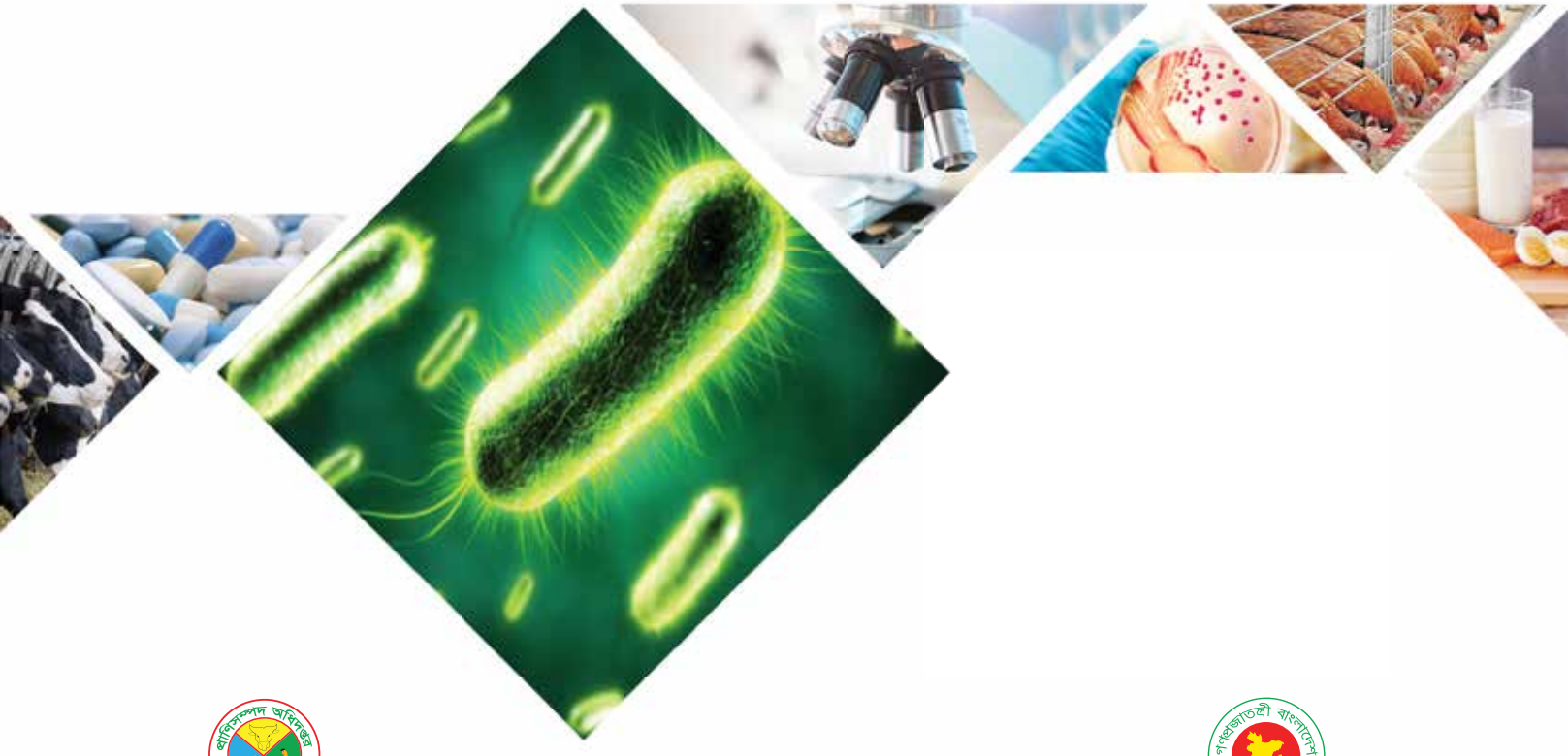
Training Module

on

Anti Microbial Resistance (AMR) and Surveillance

Training Duration-5 Days



Livestock and Dairy Development Project (LDDP)
Department of Livestock Services, Bangladesh
Ministry of Fisheries And Livestock

Training Module

on

Anti Microbial Resistance (AMR) and Surveillance

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Minister
Ministry of Fisheries and Livestock
Government of the People's Republic of Bangladesh

Message

Father of the Nation Bangabandhu Sheikh Mujibur Rahman wanted to build a happy, prosperous and self-reliant Bangladesh, which was achieved through the sacrifices of three million martyrs. Bangladesh is moving forward at an unstoppable pace due to the dedicated efforts of Hon'ble Prime Minister Sheikh Hasina, his worthy successor, who dreamed of a hunger and poverty free Bangladesh. New projects based on modern technology are being taken up in the larger agricultural sector. The Livestock and Dairy Development Project (LDDP) has been taken up with the joint funding of the World Bank and the Government of Bangladesh for the development of the livestock sector with the wistful desire of the Hon'ble Prime Minister.

Currently, about 20 percent of the population is directly and about 50 percent indirectly dependent on livestock. Sustainable development of the livestock sector through the implementation of livestock and dairy development project, creation of new employment in the livestock sector at the grassroots level, will meet the demand for animal protein, milk, eggs and meat. The Livestock and Dairy Development Project will play a pioneering role in this radical change in the livestock sector between 2019-2023 in implementing the election promise of the present government "My Village, My City". Currently, grassroots farmers, entrepreneurs and stakeholders are receiving advice and various subject based services from the livestock sector. In addition to ensuring sustainable development of animal protein, the Department of Livestock Services is working to empower women, create employment, achieve the targets of SDG 2030 and implement the current government's Vision 2041.

There is no substitute for training of Livestock Department officials in skills development, familiarity with modern livestock technology, disease control and sustainable development, and above all in creating new entrepreneurs in the livestock sector. I am very happy to know that a guideline module has been developed for both trainers and trainees to improve the skills of the officers. I hope the module will make efforts more dynamic in new initiatives to train those concerned.

Officers will make themselves efficient and trained by using the module to conduct training activities smoothly. As a result, they will be self-reliant as well as provide services to farmers at the grassroots level and help implement the project objectives. I would like to express my sincere thanks to all those who have contributed their talent, thinking and labor in composing, editing and publishing this timely module.

Allah Hafez

Joy Bangla, Joy Bangabandhu
Bangladesh live forever

S M Rezaul Karim, **MP**

Secretary
Ministry of Fisheries and Livestock
Government of the People's Republic of Bangladesh

Message

Our country, which was formed in the Gangetic floodplain, is the Lilaniketan of ancient civilization and culture. Going through various stages of history, Sonar Bangla, the dream of Father of the Nation Bangabandhu Sheikh Mujibur Rahman, under the visionary and strong leadership of his worthy daughter Hon'ble Prime Minister Sheikh Hasina, is today recognized and inaugurated as a role model for the development of the international arena. Bangladesh has shown immense capability and success in the successful implementation of the MDGs declared by the United Nations. Achieving the Sustainable Development Goals (SDGs) by 2030 and its continuation, gaining the status of a developed country by 2041 and above all, all the activities of the government are being carried out as per the plan to implement Delta Plan-2100. As part of this plan, the government has given utmost importance to infrastructure development as well as human resource development and livestock development. The launch of Bangabandhu Satellite has opened the door to the best use of information and communication technology as well as infrastructural development through the implementation of Padma Multipurpose Bridge, Dhaka Mass Rapid Transit (Metrorail) and extensive development of livestock development under the Ministry of Fisheries and Livestock. .

Under the able leadership of Hon'ble Prime Minister Sheikh Hasina, the Department of Livestock has achieved unimaginable success in the last decade in advancing sustainable development and socio-economic development of Bangladesh. In order to meet the growing demand for animal protein in the country, sustainable breeds of cattle and poultry have been developed and production has been increased through disease control. The Ministry of Fisheries and Livestock has undertaken the World Bank-funded "Livestock and Dairy Development Project" to accelerate the growth of milk, meat and egg production, the main sources of animal protein. Significant activities of the project include increasing the productivity of the livestock sector, formation of producer organizations, building market linkages and accelerating sustainable investment in the development of value chain. In order to successfully implement all these activities, special emphasis has been laid on appropriate training and research. The project has a significant role to play in enhancing the efficiency of farmers through advanced technology innovation and technology demonstrations, market connectivity for milk marketing, product diversification, value addition, entrepreneurship development at the local level, job creation and increasing animal meat production as well as ensuring food security. In view of the Covid-19 situation, under the Emergency Action Plan, a total of 620,000 beneficiary farms in the dairy and poultry sector will be selected and incentives will be provided to the selected farmers.

The role of field level officials is important in managing the multifaceted activities of Livestock and Dairy development projects. An up-to-date training support module has been developed to guide the development of the skills of the officers to deliver extension services in the field, which will be fruitful in the implementation of the project activities. I hope that the module will play an effective role in achieving the desired goal as a thematic training guide designed for the officers of the Department of Livestock Services. I sincerely thank everyone involved in composing, editing and publishing this module.

Allah Hafez

Bangladesh live forever

Rawnak Mahmud

Director General
Department of Livestock Services
Government of the People's Republic of Bangladesh

Message

Under the able leadership of Hon'ble Prime Minister Sheikh Hasina, the Department of Livestock Services has achieved unimaginable success in advancing sustainable development and socio-economic development of Bangladesh. The Department of Livestock Services is always striving for the overall development, expansion and implementation of technology-based activities in the livestock sector, which has immense potential in our agro-based economy. The importance of the livestock sector in nutrition security, poverty alleviation and socio-economic development is immense.

The need for animal protein to build a talented and intelligent nation is undeniable. Vision 2021 has set a target of ensuring nutritious food for 85% of the people of the country. The total annual demand for milk, meat and eggs is increasing with the supply of per capita daily 250 ml of milk, 120 grams of meat and two eggs a week. Milk availability has increased almost 4 times in the last 10 years. The shortage of essential animal protein and nutritious food for the people of the country is now gradually decreasing. The Ministry of Fisheries and Livestock, with the assistance of the World Bank, has adopted the Livestock and Dairy Development Project (LDDP) to bring this deficit to zero quota. A five-day training program has been organized to enhance the skills and capabilities of the DLS officials. I believe that this module, which has been designed for the smooth implementation of this training program, will be helpful in acquiring thematic and knowledge of the people concerned.

I sincerely thank all the officials involved in composing, editing and publishing the module. I hope that the proper use of this module will accelerate the implementation of the project goals.

Allah Hafez

Bangladesh live forever

Dr. Abdul Jabbar Sikder

Project Director
Livestock and Dairy Development Project (LDDP)
Department of Livestock Services
Government of the People's Republic of Bangladesh

Preface

Educated and skilled manpower is the main controller of building a developed nation. And quality education and appropriate training are needed for skill development. Father of the Nation Bangabandhu Sheikh Mujibur Rahman has established an independent and sovereign Bangladesh through continuous movement and struggle to realize his childhood dream of building a golden Bengal. His worthy daughter, Hon'ble Prime Minister Sheikh Hasina, is constantly engaged in the task of building the golden Bengal of Bangabandhu's dream by gaining the status of a developed nation by 2041 and implementing the Delta Plan-2100. The Hon'ble Prime Minister has therefore attached immense importance to the creation of skilled manpower. Bangladesh has already received international acclaim for its successful implementation of the MDGs announced by the United Nations. Following this, Bangladesh is moving fast in proper implementation of SDG-2030.

A review of the evolution of human civilization shows that livestock has played an important role in laying the foundations of civilization and culture. The first human vehicle, starting from the dog, has given more impetus to the instinctive mobility of fast-moving humans. In the age of animal husbandry, the animal kingdom was also the main source of human food. Agricultural civilization has evolved through the different uses of animal energy. In the age of industrial revolution, modern people have given utmost importance to animal food in compiling the list of balanced diet. Animals are therefore considered an important resource in the history of the human race. Animals and plants are interdependent in the food cycle.

The World Bank-funded "Livestock and Dairy Development Project" of the Department of Livestock Services under the Ministry of Fisheries and Livestock has therefore undertaken various activities for the development of the country's livestock. Currently data considered as synonymous with capacity. DLS officers working in the field will developed knowledge on livestock database, provided advice to farmers on livestock development and introduced them to advanced technology through receiving the training. Development skills of extension workers and increase in livestock production and productivity are tied to the same formula. Regular training will enable those concerned to perform their activities more efficiently. Therefore, special emphasis has been laid on the preparation and implementation of training programs. Special importance should be given to the training program in the management of the project so that the trainers can play a helpful role in preparing and teaching the lesson plan and the trainees can take effective lessons.

I would like to express my sincere gratitude and appreciation to all the officers and employees of the project who have involved in carrying out this task.

Allah Hafez

Bangladesh live forever

Md. Abdur Rahim

Acronyms

AMR & Surveillance Related:			
AMR	Anti Microbial Resistance	HP-CIA	Highest Priority Critically Important Antibiotics
AMC	Anti Microbial Consumption	IACG	Interagency Co-ordination Group on AMR
AMU	Anti Microbial Use	JPIAMR	Joint Programming Initiative on Anti Microbial Resistance
ARB	Antibiotic Resistant Bacteria	MMR	Molecular Mechanisms of Resistance
AGISAR	Advisory Group on Integrated Surveillance of Antimicrobial Resistance	MDR	Multiple Drug Resistance
BARA	Bangladesh AMR Response Alliance	NRTI	Nucleotide Reverse Transcriptase Inhibitors
CIA	Critically Important Antimicrobials	RFID	Radio-Frequency Identification
ECDC	European Centre for Disease Control	SRA	Strategic Research Agenda
GLASS	Global AMR Surveillance System	STG	Strategic Treatment Guideline
GARDP	Global Antibiotic Research and Development Partnership	VIA	Veterinary Important Antimicrobial Agents
LDDP Related:			
ABs	Agri Business	MGS	Matching Grant Scheme
BSTI	Bangladesh Standard and Testing Institute	MoU	Memorandum of Understanding
BDRI	Bangladesh Dairy Research Institute	MDG	Millennium Development Goal
BPRI	Bangladesh Poultry Research Institute	NDDB	National Dairy Development Board
CSA	Climatic Smart Agriculture	NLID	National Livestock Identification Database
CTC	Chief Technical Coordinator	NLDP	National Livestock Development Policy
DH	Dairy Hubs	OIE	Office of the International Epizootic
DPP	Development Project Proposal	PMU	Project Management Unit
DDB	Dairy Development Board	PIU	Project Implementation Unit
EMF	Environment Management Framework	PG	Producer Group
FFS	Farmers Field School	PPP	Public Private Partnerships
FOs	Farmer Organizations	PO	Producer Organization
GHG	Green House Gas	PPs	Project Proposals
MVC	Mobile Veterinary Clinic	VMCC	Village Milk Collection Centre
MIS	Management Information System	VC	Value Change
SOPs	Standard Operation Procedures	SORT	Systematic Operations Risk-rating Tool
TMR	Total Mix Ration	TOR	Terms of Reference

Index

Session- 1

Introduction of AMR and Surveillance. How Bacteria Become AMR? Types of commonly used Antibiotics in Livestock and poultry.

Key points of this session:

- *Overview of AMR and Surveillance.*
- *Common causes of AMR.*
- *How Resistance Develop and Spread.*

Overview of AMR and Surveillance:

What is AMR ?

- Antimicrobial resistance (AMR) is the ability of microorganisms that cause disease to withstand attack by antimicrobial medicines.
- The ability of pathogens that works against the antibiotics, is termed Antibiotic Resistance.
- Antimicrobials like antibiotics, antivirals, and others are losing their effectiveness because of antimicrobial resistance.
- Up to half of the antibiotic prescriptions is unnecessary or inappropriate use.

Antimicrobial Resistance (AMR) Antibiotic resistance:

- AMR is a global health crisis
- Major Public health challenges
- Everyone is affected-poor, rich
- Animal
- Human
- Plants
- Environment, etc.

AMR- the Economic Burden:

- Increase in mortality and disability
- Socioeconomic consequences and productivity loss
- Additional burden to health systems
- Cost increase through
  - -Prolonged and costlier treatment
  - -Extra health personal
  - -Extra hospital days
  - -Costly medicine

AMR Monitoring:

- Effective AMR monitoring/surveillance should be coordinated and complementary
- Should cover all components of One Health
  1. Human
  2. Animal
  3. Agriculture (e.g., Environment)

AMR monitoring is a major critical task recommended by Global Action Plan (GAP) through monitoring, we can-

- Collect data on AMR prevalence
  -Antimicrobial use (AMU) and consumption (AMC)
  -Detect emergence of AMR
  -Identify populations at risk
  -Provide guideline for better treatment
  -Inform policy development and assess the impact of interventions

How to Fight /Combat AMR in Livestock Sector?

Uses antibiotics when prescribed by a licensed veterinarian

- Maintain withdrawal period
- Good animal husbandry practices
- Improve sanitation
- Hygiene
- Biosecurity

How Bacteria Become AMR?

- It develops through-
  -Mutation of DNA that makes them resistant to certain drugs.
  -This resistant DNA can transfer horizontally to another bacteria, which increase speed of transformation.

Antibiotic resistance has potentiality to affect all the people at any stage of life, as well as the healthcare, veterinary, and agriculture industries, making it one of the world's most urgent public health problems. Each year only in the U.S., at least 2 million people are infected with antibiotic- resistant bacteria, and at least 23,000 people die as a result.

Common Causes of Antimicrobial Resistance (AMR):

1. Overuse:

Physicians incorrect diagnosis by physicians and prescribing antibiotics for viral infections, 2 or more antibiotics together, unnecessary long courses of antibiotics kill resident bacteria's (Normal flora)

2. Misuse:

Patients/ Animal owners → Incomplite course of antibiotics, Misuse → Leaving 1 or 2 doses → Some bacteria not killed → Resistance developed to future antibiotic treatment.

3. OTC antibiotics:

Antibiotics → Available as OTC medicines → Inappropriate use → Overuse or Misuse →Antibiotic resistance.

4. Healthcare Workers:

Hospital → Healthcare Workers → Not following infection control protocols → Resistance transferred by bacteria swapping genes → Antibiotic Resistance.

5. Hospitalized Patients :
Hospital → Patients with compromised health → Exposed to pathogenic organisms
→ Increased usage of different antibiotics → Rapid development of resistance

6. Animal Feed:
Animal → Feed mixed with antibiotics to prevent infections and to promote growth
→ Resistant organisms in animals → Spread to Human → Antibiotic Resistance.
How Resistance Develops and Spreads:

Fertilizing with "Antibiotic Resistant Manure". Manure encourages the proliferation of antibiotic resistant bacteria when applied as a fertilizer in Agriculture. Fifty parcent of all antibiotics given to humans are prescribed unnecessarily of used inappropriately. Consumption of Livestock and grain treated with multi-use antibiotics significantly increases the spread of resistance in bacteria. More than 50% of all antibiotics are given to livestock, mostly to speed their growth and
prevent on diseases.

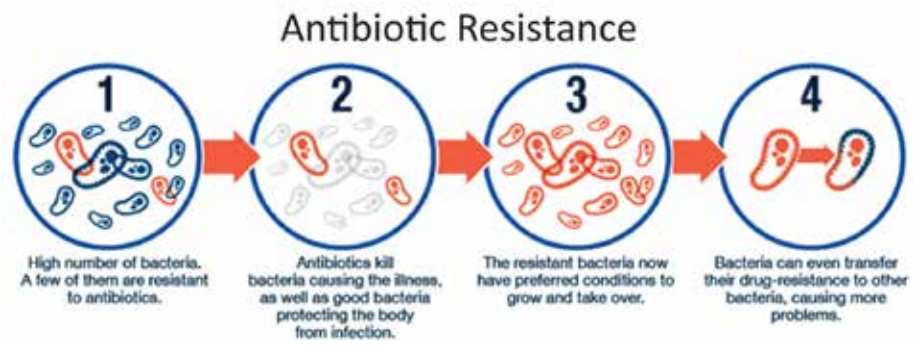
AMR In Fishes:

- Antibiotics, Probiotics & Prebiotics
- Fish for food Production & fish Food
- Waste products used as fertilizer for crops or fish food.
- AMR genes released into water system and sediments.

What is Surveillance?
Surveillance is a process of monitoring disease, involving systematic collection, analysis and interpretation of disease/health-related data needed for the planning, implementation, and evaluation of disease/health related issues

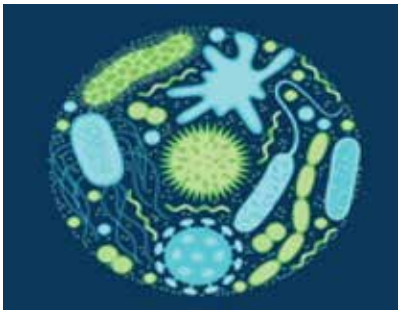
Disease Surveillance
- Information-based activity involving the
- Collection
- Analysis
- Interpretation of large volumes of data originating from a variety of sources (survey)

Informations are used to:
- Intervention
- Evaluation the effectiveness of disease control
- Preventative health measures



Session-2

Groups of Antibiotics & How Antibiotic Works in Living Body



Key points of this session:

- *Types of Antibiotics.*
- *Groups of Antibiotics*
- *How antibiotic works in living body.*

Types of Antibiotics:

There are seven types of antibiotics.

1. Penicillins such as Procaine Penicillin, Benzathine Penicillin, Amoxicillin.
2. Cephalosporins such as Cephalexin (Keflex).
3. Macrolides such as Erythromycin (E-mycyn), Clarithromycin and Azithromycin.
4. Fluroquinolones such as Ciprofloxacin, Levofloxacin and Ofloxacin (Floxin).
5. Sulfonamides such as Cotrimoxazole (Bactrim), Trimethoprim.
6. Tetracyclines such as Sumycin, Panmycin and Doxycycline (Vramycin).
7. Aminoglycosides such as Gentamycin and Tobramycin.

There are three groups of antibiotics in relation to AMR.

1. RESERVE ANTIBIOTICS:

- The reserve group includes the antibiotics that should be considered as the last resort options or tailored to highly specific patients and settings i.e. when other alternatives are inadequate or have already failed (eg. MDR infections).
- These antibiotics have a high resistance potential and their restricted use of these antibiotics is designed to reduce the risk of AMR.
- These antibiotics should be protected by national and international stewardship programmes.
- Not to be used in livestock.
- New antibiotics that enter the marked are to be added to the reserve group.
- 4th-generation Cephalosporins e.g. cefepime.
- 5th-generation Cephalosporins e.g. ceftaroline.
- Polymyxins e.g. colistin, polymyxin B.
- Oxazolidinones e.g. linezolid.
- Monobactam e.g. aztreonam.
- Other fosfomycin (IV) trigecycline daptomycin.

2. WATCH ANTIBIOTICS LIST:

- Antibiotics that are considered to have a significant resistance potential
- Recommended for first and second choice for a limited number of treatments Includes highest priority agents on the list of critically important antimicrobials for human medicine.
- Ureidopenicillin with beta-lactamase inhibitor piperacillin + tazobactam
- 3rd-generation Cephalosporins e.g. cefixime, cefotaxime, ceftriaxone, ceftazidime
- Carbapenems, ertapenem, meropenem, imipenem + cilastatin
- Quinolones/ Fluoroquinolones ciprofloxacin, levofloxacin, moxifloxacin
- VET use: enrofloxacin, marbofloxacin, orbifloxacin
- Macrolides azithromycin, clarithromycin, erythromycin, tylosin (vet)

- Glycopeptides - vancomycin (oral), vancomycin (parental), teicoplanin
- Penems, faropenem

3. ACCESS ANTIBIOTICS:

- Empirical first and second choice for common infectious syndromes
- Should be widely available, at affordable price, in appropriate formulations, and of assured quality
- First choices are narrow spectrum with low AMR risk
- Second choices are generally broader spectrum with higher AMR risk
- Penicillin's- benzathine benzylpenicillin, benzylpenicillin, phenoxymethylpenicillin, procaine benzyl penicillin
- Penicillinase-resistant penicillin's- cloxacillin
- Aminopenicillins amoxicillin, amoxicillin + clavulanic acid, ampicillin
- 1st-generation Cephalosporins- cefazolin, cephalexin, cephradine
- Aminoglycosides amikacin, gentamycin,
- Vet neomycin, streptomycin
- Lincosamides, clindamycin
- Vet lincomycin
- Tetracyclines, doxycycline
- Vet tetracycline, oxytetracycline
- Sulfonamides (vet) sulfadimethoxine, sulfamerazine, sulfamethazine, sulfaquinoxaline, sulfathiazole

Other :

- Chloramphenicol
- Metronidazole
- Spectinomycin (EML only)
- Sulfamethoxazole + trimethoprim

How Antibiotics work:

Bacteria are simple organisms and can be attacked by-

1. Disrupting the cell wall
2. Disrupting DNA/RNA synthesis
3. Protein synthesis and
4. Disrupting folic acid production

Several antibiotics have the same mode of action despite not being related.

General Resistance Information:

In most cases, the drug resistance genes of bacteria are carried on plasmids (specifically, the R or resistance plasmid), which replicate separately from the cell's circular DNA. These plasmids can be passed from cell to cell, allowing for a drug resistance to be passed to a large group of bacteria and to different types of bacteria. These resistance genes are also carried on transposons, which allow for these genes to move from one strand of genetic material to another. Because of this, a cell can receive multiple plasmids with resistance genes and then integrate all of the resistances onto one plasmid. Some R plasmids have as many as 8 drugs resistances on them.

Development of Drug Resistance:

The development of a drug resistance is not orchestrated specifically to counteract a drug. Rather, drug resistances arise because of spontaneous genetic mutations within a gene sequence. By chance, these mutations happen to produce some change in the cell that allows for drug resistance. This mutated

bacteria then has a selective advantage over other non-resistant bacteria. The addition of antibiotics to the environment (the host organism) then selects for the resistant bacteria by killing off all of the non-resistant bacteria. This allows for the resistant cells to grow and divide, creating a large population of resistant bacteria. The larger population then increases the likelihood that plasmid transfer will occur to other, non-resistant bacteria of various strains. This attained resistance has little effects on the host organism until plasmid/resistance transfer to a particularly virulent bacteria occurs. Then, the host is susceptible to infection from this organism without the benefit of treatment with the antibiotic that the bacteria is now resistant to.

Mechanisms of Resistance:
There are several general methods through which a cell can become resistance to an antibiotic. These mechanisms are:

1. Decreased cell permeability to the drug - the cell can change its membrane structure so that the drug cannot enter the cell and perform its function
2. Alter the drug binding/recognition site - by changing the structure of the membrane suface, the site which previously allowed the drug to bind to the cell can no longer do so.
3. Chemical modification of the antibiotic - by cleaving a portion of the molecule or adding a substituent group, the properties of the active molecule in the antibiotic can be altered such that it is rendered harmless to the cell
4. Active transport - the transport of drug molecules out of the cell. In many cases, this is done via a drug/proton antiport system. With this mechanism, H+ ions are pumped into the cell as drug molecules are pumped out.
5. Enzyme or pathway alteration - the cell can change the pathway or enzyme used to carry out a cell process occurs. By doing this, the cell can bypass the enzyme that is affected and cause the drug effects to have no bearing on the functioning of the cell.

Drug Rasistance Transfer:
There are three main ways in which genetic material (in this case, drug resistance genes) can be exchanged between bacteria. They are as follows

1. Conjugation - a direct, cell-to-cell, contact transmission method. The plasmid containing cell generate a small tubule that connects the two cells (the sex pili). This tube then allows for the passage of DNA strands between the two cells

2. Transformation - the absorption of "naked", free-floating DNA by a cell. Upon the death of a bacterial cell the cell components degrade, leaving the DNA and cell materials to disperse in the environment. If a cell with antibiotic resistance dies and breaks down, the resistance gene may be released into the environment and absorbed by another bacterial cell.

3. Transduction - the transportation of genetic material by a bacteriophage. When a bacteriophage infects and replicates in a cell, some new phages may be filled with cellular genetic material, rather than viral genetic material. In some cases, this cellular material is a resistance gene. When the phage containing the resistance gene infects another cell, the infected cell then gains the bacterial resistance.

Economic Impact:
The economic impact is difficult to measure, partly because extensive searching could not turn up exact figures for employees and profits specifically in feed additives.

Session-3

Bacterial Resistance Strategies. The natural resistance and its mechanism for specific bacteria.

