Antibiotics In Veterinary Medicine: Resistance To Antibiotics And its Multiple Effects

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It is of utmost importance, how consciously veterinary drugs, especially antibiotics, are used. Antibiotics are chemical agents synthesized by various organisms such as; bacteria, fungi, actinomycetes either to kill or inhibit the growth of other organisms. Main principle in antibiotic therapy is, to paramount enough poisonous/hazardous or fatal effect on the disease agent with a chemical substance that has limited or no poisonous/hazardous effect on the host.

Resistance to antibiotics is an ability of bacteria and other microorganisms and, in general used to describe their impervious nature. Clinically, resistance describes the inefficiency of achieved chemotherapeutic serum dosage on the pathogenic microorganism or strain. Development of resistance to antibiotics in bacteria still is and will be an important issue. Thus it has been preferential concern of the world, leaving AIDS and AI behind. Last year, in April, EU Commission and WHO conducted a conference as “Towards a Strategy on Containment of Antibiotic Resistance in the WHO European Region” in Russia. Especially, dispersion of multidrug resistant Tb and the fast emergence of resistance against artemicin in malaria is alarming. MRSA continues to disperse. In order to solve this problem, EU launched a five year program. Establishment of antibiotic resistance surveillance net, development of resistance prevention strategies, registration of resistance in indicator microorganism by authorities and preparation of a national project is needed in our country.

Emphasizing the subject, “Antimicrobial Resistance” has been chosen as the theme of 2012 World Veterinary Day and this brochure was prepared by Turkish Veterinary Society and Veterinary Pharmacology and Toxicology Association to update public opinion. Furthermore, an international conference on “Multidrug Resistance” is being planned towards the end of this year.

In wish of usefulness to our colleagues and public,

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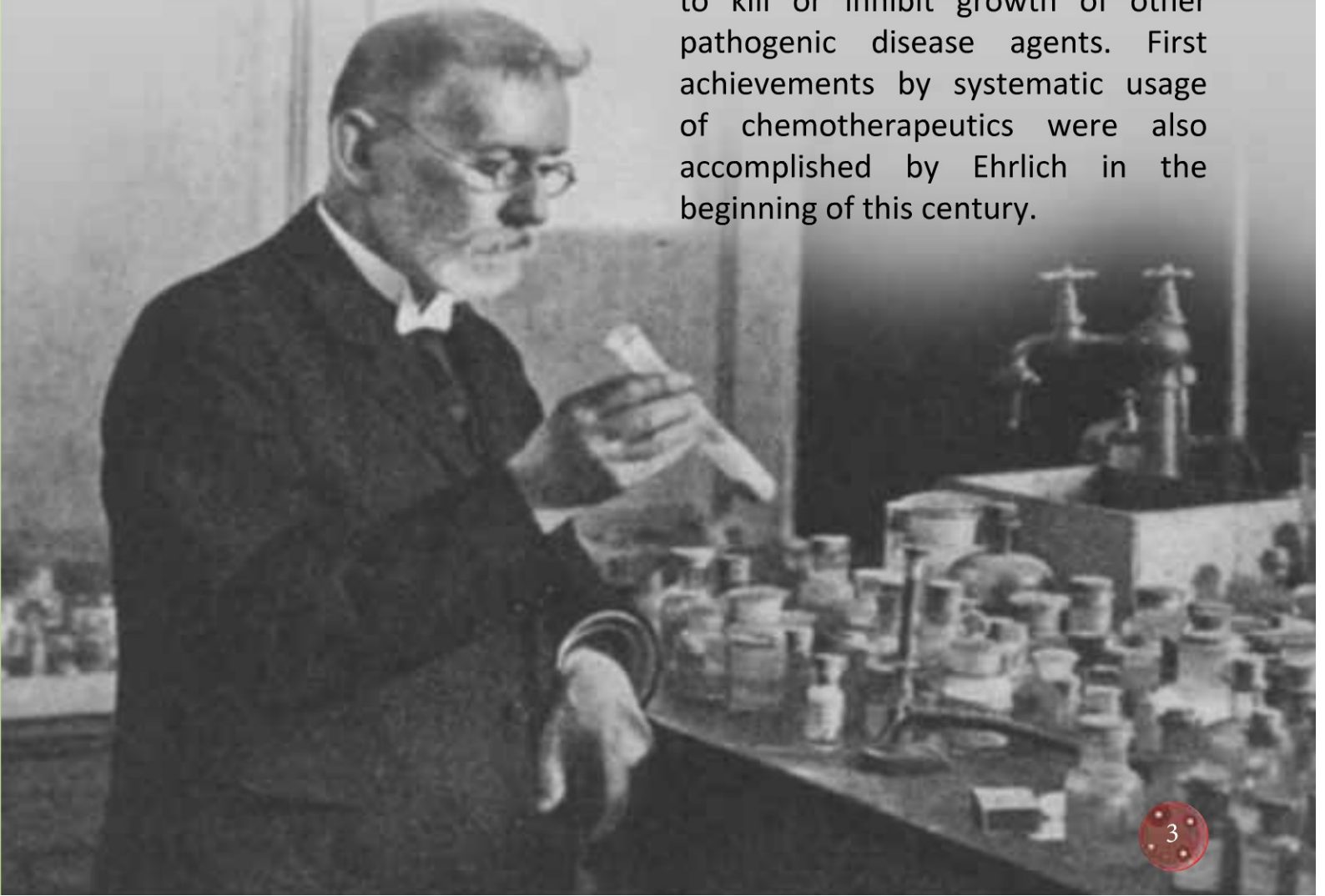
Chemotherapy

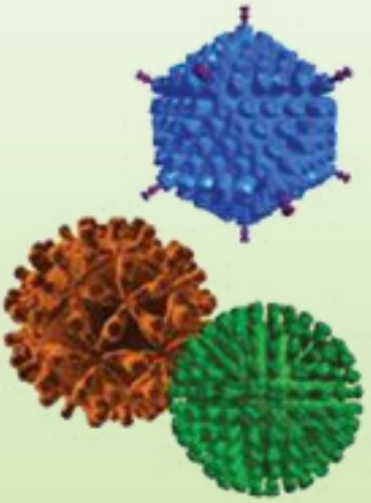
Chemotherapy is a term brought forward by German scientist Paul Ehrlich at the end of 19th century. It is described as "fatal or growth inhibiting therapy of pathogens such as; bacteria, internal or external parasites, viruses and protozoa found in the host, with a slight or no harm to the host". There are many agents such as; helminths, protozoa, fungi, bacteria, virus, insects and cancer cells that can give rise to diseases and in accordance chemotherapeutics are as much diverse. The aim of chemotherapy is to use a substance that has no or slight undesirable effects on the host, in order to maintain a sufficient impact (growth inhibitory or fatal effect) on the disease agent. Substances used in chemotherapy are examples of either selective or exclusive effects. Exclusive effect results from the differences in structural and biochemical natures of mammalian cells and microorganisms (parasites and fungi included).

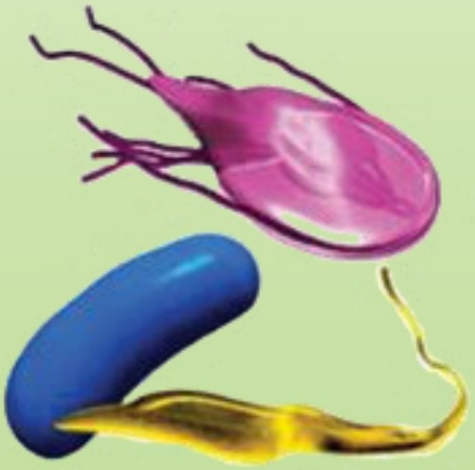
"Antibiotics" which was referred by Pasteur in 1871, was used to describe the substances that are synthesized and liberated to the culture medium by various microorganisms in order to kill or inhibit growth of other pathogenic disease agents. First achievements by systematic usage of chemotherapeutics were also accomplished by Ehrlich in the beginning of this century.



