrobial resistant organisms into the environment **such as the use of antimicrobials to treat infection and promote growth**, use of reclaimed wastewater for irrigating crops, use of manure as fertilizer and inadequate waste management'

- 'Unless broader steps are taken towards making food systems more sustainable and **curbing the use of antimicrobials in animal husbandry practices**, the use of antimicrobials in food production will continue to grow'

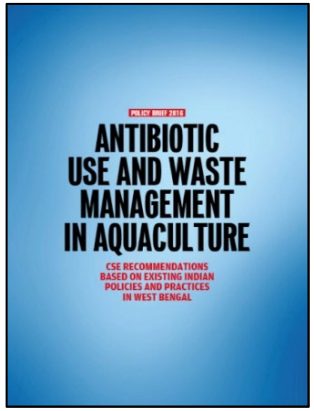
- 'In intensive animal production systems, **antimicrobials are frequently relied upon to maintain livestock health, welfare and productivity, including for control of diseases**. In some jurisdictions, antimicrobials are still used as growth promoters'

- 'Management options to address releases, effluent and waste from animal production:
  - **Reduce antimicrobial use in food animals by improving animal health through implementing biosafety, biosecurity, vaccination and good animal husbandry programmes**
  - Develop market incentives that would help motivate aquaculture producers to invest and **adopt alternative management practices that curb the use of antimicrobials'**

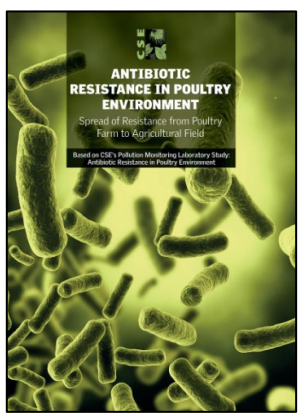
CSE's work on food and environment aspects of AMR in India (few examples)

Antibiotics in honey, 2010

Antibiotic use in poultry, 2014

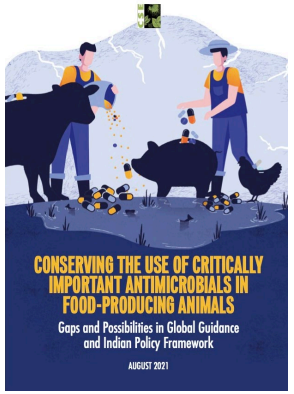


Antibiotic use in aquaculture, 2016



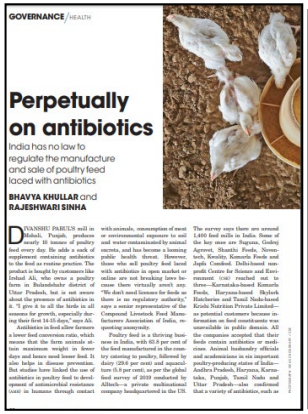
AMR in poultry environment, 2017

Antibiotic use in fast food supply chain, 2017



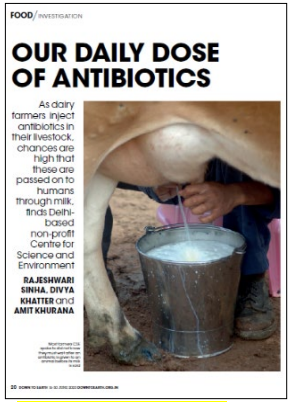
Conserve the use of critically important antimicrobial, 2021