Key points of this session:

- *Bacterial Resistance strategy.*
- *Mechanism development of AMR.*
- *Molecular change in structural level of antimicrobials.*

Bacterial Resistance Strategies:

Several different mechanisms may work together

(1) Prevention of the antimicrobial from reaching its target by reducing its ability to penetrate into the cell

(2) Expulsion of the antimicrobial agents from the cell via general or specific efflux pumps

(3) Inactivation of antimicrobial agents via modification or degradation

(4) Modification of the antimicrobial target within the bacteria

The five main mechanisms by which bacteria exhibit resistance to antibiotics are:

1. **Drug inactivation or modification:** for example, enzymatic deactivation of penicillin G in some penicillin-resistant bacteria through the production of β- lactamases. Most commonly, the protective enzymes produced by the bacterial cell will add an acetyl or phosphate group to a specific site on the antibiotic, which will reduce its ability to bind to the bacterial ribosomes and disrupt protein synthesis.

2. **Alteration of target- or binding site:** for example, alteration of PBP—the binding target site of penicillins-in MRSA and other penicillin-resistant bacteria. Another protective mechanism found among bacterial species is ribosomal protection proteins. These proteins protect the bacterial cell from antibiotics that target the cell's ribosomes to inhibit protein synthesis. The mechanism involves the binding of the ribosomal protection proteins to the ribosomes of the bacterial cell, which in turn changes its conformational shape. This allows the ribosomes to continue synthesizing proteins essential to the cell while preventing antibiotics from binding to the ribosome to inhibit protein synthesis.

3. **Alteration of metabolic pathway:** for example, some sulfonamide-resistant bacteria do not require para-aminobenzoic acid (PABA), an important precursor for the synthesis of folic acid and nucleic acids in bacteria inhibited by sulfonamides, instead, like mammalian cells, they turn to using preformed folic acid.

4. **Reduced drug accumulation:** by decreasing drug permeability or increasing active efflux (pumping out) of the drugs across the cell surface These pumps within the cellular membrane of certain bacterial species are used to pump antibiotics out of the cell before they are able to do any damage. They are often activated by a specific substrate associated with an antibiotic. as in fluoroquinolone resistance.

5. **Ribosome splitting and recycling:** for example, drug-mediated stalling of the ribosome by lincomycin and erythromycin unstalled by a heat shock protein found in Listeria monocytogenes, which is a homologue of HflX from other bacteria. Liberation of the ribosome from the drugm

allows further translation and consequent resistance to the drug. A number of mechanisms used by common antibiotics to deal with bacteria and ways by which bacteria become resistant to them.

In gram-negative bacteria, plasmid-mediated resistance genes produce proteins that can bind to DNA gyrase, protecting it from the action of quinolones. Finally, mutations at key sites in DNA gyrase or topoisomerase IV can decrease their binding affinity to quinolones, decreasing the drug's effectiveness.

Viruses:
Specific antiviral drugs are used to treat some viral infections. These drugs prevent viruses from reproducing by inhibiting essential stages of the virus's replication cycle in infected cells. Antivirals are used to treat HIV, hepatitis B, hepatitis C, influenza, herpes viruses including varicella zoster virus, cytomegalovirus and Epstein-Barr virus. With each virus, some strains have become resistant to the administered drugs.

Antiviral drugs typically target key components of viral reproduction; for example, oseltamivir targets influenza neuraminidase, while guanosine analogs inhibit viral DNA polymerase. Resistance to antivirals is thus acquired through mutations in the genes that encode the protein targets of the drugs.

Resistance to HIV antivirals is problematic, and even multi-drug resistant strains have evolved. One source of resistance is that many current HIV drugs, including NRTIs and NNRTIs, target reverse transcriptase; however, HIV-1 reverse transcriptase is highly error prone and thus mutations conferring resistance arise rapidly. Resistant strains of the HIV virus emerge rapidly if only one antiviral drug is used. Using three or more drugs together, termed combination therapy, has helped to control this problem, but new drugs are needed because of the continuing emergence of drug- resistant HIV strains.

Fungi:
Infections by fungi are a cause of high morbidity and mortality in immunocompromised persons, such as those with HIV/AIDS, tuberculosis or receiving chemotherapy. The fungi candida, Cryptococcus neoformans and Aspergillus fumigatus cause most of these infections and antifungal resistance occurs in all of them. Multidrug resistance in fungi is increasing because of the widespread use of antifungal drugs to treat infections in immunocompromised individuals.

Of particular note, Fluconazole-resistant Candida species have been highlighted as a growing problem by the CDC. More than 20 species of Candida can cause Candidiasis infection, the most common of which is Candida albicans. Candida yeasts normally inhabit the skin and mucous membranes without causing infection. However, overgrowth of Candida can lead to Candidiasis. Some Candida strains are becoming resistant to first-line and second- line antifungal agents such as azoles and echinocandins.

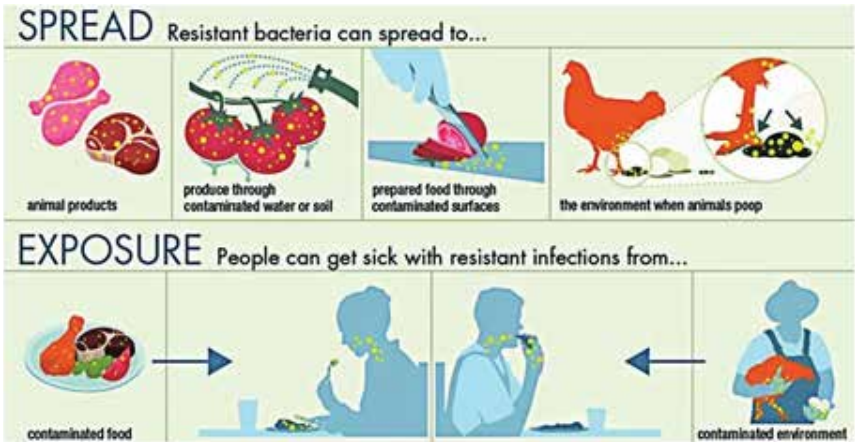
Parasites:
The protozoan parasites that cause the diseases malaria, trypanosomiasis, toxoplasmosis, cryptosporidiosis and leishmaniasis are important human pathogens. Malarial parasites that are resistant to the drugs that are currently available to infections are common and this has led to increased efforts to develop new drugs. Resistance to recently developed drugs such as artemisinin has also been reported. The problem of drug resistance in malaria has driven efforts to develop vaccines.

Trypanosomes are parasitic protozoa that cause African trypanosomiasis and Chagas disease (American trypanosomiasis).There are no vaccines to prevent these infections so drugs such as pentamidine and suramin, benznidazole and nifurtimox are used to treat infections. These drugs are effective but infections caused by resistant parasites have been reported.

Leishmaniasis is caused by protozoa and is an important public health problem worldwide, especially in sub-tropical and tropical countries. Drug resistance has "become a major concern". Tuberculosis????

A table to show the natural resistance and its mechanism for specific bacteria.

Intrinsic resistance against antimicrobial agents	Organism	Mechanism	Ref.
Aminoglycoside	Anaerobic bacteria	No oxidative metabolism for uptake of antibiotic	
Chloramphenicol	Lactobacilli and leu-conostoc	Lack of appropriate cell wall precursor target to allow binding and inhibit cell-wall synthesis	
Metronidazole	Aerobic bacteria	Unable to reduce drug to its active form	
Vancomycin	Gram-negative bac-teria	Outer membrane is impermeable to large glycopeptide	
Vancomycin	Enterococci	Lack of sufficient oxidative metabolism to drive uptake of glycopeptide antibi-otics	
β-lactams	Enterococci	Lack of penicillin binding proteins that effectively bind and are inhibited	
β-lactams	Gram-positive bac-teria	Lack of penicillin- binding proteins that bind and are inhibited by the antibiotic	
β-lactamases	Stenotrophomonas, maltophilia	Antimicrobial agents that production of enzymes (β- lactamases) that destroy imipenem before the drug can reach the PBP targets	
Ampicillin	Klebsiella	Produces β- lactamase that destroy drug before it reaches penicillin-binding protein targets	
Carbenicillin	Pseudomonas aerugi-nosa	Lack of uptake causing a lack of intra-cellular concentration and an inability of antibiotics to achieve effective concentration	



Session-4

Veterinary Drugs Control, Legal and Institutional Issues

Key points of this session:

- *Animal health and veterinary drugs.*
- *Animal production and veterinary drugs.*
- *Public health and veterinary drugs.*

The goals of veterinary drugs control are to be met within a wider framework of international obligations, and a national framework of a country's domestic laws on animal health, animal production and human health. With respect to the drugs themselves, it is widely recognized that the goals of regulating the supply of veterinary drugs are to guarantee their quality, safety and efficacy at the time of their administration to the animal. In a 1993 FAO publication, these terms were defined as follows:

Quality: means that medicines must be manufactured with appropriate quality control procedures, in premises that are inspected and licensed; the ingredients must be of appropriate purity, in the correct proportions and correctly processed; the containers must be robust with secure closures; and the labelling must be accurate and informative.

Safety: is interpreted widely, to include the animal being treated and in-contact animals; the user, including the veterinarian, farmer or pet owner administering the medicine; the consumer of livestock products from treated animals; and the environment.

Efficacy: means that the medicines must be effective against the diseases, in the species of animals, at the dose rate, frequency and duration of treatment, and by the route of administration claimed by the manufacturer.

The legal and institutional issues:
The main legal and institutional issues involved in the regulation of veterinary drugs arise with respect to the following:

i) scope of the law;
ii) definition of the key concepts;
iii) drug administration;
iv) drug registration;
v) classification of veterinary drugs;
vi) manufacture, import, distribution and sale;
vii) enforcement.

Scope of the law: The scope of a veterinary drugs law should –

- Include all drugs (including insecticides) manufactured for administration to animals;
- Not include hazardous drugs and dangerous substances, where these are already covered by their own legislation;
- Not include traditional animal remedies administered in accordance with customary usage;
- Not include aspects of veterinary practice, beyond what is involved in limiting the availability of certain drugs.

Definition of the key concepts: the key concepts are "animal" and "veterinary drug".

" Animal": If the scope of the proposed law is confined to veterinary drugs, then it should be clear that it applies only to drugs intended to be used on animals. Some countries prefer to list those species covered by the definition.

"Animal" means cattle, buffalo, sheep, goat, pig, fish, horse, mule, ass, dog, cat, bird, bee and includes any other animal domesticated or wild whether kept in captivity or wild or under control or otherwise.

"Animal" means any living stage of any member of the animal kingdom except human beings.

" Veterinary drug": The term used varies; sometimes "veterinary medicine" is used, and in some countries (e.g., Sri Lanka) a division is made between "veterinary drugs" and "veterinary biological products". Some definitions are lengthy, but the Zimbabwean definition is concise, clear and comprehensive

"Veterinary medicine" means any substance or mixture of substances which is used, or is manufactured, sold or represented as suitable for use, in

(a) the diagnosis, treatment, mitigation or prevention of disease or abnormal physical or mental state or the symptoms thereof in an animal;

(b) restoring, correcting or modifying any physical, mental or organic function in an animal.
"Medicine" means drugs, vaccines and biological supplies for the prevention, treatment, control or eradication of disease in production animals.

"Manufacture":

- "Manufacture" includes all operations involved in the production, compounding, formulation, filling, packaging, re-packing and labelling of a veterinary drug".
- The point of this extended definition is that any such processing of the drug is also covered by the requirements which apply to its manufacture.
- "Animal" should be widely defined, to include all commercial, domestic and wild animals, fish and insects which are likely to be treated with veterinary drugs;

"Veterinary drug" should also be widely defined, to include:

- drugs, insecticides, vaccines and biological products,
- used or presented as suitable for use,
- to prevent, treat, control or eradicate animal pests or diseases, or
- to be given to animals to establish a veterinary diagnosis, or
- to restore, correct or modify organic functions.

"Manufacture" should be widely defined, to include formulation, filling, packaging, re- packing and labelling of veterinary drugs.

Drug administration:

- International practice varies, between having a single agency to administer all drugs and having separate agencies for animal drugs and human drugs;
- Having a single agency for both offers greater opportunity for rationalising drug administration,

avoiding duplication and gaining practical benefits (e.g., sharing facilities); at the same time, these advantages can largely be achieved under separate agencies, provided that there is good co-operation between them;

- Whether a country adopts a single or a separate agency approach is, therefore, mainly a matter of what fits in best with the existing laws, local institutions and informed choice;
- If a single agency approach is adopted, it is essential that the decisions on veterinary drugs be made by a specialist body, to take into account the special considerations which apply to veterinary drugs.

Drug registration:

The general international practice is for drugs to be registered, before they can be introduced to a country for any manufacture, importation, distribution and sale there. Many countries operate a system for registering the drugs, while others issue product licences. Some countries give priority for registration to products contained in an "Essential List of Veterinary Drugs", that is, a list of the drugs considered to be essential for the country concerned, based on its livestock needs and circumstances. The main steps involved are application for registration; evaluation of the application and decision whether to register the drug; and registration of approved drugs. Before discussing each of those steps, however, it should be emphasised that registration is the critical step in a country's drug administration system, and, with a few exceptions to deal with emergencies or special circumstances, everything important (manufacture, importation, distribution and sale) depends on whether a drug has been registered under the process prescribed by the law or not.

(a) Application for registration:

There is a fairly standard set of details which a person must provide, when applying to register a drug. Apart from details of the applicant (name, address, contact details, etc.), detailed information is commonly required in order to compile a dossier on the drug, in particular –

- Its name, ingredients, manufacture, pharmacology, toxicology;
- Its registration details elsewhere;
- Its purpose, route of administration, dosage, side effects, contra-indications;
- Its container, packaging and labelling.

(b) Evaluation of the application and decision:

Applications for registration are considered by the drug administration agency or its specialist committee on veterinary drugs, and a decision is made on whether trials or testing must be conducted in the country concerned. Because the membership of this body represents the technical and other interest-groups qualified to make decisions on drug registration, it is not necessary for the law to spell out in detail the matters they must address.

The only risks and benefits relevant to that decision are –

(a) Risks to trade and market access for primary produce containing any substance, mixture of substances, or biological compound that forms a part of the trade name product;
(b) risks to agricultural security;
(c) risks to the welfare of animals which result from treatment with or exposure to any substance, mixture of substances, or biological compound that forms a part of the trade name product;
(d) risks to domestic food residue standards;
(e) the benefits of the trade name product and the likely consequences of the public not having access, or having restricted access, to the trade name product, including consideration of whether alternative means of achieving the stated purpose of the trade name product is available.

(c) Registration:

The final step after evaluation is the registration of approved drugs. This is a simple legal step, and some provision may be made for veterinary drugs to be given the prefix "V" (to distinguish them from the same drugs registered for use on humans), and a unique number for each registered drug.

In many countries, all registered drugs are included in a "National Formulary of Veterinary Drugs". The contents of a National Formulary are apparent from Nepal's proposed provision – In compiling the National Formulary, the Veterinary Drugs Advisory Committee shall-

(a) include all veterinary drugs which are registered at the time of its compilation;

(b) designate the veterinary drugs by their generic name or international common denomination;

(c) adopt a recognised form of pharmacological classification;

(d) show for each veterinary drug, such information on its use, including its classification, active ingredients, route of administration, indications, dosage, counter- indications, side effects and other matters, which the Committee considers are important for users to know.

On drug registration –

- registration (or issue of a product licence) is the critical step in veterinary drug administration;
- an Essential List of Veterinary Drugs is a handy tool for prioritising drug registration;
- decisions on applications for drug registration are made by the statutory body of technical experts, based on a dossier providing the necessary information on the drug and its uses;
- registration is a "public good", and does not by itself confer sole rights over the drug on the person registered;
- it is helpful for good drug administration for all registered veterinary drugs to be included in a National Formulary of Veterinary Drugs, together with the basic information on their use;
- in general, only drugs included in the National Formulary should be authorised for manufacture, importation, distribution and sale in a country.

Classification of veterinary drugs:

classification –

- veterinary drugs should be classified at the time of their registration, so as to indicate the restrictions which apply to their prescription and dispensing;
- the different categories provided by the law should reflect the main options for drug availability, having regard to the nature of the drugs and the outlets through which they can be made available;
- veterinary drug classification requires a balance to be struck between the goals of guaranteeing the quality, safety and efficacy of the drugs, and the goal of making the drug available in the country concerned;
- the most suitable body to strike that balance in registering any drug is the technical body, which should make its decisions taking account of the country's particular needs and circumstances.

Manufacture, import, distribution and sale:

These are the main activities which a veterinary drugs control law aims to regulate. The law must ensure that the drugs are of good quality, are safe and efficacious at the time of their manufacture or their importation to the country, while they are being distributed around the country to the drug retailers, and when they are sold to the eventual consumers. If the country concerned has a drug export industry, the law must also concern itself with exportation of veterinary drugs. As discussed above, none of these stages in manufacturing, importing or exporting, distributing or selling a veterinary drug can take place legally unless the drug has already been registered.

(a) Manufacture:
Most countries have a drug manufacturing industry, no matter how small. Often its main purpose is the production of priority drugs for treatment of common human illnesses, so the industry is usually regulated under human drugs legislation. In many cases, drug manufacturers will be producing drugs for both human and animal use – frequently, in fact, the same drugs. As discussed above, there are some special considerations which apply to veterinary drugs. Their packaging and labelling will reflect those differences, but not their manufacture; in each case, whether drugs are for use on animals or on humans, the manufacture concerns are the same – the quality, safety and efficacy of the drug. So, the common practice is to "piggy back" the veterinary drug manufacture requirements onto those for human drugs.

(b) Import :
For many countries, the main sources of their veterinary drugs lie outside the country. Drug importers will normally require an import licence under the country's Customs legislation, but they should also hold a licence under the veterinary drugs law to import the drugs concerned. The same requirement should also apply to the export of veterinary drugs, in countries which have a drug exporting industry.

(1) The import/export of veterinary drugs is only allowed by establishments which have a technical director with skills recognised by the Department [of Livestock Services] and which have been licensed under this section.

(2) Upon an application in writing and payment of the prescribed fee, the Department may grant a licence to an appropriate establishment to import, export or import and export the veterinary drugs specified in the licence.

(3) The period, terms and conditions of an import/export licence under this section shall be specified in the licence.

(4) The form to be used for the application and grant of an import/export licence may be prescribed.

(5) A person travelling with a registered veterinary drug for use on his or her own animal is exempted from the requirement for an import licence under this section.

(6) His Majesty's Government may, by special licence, authorise the import of an unregistered veterinary drug for a special purpose.

(c) Distribution:
Distribution is the stage between a drug's introduction to the country (by manufacture or importation), and its sale to the general public. Distributors buy the drugs from manufacturers or importers, and sell them to the retailers. Some countries require such distributors to be specially licensed, but others feel that the need to regulate such "middle men" can be met by the general requirements for storage and transport of veterinary drugs,and by controls on packaging, labelling and advertising.

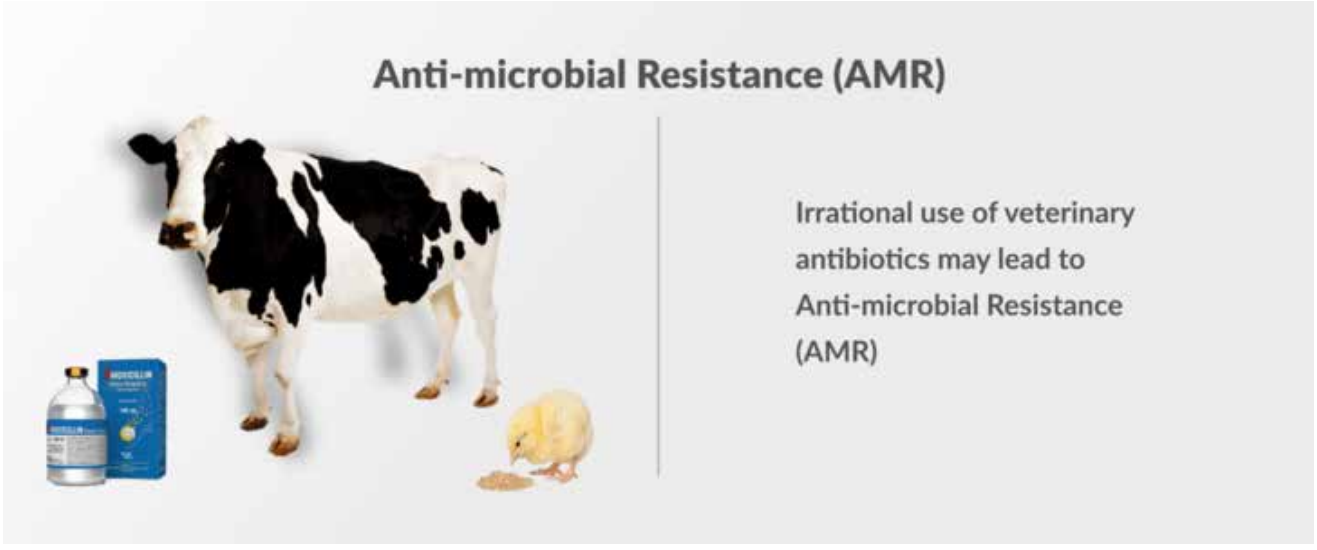
(d) Sale:
Assuming that the quality, safety and efficacy of the drugs have been protected so far by the foregoing controls on manufacture, import and distribution, the final stage of the marketing process at which quality control must be guaranteed is when the drugs are actually sold to the buying public. The main categories proposed above are –

- Prescription only;
- Pharmacy;
- Authorised dealer;
- General sale.

The terms Prescription only, Pharmacy and General sale (sometimes called "over the counter", or "OTC") are understood by the drugs trade, but the veterinary drugs law should specify how a person can qualify as an "Authorised dealer" for the purposes of the law.
What is required is a simple procedure for persons to be authorised in writing by the appropriate official (e.g., the Minister of Agriculture, or Director of Livestock Services) to deal in veterinary drugs which are classified as "Authorised dealer" drugs, on conditions relating to the storage of the drugs, and the giving of necessary advice on their use to the buying public.

e) Enforcement:
on enforcement –

- the enforcement provisions must be realistic, and not impose unnecessary burdens onthe public or the law enforcement authorities;
- sometimes the cancellation of a licence to operate (e.g., to import veterinary drugs) can be a more effective measure than prosecution for an offence;
- some breaches of the requirements are sufficiently serious, however, as to warrant prosecution for an offence.



Session-5

Surveillance, Methods and Common Forms of Surveillance, How we can reduce AMU in animal production

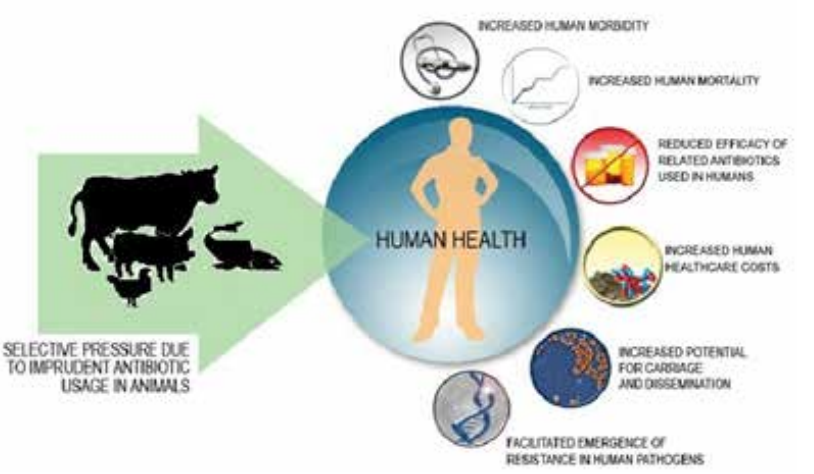
Key points of this session:

- *What is Surveillance?*
- *Methods of surveillance.*
- *Common Forms of Surveillance.*
- *AMu in Animal Production.*

Surveillance is the monitoring of behavior, activities, or information for the purpose oinformation gathering, influencing, managing or directing. This can include observation from a distance by means of electronic equipment, such as closed-circuit television (CCTV), or interception of electronically transmitted information, such as Internet traffic. It can also include simple technical methods, such as human intelligence gathering and postal interception.

Methods:

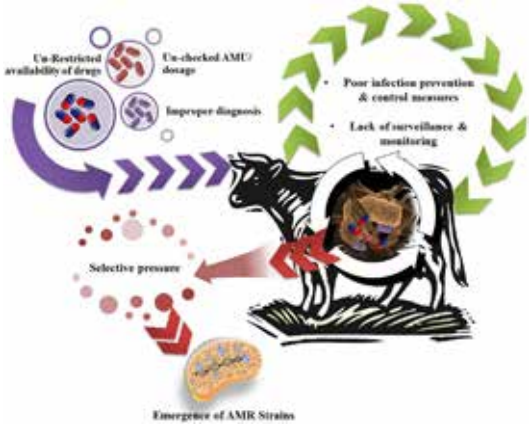
1.1 Computer
1.2 Telephones
1.3 Cameras
1.4 Social network analysis
1.5 Biometric
1.6 Aerial
1.7 Corporate
1.8 Data mining and profiling
1.9 Human operatives
1.10 Satellite imagery
1.11 Identification and credentials
1.12 Wireless Tracking
1.12.1 Mobile phones
1.12.2 RFID tagging
1.12.3 RFID tagging on humans
1.13 Geolocation devices
1.13.1 Global Positioning System
1.14 Devices
1.15 Postal services
1.16 Stakeout
1.17 Internet of things



2. Controversy

2.1 Support
2.2 Opposition
2.2.1 Totalitarianism
2.2.2 Psychological/social effects
2.2.3 Privacy

3 Countersurveillance, inverse surveillance, sousveillance
4 Popular culture
4.1 In literature
4.2 In music
4.3 Onscreen
5 See also
6 References
7 Further reading
7.1 General information
7.2 Historical information
7.3 Legal resources



Common Forms of Surveillance:

- Many security firms offer a variety of investigatory packages and services. However, when stripped down to the essentials, surveillance can be broken down into four distinct disciplines.
- Interviews – For a missing person investigation, interviews are paramount to understanding the subject. Most often family members, co-workers, friends and neighbors will be talked to in an attempt to discover information and insight.
- Physical observation – Physical observation is common for spousal investigations. This type of surveillance involves the actual viewing and following of a subject, and it may include stakeouts, disguises and multiple investigators.
- Electronic – Electronic monitoring is often the tool of choice among investigators. This involves the use of electronic equipment to record and document activity. For instance, wiretaps, radios and televisions are often used.Technical – Technical surveillance can also be referred to as A/V surveillance.

This involves the use of audio and visual equipment, like digital cameras, to record and document investigations.

Any good strategy likely utilizes a variety of these techniques and tools. However, the tools used probably depend on the purpose of the investigation and the methodologies used.

AMU in animal production:

Substantially reduced in high income countries in recent years but AMU will continue to increase in low- and middle-income countries due to the growing demand of animal protein.

How we can reduce AMU in animal production?

By good farm practice

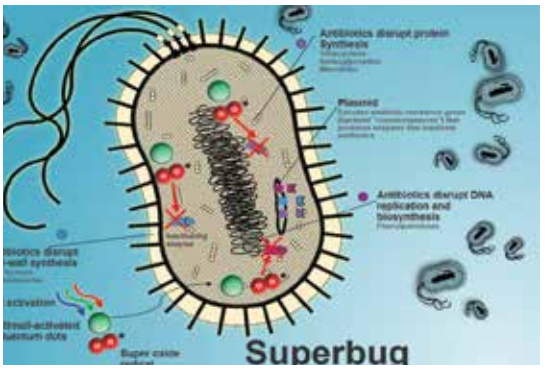
a. Awareness
b. Improving farm biosecurity
c. Using more vaccine to control infectious diseases Advice
    i) Livestock sector (animal and aquaculture) has banned the use of growth promoter
    ii) Tier-wise STG (strategic treatment guideline) for infectious diseases needs
d. As a country, antibiotic production (enforcing good manufacturing practices)

Session-6

Development of Superbug in living body. Disinfectants: A best way to use and link to AMR.

Key points of this session:

- *What is Superbug?*
- *Factor Predisposing for resistance*
- *Superbugs resistance mechanism.*
- *Effect of superbugs in Livestock Value chain.*
- *List of some superbugs.*
- *Guideline of FAO to mitigate AMR.*
- *Disinfectants: A best way to use and link to AMR.*



Superbug:
Antibiotic-resistant bacteria are on the rise, but faster testing and new drugs may help stave off the threat. Credit: Rafe Swan / Getty.
A superbug is usually defined as a microorganism that's resistant to commonly used antibiotics – but not all superbugs are created equal.
The number of different antibiotics to which it can be resistant determines the degree of the superbug. Some are resistant to one or two, but others can be resistant to multiple drugs. So, if a bug is resistant to every available antibiotic, it would be the superbug of all superbugs. Cases where people die from antibiotic-resistant infections are still comparatively rare, particularly in places like Australia, which doesn't allow antibiotics to be sold without a doctor's prescription. But around the world, the number of people dying because their infection can't be treated by any available antibiotic is increasing.