Classification of Chemotherapeutics

- **Antibiotics:** Also known as antimicrobials, they are effective on bacteria, rickettsia, chlamydia, and some internal and external parasites.
- **Antihelmintics:** Substances those are effective on round and flatworms.
- **Antiprotozoal drugs:** Effective on coccidea, babesia, theileria, histomonas, trypanasoma, anaplasma and other protozoan species.
- **Pesticides:** Effective on lice, flea, tick, flies and other parasites.
- **Antifungal drugs:** Effective on fungi.
- **Antiseptics-disinfectants (effective on germs):** Substances which are used to decontaminate alive or non-living surfaces.
- **Antiviral drugs:** Substances that effect viruses.
- **Anticancer drugs:** Harbors the drugs used in cancer therapy.





Antibiotics

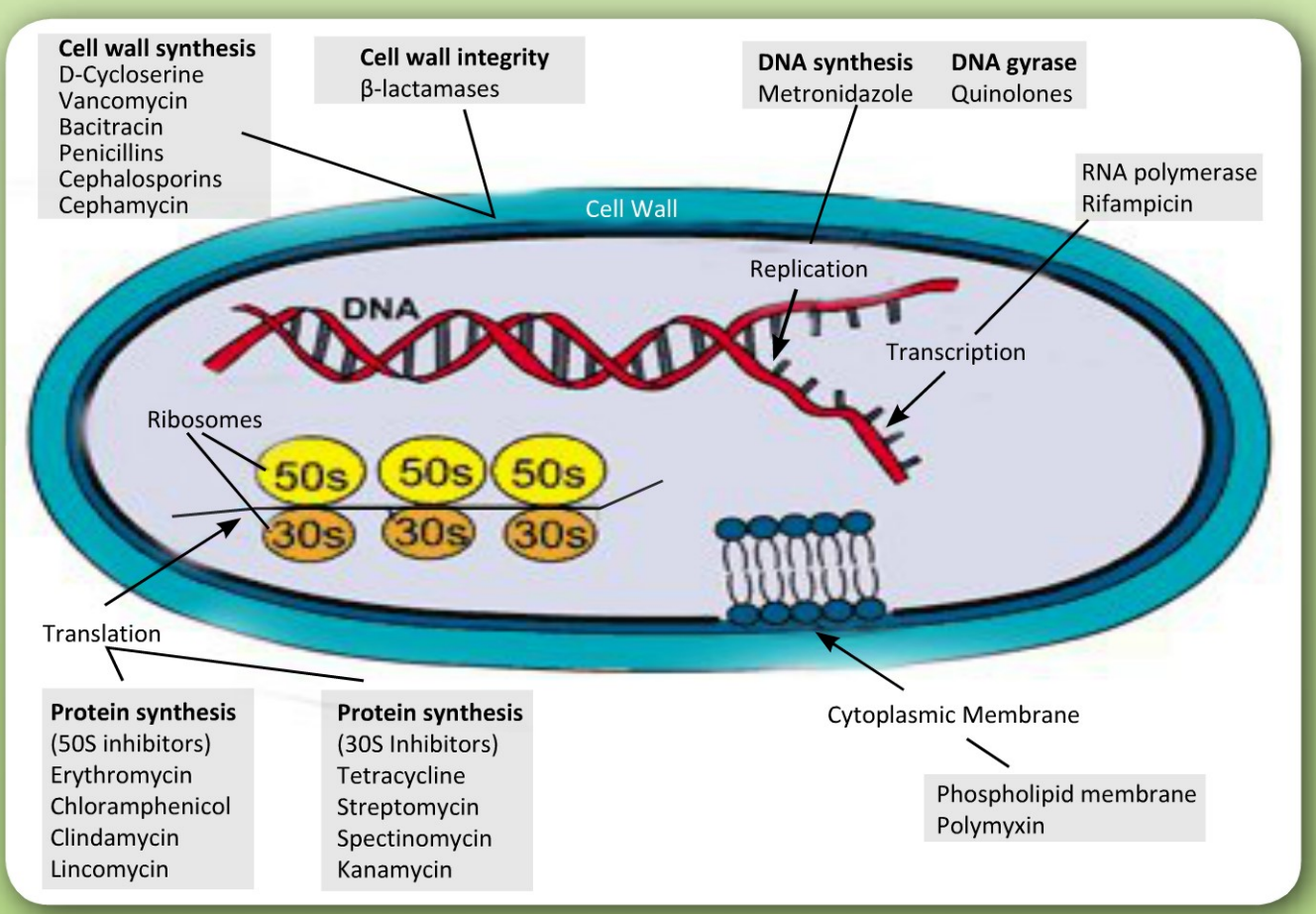
The term antibiotic is described as; substances that are either synthesized artificially or naturally by bacteria, fungi or actinomycetes, which are capable of killing or inhibiting growth of bacteria even in very small concentrations.

- **Antibacterial efficacy:** Antibiotics can be divided into two groups when their efficacies are concerned.
  - **Antibiotics that inhibit or stop the growth/propagation of bacteria (bacteriostatic agents):** These agents either slow down or prevent the growth of bacteria. Tetracyclines, macrolides, fenicoles, sulfonamides, quinolones can be presented as examples to this group.
  - **Antibiotics that kill bacteria (bactericidal agents):** These drugs directly kill the bacteria and preferred in therapy of peracute/acute diseases. Drugs that kill bacteria also

Antibiotics

prevent the growth of bacteria. Beta-lactams, nitrofurans, aminoglycosides, polymyxins and novobiocin can be presented as examples to this group.

- **Spectrum:** The groups of species those are sensitive to that antimicrobial constitute the spectrum of that antibacterial.
  - **Narrow-spectrum:** Penicillin and bacitracin, besides their semi-synthetic derivatives, that act mainly on Gram-positive and polymyxins that act only on Gram-negatives are considered in this group.
  - **Broad-spectrum:** Compounds effective on Gram-positives and - negatives, rickettsia, viruses, helminths, protozoa and even external parasites. Semi-synthetic and synthetic penicillins, including ampicillin and amoxicillin, tetracyclines, fenicoles, quinolones, and sulfonamide-trimethoprim mixtures are included in this group.