Antibiotic use in crops, 2019



Antibiotic use in feed, 2020

Antibiotic use in fast food supply chain, 2020

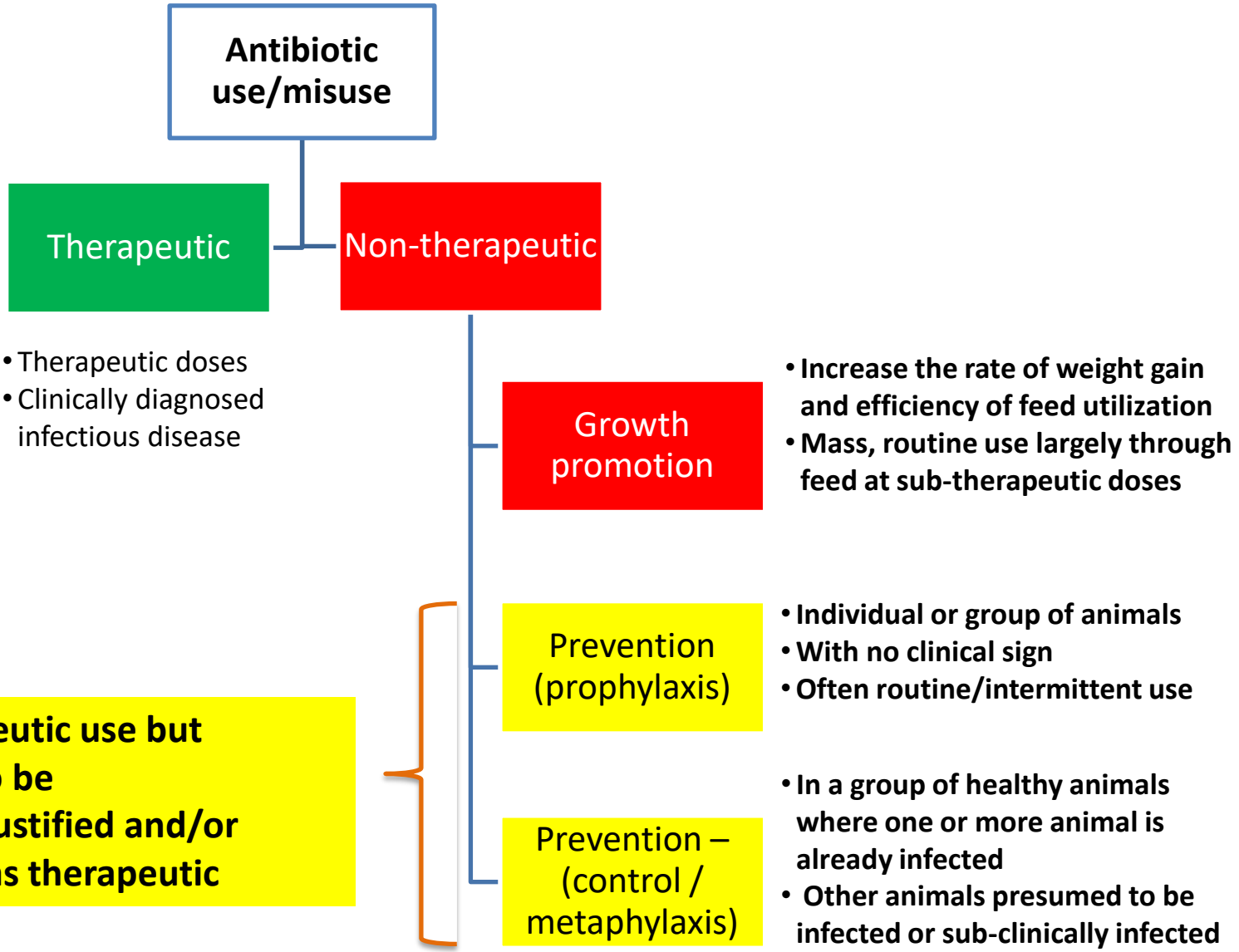


Antibiotic use in dairy, 2020

Use of ethnoveterinary medicines in dairy sector, 2021

Use of ethnoveterinary medicines in dairy sector, 2022

Antibiotic use/misuse/overuse in food systems

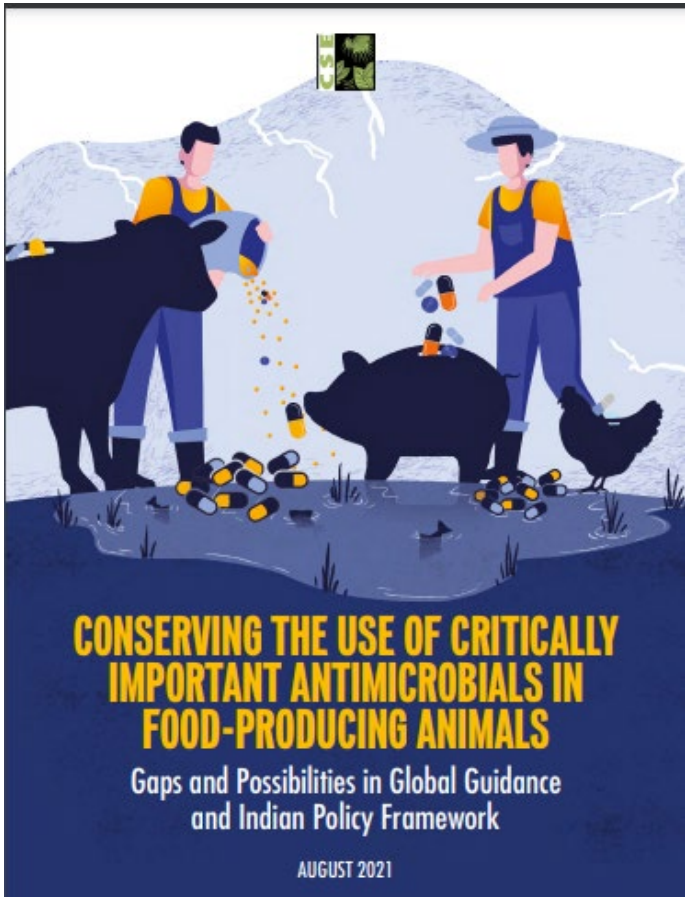


Key problems w.r.t antibiotic use in food systems (animal systems in particular)…

- Problem 1: **antibiotic use/misuse is very high**
  - Due to non-therapeutic purposes (e.g. growth promotion), large animal population, ease of antibiotic availability/use as a cheap substitute
- Problem 2: **use/misuse of critically important antimicrobials (antibiotics)**
  - Life-saving antibiotics in hospitals/ICUs are misused to grow meat in farms (for multiple reasons but some of which are avoidable)
- Problem 3: **antibiotic use/misuse to prevent diseases**
  - Whereas prevention with chemicals/antibiotics is no real prevention; but antibiotics pushed/promoted/justified as therapeutic use for prevention
- Problem 4 (the biggest): **antibiotic use/misuse is fueling intensive practices to rear animals for food**

CSE's latest report on conserving the use of critically important antimicrobials in food-producing animals

- **India**
  - Presents the **on-the-ground situation** in India wrt use of critically important antimicrobials in food-animal sector
  - Provides **a series of policy measures** including a roadmap to contain the misuse of critically important antimicrobials in food-animal production
- **Global**