How it develops?
Mutation of DNA that makes them resistant to certain drugs. This resistant DNA (plasmid) can transfer horizontally to another bacteria which increase speed of transformation.

Factor predisposing for resistance:
- Use of under dose or over dose of antibiotics.
- Improper use of antibiotics.
- Use of antibiotics for non-therapeutics purpose.
- Incorrect diagnosis.
- Not completing coarse.

Superbugs resistance mechanism:
- Act like camouflage.
- Act like shield against drugs.
- Act as biological pump (reflux).
- By using own enzyme decreases drug level.

What can we do?
- Wash hand properly.
- Use alcohol-based sanitizer

- Eating healthy diet.
- Healthy lifestyle
- Getting enough exercise
- Good sleeping pattern
- Using antibiotics as directed by physician when needed.
- Completing course of treatment.
- Never use leftover prescription.
- Never share antibiotics with other.
- Maintaining withdrawal period drugs.
- Establishment of slaughter house.
- Strong sanitary practice in slaughter house and all steps of food chain.
- Proper regulation of antibiotic dispensing.
- Proper disposal of hospital waste.
- Proper disposal of pharmaceutical waste.

Where these Superbugs can remain?

- Soil.
- Water.
- Body Surface and
- Most of the hospitals.

Effect of superbugs in Livestock Value chain:

- Treatment will become expensive.
- Prolonged treatment time.
- Decreased animal production.
- Death of animals.
- Superbugs with public health importance can threaten human life.
- Residues of antimicrobials become health hazard to consumer.

List of some superbugs:

- Neisseria gonorrhoea.
- E. coli.
- Enterobacter aeruginosa.
- Staphylococcus aureus.
- Klebsilla.
- Cl. difficile.
- Candida auris (mortality 30-60%).
- Streptococcus pneumoniae.

Superbug scenario in BD :

- E. coli, resistant to ampicillin 94.6%, ciproflxoacillin 65.20%, Amoxiclav 67.10%, cotrimox azole 100%.
- Klebsilla sp. Cotrimoxazol 86.60%
- Pseudomonas sp. Do 87.50%
- Enterococcus sp. Ciprfloxacillin 66%
- Almost same scenario in Africa.

Some important information :

- E. coli is available in jar water and street food in Dhaka.
- At least 22% patient of MDR TB don't take treatment in BD. (report of WHO)
- In Europe 33 thousand people die every year due to AMR (ecdc 2018),

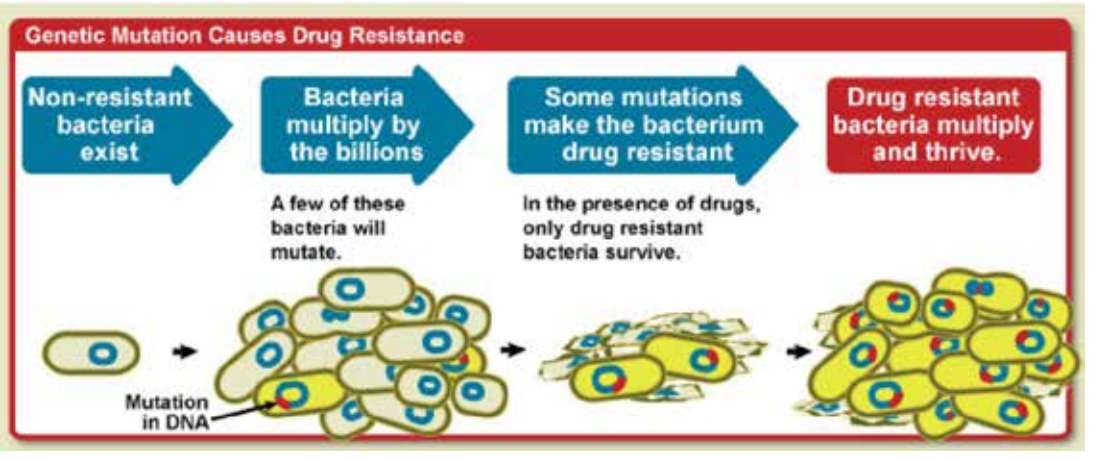
25 thousand died in 2007.
- In India 60 thousand infant are dyeing due to AMR annually.

Strategy OIE:
- Improve awareness and understanding.
- Strengthen of knowledge through surveillance and research.
- Support good governance capacity building.
- Encourage implementation of international standard.

Guideline of FAO to mitigate AMR:
- Strengthening of regulatory capacity of the country.
- Strengthening the capacity of AMR surveillance and monitoring.
- Awareness advocacy regarding food safety.
- Promoting prudent use of antimicrobials.
- Reduction of antimicrobial for vet. Use that are critically important in human use.

Disinfectants: A best way to use and link to AMR.

Sanitizers, disinfectants, and cleaning agents are vital to food hygiene assurance and are a major public health protection measure. Limiting microbial antibiotic resistance is also a global public health priority. Although many factors contribute to the rise in antimicrobial resistance in bacteria infecting humans, antibiotic use in both human clinical settings and for food producing animals are primary contributors. Some concerns have been raised about the possibility of co-selection between food hygiene chemicals and reduced antimicrobial susceptibility. This article reviews available evidence from individual studies purporting to demonstrate a possible risk of antimicrobial resistance development, following biocide usage. Furthermore, the conclusions of several key expert reports and meta-analysis publications were assessed for supportive evidence of a relationship between biocide usage in food production and resistance development. Although many studies report on the isolation of antimicrobial-resistant bacterial strains in food, evidence is lacking on the attribution of this resistance to biocide usage. Also, although a theoretical risk of causality exists, many of the studies performed to demonstrate this are in vitro studies using laboratory-grown or -trained bacterial isolates, challenged with sublethal (below the recommended food industry) disinfectant or sanitizing agent concentrations. The proper use of, and adherence to biocide manufacturer's instruction for use, and the avoidance of biocide active agent dilution (e.g., through biofilm presence) must be ensured in food production environments. It is recommended that in situ studies should be performed to further assess causality, ensured a clear differentiation between interpretation of stable antimicrobial resistance and phenotypic adaptation. Furthermore, authorization of new biocidal active substances should take a scientific and risk-based approach regarding the potential for driving microbial resistance.



Session-7

Livestock Production, it's Availability in Food Security and Nutrition Safety in Bangladesh.

Key points of this session:

- *Functions of Department of Livestock Services (DLS).*
- *Policy of Department of Livestock Services (DLS).*
- *Contribution of Livestock in National economy.*
- *Contribution in compare to Animal protein Demand with livestock and fish.*

Food Security.

Nutrition Functions of Department of Livestock Services (DLS):

1. Implementation of, laws, rules regarding livestock and poultry.
2. Increase of milk, meat and egg production.
3. Control, Treatment and Immunization of livestock and poultry.
4. Extension of Artificial Insemination.
5. Development of nutrition for livestock and poultry.
6. Dairy and poultry Breed up-gradation.
7. Quality control of Livestock product & byproduct and earning foreign currency.
8. Human resource development and poverty reduction.
9. Preservation of genetic value of livestock.
10. Livestock development by improving health management and diseases control.
11. Self-employment generation through improvement of productivity of livestock and poultry
12. Skill development and technology transfer through education, training and research.
13. Women empowerment by employment generation.
14. Ensure safe and healthy animal protein for the people.
15. To protect people from the food risk issues including zoonotic diseases originating from animals

Policy of Department of Livestock Services (DLS):

1. Livestock development by improving health management and diseases control.
2. Livestock and poultry breed development and preservation
3. Self-employment generation through improvement of productivity of livestock and poultry
4. Skill development and technology transfer through education, training and research.
5. Women empowerment by employment generation.
6. Ensure safe and healthy animal protein for the people.
7. To protect people from the food risk issue originating from animals
8. Develop marketing facilities by processing & improving food from animal origin.
9. Quality assurance of food for exporting purpose.
10. Bio security of livestock animal and environmental conservation.
11. Preparation of policies, laws, rules regarding livestock and poultry.
12. Animal welfare activities.

Contribution of Livestock in National Economy

How Much Protein Should You Eat Per Day? (0.8 to 1.3 gram per kg body wt.)

About 20% of the human body is made up of protein.

✓ 56-91 grams per day for the average male.

✓ 46-75 grams per day for the average female.

Sources of Amino Acids:

1. Twenty-two amino acids are naturally incorporated into polypeptides and are called proteinogenic or natural amino acids. Of these, 20 are encoded by the universal genetic code. The remaining 2, selenocysteine and pyrrolysine, are incorporated into proteins by unique synthetic mechanisms.

2. Essential amino acids cannot make by the body. As a result, they must come from food.

Essential Amino Acids	Non Essential Amino Acids
Isoleucine	Alanine
Lysine	Arginine
Histidine	Asparagine
Phenylalanine	Aspartic Acid
Leucine	Cysteine
Tryptophan	Glutamic Acid
Methionine	Glutamine
Threonine	Glycine
Valine	Tyrosine
	Proline
	Serine

CONTRIBUTION IN COMPARE TO FISH PROTEIN DEMAND

ITEMS OF PROTEINS	:	DEMAND	SUPPLY (gm)	PROTEIN DEMAND (gm)	PROTEIN SUPPLY (gm)	TOTAL SUPPLYED PROTEIN (gm)	CONTRIBUTION
Milk (ml/day/head)	:	250	157.97	8.75	5.53	31.10	75%
Meat (gm/day/head)	:	120	121.74	25.20	25.57		
Egg (pcs/year/head)	:	104	15.25	0.04	0.01		
Fish (gm/day/head)	:	60	60	10.20	10.20	10.20	25%
TOTAL						41.30	

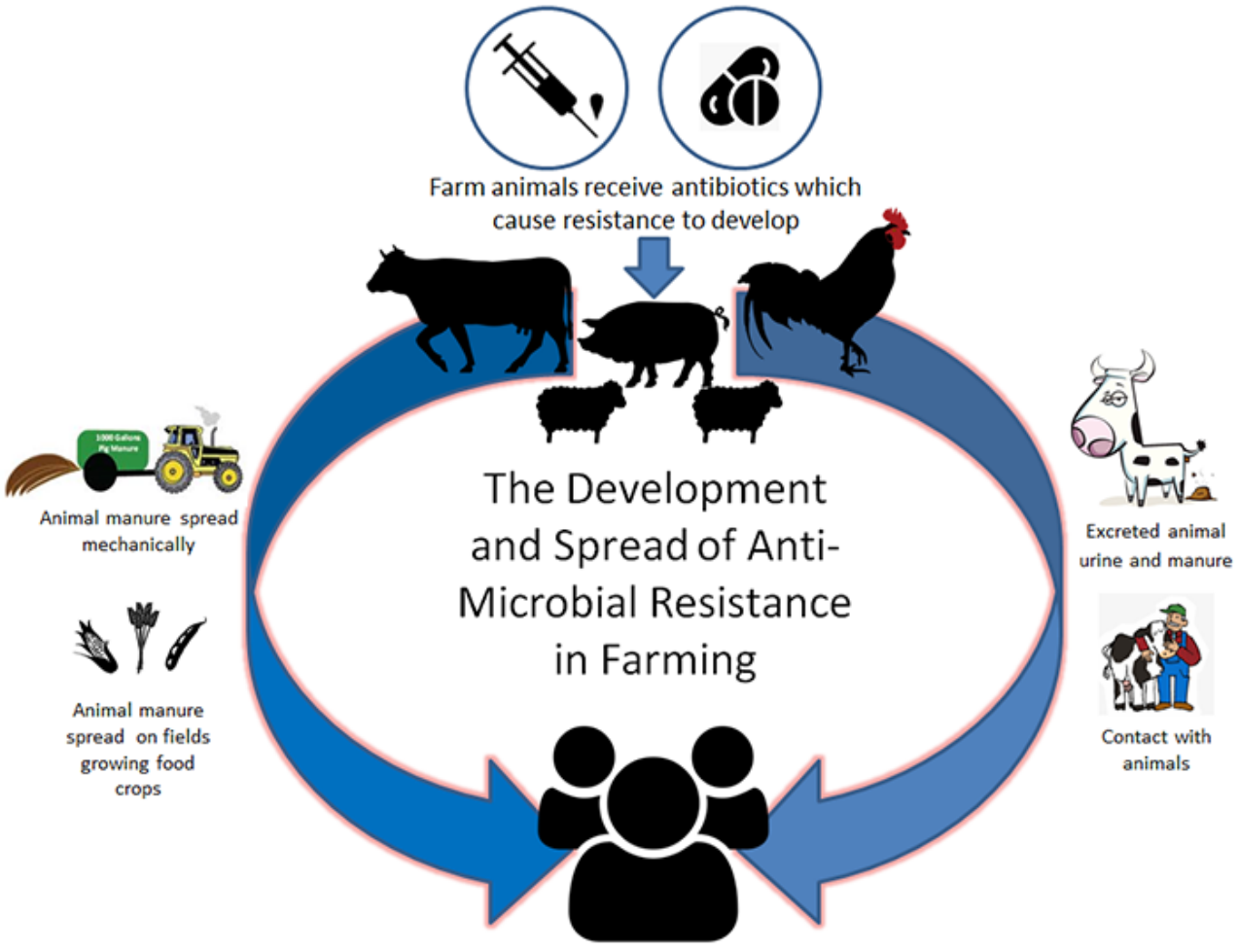
What is Food?

Material, usually of plant or animal origin, that contains or consists of essential body nutrients, such as carbohydrates, fats, proteins, vitamins, or minerals, and is ingested and assimilated by an organism to produce energy, stimulate growth, and maintain life.

Food Security:
The World Food Summit of 1996 defined food security as existing "when all people at all times have access to sufficient, safe, nutritious food to maintain a healthy and active life".
Commonly, the concept of food security is defined as including both physical and economic access to food that meets people's dietary needs as well as their food preferences.

Food Safety:
Food safety is a scientific discipline describing handling, preparation, and storage of food in ways that prevent foodborne diseases. This includes a number of routine works that should be followed to avoid potentially severe health hazards.

Nutrition:
The process by which a living organism assimilates food and uses it for growth, liberation of energy, and replacement of tissues; its successive stages include digestion, absorption, assimilation, and excretion. The science or study that deals with food and nourishment, especially in humans.



Session-8

Advocacy, Professional Public Communication and Education on AMR.

Key points of this session:

- *What is advocacy?*
- *Advocacy on AMR.*
- *Significance of Advocacy.*
- *Types of Activities in Advocacy.*
- *Toolkit on Advocacy for AMR Regulations.*
- *Advocacy activities generally try to achieve one or more.*

Advocacy:

• Advocacy is a systematic and strategic approach to influencing governmental and institutional policy and practice change - an activity (or series of activities) targeting governmental representatives towards implementing change in the law and regulations of laws.

Advocacy on AMR:

• a systematic and strategic approach to influencing governmental and institutional policy and practice change towards implementing change in the law and regulations of laws about AMR.

Significance of Advocacy:

• Advocating for change of a national law or local regulation is one of the possible approaches towards implementing change in the communities.
• As an emerging issue globally.
• Antimicrobial (incl. Antibiotic) Drug Resistance needs to be tackled on all fronts.

Types of Activities in Advocacy:

Different kinds of activities conducted by an organization or group of individuals

These could include:

- Press conference
- Strike March
- Court cases
- Poster campaign
- Round table
- Pamphlets
- Survey/Opinion Poll
- Theatre Workshop
- TV or radio drama
- Letter writing
- Petitions
- Public forum
- Conference

Policy research:

- Exposure tour
- Website Networking
- Newsletter
- Lobbying, Flyers
- Coalitions or networks,

Toolkit on Advocacy for AMR Regulations:

Five key questions to ask when thinking about advocacy and developing an advocacy strategy

A. What do you want to change?
B. How will change happen?
C. What is your core argument/message?
D. How are you going to win the argument or deliver the message?
E. How will you know if you are making progress or have succeeded?

A. What do you want to change?

- Being clear about what you want to change is critical to advocacy.
- Advocacy can be time consuming
- Make a long-term commitment in order to see the change
- Thus, don't spread your attention too thinly.
- If working with others on problem analysis, use the problem tree tool
- Understanding who will be involved in change

First list all of the potential Stakeholders

- National Government
- Local Government
- Business and the private sector
- Non-governmental (Civil society) organizations (NGOs)
- Professional bodies such as physicians, veterinarians, etc.
- Religious or community leaders
- Media
- International donors and organizations

Advocacy activities generally try to achieve one or more of the following:

- Develop and evidence your argument(or core message) e.g. research, networking, policy analysis, attending conferences, engaging with experts and academics
- Putting your case to decision makers directly e.g. lobbying, meetings, events and roundtables.
- Build pressure or momentum for change e.g. alliance or coalition building, media briefings, marches.

Session-9

Sustainable Development Goal (SDG) Relation to AMR.

Key points of this session:

- *SDG and its Goal.*
- *Why is SDG important?*
- *What are SDGs targets?*

MoFL-SDGs Implementation Progress

SDG : The 2030 Agenda for Development

- The SDGs are a bold, universal agreement to end poverty in all its dimensions and craft an equal, just and secure world -for people, for prosperity and for the planet by 2030.
- SDGs were adopted by 193 member states at the UN General Assembly Summit in September 2015.
- It came into effect in January 1, 2016.
- There are 17 Goals, 169 targets and 232 indicators (244 indicators?)
- SDG Theme: Leaving No One Behind (eg. Women, youth, children, elderly people, tribal, autistic etc.)

The SDGs are …

- A set of 17 goals for the world's future, through 2030
- Backed up by a set of 169 detailed Targets
- Emerged from the most inclusive process in the UN's history, with the involvement of approximately 8.5 million people.
- Negotiated over a two-year period at the United Nations (March 2013 to August 2015)
- 136 Heads of State or Government was present (25th September 2015).

The 17 sustainable development goals (SDGs) to transform our world:

GOAL 1: No Poverty
GOAL 2: Zero Hunger
GOAL 3: Good Health and Well-being
GOAL 4: Quality Education
GOAL 5: Gender Equality
GOAL 6: Clean Water and Sanitation
GOAL 7: Affordable and Clean Energy
GOAL 8: Decent Work and Economic Growth
GOAL 9: Industry, Innovation and Infrastructure
GOAL 10: Reduced Inequality
GOAL 11: Sustainable Cities and Communities
GOAL 12: Responsible Consumption and Production
GOAL 13: Climate Action
GOAL 14: Life Below Water
GOAL 15: Life on Land
GOAL 16: Peace and Justice Strong Institutions
GOAL 17: Partnerships to achieve the Goal

Why is SDG important?

The SDGs are extremely important because they are a powerful advocacy platform to support the implementation and the monitoring of the UN Convention on the Rights of Persons with Disabilities.

What are SDGs targets?

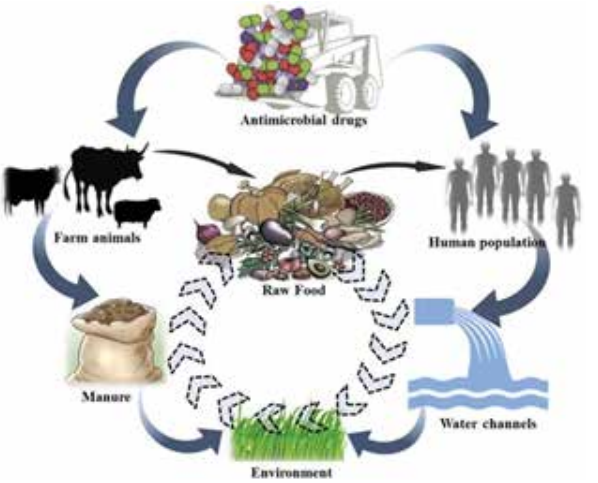
targets. 1.1. By 2030, eradicate extreme poverty for all people everywhere, currently measured as people living on less than $1.25 a day. 1.2. By 2030, reduce at least by half the proportion of men, women and children of all ages living in poverty in all its dimensions according to national definitions.

Session-10

Livestock Industry Perspectives and implementations on AMR.

Key points of this session:

- *The legal and institutional issues on AMR*
- *The goals of veterinary drugs control*
- *Definition of the key concepts*
- *Scope of the law*
- *Definition of the key concepts*
- *Drug administration*
- *Drug registration*
- *Classification of veterinary drugs*
- *Manufacture, import, distribution and sale*



The legal and institutional issues on AMR

Quality, safety and efficacy (or effectiveness) – these are the three main concerns of veterinary drugs control. Among the risks for a country of the ineffective regulation of its drug supply are:

- Introduction of drugs of unknown quality – in some cases counterfeit, unlabeled or expired drugs, drugs withdrawn from sale in other countries and dumped or drugs produced cheaply without the necessary regard for quality;
- Inadequate labelling of drugs (a particular problem where many people are illiterate), so that users are not properly informed on dosage, expiry date, dangers and precautions;
- Breach of special requirements (e.g., refrigeration) for storage of certain drugs;
- Failure to observe withholding periods, that is, the period after an animal has been treated with a drug, during which its products (meat, milk, eggs) must be withheld from the market;
- Use of drugs after their expiry (or "use by") date;
- Drug residue build-ups in livestock products – a threat to local consumers and to export markets.

The goals of veterinary drugs control:

- Animal health and veterinary drugs.
- Animal production and veterinary drugs.
- Public health and veterinary drugs.

The goals of veterinary drugs control are to be met within a wider framework of international obligations, and a national framework of a country's domestic laws on animal health, animal production and human health. With respect to the drugs themselves, it is widely recognised that the goals of regulating the supply of veterinary drugs are to guarantee their quality, safety and efficacy at the time of their administration to the animal. In a 1993 FAO publication, these terms were defined as follows:

- Quality means that medicines must be manufactured with appropriate quality control procedures, in premises that are inspected and licensed; the ingredients must be of appropriate purity, in the correct proportions and correctly processed;the containers must be robust with secure closures; and the labelling must be accurate and informative.

- Safety is interpreted widely, to include the animal being treated and in-contact animals; the user, including the veterinarian, farmer or pet owner administering the medicine; the consumer of

livestock products from treated animals; and the environment.

- Efficacy means that the medicines must be effective against the diseases, in the species of animals, at the dose rate, frequency and duration of treatment, and by the route of administration claimed by the manufacturer.

The legal and institutional issues:
The main legal and institutional issues involved in the regulation of veterinary drugs arise with respect to the following:

i) scope of the law;
ii) definition of the key concepts;
iii) drug administration;
iv) drug registration;
v) classification of veterinary drugs;
vi) manufacture, import, distribution and sale;
vii) enforcement.

Scope of the law :
the scope of a veterinary drugs law should –
- Include all drugs (including insecticides) manufactured for administration to animals;
- Not include hazardous drugs and harmful substances, where these are already covered by their own legislation;
- Not include traditional animal remedies administered in accordance with customary usage;
- Not include aspects of veterinary practice, beyond what is involved in limiting the availability of certain drugs.

Definition of the key concepts:
the key concepts are "animal" and "veterinary drug".
- " Animal": If the scope of the proposed law is confined to veterinary drugs, then it should be clear that it applies only to drugs intended to be used on animals.3 Some countries prefer to list those species covered by the definition.
- "Animal" means cattle, buffalo, sheep, goat, pig, fish, horse, mule, ass, dog, cat, bird, bee and includes any other animal domesticated or wild whether kept in captivity or wild or under control or otherwise.
- "Animal" means any living stage of any member of the animal kingdom except human beings.
- " Veterinary drug": The term used varies; sometimes "veterinary medicine" is used, and in some countries (e.g., Sri Lanka) a division is made between "veterinary drugs" and "veterinary biological products". Some definitions are lengthy, but the Zimbabwean definition is concise, clear and comprehensive –
- "veterinary medicine" means any substance or mixture of substances which is used, or is manufactured, sold or represented as suitable for use, in –

(a) the diagnosis, treatment, mitigation or prevention of disease or abnormal physical or mental state or the symptoms thereof in an animal; or

(b) restoring, correcting or modifying any physical, mental or organic function in an animal.

- "Medicine" means drugs, vaccines and biological supplies for the prevention, treatment, control or eradication of disease in production animals.

Manufacture:

- "Manufacture" includes all operations involved in the production, compounding, formulation, filling, packaging, re-packing and labelling of a veterinary drug".
- The point of this extended definition is that any such processing of the drug is also covered by the requirements which apply to its manufacture.
- "Animal" should be widely defined, to include all commercial, domestic and wild animals, fish and insects which are likely to be treated with veterinary drugs;
- "Veterinary drug" should also be widely defined, to include:
- Drugs, insecticides, vaccines and biological products,
- Used or presented as suitable for use,
- To prevent, treat, control or eradicate animal pests or diseases, or
- To be given to animals to establish a veterinary diagnosis, or
- To restore, correct or modify organic functions.
- "Manufacture" should be widely defined, to include formulation, filling, packaging, re-packing and labelling of veterinary drugs.

Drug administration:

On drug administration

- International practice varies, between having a single agency to administer all drugs and having separate agencies for animal drugs and human drugs;
- Having a single agency for both offers greater opportunity for rationalising drug administration, avoiding duplication and gaining practical benefits (e.g., sharing facilities); at the same time, these advantages can largely be achieved under separate agencies, provided that there is good co-operation between them.
- Whether a country adopts a single or a separate agency approach is, therefore, mainly a matter of what fits in best with the existing laws, local institutions and informed choice;
- If a single agency approach is adopted, it is essential that the decisions on veterinary drugs be made by a specialist body, to take into account the special considerations which apply to veterinary drugs.

Drug registration:

The general international practice is for drugs to be registered, before they can be introduced to a country for any manufacture, importation, distribution and sale there. Many countries operate a system for registering the drugs, while others issue product licences. Some countries give priority for registration to products contained in an "Essential List of Veterinary Drugs", that is, a list of the drugs considered to be essential for the country concerned, based on its livestock needs and circumstances. The main steps involved are application for registration; evaluation of the application and decision whether to register the drug; and registration of approved drugs. Before discussing each of those steps, however, it should be emphasised that registration is the critical step in a country's drug administration system, and, with a few exceptions to deal with emergencies or special circumstances, everything important (manufacture, importation, distribution and sale) depends on whether a drug has been registered under the process prescribed by the law or not.

(a) Application for registration:

There is a fairly standard set of details which a person must provide, when applying to register a drug. Apart from details of the applicant (name, address, contact details, etc.), detailed information is

commonly required in order to compile a dossier on the drug, in particular –

- Its name, ingredients, manufacture, pharmacology, toxicology;
- Its registration details elsewhere;
- Its purpose, route of administration, dosage, side effects, contra-indications;
- Its container, packaging and labelling.

Applications for registration are considered by the drug administration agency or its specialist committee on veterinary drugs, and a decision is made on whether trials or testing must be conducted in the country concerned. Because the membership of this body represents the technical and other interest-groups qualified to make decisions on drug registration, it is not necessary for the law to spell out in detail the matters they must address.

The only risks and benefits relevant to [that decision] are –

(a) risks to trade and market access for primary produce containing any substance, mixture of substances, or biological compound that forms a part of the trade name product;

(b) risks to agricultural security;

(c) risks to the welfare of animals which result from treatment with or exposure to any substance, mixture of substances, or biological compound that forms a part of the trade name product;

(d) risks to domestic food residue standards;

(e) the benefits of the trade name product and the likely consequences of the public not having access, or having restricted access, to the trade name product, including consideration of whether alternative means of achieving the stated purpose of the trade

name product is available.

(c) Registration

The final step after evaluation is the registration of approved drugs. This is a simple legal step, and some provision may be made for veterinary drugs to be given the prefix "V" (to distinguish them from the same drugs registered for use on humans), and a unique number for each registered drug.
In many countries, all registered drugs are included in a "National Formulary of Veterinary Drugs". The contents of a National Formulary are apparent from Nepal's proposed provision –
In compiling the National Formulary, the Veterinary Drugs Advisory Committee shall
–

(a) include all veterinary drugs which are registered at the time of its compilation;

(b) designate the veterinary drugs by their generic name or international common denomination;

(c) adopt a recognised form of pharmacological classification;

(d) show, for each veterinary drug, such information on its use, including its classification, active ingredients, route of administration, indications, dosage, counter- indications, side effects and other matters, which the Committee considers are important for users to know.