Issues to Be Considered in Antibiotic Therapy

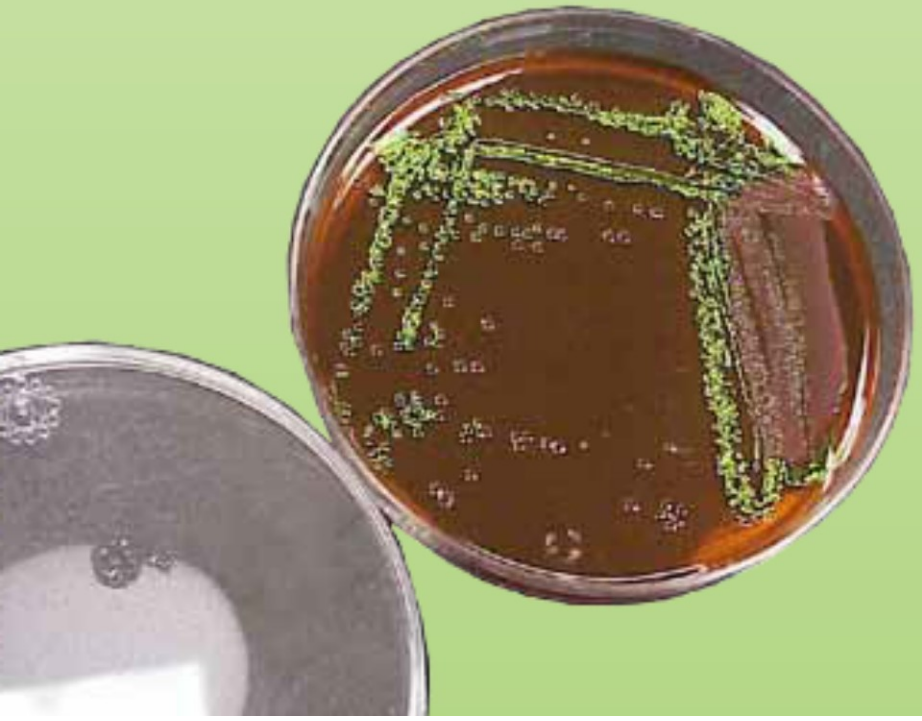
- Immunodeficiency in patient or inflammation of meninges, pericardium and bone marrow (as well render immunodeficiency) make it necessary to use drugs that kill bacteria.

- Following the fastest diagnosis, most efficient drug must be used.
  - *While it is important to use drugs that effect the logarithmical growth period of bacteria, determination of the sensitivity against the drug of choice is important as well..*
  - *Thus, if it is possible, an antibiogram would help determining the susceptibility array of the agent(s).*

- If it can be understood weather the agent of the disease belongs to one species or not, it would be possible to treat without waiting the results of antibiogram.

- In order to achieve a plasma concentration that can kill or inhibit the growth of all or some of the bacteria, drugs of initial choice should be applied in high (aggressive) dosages.

- If no prognosis is observed with antibiotic therapy in 2-3 days, diagnosis and drug choice of therapy should be reconsidered.



Issues to Be Considered in Antibiotic Therapy

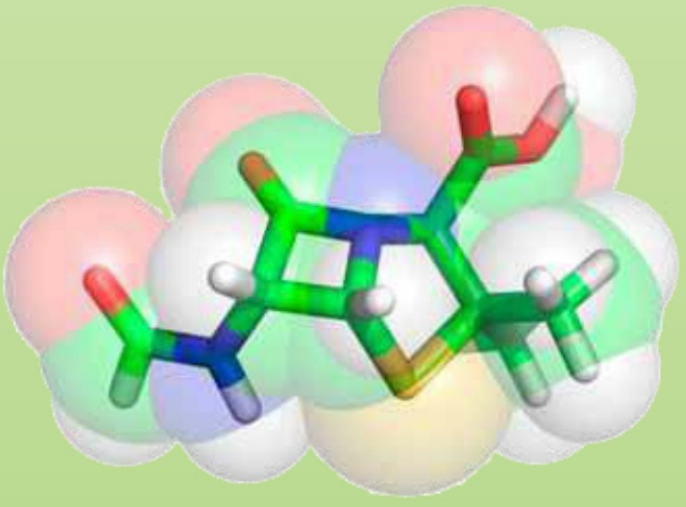
- In the course of antibiotic therapy, sensitivity of latent bacteria to drugs are generally low, thus, therapy should continue until bacteria are totally eliminated from the body.

- Application route of the drug has an important influence on how fast the impact develops.
  - In treatment of systemic-acute cases, the initial drug should be an easily dissolving, fast-absorbed preparation which would lead to a fast desirable concentration in the tissues and plasma.
  - Achieved efficient concentration should continue for a while.

- If possible, treatment of various diseases due to common species should be with one drug. However, if multiple-species are causative agents, usage of either broad-spectrum drugs or drug mixtures is recommended.

- It is a possibility that an in vitro efficient (sulfonamides, aminoglycosides and chloramphenicol against Mycoplasma; aminoglycosides, tetracyclines and cephalosporins against *S.typhi*) drug may be hampered in vivo.

- Factors such as; efficiency of drug on the disease agent, the amount of undesirable effects it causes on host and contraindicated situations should be considered well.



Factors Affecting the Use of Antibiotics

Efficient blood concentration

Achieved blood and tissue concentration of a drug has great importance when efficiency against bacteria is concerned. Fast achievement and maintenance of enough blood and tissue concentration of a drug is influenced by application route, formulation and solubility of that drug. In acute cases, in order to achieve a fast and effective blood drug concentration, highly soluble and absorbable drug formulations must be combined with one of the paranteral routes. Afterwards, therapy continues with the long effective drug versions, either orally or paranterally.

Tissue debris and pus

The efficacy of drugs such as; aminoglycosides, polymyxins and sulfonamides are decreased with the presence of pus, tissue-cell debris, fibrin, exudates etc. in the environment. Since body cavities contaminated with pus or bacteria has slightly more acidic pH, aminoglycosides, macrolides and lincosamides lose their efficiency to a great extent. The efficiency of penicillins and cephalosporins however, generally do not change, on the contrary slightly increases.

Application route and absorption

After orally applied, some of the enzymes throughout the gastrointestinal system may hamper the absorption of some antibiotics. When applied paranterally, depending on the site applied, they may generally be absorbed in few seconds to 2-3 hours. Penicillins, tetracyclines and spiramycins are examples of fastest absorbed drugs.

Natural barriers

Antibiotics applied by any route, may or may not be capable of reaching to some parts of the body. This is either related to the physicochemical nature of the drugs or the natural barriers found in the body.

The intestinal barrier: Following oral administration, due to low absorption (%1-3) from the intestinal canal, aminoglycosides fail to maintain an effective blood concentration and thus, in treatment of systemic infections they paranterally applied. Likewise, oxytetracycline is limitedly absorbed from the gastrointestinal system of poultry.

Serous membranes: Antibiotics show great difference with

Factors Affecting the Use of Antibiotics

regards to passage through these membranes.

Placenta: Normally, antibiotics can easily pass through placenta and provide a close concentration to that of mother's in blood of youngster. Good solubility in lipids and small molecular weights induces absorption.

Aqueous humor: Ampicillin can pass to the aqueous humor in a concentration that is close to that in plasma while chloramphenicol, sulfonamide-trimethoprim mixture and fluoroquinolones can pass to some extent.

Blood-brain barrier: This barrier is found between blood and cerebrospinal fluid.

Mammary gland: Most of antibiotics pass to the milk through mammary gland epithelia.

Routes of excretion

With regards to the treatment of diseases, the excretion routes of drugs are significantly important. Kidneys are one of the main excretion routes of antibiotics while one other important is bile.

Ecological factors

Especially in human medicine, usage of broad-spectrum drugs or drug mixtures cause alternation of the apathogen microflora in the intestinal system into pathogen agents such as; Staphylococcus and Proteus spp., Clostridium spp., fungi and yeasts. Due to this alteration, prevalence of intestinal and other infections (known as superinfections) are reported to be higher. Due this change of equilibrium between bacteria in the intestines likewise situations can also be found in veterinary medicine.

Immune system

Some diseases do not repeat once they are treated. This is important especially in some protozoan diseases like coccidiosis which are treated and prevented by drugs.