  - Analyses the **global guidance of the Tripartite organizations** with regard to critically important antimicrobials
  - **Calls for coherence and uniformity in global guidance** on use of critically important antimicrobials in food-animals



Key findings: Critically important antibiotics are misused and overused in Indian food-animal production sector

- 27 critically important antimicrobials from seven classes were found to be used in dairy, poultry and aquaculture for both therapeutic and non-therapeutic purposes
- Eighteen were from three highest priority critically important antimicrobial classes, i.e. macrolides and ketolides; third-, fourth- and fifth-generation cephalosporins; and quinolones and fluoroquinolones
- Antimicrobials, apart from **treatment** used for **prevention and control of diseases; in viral and fungal infections, along with feed (poultry sector)**

Dairy	Poultry	Aquaculture
21 CIAs from 6 Classes **13 HPCIAs from 2 classes**	**14 CIAs from 4 Classes** **8 HPCIAs from 2 classes**	**3 HPCIAs from1 class**
HPCIAs • **Third-, fourth- and fifth- generation cephalosporins**, Eg: Cefotaxime • **Quinolones and fluoroquinolones**, Eg: Levofloxacin **CIAs** • **Aminoglycosides**, Eg: amikacin • **Penicillins** • **Ansamycins**, Eg: Rifampicin • **Drugs used solely to treat tuberculosis or other mycobacterial disease**	**HPCIAs** • **Macrolides and ketolides**, Eg: Erythromycin • **Quinolones and fluoroquinolones**, Eg: Ciprofloxacin **CIAs** • **Aminoglycosides**, Eg: streptomycin • **Penicillins**	**HPCIAs** • **Quinolones and fluoroquinolones,** Eg: Ciprofloxacin