Classification of veterinary drugs:

- veterinary drugs should be classified at the time of their registration, so as to indicate the restrictions which apply to their prescription and dispensing;
- the different categories provided by the law should reflect the main options for drug availability, having regard to the nature of the drugs and the outlets through which they can be made available;
- veterinary drug classification requires a balance to be struck between the goals of guaranteeing

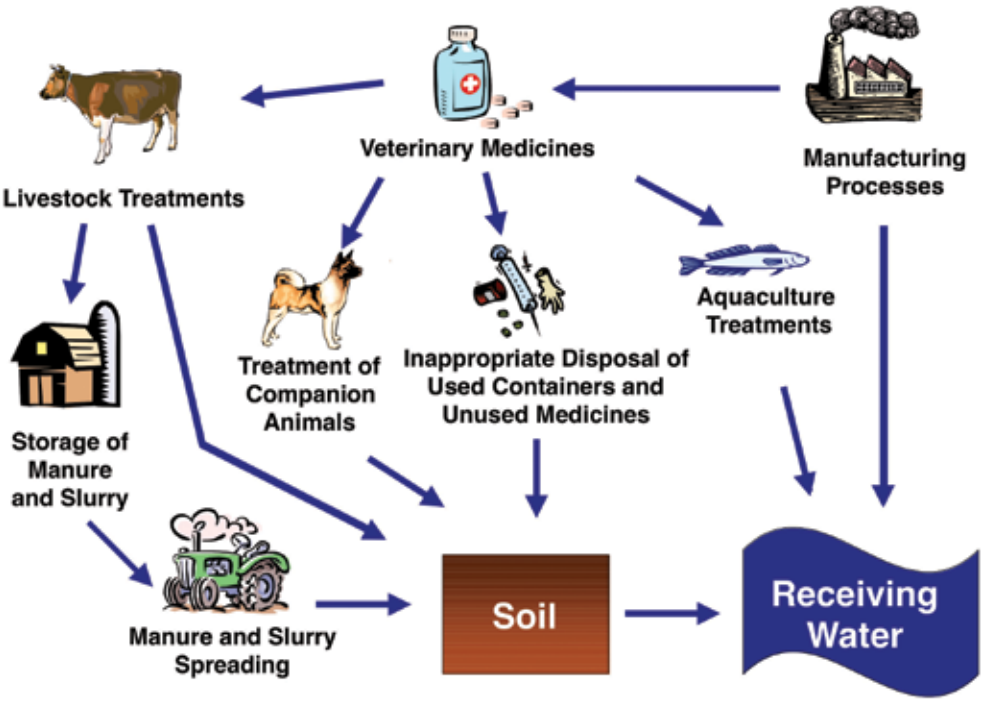
the quality, safety and efficacy of the drugs, and the goal of making the drug available in the country concerned;

- the most suitable body to strike that balance in registering any drug is the technical body, which should make its decisions taking account of the country's particular needs and circumstances.

Manufacture, import, distribution and sale:

These are the main activities which a veterinary drugs control law aims to regulate. The law must ensure that the drugs are of good quality, are safe and efficacious at the time of their manufacture or their importation to the country, while they are being distributed around the country to the drug retailers, and when they are sold to the eventual consumers. If the country concerned has a drug export industry, the law must also concern itself with exportation of veterinary drugs. As discussed above, none of these stages in manufacturing, importing or exporting, distributing or selling a veterinary drug can take place legally unless the drug has already been registered.

Veterinary Medicines in the Environment



Session-11

AMR in Veterinary Services and Responsible of use of Antibiotics.

Key points of this session:

- *Responsible use of antibiotics.*
- *What is antimicrobial?*
- *AMR in Veterinary Service.*

Responsible use of antibiotics

AMR: How do we define?

"Antimicrobial resistance (AMR) is the ability of a microorganism (like bacteria, viruses, and some parasites) to stop an antimicrobial (such as antibiotics, antivirals and anti-malarials) from working against it. As a result, standard treatments become ineffective, infections persist and may spread to others" (WHO).

What is antimicrobial?

Antimicrobial is a general term that refers to a group of drugs that includes:

Antibiotics,
Antifungals,
Antiprotozoals, and
Antivirals

Bangladesh AMR Response Alliance (BARA):

- Community of practice committed to responsible use of antimicrobials
- Animal and human health professionals
  - Clinicians and surgeons
  - Pharmacologists
  - Microbiologists
- Independent of employers/sectors/affiliations
- Willing to make recommendations on usage right now based on currently available data
- Kothakom, kajbeshi

WHO Aware classification of antibiotics

Key ACCESS

- Tend to be narrow spectrum
- Not associated with driving resistance
- Frequently recommended as 1st or 2nd empirical choice

WATCH

- Broader spectrum
- Can drive resistance
- Still necessary as 1st or 2nd empirical choice for a limited number of infections

RESERVE
- Last resort!
- Only used for confirmed multi-drug resistant infections
- Cipro, colistin and fosfomycin: yesterday's solution = today's problem

Ciprofloxacin (WATCH list):
- Broad spectrum fluoroquinolone antibiotic providing coverage against both gram-negative and gram-positive aerobic bacteria
- Excellent safety profile in adults and wide therapeutic index
- First choice antibiotic for a number of high consequence infections in humans, particularly gram-negative
- Apparently now the most common antibiotic for disease prevention/growth promotion on poultry farms

- **Colistin (RESERVE list):**
- Historically used as a growth promoter/disease prevention in livestock
- Has become a last resort antibiotic for multi-drug resistant bacteria in humans
- Now banned for use in livestock in many countries
- Use in veterinary medicine no longer justified

Responsible use of antibiotic:
1. Use as narrow spectrum as possible against the pathogen causing the infection.
2. Avoid using WATCH antibiotics as much as possible.
3. Don't use RESERVE antibiotics!

Colibacillosis
- Etiology
- Bacterium Escherichia coli, a gram-negative, motile, coliform in the family Enterobacteriaceae
- Epidemiology
- Ubiquitous organism, high numbers in poultry house environment through fecal contamination
- Environmental factors (humidity, poor air quality, high ammonia and dust) and the stress of other diseases (IBV, NDV, Mycoplasma) are major predisposing factors for systemic infection

Colibacillosis
- Clinical signs and lesions
- Variable depending upon age, systems or organs involved and concurrent infection
- Respiratory–airsacculitis along with mycoplasma or virus infection.
- Omphalitis (embryo and early chick mortality) - egg transmitted due to penetration from contact with contaminated environment (dirty nest, floor eggs, egg washing, sweating after refrigeration, and dirty hatching equipment). This is a major chick quality problem.
- Coligranuloma–nodular lesions liver and intestine and uterus in layers, enlarged congested liver
- Treatment strategy
- Control predisposing infections or environmental factors
- Management procedures

- Good management and sanitation practices are the best way to avoid colibacil losis
- Obtain new birds from well managed breeding flocks and hatcheries
- Reduce all stress factors (ventilation, density, dust and ammonia), and other disease agents

Medications

- Narrow spectrum is preferred to avoid unnecessary resistance pressure on gram-positive organisms
- Neomycin 1g/L drinking water for 5 days, mixed with acidifier 1 ml/3 L drinking water

OR

- Tetracycline 100g/ton feed or chlortetracycline 500mg/gal water for 5 days
- NOT fluoroquinolones!

AMR in Veterinary Service:

Veterinarians are part of the solution; but they must be well trained and well supervised by the statutory veterinary bodies created by law

Antimicrobial resistance in animal and public health.

Antimicrobial agents are medicines used to treat infections, particularly those of bacterial origin. These medicines are essential to protect human and animal health, as well as animal welfare. Excessive or inappropriate use can lead to the emergence of resistant bacteria which do not respond to antibiotic treatment, as seen in recent decades. This phenomenon, called antimicrobial resistance, which poses a threat to disease control throughout the world, is a primary concern for human and animal health.

It is by ensuring the responsible and prudent use of these invaluable medicines in animals, in accordance with the intergovernmental standards of the OIE that we will be able to safeguard their efficacy.

To achieve this, coordinated action between the human and animal health and environmental sectors is crucial.

Veterinarians are part of the solution; but they must be well trained and well supervised by the statutory veterinary bodies created by law.

Antimicrobial agents are a global public good.

We have a role to play in the fight against antimicrobial resistance and, in so doing, can protect the efficacy of these vital treatments and, by the same token

Session-12

Consequences of AMR on Livestock and Poultry Industry in relation to Animal Feed Act and Rules

Key points of this session:

- *Livestock & Poultry Sector at a glance.*
- *The fish and Animal Feed act, 2010 & Animal feed rules, 2013.*
- *Consequences of AMR.*

Livestock Sector at a glance:

- Contribution of Livestock to National GDP: 1.47
- GDP Growth rate of Livestock: 3.47%
- Share of Livestock in Agricultural GDP: 13.46%
- Annual meat production: 7.51 million tons
- Annual milk production: 9.92 million tons
- Annual egg production: 17,110 million
- No. of registered Grand Parent Farms in Operation: 16
- Production of Parent Stock per Week: 70,000-80,000
- No. of Listed Breeder Farms: 140

Poultry Sector at a glance:

- Production of Broiler DOC: 15 Million/Week
- No. Registered of Feed Mills: 209
- Production of Industrial Feeds: 4.45 Million Tons
- No. of Commercial Farms: 1,40,000-1,50,000
- Production of Commercial Layer Eggs: 20 Million/Day
- Per Capita Broiler Meat Consumption is: 5.50 Kg (approx.)
- Share of Broiler Meat out of Total Meat Consumption: 54%
- In 2021 Per Capita Poultry Meat Consumption is expected to be reached: 8.42 Kg
- In 2021 the Expected Contribution of Poultry Meat could Increase to: 78%
- In 2021 Total Energy Intake from Animal Sources could improve up to: 7.5%

Consequences of AMR

- A report from the European Union (EU) indicated that about twenty five thousand patient died each year from infections by drug resistant bacteria, which is equivalent to €1.5 billion of hospital cost.
- This report indicates the seriousness of the problem throughout the globe. In case of Bangladesh, these Antimicrobial Resistance (AMR) effects are more alarming due to serious misuse of antibiotics in humans as well as in animals.
- As a consequence of public health safety concern, several countries including
- Bangladesh have banned or restricted the use of human health related antibiotics in food animal production.
- Presence of antibiotic in raw milk: A nationwide debate

The Fish and Animal Feed Act, 2010
Animal Feed Rules, 2013

মৎস্যখাদ্য ও পশুখাদ্য আইন, ২০১০

(২০১০ সনের ২ নং আইন)

[জানুয়ারি ২৮, ২০১০]

সংক্ষিপ্ত শিরোনাম ও প্রবর্তন

১। (১) এই আইন মৎস্যখাদ্য ও পশুখাদ্য আইন, ২০১০ নামে অভিহিত হইবে।

(২) ইহা অবিলম্বে কার্যকর হইবে।

সংজ্ঞা

২। বিষয় বা প্রসঙ্গের পরিপন্থী কোন কিছু না থাকিলে, এই আইনে-

(১) 'অধিদপ্তর' অর্থ মৎস্যখাদ্য সম্পর্কিত বিষয়ে মৎস্য অধিদপ্তর এবং পশুখাদ্য সম্পর্কিত বিষয়ে পশুসম্পদ অধিদপ্তর;

লাইসেন্স ব্যতীত মৎসখাদ্য ও পশুখাদ্য উৎপাদন, প্রক্রিয়াজাতকরণ ইত্যাদি নিষিদ্ধ সংক্রান্ত বিধি-নিষেধ

৪। এই আইন কার্যকর হইবার পর কোন ব্যক্তি ধারা ৬ এর অধীন লাইসেন্স গ্রহণ ব্যতীত মৎস্যখাদ্য ও পশুখাদ্য উৎপাদন, প্রক্রিয়াজাতকরণ, আমদানি, রপ্তানি, বিপণন, বিক্রয়, বিতরণ এবং আনুষঙ্গিক কার্যাবলী সম্পাদন করিতে পারিবেন না।

লাইসেন্সিং কর্তৃপক্ষ

৫। এই আইনের অধীন মৎস্যখাদ্য সংক্রান্ত বিষয়ে মৎস্য অধিদপ্তরের মহাপরিচালক বা মহাপরিচালক কর্তৃক এতদুদ্দেশ্যে ক্ষমতাপ্রাপ্ত অধিদপ্তরের প্রথম শ্রেণীর কোন কর্মকর্তা এবং পশুখাদ্য সংক্রান্ত বিষয়ে পশুসম্পদ অধিদপ্তরের মহাপরিচালক বা মহাপরিচালক কর্তৃক এতদুদ্দেশ্যে ক্ষমতাপ্রাপ্ত অধিদপ্তরের প্রথম শ্রেণীর কোন কর্মকর্তা লাইসেন্সিং কর্তৃপক্ষ হিসাবে গণ্য হইবেন।

আদর্শমাত্রা

১০। (১) সরকার বাণিজ্যিকভিত্তিতে উৎপাদিতব্য মৎস্যখাদ্য ও পশুখাদ্যের গুণগতমান বজায় রাখিবার লক্ষ্যে বিধি দ্বারা মৎস্যখাদ্য ও পশুখাদ্যের বিভিন্ন উপাদানের আদর্শমাত্রা নির্ধারণ করিয়া দিবে এবং বাণিজ্যিকভিত্তিতে মতস্যখাদ্য ও পশুখাদ্য প্রস্তুতকালে উক্ত আদর্শমাত্রা অনুসরণ বাধ্যতামূলক হইবে।

(২) মান নিয়ন্ত্রণ ল্যাবরেটরীতে ও পরীক্ষায় কোন মৎস্যখাদ্য বা পশুখাদ্যে উপ-ধারা (১) এ উল্লিখিত আদর্শমাত্রা না পাওয়া গেলে বা পুষ্টি বিরোধী কোন উপাদানের উপস্থিতি প্রমাণিত হইলে বা উহাতে মৎস্যখাদ্য ও পশুখাদ্যের অযোগ্য বা ক্ষতিকর কোন দ্রব্যের মিশ্রণ পাওয়া গেলে উক্ত মৎস্যখাদ্য বা পশুখাদ্য প্রস্তুতকারী প্রতিষ্ঠানের লাইসেন্স বাতিল করা যাইবে।

মৎস্যখাদ্য ও পশুখাদ্যের মান নিশ্চিতকরণ

১১। (১) আমদানিকৃত ও দেশে উৎপাদিত যে কোন মৎস্যখাদ্য ও পশুখাদ্য বাজারজাত করিবার যে কোন পর্যায়ে উহার মান যাচাইয়ের উদ্দেশ্যে ক্ষমতাপ্রাপ্ত কর্মকর্তা কোন উৎপাদক, আমদানিকারক বা বিক্রেতার নিকট হইতে নমুনা সংগ্রহ করিয়া উহা মান নিয়ন্ত্রণ ল্যাবরেটরীতে পরীক্ষা করাইতে পারিবে।

(২) উপ-ধারা (১) এর অধীন পরীক্ষায় মৎস্যখাদ্য ও পশুখাদ্য ব্যবহারের অনুপযোগী প্রমাণিত হইলে উক্ত মৎস্যখাদ্য ও পশুখাদ্য বাজেয়াপ্ত করা হইবে এবং উহার আমদানীকারক, উৎপাদনকারী ও বাজারজাতকারী এই অধ্যাদেশের অধীন অপরাধ করিয়াছে বলিয়া গণ্য হইবে।

(৩) মৎস্যখাদ্য ও পশুখাদ্যের যে সকল উপকরণ বিপণন হইয়া থাকে উহা পরীক্ষা-নিরীক্ষার পদ্ধতি বিধি দ্বারা নির্ধারিত হইবে।

ক্ষতিকর ও ভেজাল মৎস্যখাদ্য ও পশুখাদ্য উৎপাদন, আমদানি, রপ্তানি, বিক্রয়, পরিবহন ও বিপণন নিষিদ্ধ

১২। (১) কোন ব্যক্তি, প্রত্যক্ষ বা পরোক্ষভাবে অথবা উহার পক্ষে অন্য কোন ব্যক্তি, প্রতিষ্ঠান বা কোম্পানীর মাধ্যমে এমন কোন মৎস্যখাদ্য ও পশুখাদ্য উৎপাদন, প্রক্রিয়াজাতকরণ, আমদানি, রপ্তানি, বিক্রয়, পরিবহন বা বিতরণ করিতে পারিবেনঃ

(ক) যাহাতে মানুষ, পশু, মৎস্য বা পরিবেশের জন্য কোন বিষাক্ত বা ক্ষতিকর পদার্থ থাকে; এবং

(খ) যাহা আদর্শমাত্রার সঙ্গে অসংগতিপূর্ণ।

(২) মৎস্যখাদ্য ও পশুখাদ্য আমদানির ক্ষেত্রে রপ্তানিকারক দেশের উপযুক্ত কর্তৃপক্ষ কর্তৃক প্রদত্ত তেজস্ক্রিয়তা পরীক্ষণ সম্পর্কিত প্রত্যয়নপত্র এবং উক্ত খাদ্যদ্রব্য মৎস্য ও পশুর খাওয়ার উপযোগী মর্মে প্রত্যয়নপত্র শিপিং ডকুমেন্টের সহিত বাধ্যতামূলকভাবে সংযুক্ত করিতে হইবে।

(৩) কোন ব্যক্তি উপ-ধারা (১) এর বিধান লংঘন করিলে উহা এই আইনের অধীন অপরাধ হিসাবে গণ্য হইবে।

Session-13

Critically Important Antimicrobial (CIA)
Slow down the process of AMR and Antimicrobial Stewardship

Key points of this session:

- *Background of CIA.*
- *Meaning of CIA is Critically important antimicrobials.*
- *Types of CIA.*

The World Health Organisation (WHO) categorises antimicrobials used in human health as 'critically important', 'highly important' and 'important' to human health The critically important antimicrobials are therefore the most important to human health. The WHO CIA antimicrobial group contains products licensed for use in veterinary medicine including aminoglycosides, 3rd and 4th generation cephalosporins, fluoroquinolones, glycopeptides, macrolides, certain penicillins and polymixins.

Back ground of CIA:

- The 1st WHO Expert Meeting on Critically Important Antimicrobials (CIA) for Human Health was held in Canberra, Australia, in 2005.
- Participants considered the list of all antimicrobial classes used in human medicine and categorized antimicrobials into three groups, based on their importance to human medicine:
    1. Critically important,
    2. Highly important, and
    3. Important

- The 2nd WHO Expert Meeting on Critically Important Antimicrobials for Human Health was held in Copenhagen, Denmark, in May 2007. During the second meeting, participants reviewed the two criteria and re-examined the categorization of all human antibacterial classes in light of new drug development and scientific information since 2005.
- Participants were also requested to prioritize agents within the critically important.
- These antimicrobial classes were fluoroquinolones, 3rd and 4th generation cephalosporins and macrolides

- The WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR) was formed in 2008, following a worldwide solicitation of experts from a variety of relevant fields, including human health and veterinary medicine, to serve as members.
- Reviewing and updating the WHO CIA list according to AGISAR's.
- At the 3rd AGISAR meeting held in Oslo, Norway, in June 2011,
- Veterinary drugs falling in the same classes of antimicrobials as those in the human medicine list

- Certain antibiotic classes are categorized by the World Health Organization (WHO) as critically important antibiotics for human use, of which several are designated as 'highest priority critically important antibiotics' (HP-CIA).
- In December 2014, the European Medicines Agency published scientific advice on the risk to humans from antibiotic resistance caused by the use of HP-CIAs in animals.

- This advice classed macrolides as category 1, where the risk of use in animals to public health is low or limited, whereas fluoroquinolones and 3rd and 4th generation cephalosporins were classified as category 2, where the risk for public health is considered higher.

- In November 2015, this advice was updated, and the expert group recommended that colistin was moved to category 2, alongside fluoroquinolones and 3rd and 4th generation cephalosporins

Meaning of CIA is Critically important antimicrobials:

- The World Health Organisation has designated some antimicrobial drugs as "critically important".

- The drug is the only, or one of the only, ways of treating a serious human disease, where the disease itself can be transmitted to humans from animals or where resistance of the disease to the drugs used to treat it can be transmitted to humans from animals.

According to WHO list :

- Critically important antimicrobials (CIA)
- Highly important antimicrobials
- Important antimicrobials

CIA are two type :

- 1. HP-CIA
- 2. High-priority CIA

Highest Priority Critically Important Antimicrobials:

- The World Health Organization has classified certain antimicrobial classes as "Highest Priority Critically Important Antimicrobials"for human medicine in the so called WHO list of critically important antimicrobials for human medicine (WHO CIA list).

- The CIA list is intended for public health and animal health authorities, practicing physicians and veterinarians, and other interested stakeholders involved in managing antimicrobial resistance to ensure that all antimicrobials, especially critically important antimicrobials, are used prudently both in human and veterinary medicine. It is intended as a reference to help formulate and prioritize risk assessment and risk management strategies for containing antimicrobial resistance mainly due to non-human antimicrobial use.
- In the latest version of the CIA list (6th revision, 2018), the "Highest Priority Critically Important Antimicrobials" are : quinolones, 3rd and higher generation cephalosporins, macrolides and ketolides, glycopeptides, and polymyxins.

HP-CIA :

Quinolones : Quinolones are known to selects for quinolone resistant Salmonella and E. coli in animals. At the same time quinolones are one of few available therapies for serious Salmonella and E. coli infections. Given the high incedence of human disease due to salmonella and e coli. The absolute number of serious cases is substantial.

HP-CIA :
Cephalosporin's (3rd and higher generation):
Cephalosporin's (3rd and higher generation) are known to selects for quinolone resistant Salmonella and E. coli in animals. At the same time Cephalosporin's (3rd and higher generation) are one of few available therapies for serious Salmonella and E. coli infections in human. Given the high incidence of human disease due to salmonella and e coli. The absolute number of serious cases is substantial.

HP-CIA :
Macrolides and Ketolides:
Macrolides and Ketolides are known to selects for the macrolides- resistant Camphylobacter spp in animals especially Camphylobacter jejuni in poultry. At the same time Macrolides are one of the few available therapies for serious Camphylobacter , particularlly in children for whom qunolons are not recommended for treatment. Given the high incedence of human disease due to Camphylobacter spp in animals especially Camphylobacter jejuni absolute number of serious cases is substantial.

Highly Important Antimicrobials:
- Amphenocols
- Cephalosporins (1st and 2nd generation)
- Lincosamides
- Penicillins (Amidinopenicillins)
- Penicillins (anti-stapphylococcal)
- Penicilline (narrow spectrum)
- Pseudomonic acids
- Riminofenazines
- Streiodantibacterials
- Streptogramins
- Sulfonamides
- Dihydrofolatereductase inhibitors and combinations
- Sulfones
- Tetraclyclines

Concept of CIA in veterinary medicines should be changed:
- The concept of "critically important" classes of antimicrobials for humans should be pursued by WHO and antimicrobials that are critically important in veterinary medicine should be identified by OIE.
- The overlap of critical lists for human and veterinary medicine can provide further information, allowing an appropriate balance to be struck between animal health needs and public health considerations.

Development of the OIE list:
- The OIE list was developed on the basis of replies to a questionnaire sent to all
- 167 OIE member countries and four international organizations that have signed a cooperation agreement with OIE.
- In this questionnaire the following four basic topics were explored:
- Animal species.
- Disease treated and causative microbes.
- Seriousness Economic importance.

- Antimicrobials used.
- Type of use (treatment/prevention/control) Route
- Accessibility of the product
- Quality of the substance.
- Specific rules of usage for the country concerned.

Criteria used for categorization of veterinary antimicrobials criteria were selected to determine the degree of importance for classes of veterinary antimicrobials.

Criterion 1
Response rate to the questionnaire regarding Veterinary Critically Important Antimicrobials. This criterion was met when a majority of the respondents (more than 50%) identified the importance of the antimicrobial class in their response to the questionnaire.

Criterion 2
Treatment of serious animal disease and availability of alternative antimicrobials. This criterion was met when compounds within the class were identified as essential against specific infections and there was a lack of sufficient therapeutic alternatives. On the basis of these criteria, the following three categories were established:

VCIA/VIA/VHIA
VCIA: Veterinary Critically Important Antimicrobial Agents
VHIA: Veterinary Highly Important Antimicrobial Agents
VIA: Veterinary Important Antimicrobial Agents

Categorization of antimicrobials used in veterinary medicine according to their importance in reatment of disease

- Veterinary critically important antimicrobials: Aminoglycosides, Cephalosporins, Macrolides, Phenicols, Quinolones and Sulfonamides
- Veterinary highly important antimicrobials:Rifamycins, Fosfomycin, Ionophores, Lincosamides, Pleuromutilins and Polypeptides
- Veterinary important antimicrobials:
- Bicyclomycin, Novobiocin , Orthosomycins, QuinoxalinesFusidic Acid and
- Streptogramins

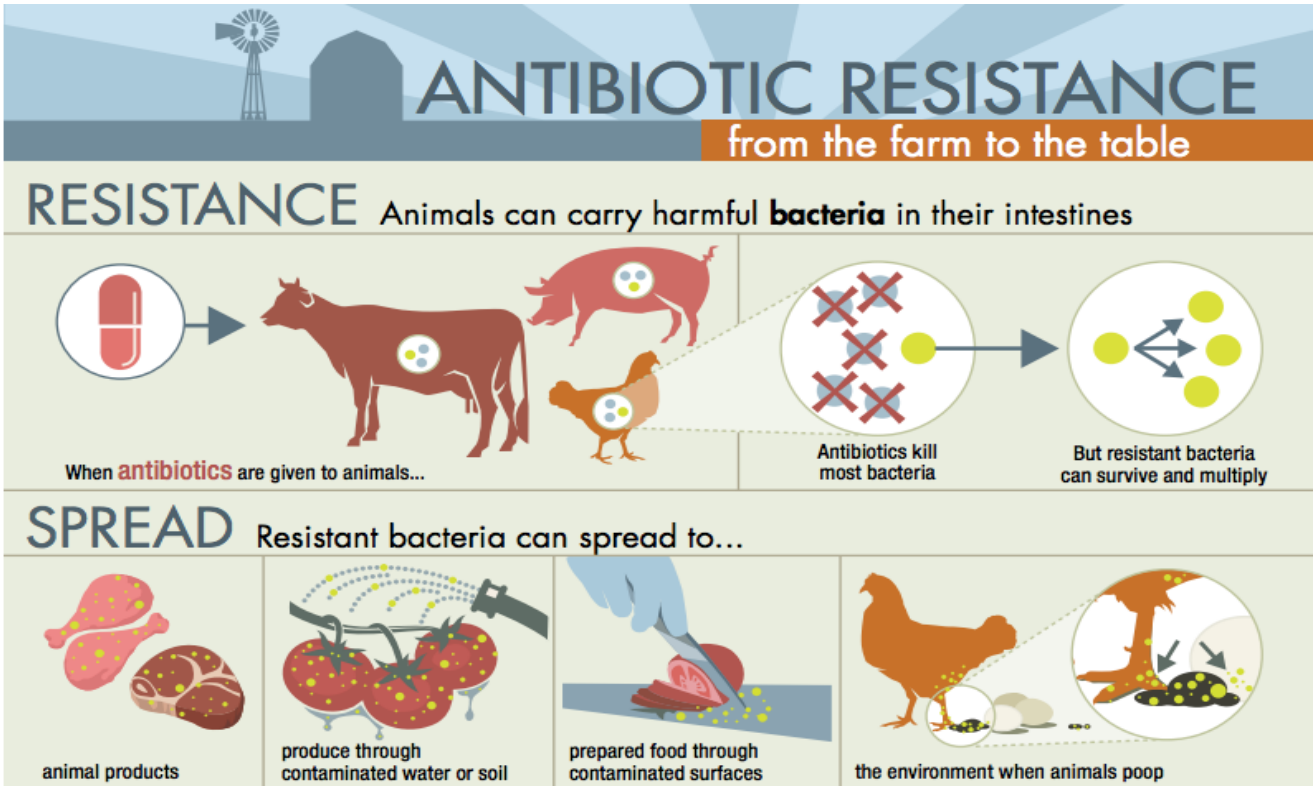
Critically important antimicrobials use in human medicine:
- Aminoglycosides, Cephalosporins (3rd and 4th generation), Macrolides, Penicillins (natural, aminopenicillins and antipseudomonal), Quinolones Tetracyclines (only tigecycline) Ansamycins, Carbapenems,Glycopeptides,Oxazolidinones,Streptogramins and Drugs used solely to treat tuberculosis or other mycobacterial diseases
- Critically important antimicrobials use in human medicine: Aminoglycosides, Cephalosporins, Macrolides, Penicillins,Quinolones ,Tetracyclines , Phenicols and Sulfonamides

How WHO, OIE and FDA mitigate the confusion of CIA list:
- There is growing agreement in animal agriculture that antimicrobials are Critically Important to human medicine – or CIAs - should be treated as a special category when finding ways to tackle

the threat of antimicrobial resistance. However, there are some differences in the current categorisation of CIAs between the World Health Organisation (WHO), the World Organisation for Animal Health (OIE) and the US Food and Drug Administration (FDA), which can lead to confusion over the exact meaning of the term 'critically important.'