Intracellular bacteria

Since most of the drugs are hardly internalized into mammalian cells, diseases of intracellular agents do not answer the treatments in desired levels.

Conscious Usage of Antibiotics

- The conscious use of antibiotics in veterinary medicine is vey important.
- Usage antibiotics should be considered from a greater frame and should not be considered separate from breeding, welfare, hygiene, nutrition and insemination.
- In order to decrease the demand for antibiotics, diseases should be controlled and approached holistically.

AIM

- Increasing the treatment efficiency of antibiotics
- Decrease the emergence of resistant microorganisms

Fundamentals in Conscious Use of Antibiotics

Choosing the correct antibiotic

- Definitive diagnosis
- Use of drugs that are approved for that disease and species
- Use of drugs that are proved by field studies
- Pharmacokinetics and dissemination of the drugs throughout the tissues
- Effects on immune system
- Spectrum
- Antibiotic combinations

Correct antibiotic applications

- Dosage
- Treatment period
- Group therapy
- Strategic treatment
- Prescribing and keeping records

Failure in Antibiotic Therapy

- Wrong diagnosis
- Bacteria may not have desired sensitivity to the drug of choice
- Previously sensitive bacteria may have developed drug resistance
- A superinfection with insensitive or resistant bacteria, fungi or yeast may develop
- Drug may not penetrate to focus of infection due to debris, pus and inflammation
- Especially in use of bacteriostatic drugs, immune system may be deficient
- Due to the oxygenation and pH of the body, the efficiency of the drug may be altered
- Application route and dosage may be wrong or insufficient
- There may be adverse interactions between antibiotics or other drugs used
- Supporting treatment may be insufficient

Undesirable Effects of Antibiotics

Drug allergy may develop.

The severity and frequency of undesirable effects may increase due to the interactions with other drugs.

Normal microflora equilibrium may alter in the patient (superinfection).

Resistance may occur.

Immune system of patient may deteriorate or be suppressed.

Tissue damage develops in the application area.

Cause drug residues in edible tissue and organs.

Allergic Effects

Even though all drugs may cause allergy, it is of importance for penicillin and chloramphenicol. In April of 1993, due to the risk of allergic aplastic anemia in bone marrow, chloramphenicol was banned in Turkey for animals with nutritional value.

Teratogenic Effects

Since benzimidazole derivative antihelmintics such as; albendazole, cambendazole, mebendazole, oxbendazole, oxfendazole and parbendazole are teratogenic in 1-1.5 months of pregnancy, they should be used.

Carcinogenic Effects

Due to their carcinogenic effects, some drugs are not allowed to be used in animals with nutritional value in United States, European Union and Turkey. Some examples are; nitrofurans (furazolidone, nitrofurazone), imidazole antibiotics (dimetridazole, ronidazole, metronidazole), chloroform, chlorpromazine, chloramphenicol, some sulfonamides (sulfodimidine).

Undesirable Effects of Antibiotics

Bacterial community of digestive tract

Some antibiotics are capable of deteriorating the bacterial community of digestive tract that endanger the health of the animal or even may cause the death of the animal; an event known as **superinfection**.

Avoid use of: aminopenicillins in horses, some laboratory animals (guinea, hamster, rabbit, and gerbil), geese and ducks; erythromycin and spiramycin in horses and ruminants; tetracyclines especially in horses; lincomycin and clindomycin in horses and ruminants and lincomycin in rabbits.

Susceptibility to drugs

Some animals for known or unknown reasons are highly susceptible to some drugs:

Guinea, gerbil, hamster and rabbits to penicillins and macrolides,

Horses to tetracyclines and levamisole,

Turkeys to salinomycin,

Fishes to piretroides,

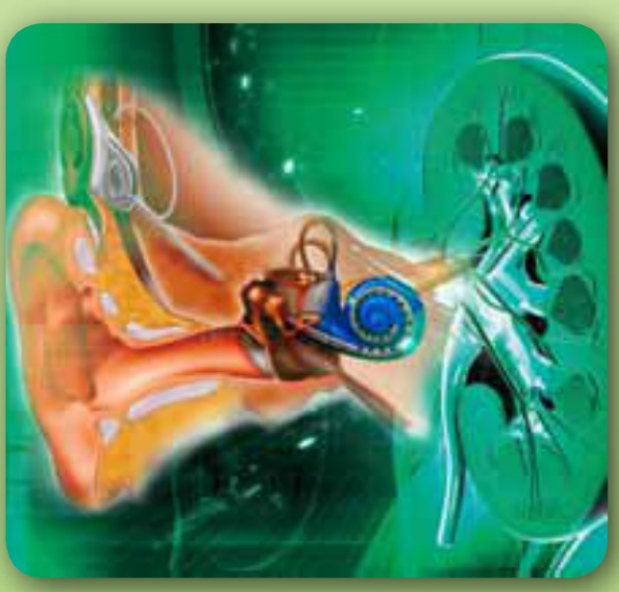
Birds and cats to DDT,

Especially horses and songbirds to ionophore antibiotics,

Some dog breeds (Collie etc.)