Critically important antimicrobials used in the Indian dairy sector to prevent, control or treat diseases		
Antimicrobial	Antimicrobial class	Disease
Highest priority critically important antimicrobials considered veterinary critically important antimicrobials		
Cefoperazone	Third-, fourth- and fifth- generation cephalosporins	Mastitis
Ceftiofur		Mastitis, haemorrhagic septicaemia, anthrax
Ceftriaxone		Mastitis, haemorrhagic septicaemia; viral disease: footand mouth disease
Cefquinome		Mastitis
Ciprofloxacin	Quinolones and fluoroquinolones	Anthrax, diarrhoea; viral disease: foot and mouthdisease
Enrofloxacin		Mastitis, haemorrhagic septicaemia, diarrhoea; viraldisease: foot and mouth disease, infectious bovine rhinotracheitis
Norfloxacin		Diarrhoea
Ofloxacin		Diarrhoea
Critically important antimicrobials considered veterinary critically important antimicrobials		
Amoxicillin	Penicillins	Mastitis; viral disease: foot and mouth disease
Ampicillin		Mastitis, black quarter, brucellosis; viral disease: footand mouth disease, infectious bovine rhinotracheitis
Amikacin	Aminoglycosides	Mastitis, brucellosis
Gentamicin		Mastitis, diarrhoea; viral disease: foot and mouthdisease
Streptomycin		Mastitis, black quarter, brucellosis, tuberculosis; viraldisease: foot and mouth disease
Critically important antimicrobials considered veterinary highly important antimicrobials		
Rifampicin	Ansamycins	Brucellosis, tuberculosis
Highest priority critically important antimicrobials not mentioned in OIE list		
Cefotaxime	Third-, fourth- and fifth- generation cephalosporins	Mastitis, haemorrhagic septicaemia
Ceftazidime		Mastitis
Ceftizoxime		Mastitis
Levofloxacin	Quinolones and fluoroquinolones	Mastitis
Moxifloxacin		Mastitis
Critically important antimicrobials not mentioned in OIE list		
Ethambutol	Drugs used solely to treat tuberculosis or other mycobacterial disease	Tuberculosis
Isoniazid		Tuberculosis

Dairy sector

Note: In addition to the above, antimicrobials which are not critically important and used in Indian dairy sector include tetracycline, oxytetracycline, doxycycline, trimethoprim, sulfamethoxazole, sulfadimidine, cloxacillin, benzylpenicillin, nitrofural, cefalexin, ornidazole and metronidazole.

Critically important antimicrobials used in the Indian poultry sector to prevent, control or treat diseases		
Antimicrobial	Antimicrobial class	Disease
Highest priority critically important antimicrobials considered veterinary critically important antimicrobials		
Ciprofloxacin	Quinolones and fluoroquinolones	Pullorum disease, fowl typhoid, colibacillosis,salmonellosis
Enrofloxacin		Fowl cholera, infectious coryza, pullorum disease, fowltyphoid, colibacillosis, necrotic enteritis, salmonellosis,chronic respiratory disease; viral diseases: Ranikhet disease, infectious bronchitis, avian influenza, Marek'sdisease, infectious bursal disease
Norfloxacin		Colibacillosis
Erythromycin	Macrolides and ketolides	Infectious coryza
Tylosin		Chronic respiratory disease; fungal disease:mycotoxicosis
Tylvalosin		Chronic respiratory disease
Critically important antimicrobials considered veterinary critically important antimicrobials		
Amoxicillin	Penicillin	Necrotic enteritis; viral disease: Ranikhet disease
Ampicillin		Necrotic enteritis
Amikacin	Aminoglycosides	Infectious coryza, pullorum disease, fowl typhoid,colibacillosis, salmonellosis
Gentamicin		Pullorum disease, fowl typhoid, salmonellosis
Neomycin		Pullorum disease, colibacillosis, necrotic enteritis; fungaldisease: aspergillosis, mycotoxicosis
Streptomycin		Fowl cholera
Highest priority critically important antimicrobials not mentioned in OIE list		
Azithromycin	Macrolides and ketolides	Fowl cholera
Levofloxacin	Quinolones and fluoroquinolones	Fowl cholera, Infectious coryza, pullorum disease, fowl typhoid, colibacillosis, necrotic enteritis, salmonellosis; viral disease: Ranikhet disease

Note: In addition to the above, antimicrobials that are not critically important and are used in the Indian poultry sector include tetracycline, oxytetracycline, doxycycline, trimethoprim, sulfamethoxazole, tiamulin, cefalexin, furazolidone and chloramphenico