Why is antibiotic resistance so important?

- Because without effective antibiotics, infections – like sepsis, or food poisoning cause death.
- And as more and more bacteria become resistant to antibiotics, routine medical procedures which rely on antibiotics to prevent infection – like chemotherapy, organ transplants and hip replacements – will become impossible.
- Antibiotics are not just used as a human medicine, but for diseases in animals as well. Around 45% of antibiotics used in the UK are given to animals – this includes food animals, like cattle, pigs and poultry, and pets such as dogs and cats.



Session-14

Dynamics and Capacity Building Support to reduce Antimicrobial Resistance

Key points of this session:

- The antimicrobial resistance (AMR) problem
- Collaborating to find a solution
- The priority topics

The antimicrobial resistance (AMR) problem:

History

In his 1945 Nobel prize lecture, Fleming warned of the dangers of antimicrobial resistance:
"The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily underdose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant."

Modern Medicine depends on access to effective antibiotics.

Antibiotics revolutionized medicine!

The introduction of penicilin in the 1950's increased the chance of survival for pneumonia patients from 25% to 80%.

* Antibiotic Resistance Threatens to return us to the pre-antibotic era.
* In the EU, More than 25,000 patients die from multidrug resistant bacteria annually (ema/ECDC Report)
* Extra health care costs and productivity losses of at least 1.5 billion EURO per year.

In some parts of the world, once powerful medicines against malaria and tuberculosis have now become virtually useless.

AMR is rapidly becoming a major public health risk and is threatening to undo decades of advances in treating disease.

What has led to resistance?

- Increased use of antibiotics
- Prescriptions taken incorrectly.
- Medicine sold without medical supervision
- Prophylactic use before surgery
- Antibiotics used for viral infection
- Spread of resistant microbes in hospitals due to lack of hygine.
- Patients who do not complete course.
- Antibiotics in animal feeds.

National research on AMR is dispersed.
- No common goals
- So far no success in reducing the risk of AMR
- The spread of AMR continuous.

To bring together all players in the field for a multidimensional approach.

- To Provide a platform for partners to collaborate in a tailor-made fashion on specific topics.
- To harmonise joint actions and creat greater impact.
- To improve awareness and knowledge
- To Stand a chance of actually finding a solution to the AMR problem.

What can be achieved by working together? (1)
* New preventative and therapeutic approaches.
* AMR related research elements more embedded in health service and care infrastructure.
A reduction of inappropriate consumption of antibiotics in humans and animals.

What can be achieved by working together? (2)
* A positive impact on treatment, care and quality of life.
* Increased visibility of the burden of AMR and the benefits of research.
* A catalytic effect on the development on national and international strategies.

What exactly is the Strategic Research Agenda?
* The first step to drafting future research programmes.
* A framework to begin joint actions.
* A framework for creating an extensive trans-European work programme on AMR

The priority topics-
* Will form a comprehensive approach for studies into strategies to reduce the use of antibiotics.
* will minimise the emergence and spread of antibiotics resistance genes and bacteria.
* will aim to reduce the burden of AMR by 2040.

Six Priority topics.
Therapeutics:
* Development of novel antibiotics and alternatives for antibiotics- from basic research to the market.

Diagnostics:
* Design strategies to improve treatment and prevention of infections by developing new diagnostics.

Surveillance:
* Standardisation and extension of surveillance systems to establish a global surveillance programme on antibiotic resistance and antibiotics use.

Transmission:
* Transmission dynamics.

Environment:
* The role of the environment as a source for the selection and spread.

Interventions:
* Designing and testing interventions to prevent acquisition, transmission and infection caused by AMR.

Therapeutics:
The discovery of new antibiotics has slowed in the last 40 years.

- Even the few recently development classes of antibiotics report resistance already.
- Large pharma withdraw because of huge development costs.
- Antiboitics are undervalued and underpriced.

Therapeutics: What the aims to do
Find new targets for antibiotics.
Develop new antibiotics.
Improve pharmakinetics and pharmacodynamics of neglected antibiotics.
Develop treatment protocols based on combination therapy using existing and new antibiotics.
Develop alternatives for antibiotics (vaccines)
Develop and study effect of policy measures and economic stimuli to minimize barriers for the development and introduction of new antibiotics.

Diagnostics:
Up to 70% of antibiotics are prescribe incorrectly- Physicians cannot make precise diagnosis.
Diagnostic Strategies can help identify patients and animals who really need antibiotics.
Reimbursements structures used by governments and health insurers need to allow for diagnostics.
Diagostic technologies exist but are costly and have not been developed with the current reality of health care in mind.
Behaviour change to use diagnostic technologies is needed: Clinicians, veterinarians, farmers, patients.

Diagnostics: what the aims to do?

- ***Improve existing and develop new diagnostic tools:***
- That more effectively distinguish between viral and bacterial infections.
- That can promote the use of narrow spectrum antibiotics.
- For the identification of antibiotics resistance bacteria; including their resistance profile.
- Identify and romove current barriers that inhibit the acceptance of rapid diagnostic tests.

Determine the exact role of various environmental reservoirs (e.g. surface water, soild, air) on the emergence and dessemination of AMR.

Understand the basic biological process that underlies these phenomena to develop remediative and preventative measures.

Interventions: What's the story?

- Little biomedical research on resistance has been translated into interventions to improve health care.
- Most interventions to control AMR to date have been based on experience, empiricism and common sense; rather that strong evidence.
- Lack of evidence base also in veterinary science.
- Controlled integrated studies in society, health care and agricultural setting are urgently needed.

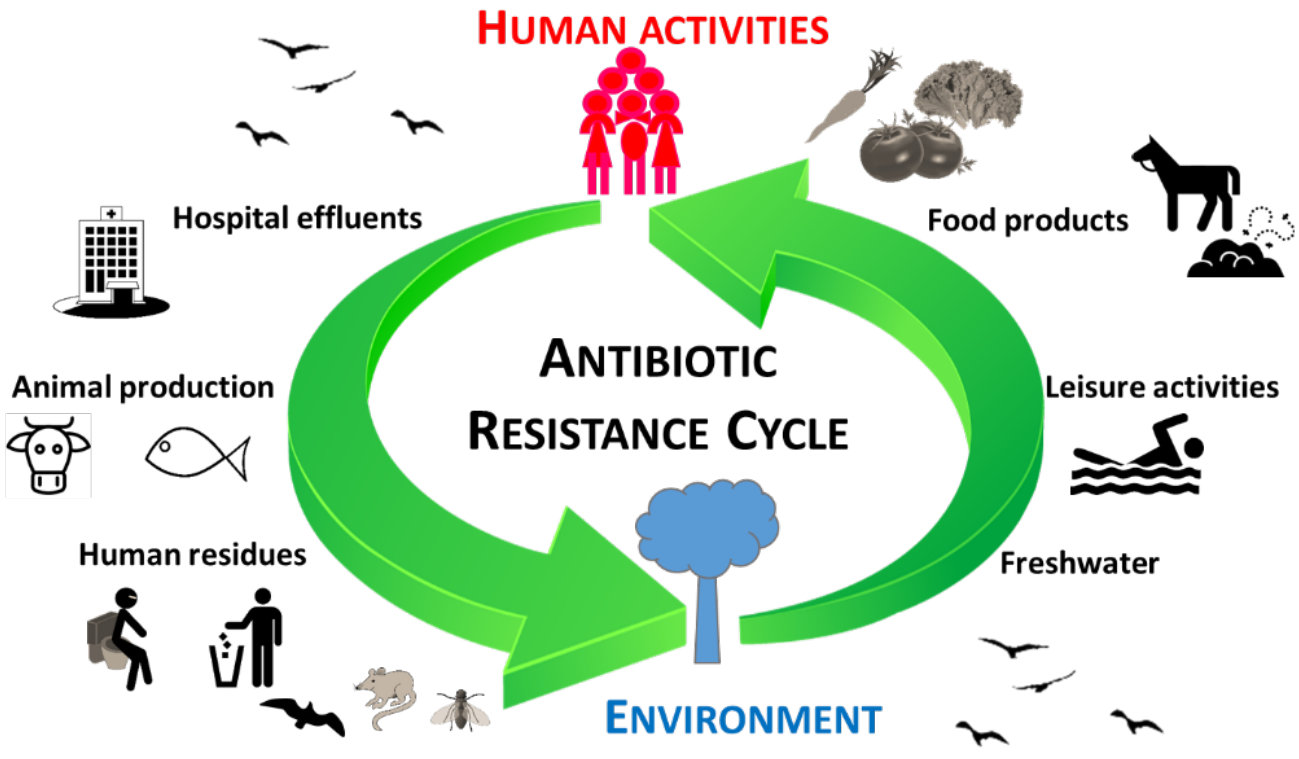
Interventions: What the SRA aims to do?

- Initiate large-scale, international projects in which interventions to prevent and control the spread

of AMR can be tested in different settings.
- Compare and combine AMR Prevention and control practices in cost efficacy trials.
- Perform research to optimize implementation strategies of interventions aimed at reducing AMR.

JPIAMR (Joint Programming Initiative on Antimicrobial Resistance) anchors the priority topics by.

- Establishing a biobank of clinical specimens and strains.
- Establishing a database containing information on on-going AMR research (including veterinary and environmental samples.)
- Collaborating with stakeholders.
- Raising awareness of AMR.
- Putting focus on antibiotics resistance in bacteria that cause life threatening infection duing hospitalization.



Session-15

Effect of AMR in Human Health and Good Medical Practice that Prevent AMR

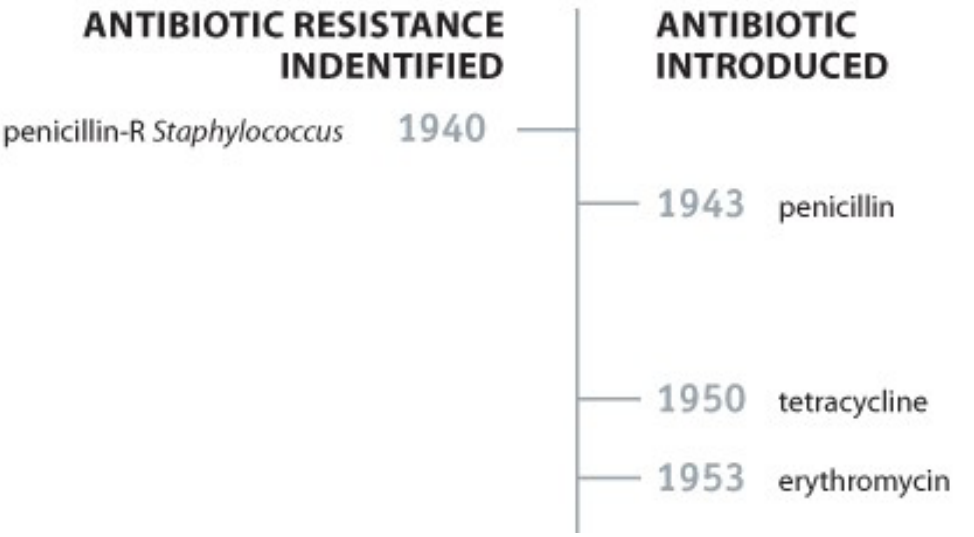
Key points of this session:

- *Brief History of Resistance and Antibiotics.*
- *Prevention of AMR*
- *Impact of AMR*

Brief History of Resistance and Antibiotics:

Penicillin, the first commercialized antibiotic, was discovered in 1928 by Alexander Fleming. Ever since, there has been discovery and acknowledgement of resistance alongside the discovery of new antibiotics. In fact, germs will always look for ways to survive and resist new drugs. More and more, germs are sharing their resistance with one another, making it harder for us to keep up.

Timeline of Antibiotic Resistance Compared to Antibiotic Development



Our Time with Antibiotics is Running Out

- Since discovery, antibiotics have served as the cornerstone of modern medicine.
- However, the persistent overuse and misuse of antibiotics in human and animal health have encouraged the emergence and spread of antibiotic resistance, which occurs when microbes, such as bacteria, become resistant to the drugs used to treat them.

Why is antimicrobial resistance a global concern?

New resistance mechanisms are emerging and spreading globally, threatening our ability to treat common infectious diseases, resulting in prolonged illness, disability, and death.

Without effective antimicrobials for prevention and treatment of infections, medical procedures such as organ transplantation, cancer chemotherapy, diabetes management and major surgery (for example, caesarean sections or hip replacements) become very high risk.

Antimicrobial resistance increases the cost of health care with lengthier stays in hospitals and more intensive care required.

Antimicrobial resistance is putting the gains of the Millennium Development Goals at risk and endangers achievement of the Sustainable Development Goals.

What accelerates the emergence and spread of antimicrobial resistance?

- Antimicrobial resistance occurs naturally over time, usually through genetic changes.
- However, the misuse and overuse of antimicrobials is accelerating this process.
- In many places, antibiotics are overused and misused in people and animals, and often given without professional oversight.
- Examples of misuse include when they are taken by people with viral infections like colds and flu, and when they are given as growth promoters in animals or used to prevent diseases in healthy animals.
- Antimicrobial resistant-microbes are found in people, animals, food, and the environment (in water, soil and air).
- They can spread between people and animals, including from food of animal origin, and from person to person.
- Poor infection control, inadequate sanitary conditions and inappropriate food- handling encourage the spread of antimicrobial resistance.

Need for coordinated action:

- Antimicrobial resistance is a complex problem that affects all of society and is driven by many interconnected factors. Single, isolated interventions have limited impact.
- Coordinated action is required to minimize the emergence and spread of antimicrobial resistance.
- All countries need national action plans on AMR.
- Greater innovation and investment are required in research and development of new antimicrobial medicines, vaccines, and diagnostic tools.

WHO response:

WHO is working closely with the Food and Agriculture Organization of the United Nations (FAO) and the World Organisation for Animal Health (OIE) in a 'One Health' approach to promote best practices to avoid the emergence and spread of antibiotic resistance, including optimal use of antibiotics in both humans and animals.

UN Declaration:

A political declaration endorsed by Heads of State at the United Nations General Assembly in New York in September 2016 signaled the world's commitment to taking a broad, coordinated approach to address the root causes
of antimicrobial resistance across multiple sectors, especially human health, animal health and agriculture.

Leading multiple initiatives to address antimicrobial resistance by WHO

- World Antibiotic Awareness Week
- The Global Antimicrobial Resistance Surveillance System (GLASS)
- Global Antibiotic Research and Development Partnership (GARDP)
- Interagency Coordination Group on Antimicrobial Resistance (IACG)

World Antibiotic Awareness Week

Held every November since 2015 with the theme "Antibiotics: Handle with care", the global, multi-year campaign has increasing volume of activities during the week of the campaign

Global Antibiotic Research and Development Partnership (GARDP)

- A joint initiative of WHO and Drugs for Neglected Diseases initiative (DNDi), GARDP encourages research and development through public-private partnerships.
- By 2023, the partnership aims to develop and deliver up to four new treatments, through improvement of existing antibiotics and acceleration of the entry of new
- antibiotic drugs.

Interagency Coordination Group on Antimicrobial Resistance (IACG)

- The United Nations Secretary-General has established IACG to improve coordination between international organizations and to ensure effective global action against this threat to health security.
- The IACG is co-chaired by the UN Deputy Secretary-General and the Director General of WHO and comprises high level representatives of relevant UN agencies, other international organizations, and individual experts across different sectors.

Mechanism of development of AMR:

- Antibiotic resistance happens when germs like bacteria and fungi develop the ability to defeat the drugs designed to kill them.
- That means the germs are not killed and continue to grow.
- Numerous biological, behavioral, economic, environmental and social factors contribute to the production and propagation of antimicrobial resistance (AMR).

Prevention of AMR: Individuals

- Prevent infections by regularly washing hands, preparing food hygienically, avoiding close contact with sick people, practicing safer sex, and keeping vaccinations up to date.
- Prepare food hygienically, following the WHO Five Keys to Safer Food (keep clean, separate raw and cooked, cook thoroughly, keep food at safe temperatures, use safe water and raw materials)
- choose foods that have been produced without the use of antibiotics for growth promotion or disease prevention in healthy animals.

Prevention of AMR: Policy makers

- Ensure a robust national action plan to tackle antibiotic resistance is in place.
- Improve surveillance of antibiotic-resistant infections.
- Strengthen policies, programmes, and implementation of infection prevention and control measures.
- Regulate and promote the appropriate use and disposal of quality medicines.
- Make information available on the impact of antibiotic resistance.

Prevention of AMR: Health professionals

- Prevent infections by ensuring your hands, instruments, and environment are clean.
- Only prescribe and dispense antibiotics when they are needed
- Report antibiotic-resistant infections to surveillance teams
- Talk to your patients about how to take antibiotics correctly, antibiotic resistance and the dangers of misuse
- Talk to your patients about preventing infections (for example, vaccination, hand washing, safer sex, and covering nose and mouth when sneezing).

Prevention of AMR: Healthcare industry

To prevent and control the spread of antibiotic resistance, the health industry can:

- Invest in research and development of new antibiotics, vaccines, diagnostics and other tools.

Prevention of AMR: Agriculture sector

- Only give antibiotics to animals under veterinary supervision.
- Not use antibiotics for growth promotion or to prevent diseases in healthy animals.
- Vaccinate animals to reduce the need for antibiotics and use alternatives to antibiotics when available.
- Promote and apply good practices at all steps of production and processing of foods from animal and plant sources.
- Improve biosecurity on farms and prevent infections through improved hygiene and animal welfare.

Impact of AMR:

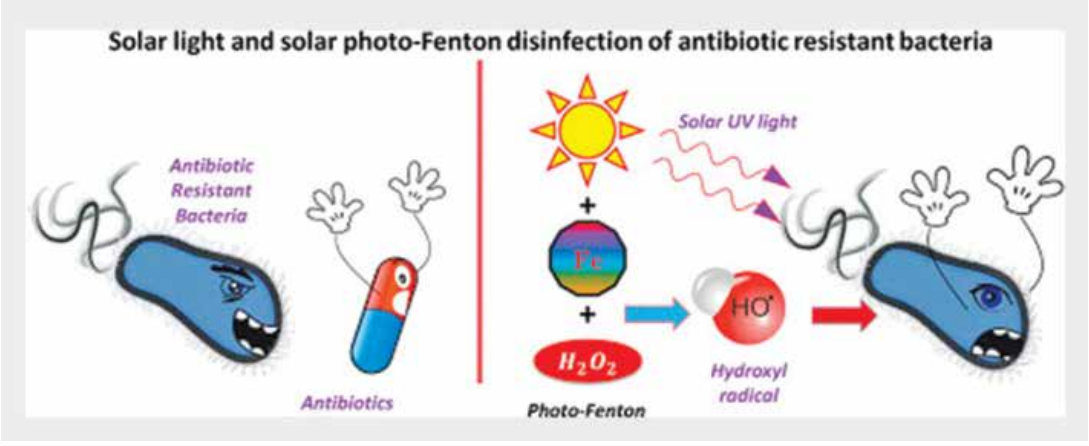
- When infections can no longer be treated by first-line antibiotics, more expensive medicines must be used.
- A longer duration of illness and treatment, often in hospitals, increases health care costs as well as the economic burden on families and societies.
- Antibiotic resistance is putting the achievements of modern medicine at risk.
- Organ transplantations, chemotherapy and surgeries such as caesarean sections become much more dangerous without effective antibiotics for the prevention and treatment of infections.

WHO response:

- A global action plan on antimicrobial resistance, including antibiotic resistance, was endorsed at the World Health Assembly in May 2015.
- The global action plan aims to ensure prevention and treatment of infectious diseases with safe and effective medicines.

Global action plan on antimicrobial resistance: It has 5 strategic objectives:

- To improve awareness and understanding of antimicrobial resistance.
- To strengthen surveillance and research.
- To reduce the incidence of infection.
- To optimize the use of antimicrobial medicines.
- To ensure sustainable investment in countering antimicrobial resistance.



Session-16

Epidemiology for AMR Surveillance. Role of Veterinary Epidemiology unit to combat AMR.

Key points of this session:

- *Epidemiology for AMR surveillance.*
- *AMR study in Bangladesh.*
- *Important issues need to be addressed.*

Epidemiology for AMR surveillance

Resulting-
More purchasing capacity and positive attitude towards fulfillment of nutritional requirement. More animal protein is required. Changes in poultry 16 grandparent farms produce 60000-70000 parent stock chicks/week. Around 206 parent stock farms produce day old chicks (15 million/week, Broiler), Layer chicks (6 lakh), eggs (25 million/day)

What should do?
Different organizations and institutes are working to identify the level of resistance and contain the resistance. WHO has recommended that countries develop antimicrobial surveillance programmes that integrate data from bacterial isolates originating from humans, food-producing animals, and retail meats.

- Strengthen knowledge and evidence through surveillance and research
- Quality of diagnosis
- Surveillance: Production of data, collection, analysis and reporting
- (≠sources) Source of resistant mechanisms
- Detection, confirmation, characterization and communication of AMR emergencies
- Measuring impact of AMR (research)
- Provide microbiological knowledge for the development of guidelines for treatment based on local epidemiology

AMR study in Bangladesh: One study revealed the use of antibiotic as follows-

- therapeutic (29.80%),
- prophylactic (15.10%),
- both therapeutic and prophylactic (45.29%) and
- growth promotion (9.80%) were observed

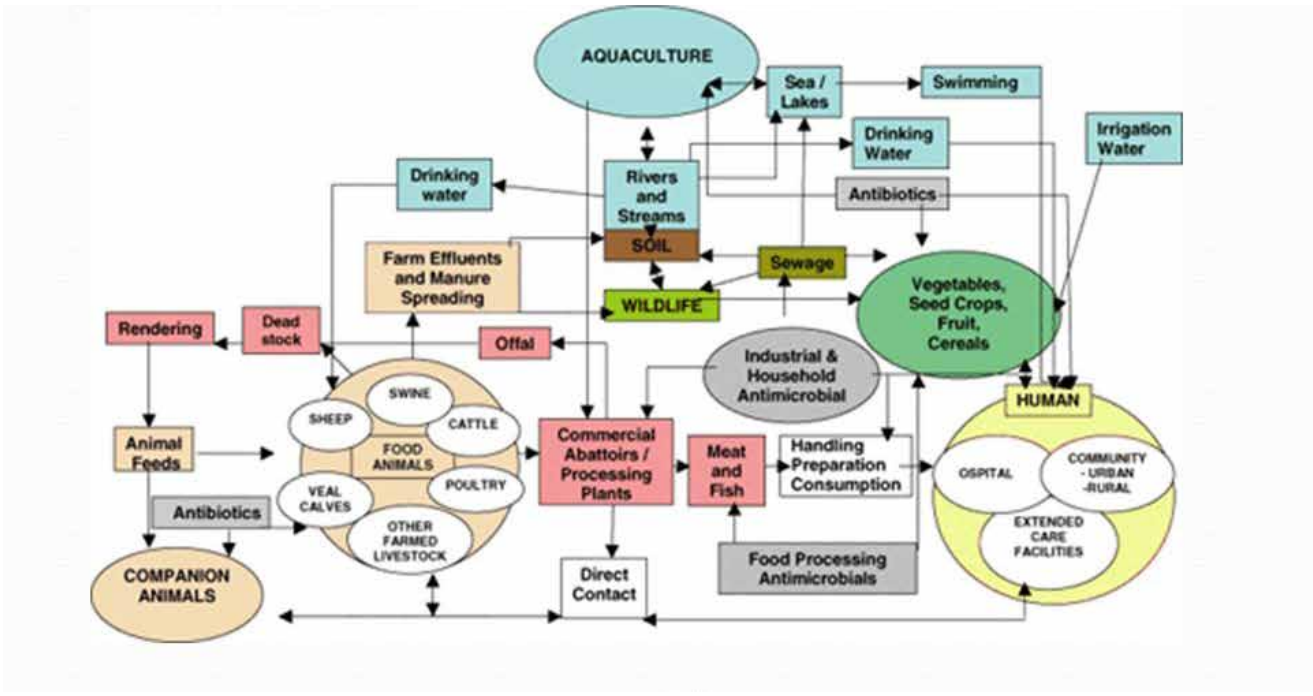
Some other studies identified the AMR isolates which are as follows-
Escherichia coli of poultry sample found resistant 88% to penicillin, 82% to ciprofloxacin, 80% to Rifampicin, 76% to Kanamycin, 70% to streptomycin, 68% to cefixine, 64% to erythromycin, 58% to ampicillin, 52% to tetracycline and 20% Chloramphenicol and Neomycin. Multidrug resistant also recorded against 6-10 antibiotics.
Salmonella of poultry sample also found multidrug resistant.

Veterinarian can play role:
- At farm level
- At animal level
- At laboratory
- And local veterinary hospital
- Feed production industries

Objective :
- To monitor trends in AMR resistance in humans, animals and fish species at the national level.
- To monitor AMR organisms in environment
- To inform policy and decision making relevant to AMU and AMR.
- To generate data for informed decisions on AMU.

Important issues need to be addressed-
- Risk assessment that is necessary to set priorities
- Assessment of veterinary AMU in Bangladesh
- Identify the veterinary (critically, highly and important) antimicrobials use in Bangladesh

Epidemiology of antimicrobial resistance



Session-17

AMR Situation in Hospital. Effect of AMR in Human Health. Good Public health practice that prevent AMR.

Key points of this session:

- *Strategic objectives of tackling AMR (WHO Recommendation):*
- *Good Public health practice that prevent AMR.*
- *Prevention of antibiotic-resistant infections:*

Collaborative NAP on Antimicrobial Resistance Containment in Bangladesh Human civilizations: constantly confronted with fatal infectious diseases AMs: most successful forms of treatment in the history of medicine.

Antimicrobial resistance is possibly the single biggest threat facing the world in the area of infectious diseases. European Centre for Diseases Control (ECDC) Microbes and vectors swim in the evolutionary stream, and they swim faster than we do. Bacteria reproduce every 30 minutes. For them, a millennium is compressed into a fortnight. They are fleet afoot, and the pace of our research must keep up with them, or they will overtake us - (Krause 1998).

Antimicrobial Resistance: Global Public Health Challenge

- Currently, 700,000 deaths recorded annually attributable to infection from AMR pathogens
- By 2050, it may rise to 10 million (Review on Antimicrobial Resistance by O' Neil)

Strategic objectives of tackling AMR (WHO Recommendation):

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

Good Public health practice that prevent AMR.

Antimicrobial-drug resistance in hospitals is driven by failures of hospital hygiene, selective pressures created by overuse of antibiotics, and mobile genetic elements that can encode bacterial resistance mechanisms. Attention to hand hygiene is constrained by the time it takes to wash hands and by the adverse effects of repeated handwashing on the skin. Alcohol-based hand rubs can overcome the time problem and actually improve skin condition. Universal gloving could close gaps left by incomplete adherence to hand hygiene. Various interventions have been described to improve antibiotic use. The most effective have been programs restricting use of antibiotics and computer-based order forms for health providers.

Prevention of antibiotic-resistant infections:

1. Not take antibiotics for viral infections.
2. Follow the course of treatment exactly as instructed healthcare provider.
3. Not take someone else's antibiotics because different kinds of antibiotics treat different types of bacterial infections.

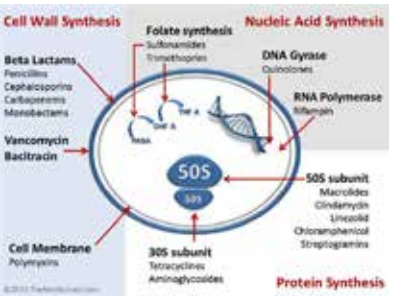
Paul Ehrlich (1854 - 1915)

Paul Ehrlich 1854-1915

- German Physician On
- Koch's Research Team
  (Helped to make Koch's dye)
- Invented Chemotherapy
- Won Nobel Prize
- Made First Magic Bullet
  (Which was Injected) -
- Called Salvarsan 606

Session-18

Antimicrobial Resistance Patterns Priority list of ARB and their Resistance Effect.