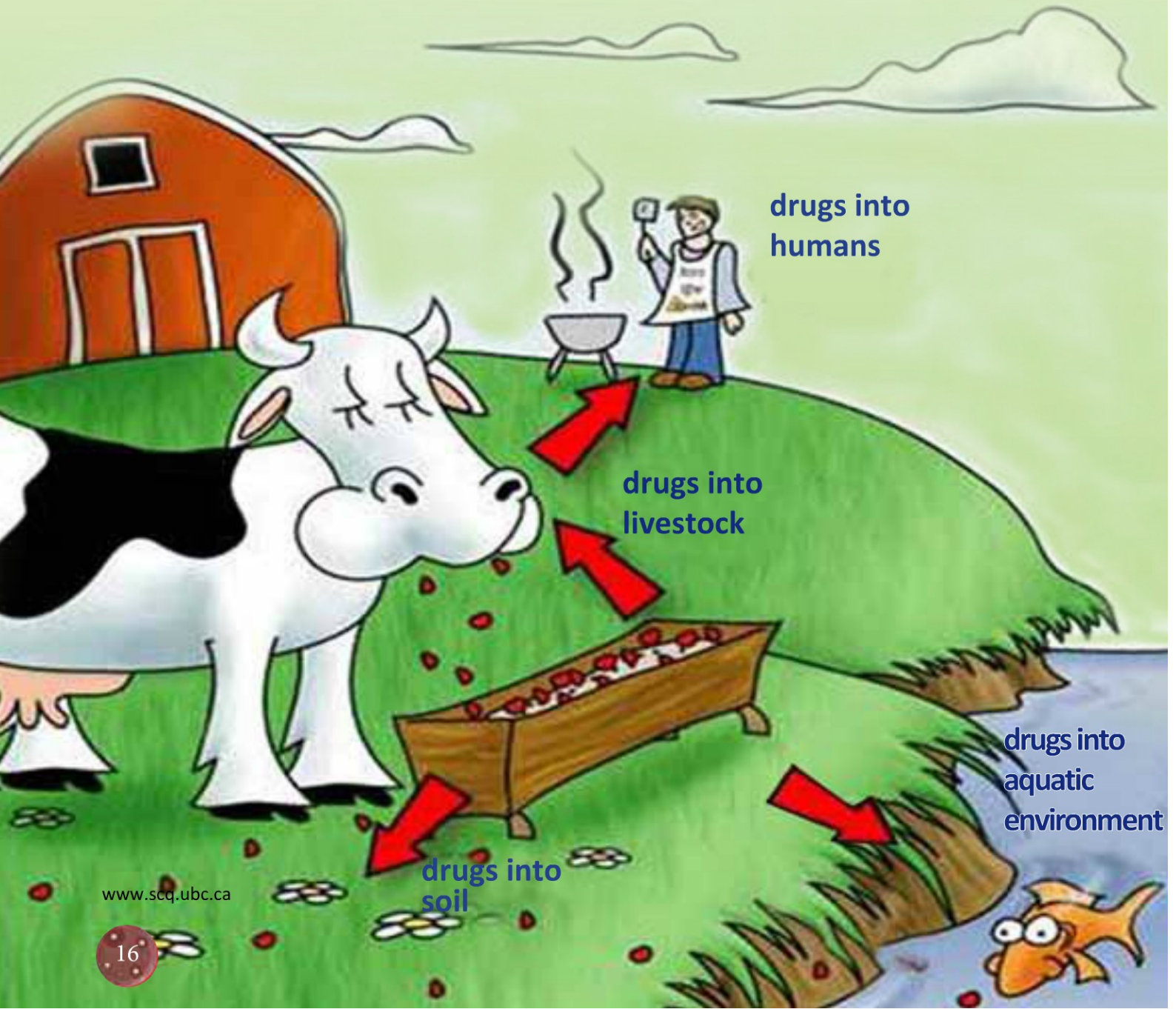
Tissue and organ damage

Aminoglycosides are highly toxic for kidneys and inner ear (hearing and balance organelle) and thus must be used with caution. Griseofulvin, cephaloridine and polymyxins are very toxic for kidneys while, polymyxins are for nerves, quinolones are for cartilage tissue.



Drawbacks in Usage Antibiotics

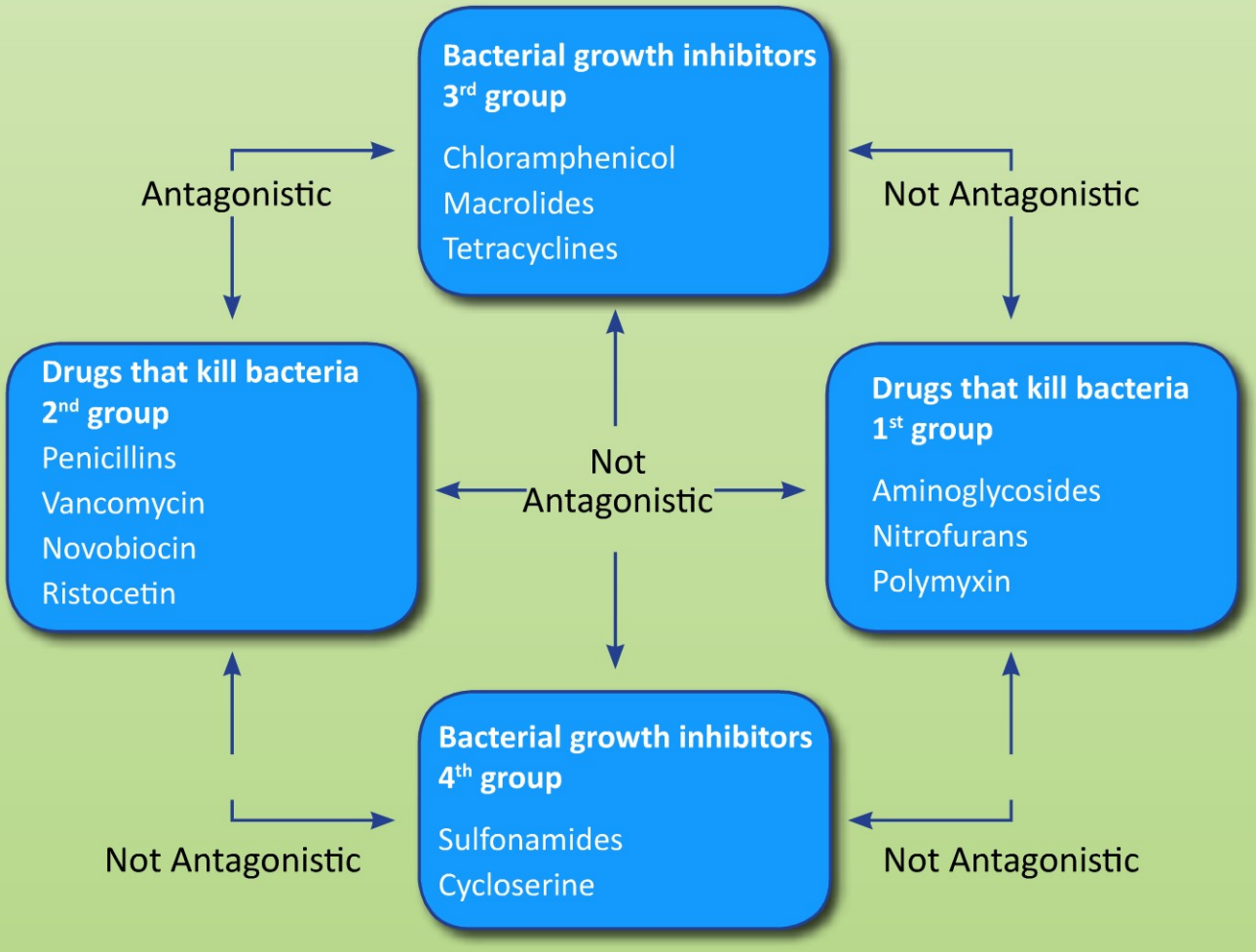
1. Possible emergence of resistant strains
2. Drug residues in foods
3. Alteration of immune response
   - Repression
   - Stimulation
4. Direct effects of drugs
5. Drug allergy
6. Endotoxic shock
7. Positive Coombs test



Antibiotic Mixtures

In multi bacterial infections or in such cases when high dosages of drugs can not be administered due to undesirable effects or simply synergism is desired, two or more drugs will be administered. It can be possible to decide the proper mixture, from an array of drugs if drug interactions are well known. Drug interactions are as well important for patients as they are for the bacteria.

When the effect and spectrum of antibiotics are known, collective effect can be anticipated. A scheme, originating from comprehensive work of Manten and Wisse that was conducted with many bacteria in 1961, describes the behavior of more than 90 % bacteria or strain against drug mixtures. According to this scheme, antibiotics are divided in to 4 groups.



Antibiotic Mixtures

1ST GROUP:

Generally affecting drugs that kill bacteria: Aminoglycosides, polymyxins, bacitracin, nitrofurans.

2ND GROUP:

Particularly affecting drugs that kill bacteria: Penicillins, cephalosporins, novobiocin, vancomycin, ristocetin.

3RD GROUP:

Fast acting bacterial growth inhibitors: Tetracyclines, macrolides, phenicoles.