Poultry sector

Critically important antimicrobials used in the Indian aquaculture sector to prevent, control or treat diseases		
Antimicrobial	Antimicrobial class	Disease
Highest priority critically important antimicrobials considered veterinary critically important antimicrobials		
Ciprofloxacin	Quinolones and fluoroquinolones	For one or more of the following: Infections caused by *Aeromonas* spp.: e.g. motile aeromonadsepticaemia, hemorrhagic septicemia, red sore, tail rot and fin rot, furunculosis Infections caused by *Vibrio* spp.: e.g. vibriosis, intestinalnecrosis, anaemia Infections caused by *Pseudomonas* sp.: e.g. pseudomonassepticaemia, fin rot Infections caused by *Flavobacterium* sp.: e.g. columnarisdisease, bacterial gill disease Infections caused by *Edwardsiella* sp.: e.g. edwardsiellosis
Enrofloxacin		
Oxolinic acid		

Note: In addition to the above, antimicrobials that are not critically important and are used in the Indian aquaculture sector include tetracycline, oxytetracycline, doxycycline, trimethoprim, sulfamethoxazole, cefalexin, furazolidone, chloramphenicol and nitrofurans.

Aquaculture sector

Indian practices reflect the collective impact of the global guidance and national policy-related actions

Analyses the **global guidance of the Tripartite organizations** with regard to critically important antimicrobials reflect three key issues

Key Issue 1: Significant overlap in antimicrobials considered critical for humans and food-producing animals

Key Issue 2: Need for coherence in position on use of critically important antimicrobials in food-producing animals

Key Issue 3: Need for clarity and strong action on use of antimicrobials for disease prevention in food-producing animals

CSE views on the draft WHO Medically Important Antimicrobial List, 7th Revision 2023

- **The overall positioning of antimicrobials that need attention (to be conserved etc.) has reduced due to changes made in categorization/prioritization**
  - Problem appears to be related to only a limited set of antibiotics
  - Frequent shifts in antimicrobials falling under HPCIA and CIA categories make it look like a less-serious exercise
  - What the stakeholders/nations are expected to interpret w.r.t. antimicrobials authorised only for humans to be made amply clear
- **The basis of using for authorization of antimicrobials is not clear and can potentially mislead. It needs to be addressed and made clear**
  - Antimicrobial authorisations can vary across countries; on-the-ground antimicrobial use practices can vary
  - Need to know/clarity on rationale to use authorisations, which national-level/global database were referred, what a country is expected to do in case a contradiction
- **Macrolides (as well as certain penicillins) getting off the radar of HPCIAs /CIAs may not be a good idea**
  - Extensively used in Indian food-animal sector as well as in human health; Becoming ineffective due to growing resistance
- **Contradiction/confusion regarding the future animal use of antimicrobials authorised only for humans currently**
- **While crops are not being considered as part of non-human use, all caution must be exercised to avoid under-playing the problem of antibiotic misuse in crops and its connections with AMR**

India should consider developing a road map and necessary policy framework to conserve the use of CIAs for both human and non-human sector initiatives

- **Use of highest priority critically important antimicrobials for treatment should also be considered for phase-out**. They should only be allowed in exceptional situations as a last resort
- **Prohibition of antibiotic growth promoters in food-producing animals** (e.g., poultry sector)
- **Antimicrobial use for disease prevention (including control) should be recognized as non-therapeutic** and all measures should be adopted and/or promoted to discourage such use in farms.
- Necessary focus should also be placed on promoting and incentivizing use of **non-antimicrobial alternatives, biosecurity, hygiene and sanitation, and good animal-rearing practices.**
- **A long-term research agenda should be developed and implemented for non-antimicrobial alternatives and their effectiveness understood in managing diseases in animal farms. Programmatic interventions should be made for their greater promotion and adoption.**
- **Setting up systems and mechanisms to gather data and enhance understanding on critically important antimicrobial use and resistance in food-producing animals. This data on sector-wise use should be analysed with resistance in animals and humans and the reports should be made public annually.**
- **Routine monitoring by the central food regulator (FSSAI) and state food regulators on antimicrobial use and residues** to ensure that withdrawal periods are followed and residue standards are met.