Key points of this session:

- *Molecular Mechanisms of Resistance*
- *Reducing Penetration:*
- *Expulsion of the Antimicrobial Agents*
- *Inactivation of Antimicrobial Agents*

Mechanism of development of AMR against antimicrobials with their molecular changes in structural and functional level Communicable diseases- infectious or transmissible diseases- result from the infection in an individual human or other animal host

Annex 9. Distribution of Member countries by OIE Region-

AFRICA (54):

ALGERIA 2. ANGOLA 3. BENIN 4. BOTSWANA 5. BURKINA FASO 6. BURUNDI 7. CAMEROON 8. CABO VERDE 9. CENTRAL AFRICAN 10. CHAD 11. COMOROS 12. CONGO 13. CONGO 14. CÔTE D'IVOIRE 15. DJIBOUTI 16. EGYPT 17. EQUATORIAL GUINEA 18. ERITREA 19. ETHIOPIA 20. GABON 21. GAMBIA 22. GHANA 23. GUINEA 24. GUINEA BISSAU 25. KENYA 26. LESOTHO 27. LIBERIA 28. LIBYA 29. MADAGASCAR 30. MALAWI 31. MALI 32. MAURITANIA 33. MAURITIUS 34. MOROCCO 35. MOZAMBIQUE 36. NAMIBIA 37. NIGER 38. NIGERIA 39. RWANDA 40. SAO TOME AND PRINCIPE 41. SENEGAL 42. SEYCHELLES 43. SIERRA LEONE 44. SOMALIA 45. SOUTH AFRICA 46. SOUTH SUDAN 47. SUDAN 48. SWAZILAND 49. TANZANIA 50. TOGO 51. TUNISIA 52. UGANDA 53. ZAMBIA 54. ZIMBABWE

AMERICAS (30):

1. ARGENTINA 2. BAHAMAS 3. BARBADOS 4. BELIZE 5. BOLIVIA 6. BRAZIL 7. CANADA 8. CHILE 9. COLOMBIA 10. COSTA RICA 11. CUBA 12. CURAÇAO 13. DOMINICAN REP. 14. ECUADOR 15. EL SALVADOR 16. GUATEMALA 17. GUYANA 18. HAITI 19. HONDURAS 20. JAMAICA 21. MEXICO 22. NICARAGUA 23. PANAMA 24. PARAGUAY 25. PERU 26. SURINAME 27. TRINIDAD AND TOBAGO 28. UNITED STATES OF AMERICA 29. URUGUAY 30. VENEZUELA

Middle East (12) :
1. AFGHANISTAN 2. BAHRAIN 3. IRAQ 4. JORDAN 5. KUWAIT 6. LEBANON 7. OMAN 8. QATAR 9. SAUDI ARABIA 10. SYRIA 11. UNITED ARAB EMIRATES 12. YEMEN

ASIA, FAR EAST AND OCEANIA (32)
1. AUSTRALIA 2. BANGLADESH 3. BHUTAN 4. BRUNEI 5. CAMBODIA 6. CHINA (PEOPLE'S

REP. OF) 7. FIJI 8. INDIA 9. INDONESIA 10. IRAN 11. JAPAN 12. KOREA (REP. OF) 13. KOREA (DEM. PEOPLE'S REP. OF) 14. LAOS 15. MALAYSIA 16. MALDIVES 17. MICRONESIA (FED. STATES OF) 18. MONGOLIA 19. MYANMAR 20. NEPAL 21. NEW CALEDONIA 22. NEW ZEALAND 23. PAKISTAN 24. PAPUA NEW GUINEA 25. PHILIPPINES 26. SINGAPORE 27. SRI LANKA 28. TAIPEI (CHINESE) 29. THAILAND 30. TIMOR LESTE 31. VANUATU 32. VIETNAM

EUROPE (53) :
1. ALBANIA 2. ANDORRA 3. ARMENIA 4. AUSTRIA 5. AZERBAIJAN 6. BELARUS 7. BELGIUM 8. BOSNIA AND HERZEGOVINA 9. BULGARIA 10. CROATIA 11. CYPRUS (+ME) 12. CZECH REP. 13. DENMARK 14. ESTONIA 15. FINLAND 16. NORTH MACEDONIA (REP. OF) 17. FRANCE (+AMER) 18. GEORGIA 19. GERMANY 20. GREECE 21. HUNGARY 22. ICELAND 23. IRELAND 24. ISRAEL 25. ITALY 26. KAZAKHSTAN 27. KYRGYZSTAN 28. LATVIA 29. LIECHTENSTEIN 30. LITHUANIA 31. LUXEMBOURG 32. MALTA 33. MOLDOVA 34. MONTENEGRO 35. NETHERLANDS 36. NORWAY 37. POLAND 38. PORTUGAL 39. ROMANIA 40. RUSSIA (+ASIA) 41. SAN MARINO 42. SERBIA 43. SLOVAKIA 44. SLOVENIA 45. SPAIN 46. SWEDEN 47. SWITZERLAND 48. TAJIKISTAN 49. TURKEY (+ME) 50. TURKMENISTAN 51. UKRAINE 52. UNITED KINGDOM 53. UZBEKISTAN (+AMER): Also member

- The quantity of antimicrobials used in agriculture globally is not known precisely.
- The amount used for food-animal production is significantly higher compared to human use.
- About 80 percent of antimicrobials are sold or distributed for use in animals in USA in 2012
- Use of antimicrobials in food-animal production will increase 67% by 2030 (Boeckel et al., 2015)

Molecular Mechanisms of Resistance
The abilities of bacterial organisms to utilize the various strategies to resist antimicrobial compounds are all Genetically Encoded

Intrinsic resistance
Acquired resistance
1. Mutation
2. Horizontal gene transfer

Intrinsic Resistance:
Resist activity of a particular antimicrobial agent through its inherent structural or functional characteristics.
Naturally coded and expressed by all (or almost all) strains of that particular bacterial species.
This can also be called "insensitivity" e.g., Natural resistance of anaerobes to Aminoglycosides and Gram-negative bacteria against Vancomycin Intrinsic Resistance due to several different mechanisms-
(1) Reduction of antimicrobial's ability to penetrate into the cell
(2) Expulsion of the antimicrobials
(3) Inactivation of antimicrobial
(4) Modification of the antimicrobial target within the bacteria

Reducing Penetration:

- Antibiotics enter into bacteria through Porin channels
- Gram-negative bacteria modify this channel

- ❖ Reduce the uptake of antibiotics
- ❖ Prevent from reaching their target site e.g., Aminoglycosides - Ribosomes

Beta-lactams - PBPs

Pseudomonas aeruginosa against Imipenem (a beta-lactam antibiotic) Enterobacter aerogenes and Klebsiella spp. against Imipenem. Many Gram-negative bacteria against Aminoglycosides and Quinolones

Expulsion of the Antimicrobial Agents

- ❖ To be effective- sufficient concentration is required
- ❖ Some bacteria expel the antibiotic via membrane proteins
- ❖ Low intracellular concentrations- insufficient to elicit an effect
- ❖ Some efflux pumps selectively expel specific antibiotics Macrolides, Lincosamides, Streptogramins & Tetracyclines, whereas others (multiple drug resistance pumps) expel a diverse anti-infectives with different modes of action.

E. coli and other Enterobacteriaceae against Tetracyclines; Enterobacteriaceae against Chloramphenicol; Staphylococci against Macrolides and Streptogramins; Staphylococcus aureus and Streptococcus pneumoniae against Fluoroquinolones

Inactivation of Antimicrobial Agents

Destroy the active component of the antimicrobial agent. Hydrolytic deactivation of the Beta-lactam ring in Penicillins and Cephalosporins by the bacterial enzyme called beta lactamase
The first antibiotic resistance mechanism described was that of Penicillinase
(Abraham and Chain in 1940; Nature 146: 837) Less than 10 years after the clinical introduction of Penicillins, penicillin-resistant S. aureus was observed In Gram- positive infections in people

Three main enzymes that inactivate antibiotics-

β-lactamases: Hydrolyze nearly all β-lactams. About 300 β-lactamases are known till date

Aminoglycoside-modifying enzymes:
- Phosphoryl-transferases
- Nucleotidyl-transferases
- Adenylyl-transferases

These enzymes reduce affinity of a modified molecule, impede binding to the 30S ribosomal subunit, and provide resistance to AG's and FQ

Chloramphenicol acetyltransferases:
Acetylates hydroxyl groups of chloramphenicol.
Modified chloramphenicol is unable to bind to a ribosomal 50S subunit properly.

Modification of the Antimicrobial Target, Reprogramming of target sites to avoid recognition, No binding or inhibition takes place

Bacterial Resistance Due to Target Site Modification

Alteration in PBPs- leading to reduced affinity of beta-lactam antibiotics (Methicillin- Resistant S. aureus, S. pneumoniae, N. gonorrheae, L. monocytogenes)

Changes in peptidoglycan layer and cell wall thickness- resulting to reduced activity of vancomycin: Vancomycin- resistant S. aureus. Changes in vancomycin precursors reducing activity of vancomycin: Enterococcus faecium and E. faecalis.

Alterations in subunits of DNA gyrase- reducing activity of Fluoroquinolones: Many Gram- negative bacteria Alteration in subunits of topoisomerase IV- leading to reduced activity of Fluoroquinolones: Many Gram-positive bacteria, particularly S. auerus and Streptococcus pneumoniae Changes in RNA polymerase- leading to reduced activity of Rifampicin: Mycobacterium tuberculosis.

Session-19

Vaccine, Types of Vaccine and Vaccination of Food Animals

Key Points of this session:

- *Definition of vaccine.*
- *Types of vaccines.*
- *Live vaccine-Avirulent strain vaccine.*
- *Inactivated or killed vaccine.*
- *Genetically Engineered vaccine.*
- *Synthetic vaccine.*
- *DNA Vaccine.*
- *Advantages and disadvantages of vaccines: Killed vaccines (KV) and Toxoids.*

Definition of vaccine:

A vaccine is a biological preparation that provides active acquired immunity to a particular infectious disease. A vaccine typically contains an agent that resembles a disease-causing microorganism and is often made from weakened or killed forms of the microbe, its toxins, or one of its surface proteins

Vaccine may be defined as an antigenic preparation which when inoculated in the body induces an active immune response at a certain level of protection against the infectious agent
OR
Microorganisms and their products, which are inoculated into animal body, can produce active immune response for the individuals' protection against the infectious agents

Types of vaccines:
Live vaccine-
a) Avirulent strain vaccine and b) Attenuated vaccine

- Inactivated or Killed vaccine
- Genetically Engineered vaccine and
- DNA Vaccine
- Subunit vaccine and toxoid
- Synthetic vaccine

Live vaccine
Avirulent strain vaccine

- The avirulent strain has the ability to induce immunity in the body but having no disease producing capacity.
- Here the condition is that the avirulent strain should be antigenically related with the challenging agent.

Live attenuated vaccine

- Modified live vaccines (MLV) contain a small quantity of virus or bacteria.
- That has been altered so that it no longer is capable of causing clinical disease.
- But are still capable of infection and multiplying in the animal.
- Live attenuated vaccine (LAV) derived by mutation from a virulent, wild type bacterium or virus i.e. making of less virulent by some suitable means.

E.g. (a) Homologous PPR and Rinderpest vaccines
(b) Rabies vaccine (c) Anthrax spore vaccine

Inactivated or killed vaccine

- Inactivated or killed vaccines are produced by inactivation of growing large amount of the bacteria or viruses in bacteriological media /tissue culture or sometimes in the intact animal.
- Inactivation is done chemically with agents such as formaldehyde, phenol, beta-propiolactone or binary ethylamine, or physically with ultra-violet light.
- Killed vaccines consist of concentrated antigen combined with adjuvant. E.g. Fowl Cholera Vaccine, FMD vaccine, NDV vaccine and Rabies vaccine etc.

Adjuvants

- Substances that have the ability to enhance humoral and cell-mediated immune responses to inactivated microorganisms or their products are termed adjuvants.
- A large number of substances can enhance the immune response as adjuvants, as carriers for antigenic material, or as vehicles in which vaccines can be administered. e.g. Aluminium phosphate, Aluminium hydroxide, Aluminium potassium sulphate, Freund's complete adjuvant, Saponins, Aviridine, and Dextran

Modes of action of adjuvants

- Retention and slow release of antigenic material from the site of injection
- Increased immunogenicity of small or antigenically weak synthetic or recombinant peptides
- Improved speed of response and persistence of response to effective antigens
- Increased immune response to vaccines in immunologically immature, immunosuppressed or ageing animals
- Stimulation of macrophage activity and the processing of antigen by antigen- presenting cells
- Modulation of humoral or cell-mediated immune responses by the subset of T lymphocytes
- Stimulation of T and B lymphocytes

Subunit vaccine and Toxoids

- Microbial products such as toxoids or subunit components are included in this type of vaccine.
- Subunit vaccines are a type of killed vaccine that contains only part of the virus or other microorganisms.
- These vaccines were developed to either isolate or engineer the most important part of the microorganism needed to produce a proper immune response and eliminate the part (s) of the microorganism that caused adverse vaccine reactions or interfered with a proper immune response

Sub-unit Vaccine

- Sub-unit vaccines may developed from crude preparations of virus/bacteria from animal tissues/ culture media.
- The peptide sites encompassing the major antigenic sites of viral/bacterial antigens, from which highly purified subunit vaccines can be produced.
- Increasing purification may lead to loss of immunogenicity, and this may necessitate coupling to an immunogenic carrier protein or adjuvant, such as an aluminum salt.
- Examples of purified subunit vaccines include the HA vaccines for influenza A and B, and HB Ag derived from the plasma of carriers.

Genetically Engineered vaccine

- Gene of desired protein for vaccine candidate be ligated with the plasmid and then transformed into the bacteria.
- The bacteria are then allowed to multiply into the media and liberate the desired protein for vaccine.
- This protein is purified and used as vaccine. E.g. Genetic engineered FMD vaccine.

Synthetic vaccine

- Synthetic vaccine is producecd by chemical alteration of microorganism.
- It contain modified live organisms that have been grown in a media containing adjusted levels of certain chemicals that trigger and amplify mutation of the organisms, changing the organisms' metabolism in such a way as to alter the ability to cause disease.

DNA Vaccine

- DNA coding for the foreign antigen is directly injected into the animal so that the foreign antigen is directly produced by the host cells.
- In theory these vaccines would be extremely safe and devoid of side effects since the foreign antigens would be directly produced by the host animal.
- In addition, DNA is relatively inexpensive and easier to produce than conventional vaccines and thus this technology may one day increase the availability of vaccines to developing countries.
- DNA vaccines can theoretically result in more long-term production of an antigenic protein when introduced into a relatively nondividing tissue, such as muscle.

Advantages and disadvantages of vaccines: Killed vaccines (KV) and Toxoids

Advantages	Disadvantages
Available for a wide variety of diseases	Killed virus does not mutiplty so that an immunizing dose has to contain for more virus than a dose of live vaccine
No risk of reverting to virulent form	As no multiplication occurs do not reach to those areas of the body where infectious virus would normally be found.
No risk of vaccine organism spreading between animals	Care must be taken in making them such that no live virulent virus is present in the vaccine
Little risk of causing abortion	More likely to cause allergic reactions and post vaccination lumps i.e. may cause hypersensitivity reaction
More stable in storage	Two initial doses required at least 10 days apart
No on-farm mixing, therefore less risk of contamination	Slower onset of immunity

Modified live vaccine (MLV)

Advantages	Disadvantages
One initial dose is usually sufficient but additional booster doses may be required	There is a risk of the virus reverting to greater virulence during multiplication
A strong, long-lasting immune response that is achieved with fewer doses	Potential to mutate to a virulent form
More rapid protection than KV vaccine	Could cause disease in immunosuppressed animals
Less likely to cause allergic reactions or post vaccination lumps than KV products	Potential for excessive immune response
Less susceptible to passive antibody vaccine block than KV vaccine	Some risk of causing abortion or transient infertility
Some risk of causing abortion or transient infertility	Must be handled and mixed with additional care

Comparisons of advantage between lives and killed vaccines

Advantages of Live vaccines	Advantages of killed vaccines
Most confer life-long protection	No danger to immuno- incompetent and malnourished patients or to foetus
Often only a single dose is required	Longer shelf life and easier storage
Protection may be transmissible	Can be given with other vaccines
Much smaller dose, therefore a) lower cost and b) less antigen from culture medium and less bacterial toxin, hence fewer allergic or toxic reactions	Still effective even if patient has another infection when vaccinated
Better at stimulating cytotoxic T cells	Less danger of contamination with another organism (e.g. SV40 virus)

Important Livestock and poultry Vaccines commonly used in Bangladesh

Animal Vaccines:

- Killed Vaccines: FMD Vaccine, BQ vaccine, HS Vaccine
- Attenuated Vaccines: Goat Pox Vaccine, Rabies vaccine, Anthrax vaccine

Poultry Vaccines:

Live vaccines found in Bangladesh used against the following poultry diseases- NDV, IB, IBD, Fowl pox, Avian encephalomyelitis, Marek's disease, Reovirus, ILT Vaccine , Dp Vaccine M. gallisepticum, Avian infectious anemia, S. gallinarum

Inactivated vaccines used for poultry diseases: ND, IB, Reovirus, IBD, FC, Avian adenovirus, Avian influenza, Avian pneumovirus, M. gellisepticum, EDS, S. enteritidis, E. coli, Infectious coryza.

Session- 20

Immunity, Types of immunity and Comparison of non-specific immunity with specific immunity

Key Points of this session:

- *Active immunity*
- *Community Immunity*
- *Herd immunity*
- *Cocooning*

Immunity is the capability of multicellular organisms to resist harmful microorganisms from entering it. An immune system may contain innate and adaptive components.
Two types of immunity exist — active and passive:

- Active immunity occurs when our own immune system is responsible for protecting us from a pathogen.
- Passive immunity occurs when we are protected from a pathogen by immunity gained from someone else.

Both of these different types of immunity can be acquired in different ways.

A third category, community immunity, does not involve physical components of the immune system for protection, but is still worth discussion in this capacity.

Active immunity
Individuals rely on active immunity more so than passive immunity. Active immunity is created by our own immune system when we are exposed to a potential disease-causing agent (i.e., pathogen).
Vaccines contribute to active immunity by providing us with a controlled way to create an immune response. When a vaccine is introduced, our immune system treats it like any other exposure. It works to stop the "assault" and, in the process, immunologic memory develops. Because vaccines are designed such that they do not cause illness, we gain the benefits of the exposure without the risks associated with fighting off a natural infection

Community Immunity:
Community immunity occurs when people are protected by those around them. This type of protection is indirect in that it does not involve physical components of immunity, such as antibodies, but rather results when a pathogen is less likely to infect a susceptible person because of the high numbers of protected people around them. Because this immunity is not based on "products" of the immune system, it is the least reliable. However, for some in our communities, such as those too young to be immunized or those with weakened immunity due to illness or treatment, community immunity is the only way they can be protected.

We generally talk about community immunity from two perspectives — that of the community, commonly referred to as herd immunity, and that of the individual, commonly known as cocooning:

Herd immunity:

When enough people in a community have been exposed to a pathogen, it cannot spread as easily. As more people become immune, the pathogen has a smaller pool of people to infect. The result is that the community overall will have fewer outbreaks. Because not all pathogens spread with the same effiiency, the community levels of immunity necessary to benefit from herd immunity vary. For example, because measles is one of the most contagious pathogens known, a community requires almost everyone to be immune in order to stop its transmission. Or said another way, it is much more difficult for an individual to benefit from herd immunity to measles than from most other infectious agents. Vaccines have made it easier for society to reap the benefits of this type of protection. Before vaccines, diseases continued to have susceptible pools of individuals — most often infants and young children not previously exposed to the disease. This is why childhood diseases and deaths were so common.

Cocooning:

This type of passive immunity is similar to herd immunity, but is more often aimed at protecting a particular individual rather than a community. Ensuring that everyone around a young infant is immune to a disease like pertussis (whooping cough) is an example of this type of indirect immunity. Another example is ensuring that everyone who visits or cares for a person being treated for cancer is healthy, so that the cancer patient whose immunity is weakened by treatment is less likely to be exposed to a pathogen.

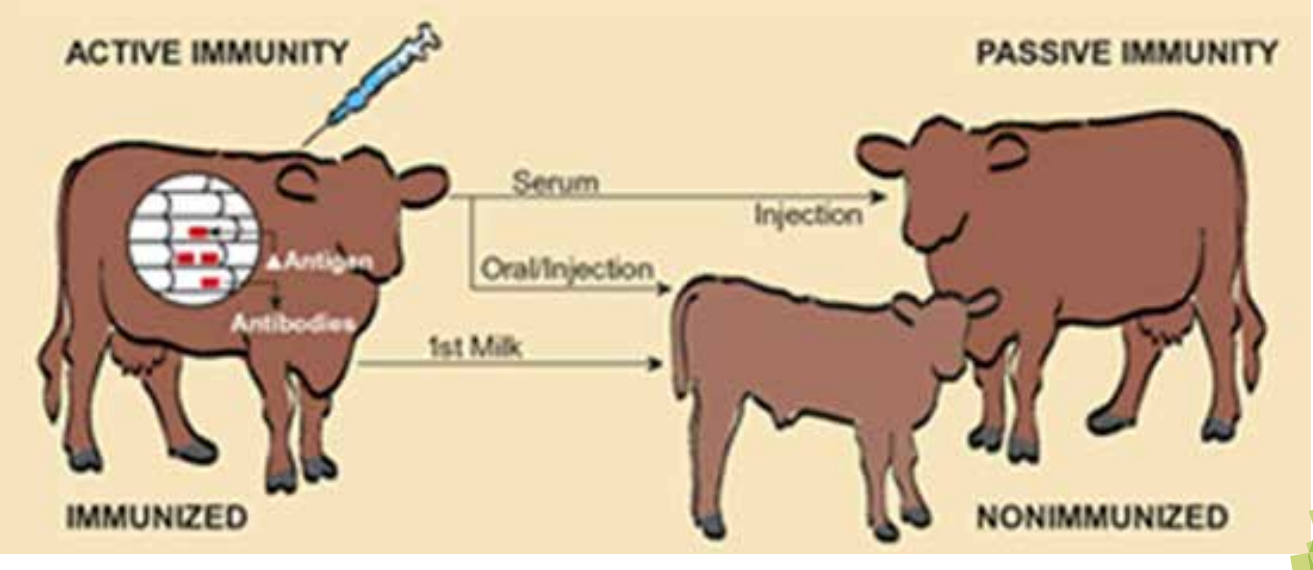
Table 1. Comparison of non-specific immunity with specific immunity

Feature	Non-specific	Specific immunity
Occurrence	Vertebrates and invertebrates	Vertebrates only
Induction	Innate	Induced by exposure to pathogens or by vaccination
Physical barriers	Skin, mucous membrances, mucociliary clearance, turbinate baffles	-
Mechanical action	Flushing activity of tears and urine, peristalsis	-
Physiological influences	Low pH values on skin, gastric acidity, bile	-
Participating cells	Macrophages, monocytes, poly-morphonuclear leukocytes, natural killer cells, mast cells	T and B lymphocytes (antigen-presenting cells required to initiate some responses)
Principal soluble factors	Complement, lysozymes, interferons, degradative enzymes	Cytokines, antibodies
Rate of response to infection	Moderately fast, minutes to hours	Relatively slow, days to weeks
Immunological memory	Absent	Present
Contribution to body defenses	First line of defence against opportunistic pathogens; offers limited protection against virulent microorganisms	Produces an effective response to a wide range of virulent microorganisms, effectiveness of the response improves with time

Comparison of T lymphocytes and B lymphocytes and their roles in specific immune responses

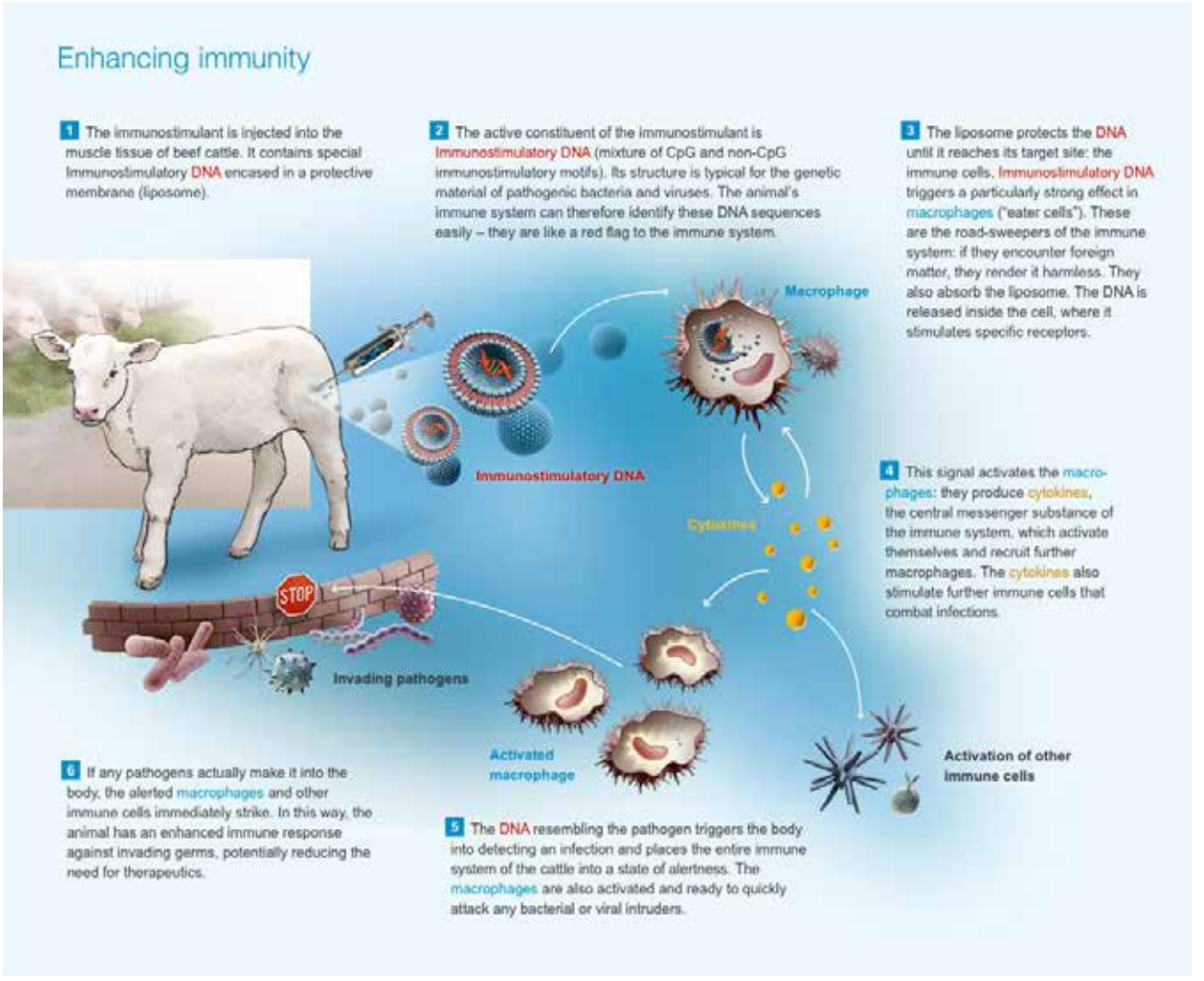
Comparison of T lymphocytes and B lymphocytes and their roles in specific immune responses:

Feature	T lymphocyte	B lymphocyte
Origin	Bone marrow	Bone marrow
Site of maturation	Thymus	Bursa of Fabricius in birds; bone marrow and gut -associated lymphoid tissue in mammals
Antigen receptors	T cell receptors	Membrane -bound immunoglobulin's Following interaction with antigen, B cells differentiate into plasma cells which produce antibody
Soluble factors produced	Cytokines	Antibodies
Protective role	Subsets of T lymphocytes participate in a wide range of cell mediated immune responses	Antibodies, which have a protective role against many infectious agents, are the effector molecules of humoral immunity
Participation in hypersensitivity	Participate in type IV reaction	Participate in types I, II and III reactions
Contribution to the development of immunological memory	Memory T cells produced	Memory B cells produced



Potential adverse reactions following vaccination:

1. Local or systemic infection caused by contamination of live vaccine with extraneous agents
2. Disease produced by the survival of infectious agents in a supposed by killed vaccine
3. Disease produced by resistant infectious agents such as prions surviving in inactivated vaccines
4. Disease production by live vaccine in immunosuppressed animals
5. Vaccine-induced immunosuppression
6. Development of hypersensitivity reactions to vaccine components (immediate or delayed responses)
7. Induction of neoplastic changes due to the presence of oncogenic infectious agents or from the action of adjuvants
8. Disease produced by the presence of infectious agents in live vaccines indictable by current conventional methods



Session-21

Antimicrobial Resistance Situation in Hospitals International

Key Points of this session:

- *Integron elements and their resistance gene cassettes*
- *Chicken meat from supermarkets*
- *Specimens from farms and human workers*
  Community
- *Future collaboration and technology transfer*

Horizontal Gene Transfer

- Transformation
- Conjugation
- Transduction

"Gram-negative" Resistance Integron:

What we should know! "Integron" was named by H. W. Stokes and Ruth Hall in 1989 (Australia) Paul H. Roy et al. was also working on these genetic elements in late 80s (Canada) Different resistance genes surrounded by conserved DNA segment encoding a putative recombinase

Integron Characteristics

-Gene capturing machine
-Useful genes are called "cassettes"
-Recombinase activity is from "integrase", an enzyme of a tyrosine recombinase family
-Non-palindromic recombination site called "attI", specific for each integrase
-Now it becomes the antibiotic resistance gene collecting machine

Basic Structure of Integron

Animals from Farms (and their bacteria!)
Multi-drug resistant Salmonella spp. may be spread throughout Thailand now.
–Most farms give antibiotic as feeding supplement banned in 2002, but no one followed
–The bacteria carry integron elements
–The one identified match with those in other regions of the world

Bacterial isolates:

E. coli Human	Food Animal 6	258
Farm env	26	
Total Salmonella	290 Food Animal	117
Human	0	
Farm env	167	
Total	284	

- Reintroduction of Antimicrobials Previously Abandoned
- Limited use in human infections primarily due to nephrotoxicity
- Pan-resistant Gram-negative organisms brought Polymyxin revisit
- No option to treat carbapenemase-producing Gram-negative bacilli, i.e. CRE

- Antimicrobial Peptide
- Polymyxins are polypeptide antibiotics
- Five compounds, polymyxin A-E
- Only two have been used clinically (polymyxin B and E)

- Polymyxin Action
- Colistin (polymyxin E) disrupts the outer membrane of bacteria
- Displacing magnesium and calcium resulting in cell death
- Acquired resistance to the polymyxins has been reported in organisms such asPseudomonas aeruginosa and Acinetobacter baumannii

- Plasmid-borne Polymyxin Resistance: MCR-1
- Mobile colistin resistance-1: November 2015

Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study. Liu, Y.-Y., Wang, Y., Walsh, T. R., Yi, L.-X., Zhang, R., Spencer, J., et al. MCR-1, a phosphoethanolamine transferase enzyme, resulting in the addition of phosphoethanolamine to lipid A Found in Enterobacteriaceae and P. aeruginosa mcr-1 has been reported on all continents from human, animal, and environmental sources Skov RL, Monnet DL. 2016. Plasmid-mediated colistin resistance (mcr-1 gene): three months later, the story unfolds. Euro Surveill21.