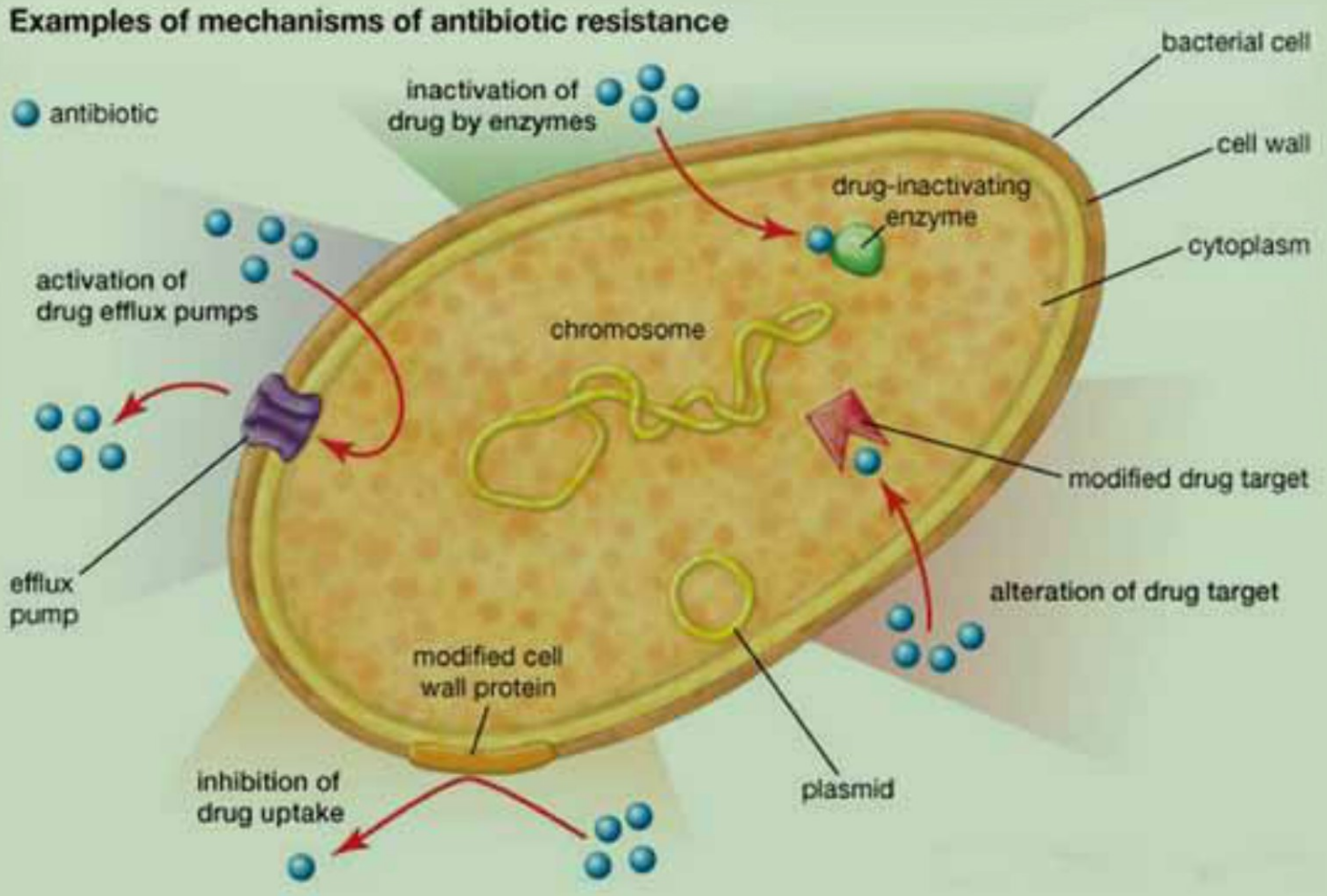
4TH GROUP:

Slow acting bacterial growth inhibitors: Sulfonamides, cycloserine.

- Generally mixtures from the same groups are not antagonistic.
- If a drug from 1st group is mixed with a drug of any other group, generally, antagonism is not observed. On the contrary, in these kinds of interactions effect of the drug that kills bacteria is more pronounced and sometimes synergisms can be observed.
- If drugs from 2nd and 3rd group are mixed, the effect of poorly affecting drug will be dominant. Thus drug mixtures from these two groups should not be considered.
- Drugs of 2nd and 4th group do not interact antagonistically and drug that kills bacteria dominates the effect which may lead to synergism.
- Drugs of 4th group can be mixed with drugs of any other group.
- Since the effect of members of 2nd group is more pronounced in the logarithmic phase of bacteria, fast acting bacterial growth inhibitors disrupt their effects while slow acting bacterial growth inhibitors does not.

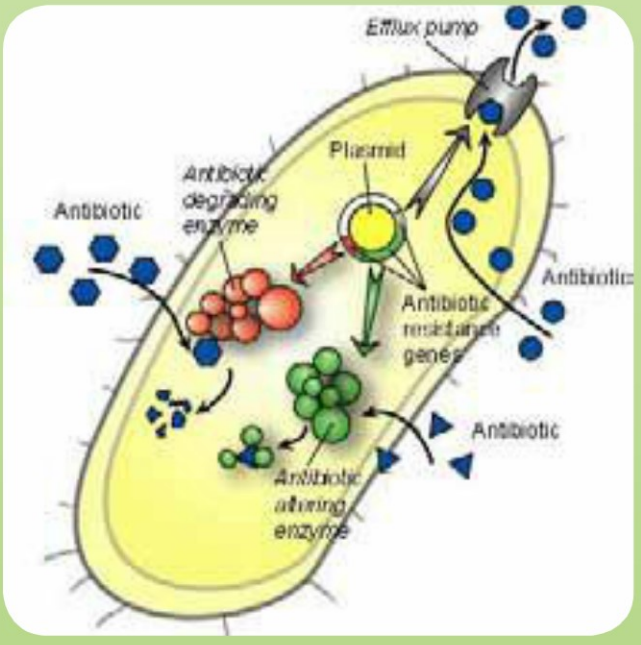
Developing Resistance Against Antibiotics

- Resistance to antibiotics is an ability of bacteria and other microorganisms and, in general used to describe their impervious nature. Clinically, resistance describes the inefficiency of chemotherapeutic dosage that was achieved in the serum, on the pathogenic microorganism or strain. Resistance may either be natural or acquired (mutation and transmissible). Bacteria that are resistant to one drug may also be resistant to others with similar structures or efficiencies. This phenomenon is known as **cross resistance.**