Ethnoveterinary Medicine in the Indian Dairy Sector

Results: effectiveness of EVM

With a few herbs and a prayer

Traditional veterinary medicines can go a long way in addressing the growing burden of antimicrobial resistance

DEEPAK BHATI AND RAJESHWARI SINHA NEW DELHI

MASTITIS CAN be debilitating both for dairy cattle and their farmers. This bacterial infection, triggered by injuries caused due to rough milking or because of unhygienic farm conditions, causes inflammation of the udder tissue and blockage of milk ducts. This causes excruciating pain to the animal and affects milk yield and quality. Left unmanaged, the disease can spread to uninfected animals in the herd and result in their death. A July 2020 study published in *BioMed Central* says 70 per cent of all losses incurred by dairy herds in India are due to mastitis.

Now call it the lack of enough field veterinarians in the country, over-the-counter access to antibiotics or the fear of losing milk and, therefore, income, most dairy farmers rush to administer high doses of antibiotics to the cattle even at the slightest sign of mastitis. In June 2020, Delhi-based non-profit Centre for Science and Environment (CSE) spoke to dairy farmers of high milk-producing states—Punjab, Haryana, Uttar Pradesh, Rajasthan, Karnataka and Tamil Nadu—to understand the prevalence of the practice. It found that more often than not dairy farmers do not consult veterinarians and indiscriminately use antibiotics that are crucial for treating infections in humans. One such is ceftriaxone, which is categorised as "highest priority critically important antimicrobial" (HPCIA) by the World Health Organization (WHO). Three others, gentamicin, streptomycin and penicillin, are categorised as "critically important antimicrobials (CIAs)" by WHO. Even the Farmers Manual by the Department of Animal Husbandry and Dairying (DAHD) recommends using these three antibiotics for treating mastitis. Worse, most dairy farmers skip the critical withdrawal period—a prescribed period during which treated animals should be excluded from the milk supply chain to allow antibiotic residues to fall to the required level. In 2018, when the Food Safety and Standards Authority of India (FSSAI) tested milk samples from organised and unorganised sectors across the country, it found antibiotic residues beyond permissible limits.

Analysts fear that such misuse of CIAs and HPCIAs could be driving the burden of anti-microbial resistance (AMR), already a pressing concern worldwide; at least 10 million people are likely to die of AMR every year by 2050, says WHO.

To understand the reasons for such misuse or overuse of antibiotics in dairy sector, CSE recently organised a national-level consul-

EASY TO SWITCH

Ethnoveterinary medicine is a low-cost alternative to reduce antibiotic use in Indian dairy sector

DEEPAK BHATI, RAJESHWARI SINHA, AMIT KHURANA

NEW DELHI

CSE assessment of the National Dairy Development Board's EVM project implemented with technical support from Trans-Disciplinary University, Karnataka

SOME LIFESAVING solutions are so simple and obvious that they remain hidden in plain sight. This is particularly true for livestock disease treatments that have evolved over generations through experiences of communities, withstood the test of time and are embedded in local culture and practices. Yet the knowledge remains untapped in the absence of standardisation and scientific validation. More often than not, dairy farmers, and some field veterinarians, indiscriminately use crucial antibiotics for treating even benign infections in animals.

Researchers with Delhi-based Centre for Science and Environment found evidence of such rampant misuse and overuse of antibiotics during consultations with dairy farmers and experts from sectors, including animal husbandry, food safety, human health, conducted in 2020 and 2021. CSE had observed that most dairy farmers also skip the critical withdrawal period—a prescribed number of days during which treated animals should be excluded from the milk supply chain to allow antibiotic residues excreted out of the body. In 2018 the Food Safety and Standards Authority of India (FSSAI) also found antibiotic residues in milk samples.