Laboratory Testing

- Challenges in laboratory testing
- Problems of specific physiochemical properties
- Lack of clinical data to correlate with isolate MICs
- Large size and amphipathic (hydrophobic and hydrophilic) nature of the polymyxins
- Unacceptable performance of disk diffusion and agar gradient diffusion

Problems in Laboratory (cont.)

- Polymyxins are also cationic increasing adsorption to plastic surfaces
- The addition of Polysorbate-80 (P-80) to broth microdilution panels decreases adsorption and leads to more accurate MICs (But P-80 may affect bacterial growth???) Use a validated broth microdilution method
- Report the MIC value with no interpretation

Centers for Disease Control and Prevention (CDC) advises

Laboratories which test Enterobacteriaceae for colistin resistance should confirm the presence of the mcr-1gene in isolates with an MIC of 4 µg/ml or greater. Not necessary to test intrinsically resistant bacteria, e.g. Proteus, Providencia, Morganella, Serratia, and Moraxella.

The Clinical and Laboratory Standards Institute (CLSI)

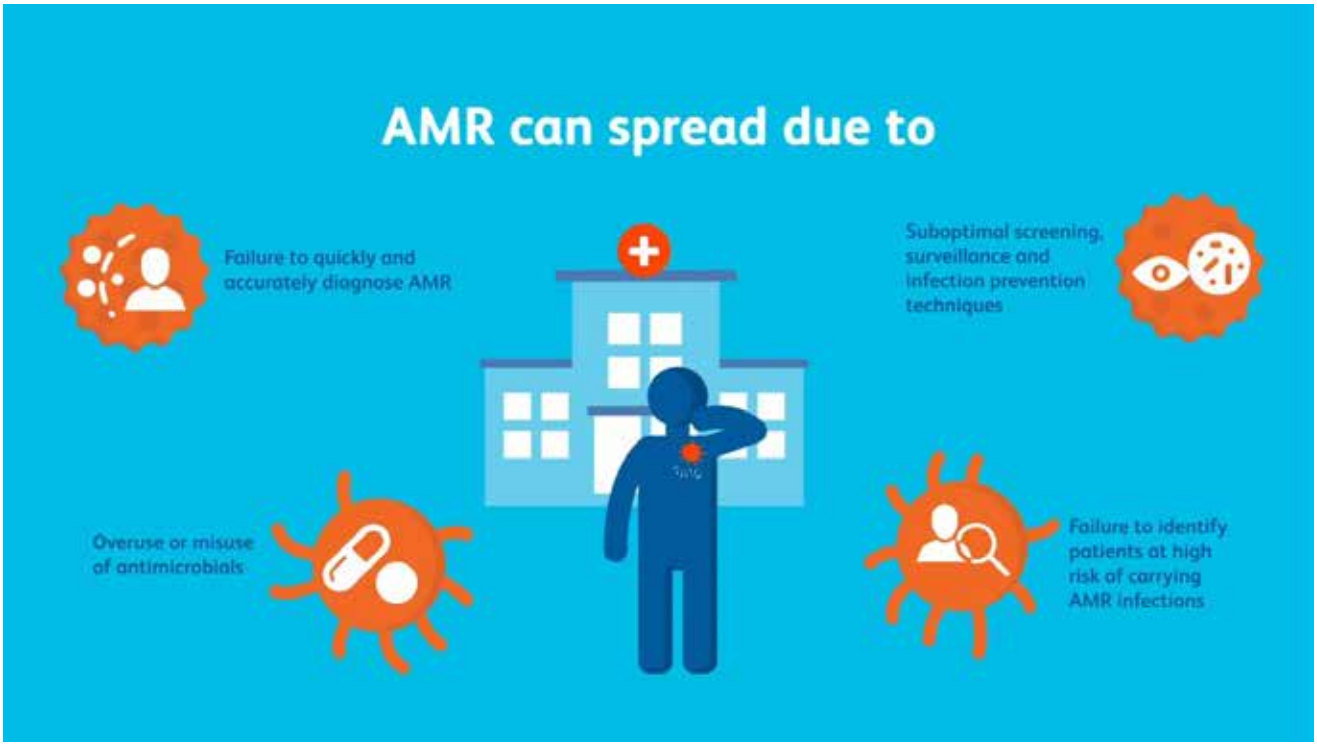
CLSI has reevaluated colistin interpretive criteria, Upcoming changes will be outlined in the M100 Performance Standards for Antimicrobial Susceptibility Testing

Epidemiology and Infection Control

- Natural interspecies spread within the Enterobacteriaceae with potential widespread of colistin-resistance, infection control should be enforced
- If mcr-1is identified from patients, local and state public health authorities should be notified immediately
- The CDC: all mcr-1-harboring isolates can safely be handled in a biosafety level-2 (BSL-2) laboratory

Future Threat

mcr-1may follow the same rapid pattern of spread that has already been observed for other plasmid-borne mechanisms of resistance, such as the Klebsiella pneumoniae Carbapenemase (KPC) and the New Delhi Metallo Beta-Lactamase (NDM) Horizontal transfer to Acinetobacter baumannii.



Session-22

Antimicrobial Use (AMU) in Hospitals

Key Points of this session:

- *Global, Regional and International policies on AMR*
- *Time line of the AMR/AMU initiatives in Bangladesh.*
- *Antibiotics smart use program*
- *Antimicrobial Use in Bangladesh*
- *National action plan (2016-2021) Objectives.*

Global, Regional and International policies on AMR

AMR Strategy	-Global Health Security Agenda (GHSA) (2014) -Global Action Plan on AMR (GAP-AMR) (2015) -FAO Action Plan on AMR 2016-2020(2016) -OIE Strategy on AMR and the Prudent Use of Antimicrobials (2016)
M&E frameworks	-WHO Monitoring and Evaluation of the Global Action Plan on AMR (in a developing process) -Joint External Evaluation on International Health Regulation (2016) -Joint External Evaluation on International Health Regulation for Human-Animal Interface (2017)
AMR resolution/ declarations	Government -WHA resolution 68.7 on GAP-AMR (2015) -FAO resolution 4/2015 on AMR (2015) -UNGA resolution 71/3 on Political declaration of the high-level meeting of the General Assembly on AMR (2016) -Alliance of champions on AMR (2015) -SEARO: Jaipur Declaration on AMR (2011), AMR as the SEARO Regional Director's Flagship (2014) -Asia Pacific: Communiqué of Tokyo Meeting of Health Ministers on AMR in Asia (2016) -ASEAN: ASEAN Leaders' Declaration on AMR: Combating AMR through One Health Approach (to be adopted in November 2017)

Non-government

-Antibiotic Resistance Coalition (2015)

-Declaration by the Pharmaceutical, Biotechnology and Diagnostics Industries on Combating Antimicrobial

Resistance (2016)

Time line of the AMR/AMU initiatives in Bangladesh.

12thNational Economic and Social Development Plan (2017-2021): focusing on aging society and AMR problems

WHO Global action plan on AMR at the WHA68 (2015) – Thailand is the leader of 11 countries in the South East Asia Regional One Voice to adopt the GAP-AMR United Nations General Assembly: Political Declaration of High-level Meeting of General Assembly on Antimicrobial Resistance

WHO GAP-AMR

Objective 4: Optimize the use of antimicrobial medicines in human and animal health

–AMR is driven by the volume of antimicrobial use; over-prescription, over-the- counter sales, and sales over the internet, etc.

–Data on antibiotic use are collected and analyzed in only high-and middle-income countries

–Lacking on antibiotic use in human beings at the point of care and from lower- income countries

WHO GAP-AMR

- Industry spending on promoting products is greater than governmental investment in promoting rational use of antimicrobials
- Decisions to prescribe antibiotics are rarely based on definitive diagnoses. Effective, rapid, low-cost diagnostic tools are needed for guiding optimal use of antibiotics in human and animal medicine
- AMR causes 700,000 death/year globally
- In 2050, it is projected to be 10 million death
- National action plan (2016-2021) objective is to control antimicrobial use in hospitals
- (drug registry and smart use program)

National action plan (2016-2021) Objectives

- Systematically manage AMR with integrated approach
- Increase capacity for Infection Control in both equipment and human resource
- Control and monitor the AMR management in healthcare facilities
- Control proper use of antimicrobials in private clinics
- Control the sales of antimicrobials in drug stores
- Short Outcomes of NAP
- Setting the National Committee for AMR Release the policy on Antimicrobials smart use
- Stop important antibiotic sales by drug stores, e.g. prescription needed.
- Control antimicrobial use in animal hospitals

Goals of National Action Plan by 2021

- 50% reduction of AMR infections
- 20% reduction of human antimicrobial use
- 30% reduction of animal antimicrobial use
- 20% increase of antimicrobial knowledge among Thai people
- Reach international level 4 for AMR management

Need to assess AMR data in Bangladesh.

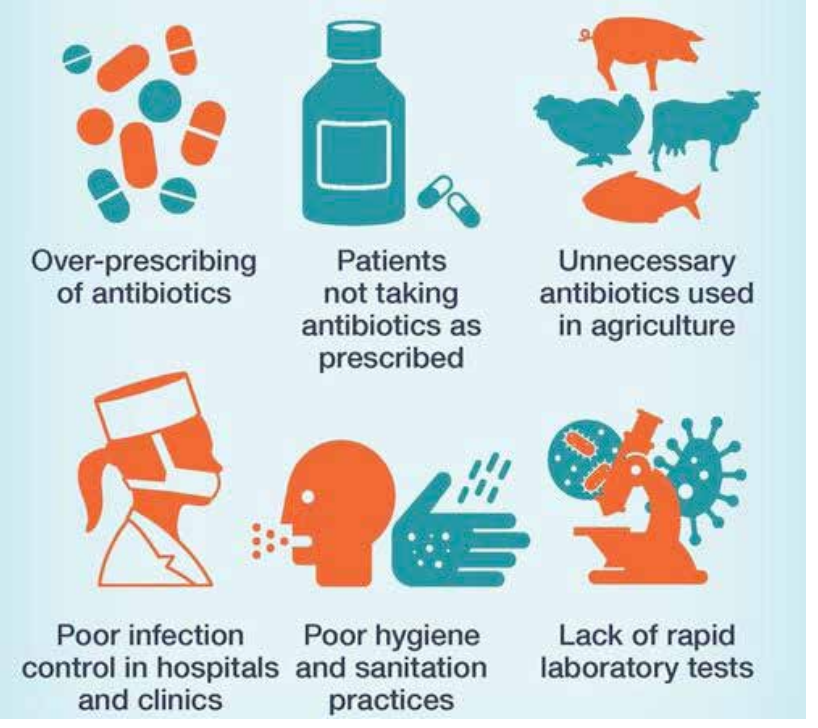
- AMU is an important risk factor for the development of AMR
- Collection of data on AMU in humans, agriculture and aquaculture is vital for understanding of The Drivers of AMR in Southeast Asia
- Economic development and population growth stimulate antimicrobial demand
- Antimicrobial usage in human medicine
- Antimicrobial awareness, knowledge and prescribing practices
- Antimicrobials in agriculture and aquaculture
- Drug access and quality
- Hospital Antibiotic Stewardship Programs
- Formal, written statement of support from leadership Financial support for antibiotic stewardship activities Physician and Pharmacist leaders are important staff

Actions to Support Smart Antimicrobial Use

In the antimicrobial order: must indicate a dose, duration, and indication for all antibiotic prescriptions Have facility-specific treatment recommendations and national guidelines Actions to Improve Antibiotic Prescribing Formal procedure to review the appropriateness of all antibiotics 48 hours after the initial orders dispensing Pharmacy-driven Interventions Automatic changes from intravenous to oral antibiotic therapy Dose adjustments in cases of organ dysfunction Pharmacokinetics/pharmacodynamics considerations Time-sensitive automatic stop orders for specified antibiotics

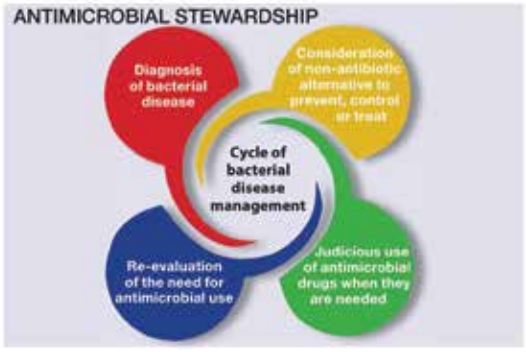
Diagnosis and Infections Specific Interventions. Solutions to the crisis:

Surveillance
Diagnostics
Stewardship
Qualitative research



Session - 23

Slowdown process of AMR and Antibiotic Stewership



Key Points of this session:

- *Slowdown process of AMR:*
- *Antimicrobial Stewardship :*
- *Building the stewardship team:*

Slowdown process of AMR:

Always wash your hands.

- Wash or sanitize your hands before every meal, using soap and water or hand sanitizer that is a gelled solution of 70% rubbing ethyl alcohol.
- Be sure to wash your hands after you go to the bathroom, not simply run your hands under water. Water doesn't wash off the germs, the soap will help with that.
- Keep your hands away from your mouth, eyes, and nose.
- This is particularly important if colds or a particular flu is hanging around your place of work or school. This way you reduce the chance of ingesting or inhaling germs and getting sick yourself. Otherwise, make sure you sanitize or wash your hands.

- Colds and flu are contagious and get spread around via airborne bacteria and viruses and contaminated objects.
- In a public place, the highest contaminated object would be stair-case handles, door handles, elevator buttons, computer keys, and even the sink taps.
- There's no avoiding touching these, but you can try to avoid taking in the "bugs" from these objects by keeping your dirty hands away from your face.
- You can also try to touch as little of these objects as possible.

Don't accept anything from someone you suspect is sick.

- But be liberal about it. Food and drink is one thing you must be careful about, and have a napkin at the ready if a glass is headed your way with the sick person's hand having been previously handled it.

Cover your mouth when you cough or sneeze.

- Do not cover your mouth with your hand! Rather, use the crook of your elbow to stop most of the spray that you would put out with a terrifically shattering sneeze, and do the same if you are coughing. The back of your hand may also work as well if it's necessary.

- If you can, try to keep the sneeze in, like sneeze quietly with your mouth closed and not a loud, "AAH-CHOO!!" This will reduce the chance of germs spreading onto other people and other things that people after you will use. To control coughing, use cough lozenges like Ricola or Fisherman's Friend cough drops as prescribed on the package or by your doctor.

Take care of runny noses properly.

- use a tissue or Kleenex, not your hand, to wipe your nose, and keep them handy, particularly if you are coming down with an illness that is leaving you with a runny, plugged-up nose. While this step goes in hand with step #2 above, this reduces germs getting to others and being spread around.

Be careful about any potential antibiotics you will have to take if you get sick.

- If you are ill with something that may resemble the flu or an infection, see your doctor as soon as possible to get it checked out. Your doctor has the expertise to tell you whether what you have is a bacterial or viral infection, and whether it
- needs treatment or simply a day of rest and lots of fluids.

Take your medicine according to the doctor's advice.

- Do not try any what is called "extra-label" use practices, like taking less or more of what is recommended.
- Skipping times to take your meds, not taking enough (stopping when you think you are feeling better and think you don't need to take anymore medication), or
- Insisting that you should take a particular medication because you've always
- taken that and it's always worked for you, even though the doctor strongly disagrees and says you need to take something different.

Hospitals are reservoirs for super-bugs.

- This is something that everyone must know, no matter how hygienic or sterile and environment they seem to be. This is also where you must be absolutely cautious about where you put your hands and what surfaces you touch.
- Sanitize as frequently as possible (even if you feel you have to hit every sanitizer station along the route you take through a hospital), touch few surfaces as possible, and certainly keep your hands off your face as often as possible.

Eat healthy and well.

- Take in foods that are known for their health capacities, such as apples, honey, broccoli, blackberries, and many other fruits and vegetables. You do not have to go vegetarian or vegan to reduce your chance of getting an antibiotic resistant bug, as majority of meat and dairy products are made with a very, very low chance of you ingesting antibiotics.

- Use your common sense with cooking meat. Ground beef and all poultry and pork meats must be cooked through or until they are well-done (no pink in the middle), and beef cooked in a similar fashion, or to the USDA recommended 145ºF for medium-cooked steaks and roasts.

- Antibiotic resistance with regards to livestock is less of a concern from the point the animal is raised to slaughter, particularly when majority of producers practice safe-use labelling and follow withdrawal times (time from last injection to when the animal is to be slaughtered or be used for milk and eggs) according to drug labelling.
- While there is controversy and questions surrounding antibiotic use in livestock, antibiotic-residue presence in the meat is tested both on farm and at random in the slaughter plant. Any antibiotic that would be present in meat, milk or eggs are at such low levels that they are not a risk to human health, and not likely to contribute to the development of antibiotic-resistant bacteria.
- There are also many antibiotics used in animals that are not approved for use in humans.

Antimicrobial Stewardship :

- Antimicrobial stewardship has been defined as "the optimal selection, dosage, and duration of antimicrobial treatment that results in the best clinical outcome for the treatment or prevention of infection, with minimal toxicity to the patient and minimal impact on subsequent resistance."

- Antimicrobial drugs have been widely used in veterinary medicine for more than 50 years. When used judiciously, antimicrobials can effectively fight infections and improve animal health. However, overuse of antimicrobials promotes the development of antimicrobial-resistant bacteria. Today, antimicrobial resistance is a worldwide phenomenon and growing problem. To slow the emergence of resistance and extend the useful life of antimicrobials, stewardship of antimicrobials in both human health and veterinary settings is essential.

- The first goal is to work with health care practitioners to help each patient receive the most appropriate antimicrobial with the correct dose and duration. Joseph and Rodvold wrote about the "4 D's of optimal antimicrobial therapy": right Drug, right Dose, De-escalation to pathogen-directed therapy, and right Duration of therapy. The optimal care of an infected patient means treating with the correct, properly dosed antibiotic and one that has the least likelihood of causing collateral damage (ie, leading to resistance in the patient or his or her contacts).

- The second goal is to prevent antimicrobial overuse, misuse, and abuse. In both the hospital and the outpatient setting, physicians use antibiotics when they are not necessary. Antibiotics are given to patients with viral infections, noninfectious processes (a classic example is the febrile patient with pancreatitis), bacterial infections that do not require antibiotics (such as small skin abscesses that will resolve with incision and drainage), and bacterial colonization (as in the case of a positive urine culture result in a patient with a bladder catheter). Antibiotics are also frequently misused, such as in the very common scenario of the use of broad-spectrum antibiotics that cover multidrug- resistant organisms in a patient whose infection was acquired in the community or the failure to

adjust antibiotics according to culture data, thus maintaining the patient on a regimen to which the organism is not susceptible. Abuse of antibiotics is more difficult to define, but the term might be used to describe the use of one particular antibiotic preferentially over others by a physician as a result of aggressive detailing by the pharmaceutical representative or worse because of financial interest.

- The third goal is to minimize the development of resistance. Both at the individual patient level and at the community level, antibiotic use changes susceptibility patterns. Patients exposed to antibiotics are at higher risk of becoming colonized or infected by resistant organisms.The most common cause of the development of Clostridium difficile diarrhea is exposure to antibiotics.Gram-negative resistance to carbapenems and cephalosporins has been shown to increase 10- to 20-fold with exposure to these broad-spectrum antimicrobials.

- The Food and Drug Administration (FDA) is committed to antimicrobial stewardship and supports several important principles that are critical to curbing or slowing the emergence of antimicrobial resistance. With respect to veterinary settings, these principles are 1) antimicrobial drugs should only be used when necessary to treat, prevent or control disease, and 2) when antimicrobials are used, these drugs should be administered in an optimal manner under the supervision of a licensed veterinarian.

BUILDING THE STEWARDSHIP TEAM:

Every hospital should work within its resources to create an effective team given its budget and personnel constraints. The stewardship team does not have to fit a particular mold, and it would be a mistake to delay implementation of a stewardship program because of a lack of availability of one or more of the typical team participants listed subsequently. Most stewardship teams include either an infectious disease physician or a pharmacist (with or without specialized training in infectious disease) or both. Sometimes a hospitalist with an interest in infectious disease serves in this role. Often the infection preventionist is an active member of the team. Close collaboration with the staff in the microbiology laboratory, hospital epidemiology, and administration is essential to a well-functioning program. A working relationship with the information specialist can be especially helpful. Engaging hospital leadership will open doors to good relationships with other physician groups. Therefore, early involvement of thought leaders from hospital administration and the various practitioner groups will improve acceptance and implementation.

Session-24

AMR in Milk, Meat, Eggs and Fish

Key points of this session:

- *Industrial livestock and poultry and fish production in Bangladesh*
- *Animal farms and animal waste release*
- *Use of veterinary drugs and feed additives in animal and fish farming*
- *Sustainability of Bangladesh's animal farming practices.*

Antibiotics are powerful medicines that fight certain infections and can save lives when used properly. They either stop bacteria from reproducing or destroy them. ... White blood cells (WBCs) attack harmful bacteria and, even if symptoms do occur, the immune system can usually cope and fight off the infection.

Antibiotics in Eggs:
After taking an antibiotic you may need to wait for up to three hours before eating or drinking any dairy products. Grapefruit juice and dietary supplements containing minerals like calcium may also work dampen the effect of antibiotics.

Antibiotic in Chicken:
One can eat chicken on a daily basis; however, it is good to use cooking methods like boiling, grilling, roasting or baking rather than frying as it can lead to various health problems.

Every year, about 63,151 tons of antibiotics are being used in livestock worldwide. In animal husbandries, antibiotics are applied for both therapeutic and prophylactic purposes. Due to some positive impacts, multiple veterinary antibiotics (VAs) have been used worldwide recently for promoting growth and treatment of the livestock. The global usage of antimicrobials in animals is double compared to humans. Many studies have shown that significant portions (30%–70%) of antibiotics are released unaltered, i.e., with potential antimicrobial activity, into the environment. Upon release into the environment, most antibiotics are persistent and biologically active. Milk is a highly consumed food item in the world which has also a great value for human health. Residues of antibiotics are mainly found in milk due to their injudicious usage in treating infectious diseases of animals. Moreover, some antibiotics are being used as feed additives indiscriminately which is another source of antibiotic residues in milk, ultimately responsible for potential public health importance.

Antibiotic residue (AR) in Milk.
Among the vital causes of presence of antibiotic residues in milk, dry cow therapy and usage in mastitis treatment are of great importance. The developing countries are in greater risk due to residues in milk than the developed ones. Poor detection facilities as well as lack of proper monitoring system of residues in foods considering the maximum residue limits (MRLs) might be taken as vital causes for higher risk of milk derived antibiotic residues.

Main causes of presence of antibiotic residues in milk

1. Therapeutical uses of antibiotics: Vital cause of presence of ARs in milk is the indiscriminate usage of antibiotics in therapy of infectious diseases, such as clinical mastitis and viral diseases.

2. Antibiotics as prophylactics: Sometimes, antibiotics are used in therapy of dry cow and management of post-surgical risk, which are also responsible for AR in milk.

3. Antibiotics in miscellaneous purposes: There may have direct or indirect pathways of contaminating milk by ARs, when used during processing and preservation of milk and related dairy products.

4. If the supplied instructions in the label are not followed accordingly, residues of antibiotics may be found in milk. When an antibiotic is approved only for humans become used injudiciously in animals, or usage in different species where it is not approved, or during a condition where it is not approved, or usage beyond the appropriate concentration, may be referred as extra-label use

.

5. Lack of maintenance of proper withdrawal time: Without proper maintenance of withdrawal time of antibiotics in milking animal, AR appears in milk at higher concentration.

6. Limited detection facilities of ARs and improper monitoring system of residues due to the crisis of strong regulatory organization, may be considered as important phenomena in this issue for developing countries.

7. Normal metabolic process of antibiotics is hampered in diseased animals, which can cause antibiotics to remain stored for a longer period of time and higher amount in tissues, ultimately impose a higher risk of residues.

8. Lack of awareness of farmers about residual effects of AR from milk in human health.

9. Improper education of farmers.

10. Inadequate literatures supplied by manufacturers.

11. Improper cleaning of antibiotics contaminated equipment after using in mixing or administering process.

12. Improper disposal of empty containers of antibiotics in the farm premises which can contaminate feeds of animals. Animals may lick those or even get exposed through contaminated feeds accidentally.

13. Insufficient identification of treated cows.

14. Miscellaneous factors those influence the presence of AR in milk:

a. Type and concentration of antibiotics
b. Excipients used during preparation of medicine
c. Frequency of milking and quantity of milk collection d. Absorbance of udder tissues
e. Milk yield (AR in milk is inversely related with milk yield). f. Individuals factors

Potential effects of ARs on public health and in dairy industry

1. Antibiotic resistance: Presence of low level of antibiotic residues in milk and other dairy products causes microorganisms to be resistant against antibiotics. The resistant microbes may be transmitted among the individuals via direct contact or indirectly by exchange of resistant genes in the environment.

2. Allergic reactions: Residues of various antibiotics are associated with multiple types of allergic reactions, including serum sickness and anaphylaxis, especially in case of penicillins.

3. Carcinogenicity: Residues of antibiotics possess potential carcinogenic impacts by interacting with cellular elements, such as DNA and RNA.