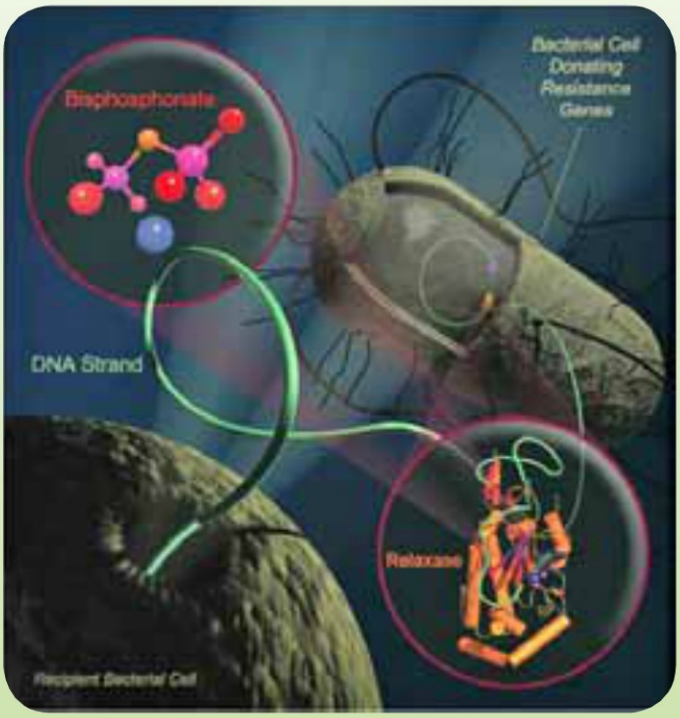


Developing Resistance Against Antibiotics

- Some bacteria may naturally be resistant to some drugs, that is known as **natural resistance**. Fundamentals of this resistance consist of either the inactive phase of bacteria or the absence of the targets for that drug. Mycoplasma spp. can be given as an example because of their insensitivity in calcified focuses due to the lack of a robust metabolism and their resistance against beta-lactam antibiotics due to the lack of cell wall. Second way of resistance is the **acquired resistance**. In this case, bacteria are formerly sensitive to drug, however during consecutive contacts they develop resistance. Development of resistance against antimicrobials can be seen anytime and indicator of resistance is the increase in minimal inhibitory and bactericidal concentrations. As a result, either in a short or long period of time, a formerly effective antimicrobial may not be as effective anymore as it primarily was in same dosages.
- Bacteria that have lost sensitivity against a particular antibiotic may also lose their sensitivity against an antimicrobial with similar chemical structure or an antimicrobial with different structure but similar impact and this phenomenon is called **cross resistance**. In example, a bacteria which has developed resistance against oxytetracycline, will be resistant against antibiotics such as; tetracycline, chlortetracycline and doxycyclin with similar chemical structure. Moreover, Gram negative bacteria that have developed resistance against tetracycline are also generally resistant to chloramphenicol which has a similar impact mechanism. Bacteria with resistance against more than one antimicrobial that are different in structure or impact mechanism are called as **multi drug resistant**.



Developing Resistance Against Antibiotics



Multi drug resistance is generally related to the existence of more than one resistance gene in the genome (chromosomes or plasmids) of the bacteria. It was shown in some multi drug resistant members of Enterobacteriaceae, that there are plasmids that can code for resistance against more than 10 antimicrobials.

- Acquired resistance results from; a mutation in the genome of the bacteria or through acquisition of the resistance genes by transduction, transformation and conjugation with other bacteria (resistance by R plasmids or transposons).

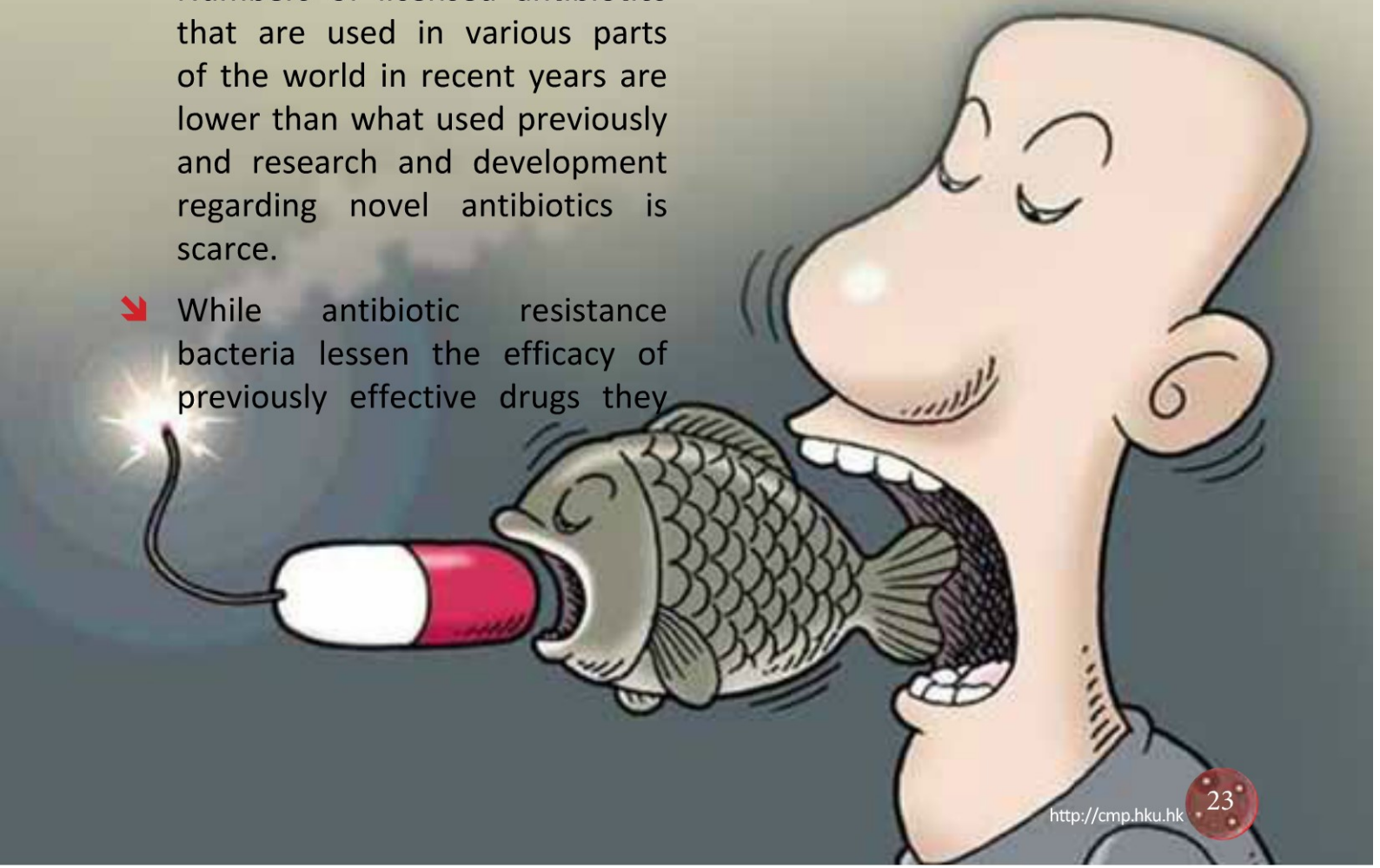
- **Acquired resistance due to chromosomal mutation:** This resistance is not related to the interaction between bacteria and the antimicrobial and generally no cause-result relation can be found. Mutation often happens spontaneously and it either succeeds in single or more than one steps.
  - **Single-step mutation:** Emerges following a single or more than one interaction of bacteria with an antimicrobial, and often called as **streptomycin-type resistance**. Following treatment with streptomycin, resistant clones may emerge in 3-4 days.
  - **Multi-step mutation:** Resistance emerges gradually and slowly and it is called **penicillin-type resistance**. In order this resistance to succeed, consecutive mutations throughout the DNA must happen. This type of resistance may develop against penicillins and tetracycline.

Developing Resistance Against Antibiotics

- **Transmissible resistance (R plasmids and transposon mediated resistance):** Plasmids are extrachrosomal genetic materials that consist of double-strainded and circular DNA molecules. Plasmids that harbors resistance genes and elicit transfer of antimicrobial resistance are called resistance plasmids (resistance factor, R plasmids). Transposons are other particular DNA particles that play role in transfer of resistance. They can either be found on chromosome or plasmids and due their high mobility, they may carry genes from plasmid to plasmid or plasmid to chromosome, increasing the dissemination of resistance traits. Mechanism that play role in transfer of resistance:
- **Transduction:** Bacteriophages accomplish the transfer of resistance trait. Bacteriophage that has infected the bacteria may intake and replicate the bacterial resistance factor and disseminate the resistance by many infectious progeny. These infectious viral particles may consecutively infect same or different species of bacteria.
- **Conjugation:** Transfer of resistance traits from bacteria to bacteria through a cytoplasmic conjugation bridge can occur, making the recipient bacteria resistant.
- **Transformation:** Following the lysis of bacterial cells, freed DNA particles can be taken up by sensitive bacteria readily existing in the surrounding environment. These bacteria become resistant.