Such abuse of antibiotics not only adds to the treatment costs, but also adds to the growing burden of antimicrobial resistance (AMR). Interaction between antibiotic residues and pathogens in various environmental matrices (soil and water) and in humans lead to the formation and spread of bacteria that are resistant to antibiotics. A study published

Mastitis Control Popularization Project: Overall results

Disease	Number of unions/producer companies treating with EVM	Total number of cases treated across unions (in thousands)	Cure rate (%)
Mastitis	25	255	78.4
Fever	18	163	82.2
Diarrhea	20	151	84.4
Indigestion	19	32	83.4
Wound	16	9	80.5
Bloat	18	7	76.0
Retention of placenta	17	6	71.2
Lumpy skin disease	8	3	66.2
Prolapse	17	2	69.6
Sub-total		628	80.9
Other ailments		152	78.3
Total	25	780	80.4

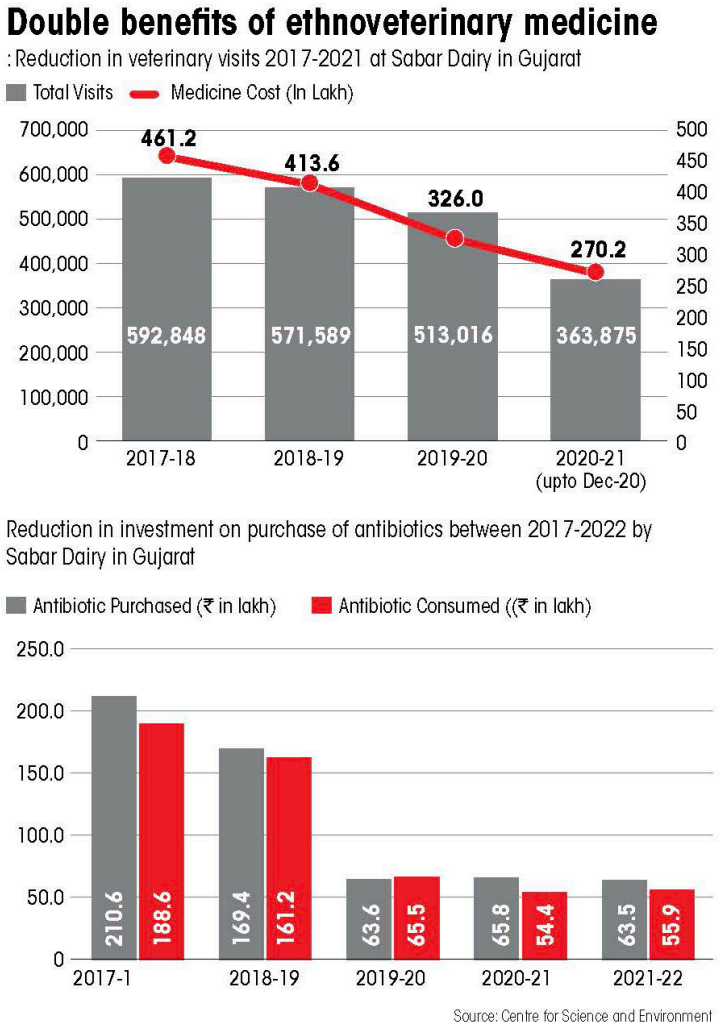
Key four diseases covering 77% (6.01 lakhs) of total cases

Key nine diseases which are otherwise treated with antibiotics

- 2016-October 2022
- 7.8 lakh disease cases across all 25 unions
- Overall 80.4% cure rate
- Nine diseases which are treated with antibiotics, 80.9% cure rate
- 4 diseases covering 77% of total cases; 81.2% cure rate
- **In general, in most disease cases, 4 out of every 5 animal were cured using EVM.**

What do these results mean?

- **Safe milk and milk products for consumer**
  - antibiotic free milk
  - cattle reared without antibiotics leading to reduction in AMR drivers/pathways through food and environment (AMR safe manure useful for growing organic movement in India)
- **Reduction in overall treatment expenses**
  - reduced consumption of antibiotics, veterinary medicines
  - reduced veterinary visits; farmer dependence on vets reduced
- **Improved livelihood of farmers**
  - reduction in loss of milk productivity
  - lesser rejection of milk at the district co-operative society level



Key problems w.r.t antibiotic use in food systems (animal systems in particular)…

- Problem 1: **antibiotic use/misuse is very high**
  - Due to non-therapeutic purposes (e.g. growth promotion), large animal population, ease of antibiotic availability/use as a cheap substitute

- Problem 2: **use/misuse of critically important antimicrobials (antibiotics)**
  - Life-saving antibiotics in hospitals/ICUs are misused to grow meat in farms (for multiple reasons but some of which are avoidable)