4. Mutagenicity: Mutagenic effect is another dangerous impact of ARs, which can cause mutation of DNA molecule or damage of chromosomes. Infertility of human being may results from this mutation.

5. Teratogenicity: Various congenital anomalies may be seen in new born child due to long term exposure of ARs during gestation period.

6. Disturbances in the normal intestinal environment: Normal habitant of the intestine coexists with others and colonizes to prevent the pathogenic microbes from producing diseases. ARs in milk resulting from usage of broad-spectrum antibiotics may kill a wide range of microflora in the intestine including the non-pathogenic organisms, which can make the disease causing microorganisms more prominent and disrupt the normal intestinal environment.

7. Effects in dairy industry: Existence of ARs in milk, even in very low concentration is of great concern in dairy industries. The residues of antibiotics can interfere with the fermentation process during production of cheese and yogurt by inhibiting the starter cultures.

Control and preventive measures to avoid ARs in milk

1. There are two basic approaches to control ARs in milk: (a) Development of highly sensitive detection tools to avoid the false negative results; (b) Usage of appropriate methods for confirmation and quantification of ARs, where possibility of false positive outcome will be minimum Simple, rapid, sensitive, specific, and economic procedures should be developed to analyze ARs in milk, followed by discarding if exceeds the MRL.

The MRLs in milk for some antibiotics, established by European Commission (mentioned in council regulation 2377/90/EC) is given below :

Antibiotics	MRLs in milk (µg/kg)	Antibiotics	MRLs in milk (µg/kg)
Benzyl penicillin	4	Gentamicin	200
Ampicillin	4	Neomycin	1500
Amoxicillin	4	Spiramycin	200
Tetracycline	100	Tylocin	100
Oxytetracycline	100	Erythromycin	40
Chlortetracycline	100	Colistin	50
Streptomycin	200	Ceftiofur	100
Dihydrostreptomycin	200		

2. The level or concentration of ARs in milk should be under regular basis monitoring and surveillance policies nationwide.

3. Following measures can be taken to inactivate some of the antibiotics: (a) Penicillin becomes inactivates following refrigeration. (b) Pasteurization can be used as an important measure to make most of the antibiotics inactive. (c) Some of the antibiotics loss their activity if treated with UV radiation, activated charcoal or resin etc.

4. Development of public awareness through arrangement of some effective activities in this field, facilitated by the expert personnel or organizations.

5. Indiscriminate uses of VAs should be strictly prohibited.

6. Herbal sources of medicines may be taken in consideration as an alternative option for treating diseases.

7. Following guidelines for an effective drug use program:
a. Paying attention to proper withdrawal times of antibiotics for milking cows. b. Label instructions should be read prior to purchasing of antibiotics to
understand the consequences of usage.

c. Drugs used for lactating and non-lactating animals should not be intermixed, rather storing those in separate places.

d. Maintaining the good hygienic management practices during antibiotic administration.

e. Proper biosecurity should be maintained in dairy farms to avoid infections.
Highest priority should be given in maintaining better health quality of dairy animals, where usage of antibiotics can be avoided in large extent.

f. Marking of antibiotics treated cows for easy identification, which will help the milkers to recognize them and withheld milk from marketing up to appropriate withdrawal time.

g. Data regarding treatment of milking cows should be preserved cautiously in written form, where date and cause of treatment, name and dosage of drugs used, withdrawal time must be included.

h. Antibiotics treated cows should be separated from the rest ones and milking lastly to minimize the risk of ARs contamination.

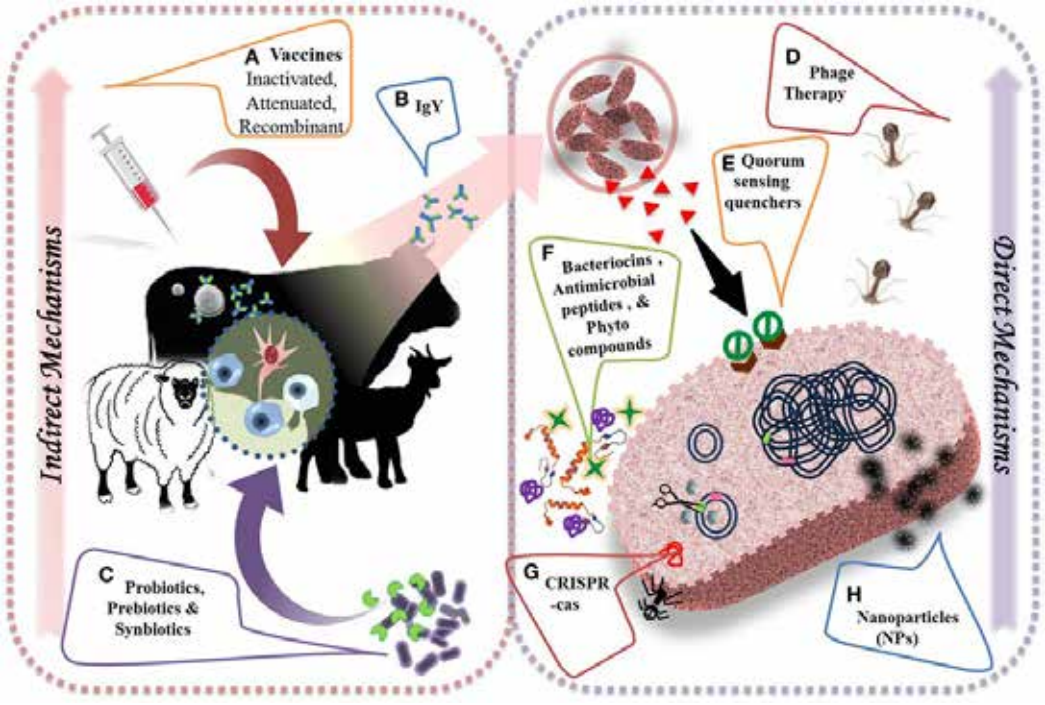
i. Milk should be withdrawn and discarded from all of the quarters following intra-mammary infusion of antibiotics, as infused drug can be disseminated through circulation easily.

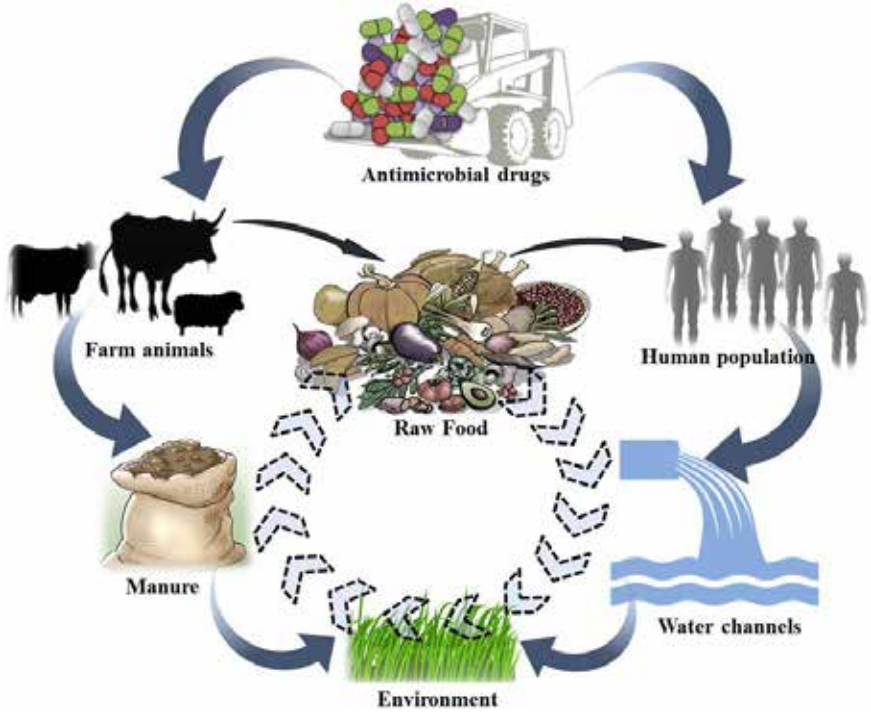
j. The dairy producers should be made competent about maintaining proper quality of milk as well as its assurance.

Therefore, the appropriate measures should be implemented to cease the ARs in milk.

Antibiotic in Fish-
The accelerated growth of aquaculture has resulted in a series of harmful effects to human health. The widespread and unrestricted use of antibiotics in this industry, to prevent bacterial infections, leads to remaining amounts in the aquatic environment. This has resulted in the emergence of antibiotic-resistant bacteria in aquaculture environments, in the increase in antibiotic resistance in fish pathogens as

well as in the transfer of these resistance determinants to human pathogens. Moreover, the use of large amounts of antibiotics may lead to the presence of residual antibiotics in fish tissue and fish products. Fluoroquinolones, tetracyclines, penicillins, sulphonamides and other antibiotics, exhibiting activity against both Gram-positive and Gram-negative bacteria, are widely used for the treatment and prevention of diseases in fish.





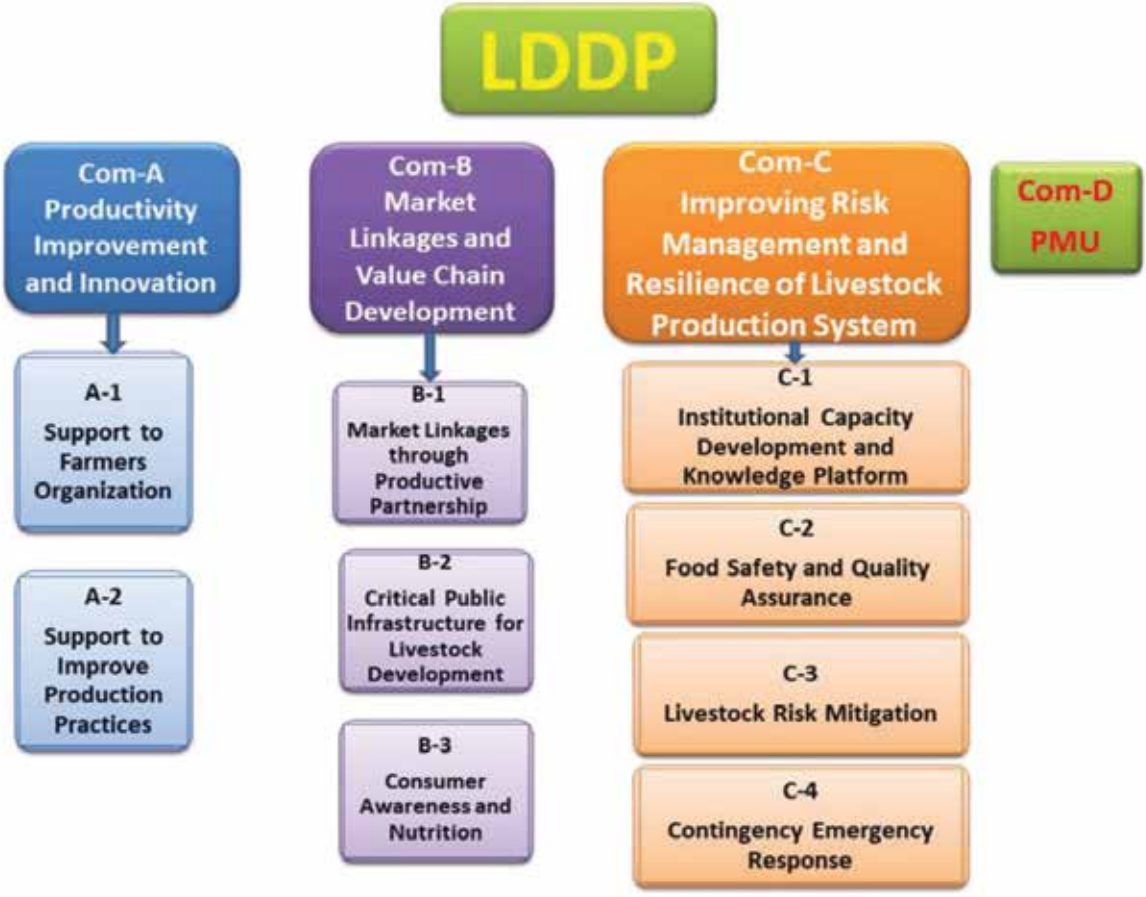
Session-25

Introduction of LDDP. Project Implementation strategy and its input output outcome

Kye Points of this session:

- *Introduction of LDDP.*
- *LDDP Implementation Strategy.*
- *Projects input and Output.*
- *Outcome of this project.*


Nov 2016
Scoping Mission
March-April 2017
Identification Mission
Sept 2017
Pre Appraisal Mission
Oct-Nov 2017
Costing Mission
April 2018
Appraisal Mission
Oct 2018
Tech Negotiation & WB Board
Decem 2018
Loan Agreement Signing

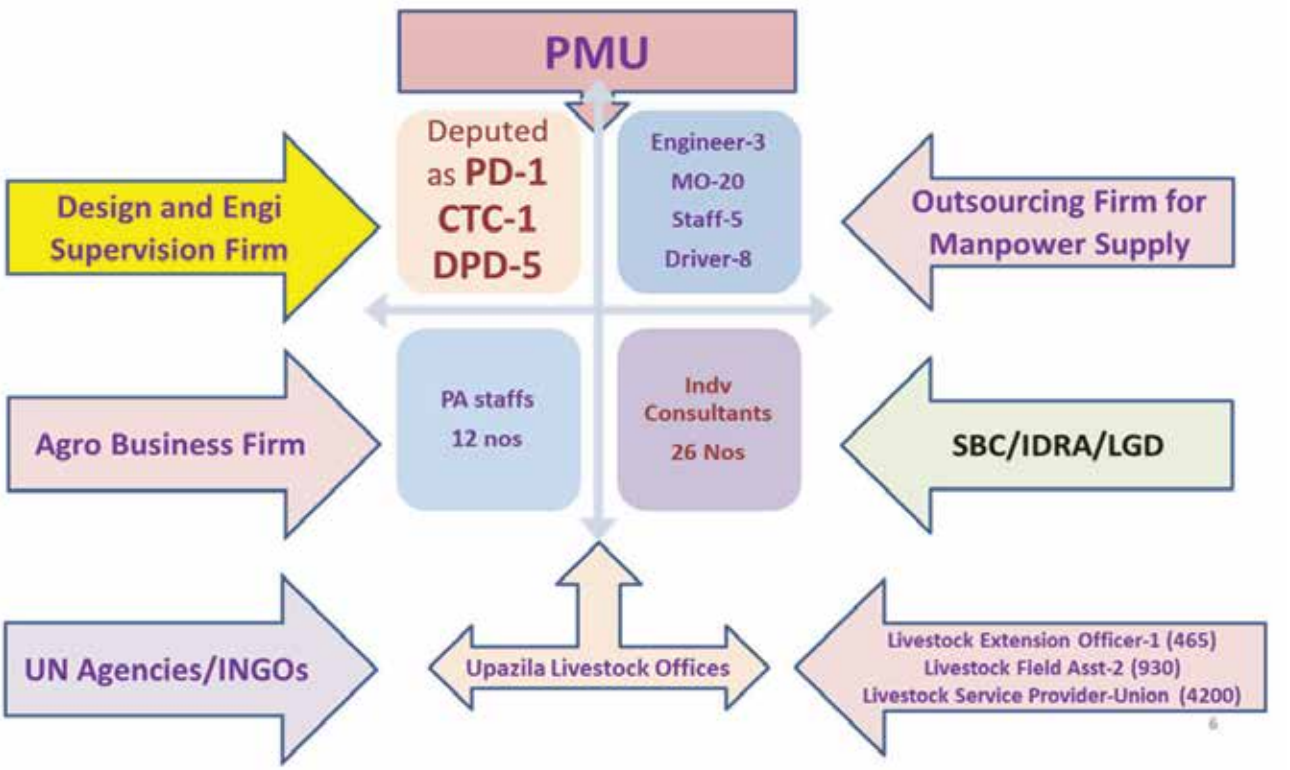

LDDP
Com-A Productivity Improvement and Innovation
A-1 Support to Farmers Organization
A-2 Support to Improve Production Practices
Com-B Market Linkages and Value Chain Development
B-1 Market Linkages through Productive Partnership
B-2 Critical Public Infrastructure for Livestock Development
B-3 Consumer Awareness and Nutrition
Com-C Improving Risk Management and Resilience of Livestock Production System
C-1 Institutional Capacity Development and Knowledge Platform
C-2 Food Safety and Quality Assurance
C-3 Livestock Risk Mitigation
C-4 Contingency Emergency Response
Com-D PMU

LDDP: Basic information

- Proposed 5 years (2019-2023)
- Total Cost: 428036.48 Lac BDT (IDA - 388573.07, GoB 39463.41)
- Project Areas – 61 districts (other than 3 hilly districts)
- Farm HH-191000: (Dairy-100000, Beef-20000, Sheep/Goat-15000, Com.Poultry-16000, Sonali-10000, Scavenger Poultry-30000)
- FO/POs-5500, LSP-4200
- Mobile Veterinary Clinic Facilities-360
- Food Safety and Quality Control
- Information System/Database/ICT
- Logistic Facilities at Upazila
- Logistic Facilities at FDIL, CDIL, DVH, CVH
- Progressive Disease Control Program

Dairy Hub-20, VMCC-300, Estd of DB-1
Cooling System at VMCC-175
School Milk-700 School, (2000 SY)
Modern Slaughter House-3
District level slaughter house-20
Upazila/growth center level WM-192
Cattle Insurance-Policies, basics, pilot.
Knowledge Platform-1 GP & Tech and R&I
Manure Entrepreneur Development-10
Product diversification-405, Feed Entrepreneurship
Office Space for PMU, Dist AI Centre-7+2
Capacity Strengthening, Training, Demo, Tour

5



6

SL No	Risks/Challanges	Mitigation Measures
1	Weak institutional capacity of DLS	Will be mitigated through (a) recruitment of manpower under project; (b) possible additional manpower under proposed organogram of DLS.
2	Lack of sufficient professional knowledge and skills of both DLS and stakeholders	Will be improved through training, tours and learning by doing process as identified by feasibility report.
3	Insufficient logistics and infrastructural capacity of DLS	Will further be strengthened through supplying logistics like Mobile Veterinary Clinics (MVC), modern equipment and machineries, and vehicles. Modern infrastructures to be built and institutions to be established.
4	Weak extension-research- academia linkages	Through establishing knowledge platform under the project will further stimulate the linkages among research- extension-farmers-academia both nationally, regionally and globally.
5	Timely PMU set up, recruitment of experts, staff and firms	As soon as project is approved, PMU will be set up as per set criteria within a shorter possible time period.
6	Timely procurement of goods, works and services	PMU will be assisted by a design and supervision consulting firm and procurement experts which will further stimulate the PMU capacity to procure and deliver inputs. A number of subject specific experts/consultants identified and kept the project for smooth execution.
7	Cooperation of relevant ministries/divisions/agencies	To implement slaughter houses constructions, insurance piloting, exhibition of dairy products to school children, registration of FO/PO need deliberate cooperation of respective ministries/divisions/agencies like FID/IDRA/SBC/LGD (RD&CD)/CCs/MoPME, etc would be ensured through proper communication and signing MOU as and where applicable.
8	Active participations of processors	Strengthening of market linkages through linking of Producers Organization to Agri Business would be ensured through development of specific selection criteria. Both competitive and pre-communication basis.

Major Interventions	Sustainability Mechanisms
Farmers Organizations/ Producers Organizations and Livestock Farmers Field School	• 5500 Farmers Organizations/Producers Organizations either to be developed or strengthened • Will be facilitated for registrations either by Polli Sanchoy Bank or dept. of cooperatives. • Members of the POs will be trained on FFS modalities and agribusiness plan development • Will also be linked to ABs and/or local traditional markets for milk and milk products marketing.
Village Milk Collection Centre (VMCC) and Dairy Hub (DH)	• The VMCC will be of 20-30 farmers society or groups supplying milk either directly to dairy hub owners or stored/processed milk to sell later on. • VMCC will be maintained and run by the registered farmers organizations as per their by-laws and it will remain functional even after phase out of the project. • 20 dairy hubs owned by private agribusiness business are to be developed/further strengthened • Project will stimulate the food safety and nutrition awareness through multi-faceted media communication
Modern Slaughter House at metro area; Slaughter House at district level; Hygienic	• 3 nos modern slaughter houses with cool chain, mechanical devices, storing and sanitary measures, effluent treatment facilities, etc. operated and owned by the selective city corporations. • 20 nos district level slaughter houses to be built and owned & operated by interested pourashovas.
Slaughter Facility at Upazila or growth centre	• 192 nos either wet market renovated and/or slaughter facilities will be developed conditional to land availability and demand by local pourashovas. • Project will only constructed/ renovated the structures.
Milk Chilling Plant	• 175 Milk Chilling Plants will be procured and distributed to farmers societies or farmers/entrepreneurs • This will also owned by them and benefit will also bestowed upon them that will ensure its sustainability.

Major Interventions	Sustainability Mechanisms
Dairy Development Board	• A Dairy Development Board Office will be constructed in the land of DLS at Savar • Will be used and maintained by the Dairy Development Board to be formed.
Officers Training Institute (OTI)	• OTI at Savar will be further restructured and capacitated and eventually run as running now.
Manure Management Plants	• Manure management plant will be established in Savar Dairy to demonstrate how farm manure to be converted into valuable resources • Will be run and maintained by the corresponding farm authorities. • Moreover, 10 entrepreneurs could get support to establish similar facilities at their farm premises • Profitable and environment friendly enterprise based-on cow-dung and farm debries.
Dairy Training Centre	• Dairy Training Centre will be established in 6 different government dairy farms • Will be run and maintained by the corresponding farm authorities mobilizing regular budgets

District Artificial Insemination Centre

• Artificial Insemination Centre under DLS will be either re-structured through dismantling existing old structures and/or renovated.

• These will be used and maintained by the corresponding offices using their regular revenue budget.

Major Interventions	Sustainability Mechanisms
Climate Resilient Housing	• Both small and medium sized climate resilient cattle shed will be established at the premises of interested farm households to demonstrated how to cope up with changing climatic condition. • These structures will be used and maintained by the corresponding farm HH for their own benefits and will be sustainable accordingly.
Mobile Veterinary Clinic (MVC)	• 360 nos modified vehicles equipped with modern veterinary logistics will be procured and delivered one in each upazila • Will be included in to TO & E for regular maintenance and fueling after ending of project in future.
Livestock Insurance	• Insurance policy will be developed and promulgated by the concern offices under BFID • Support will be borne from the project. • Other pre-conditions will be met up by the livestock department • Once insurance products developed and piloted, if farmers get benefit and weaver from risk, demand will be created that will make the insurance system sustainable.
Exhibition and Demonstration of Dairy Products Consumption by School Children	• This sort of program will produce multifaceted benefits including nutrition awareness, publicity, demonstration, exhibition, physical and mental health development and merit score, body score of students • Creation of future consumers for nutritious dairy products.

• Seeing is believing and like other social safety net program government may bring such program under safety net

• Corporate can invest their CSR to continue the beneficial scheme for further flourishing their dairy business.

প্রশিক্ষণে অংশগ্রহণকারীদের তথ্য ফরমের নুমনা

গণপ্রজাতন্ত্রী বাংলাদেশ সরকার
প্রাণিসম্পদ ও ডেইরি উন্নয়ন প্রকল্প (এলডিডিপি)
প্রাণিসম্পদ অধিদপ্তর
কৃষি খামার সড়ক, ফার্মগেট, ঢাকা-১২১৫

প্রশিক্ষণ শিরোনাম : Training on Anti Microbial Resistance (AMR) and Surveillance পেশাগত উন্নয়ন বিষয়ক প্রশিক্ষন।
প্রশিক্ষণ মেয়াদ : ৫ দিন।
প্রশিক্ষণ ভ্যানু : .....।

প্রশিক্ষণার্থীর তথ্যাবলী

[নিচের ছকটি পূরণ করুন (* চিহ্নিত স্থানটি পূরণ আবশ্যকীয়)]

প্রশিক্ষণার্থীর নাম	বাংলা*	:
	English Block Letter*	:
পিতার নাম	বাংলা*	:
	English Block Letter*	:
মাতার নাম	বাংলা*	:
	English Block Letter*	:
কর্মস্থল	বাংলা *	:
	English Block Letter*	:
পদবী*		:
জাতীয় পরিচয় পত্র নং		:
লিঙ্গ		:
বৈবাহিক অবস্থা		:
জন্ম তারিখ *		:
জাতীয়তা *		:
ভাষাগত দক্ষতা*	বাংলা	:
	ইংরেজি	:
	অন্যান্য	:
ধর্ম*		:
স্বাস্থ্যগত অবস্থা		:
রক্তের গ্রুপ		:

শিক্ষাগত যোগ্যতা*	ডিগ্রি/সার্টিফিকেট	বোর্ড/বিশ্ববিদ্যালয়	পাশের সাল	জিপিএ/বিভাগ

স্থায়ী ঠিকানা*	:
বর্তমান ঠিকানা	:
ইতিপূর্বে কোন কোন বিষয়ে প্রশিক্ষণ নিয়েছেন উল্লেখ করুন*	:
*ইমেইল/ফেসবুক/টুইটার/অন্যান্য সোস্যাল মিডিয়ার ঠিকানা (যদি থাকে)	:
টেলিফোন/মোবাইল নম্বর*	:
জরুরী যোগাযোগ *	:
অন্যান্য তথ্য	:

তারিখ

প্রশিক্ষণার্থীর স্বাক্ষর

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9. **A Textbook of Clinical Pharmacology and Therapeutics** by JAMES M RITTER, LIONEL D LEWIS, TIMOTHY GK MANT BSC FFPM FRCP ALBERT FERRO PHD FRCP FBPHARMACOLS

মুদ্রণে: দি প্রিন্ট মিডিয়া
২৫৭ ফকিরাপুর, মতিঝিল, ঢাকা-১০০০

প্রশিক্ষণার্থীদের মতামত ও পর্যালোচনা ছক

প্রশিক্ষনার্থীরা নীচে তাদের মতামত লিখবেন এবং প্রশিক্ষণ সহায়তাকারীকে ফেরত দেবেন। প্রয়োজনে আলাদা কাগজ ব্যবহার করুন।

ক্রমিক নং	বিষয়	মতামত		মন্তব্য (মতামত ব্যাখ্যা করুন)
১.	এই প্রশিক্ষণে অংশগ্রহণের আগে আপনি কি কম্পিউটার ব্যবহার করেছেন?	হ্যাঁ	না	
২.	এই প্রশিক্ষণের উদ্দেশ্য জানেন কি?	হ্যাঁ	না	
৩.	প্রশিক্ষণের উদ্দেশ্যের সঙ্গে এর বিষয়বস্তু সামঞ্জস্যপূর্ণ বলে মনে করেন কি?	০-২০% ২১-৪০% ৪১-৬০% ৬১-৮০% ৮১-১০০%	১ ২ ৩ ৪ ৫	
৪.	প্রশিক্ষণের উদ্দেশ্য কতটুকু সফল হয়েছে বলে আপনি মনে করেন?	০-২০% ২১-৪০% ৪১-৬০% ৬১-৮০% ৮১-১০০%	১ ২ ৩ ৪ ৫	
৫.	আপনার কর্মপরিধির কতটুকু প্রশিক্ষণের বিষয়বস্তুর সঙ্গে সম্পর্কিত?	০-২০% ২১-৪০% ৪১-৬০% ৬১-৮০% ৮১-১০০%	১ ২ ৩ ৪ ৫	
৬.	প্রশিক্ষণ পদ্ধতি কতটুকু গ্রহণযোগ্য বলে আপনি মনে করেন?	০-২০% ২১-৪০% ৪১-৬০% ৬১-৮০% ৮১-১০০%	১ ২ ৩ ৪ ৫	
৭.	এই প্রশিক্ষণের তিনটি সন্তোষজনক দিক উল্লেখ করুন।	১. ২. ৩.		
৮.	এই প্রশিক্ষণের তিনটি অসন্তোষজনক দিক (যদি থাকে) উল্লেখ করুন।	১. ২. ৩.		
৯.	এই প্রশিক্ষণ চলাকালে তাত্ত্বিক ও ব্যবহারিক ক্লাসের ক্ষেত্রে কোনো সমস্যা হয়েছে কি? হ্যাঁ হলে সমস্যার ধরণ ঃ	১. ২. ৩.		
১০.	এই প্রশিক্ষণের উন্নয়নে আপনার তিনটি সুপারিশ লিখুন।	১. ২. ৩.		

Notes