The Importance of Developing Resistance Against Antibiotics

- Severe infections of bacteria that are resistant to commonly used antibiotics have been a major health issue in 21 century. Though, it firstly emerged as nasocomial infections with increasing prevalence in immunosuppressed or severely diseased patients, now it has become a serious public concern with failures in diagnosis and treatment. Indiscriminative use of antibiotics in human clinics or hospitals together with the use in food industry is the major reason causing antibiotic resistance. Numbers of licensed antibiotics that are used in various parts of the world in recent years are lower than what used previously and research and development regarding novel antibiotics is scarce.
- While antibiotic resistance bacteria lessen the efficacy of previously effective drugs they cause failures in treatments. Above all, it is of utmost importance for public health that they cause an increase in the numbers of diseases that are transmitted either from animal to animal or animal to human. One of the major problems in treatment of human cases is the inefficiency of treatments with previously accustomed drugs, which may also increase mortality. Furthermore, it may need an increase in normally accustomed dosages or treatment periods



The Importance of Developing Resistance Against Antibiotics

which may also result in more undesirable effects on patients increasing the cost. Likewise, treatment of resistant bacterial infections may also need usage or combinations of more toxic and expensive drugs that are known to be effective against the agent, increasing the total cost.

- Antibacterial drugs can be used in modern production applications or metaphlactics, prophylactics or growth promoters. In recent years, worldwide microbial health threats (i.e. bioterrorism, severe acute respiratory syndrome (SARS) and avian influenza) drew much more politic and public attention than antibacterial resistance. Acute danger of bioterrorism and SARS, triggered international prevention regulations and accelerated the establishment of The European Centre of Disease Prevention of Control (ECDC).

Prevention of Antibiotic Resistance

- In order to decrease the possibility of antibacterial resistance development in bacteria, proper attention should be given to some points. Drug should only be used if either it is known or believed that the agent is susceptible. Drugs should be applied as fast as possible with adequate dosage. Inadequate dosages or prolonged treatments may facilitate development of resistance. Drug of choice should be applied after having the results of susceptibility testing of the isolated bacteria. Antimicrobial resistance prevalence in that particular region should be well known, emphasizing the research that should be conducted on the subject. Choice of antibiotic should be as narrow-spectrum as possible. Some drugs in animals, rather than treatment of infections, are mostly included in feed and water for growth

Prevention of Antibiotic Resistance

promotion increasing the frequency of prophylactic usage of antibacterials in animals than in humans. Drugs of this purpose should not have therapeutic potency in humans or favor cross-resistance.

- In order to control antibacterial resistance, emphasis should be given on some strategic subjects such as, survey of steps of antibacterial resistance development and tendencies in particular geographical regions. The emerging data from this survey can be used in eliciting appropriate antibiotics, determination of novel resistance mechanisms and intervention strategies. Emergence of antibacterial resistance is fundamentally related to use of antibiotics and thus, it is not possible to totally dodge this issue. Effective usage does not mean the decrease in the amount consumption of antibiotics but rather describes adjust (neither excessive nor less) usage of antibiotics. Through effective usage of antibiotics, long continuity of antibiotic can be elicited, leaving more time for development of novel antibiotics and approaches against antimicrobial resistance.
- One important future of effective usage of antibiotics is that they should be prescribed. Secondly, since public knowledge on antibacterial resistance is fairly limited, awareness should be raised by specialists. Control of infections is another important controlling component of antibacterial resistance emergence. While correct usage of antibiotics decreases the emergence and dissemination of resistant bacteria, infection prevention measures limits the dissemination bacteria that have already developed antibacterial resistance.
- The divergence of novel antibiotics marketed during the last decade is also an important issue. Resistance against these antibiotics can easily be developed due to their structural similarity to their former family members. Since big drug enterprises are limiting their research and development

Prevention of Antibiotic Resistance

on novel antibiotics due to many reasons, lack of novel antibiotics in the future will cause severe threats in international scale. One such limitation arises due to cost. Development of a novel antibiotic approximately costs 500 million Euros and takes around 10-15 years while additionally novel drugs face highly limiting regulations.

- Use of drugs, especially antibiotics, in veterinary medicine is very important. It is generally accepted that antibiotics are weapons that may cause serious injuries or even death when unconsciously used whereas, when used consciously, have marvelous contributions in treatment of infections. Antibacterial resistance had been pronounced after the first use of penicillins for treatment. Even today, development of antibacterial resistance in bacteria is an important concern and will continue to be. For appropriate usage of antibiotics some principals must be followed: antibiotics should be used limitedly on a rotational basis, antibiotics usage educations should be given, drug firms should be inspected, correct antibiotic should be chosen following antibiogram and resistance against antibiotics should be surveyed. One other important precaution to prevent development of resistance against antibiotics would be, saving of some antibiotics as last resort. In conclusion, for correct usage of drugs, educational quality of medical personnel should be increased; their knowledge on subject should be kept updated by in-service trainings and controlled periodically. Public should be enlightened on the risks of unconscious or uncontrolled drug usage, especially by media.

Alternatives to Antibiotics and Joint Disease Control Programs

- In order to decrease the need of antibiotic usage, development of systematic preventative applications should be emphasized.

  Preventative medicine is more important than treatment.

- In management of antibiotic usage in farm animals;

  Caution should be given also to hygiene and disinfection procedures, bio-security and herd management.

- Antibiotic usage in these control programs should be assessed periodically and usage should be decreased or terminated according to the efficiency.

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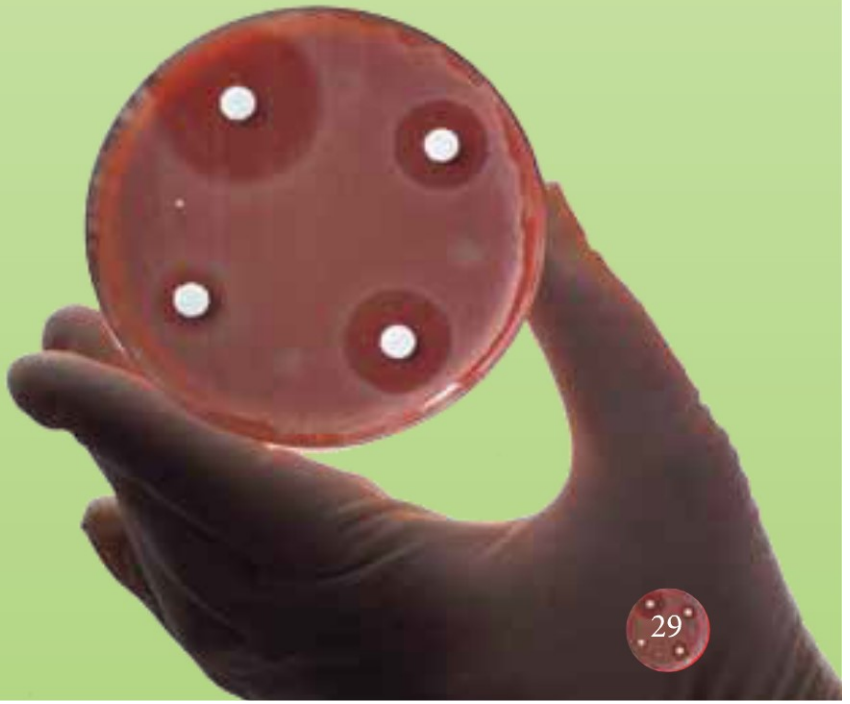

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