- Problem 3: **antibiotic use/misuse to prevent diseases**
  - Whereas prevention with chemicals/antibiotics is no real prevention; but antibiotics pushed/promoted/justified as therapeutic use for prevention

- Problem 4 (the biggest): **antibiotic use/misuse is fueling intensive practices to rear animals for food**

High stocking density in intensive animal farms

Chemical-dependent Intensive food systems – drivers, characteristics and impacts; impacts are much beyond AMR

DRIVERS OF INTENSIFICATION
(more so in LMICs/emerging economies)

- Growing food demand (protein, animal protein)
- Growing population
- Growing incomes / purchasing power
- Urbanization
- Changing food habits, evolving taste
- Less people, less land to grow food
- Political mandate for exports, livelihood opportunities
- Availability of inputs - machines, feed, drugs and chemicals

CHARACTERISTICS OF INTENSIFICATION

- Large-scale units with **high stocking density** of animals/birds/ fish
- **Genetically selected similar breeds** for productivity (not disease resilience); **amplification** of pathogens due to **monoculture effect**
- Kept under **confined conditions** and in **close proximity**; **limited focus on animal husbandry;** high stress
- **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; can bypass required regulatory attention

IMPACTS OF INTENSIFICATION

- **AMR – through two key routes – food and farm waste; untreated manure/litter/waste water application to crops, fish ponds.**
- **Zoonoses, pandemics (e.g. swine flu)**
- **Food-borne illnesses, nutritional deficiencies**
- **Loss of biodiversity/agro-diversity/dietary diversity**
- **Natural resource degradation (water quality and reserves, soil fertility, nutrient availability etc.)**
- **Growing pest attacks; loss of disease resilience; increasing dependence on chemicals (pesticides, fertilisers) and high yielding varieties**
- **Land use changes, loss of forests; often diffuses boundaries b/w human-animal-wild-life**
- **Rising GHG intensive processes, vulnerability to climate crisis**
- **Small holder farmer livelihood crisis and distress**

Post COVID-19 pandemic, One Health approach is gaining momentum to contain AMR

- **Growing realization that the way we produce our food and the way we manage our environment is connected to our health and the health of planet**

- **Importance of One Health is becoming clear:**
  - connected to development, trade, commerce etc.
  - only a true One Health AMR response on-the-ground is effective
  - **A ONE HEALTH RESPONSE TO AMR has co-benefits related to**:
    - Limiting zoonoses and pandemics
    - Ecological conservation
    - Livelihood security
    - Climate resilience

Quadripartite call to action for One Health for a safer world, March 27, 2023

There are real challenges in implementing the One Health approach
More so for emerging economies…

- **Limited resources and competing priorities** like – food, nutrition and livelihood security, access to life-saving medicines, primary healthcare and education
- There are **issues related to stakeholder ownership, denial, conflict of interest and apportioning of blame; and lack of coherent communication/ guidance**;
- **Limited understanding of connections so far**; no real estimates of cost of action as well as cost of inaction; issues around data sharing/interpretation
- **Complexity and scale of the problem and solution** also makes it hard to create public awareness and build pressure
- There are **hardly any established multi-sectoral mechanisms and implementation systems**

But we have also learned that we cannot afford AMR

- **LMICs/emerging economies cannot first pollute, chemicalize and toxify the environment and then invest in clean up, because we cannot afford the high cost of cleanup**
- **We also cannot afford the high cost of treatment when basic drugs fail**
- **So, we have to do things differently…**

We need to Re-invent …the agenda/pathways

- Conserve what we have. Ensure that antibiotics critically important for human health are conserved. We call this the Conservation agenda.
- Ensure that we can continue to increase food production without the use of antimicrobials. The Development agenda. This needs food systems to be transformed. Unlearn the dependence on chemicals. Counter commercially-driven narratives.
- Ensure that the waste from pharma/other sources is tracked and contained. The Environmental agenda. This needs cost effective waste management.
- But all this will require serious re-invention of the way we do business with our food and environment. We have to prevent pollution and overuse of chemicals – Prevention agenda.

Thank you!

For more information, contact:

Amit Khurana
Director
Sustainable Food Systems Programme
CSE
k_amit@cseindia.org

Rajeshwari Sinha
Programme Manager
Sustainable Food Systems Programme
CSE
s_rajeshwari@cseindia.org