

Goals in Teaching Basic Pharmacology in the Veterinary Curriculum/Concepts and Clinical Applications

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Introduction

Is problem solving as a basis for learning in Veterinary Medicine new? I submit that it is not. No matter what career opportunity a veterinary medical student chooses to pursue after graduation, it will constantly require that person to make decisions, make judgement "calls". I feel that we do prepare them for problem solving and that the strength and uniqueness of a degree in veterinary medicine is that our graduates are able to make sound judgements relative to all aspects of comparative medicine. I sincerely hope that we do nothing to change this. My philosophy is that if the students are given the fundamentals, that basic foundation for step by step learning, and if concepts are emphasized, the students will be able to make rational decisions.

There are different instructional methodologies to accomplish these goals. I will not attempt to speak to all of them, only to say that I feel it can be done in a lecture and laboratory setting, which is what I will discuss.

Doses cannot be "cookbooked". Some drugs disappear and new drugs appear and new uses for old drugs appear, but concepts remain. There are some fundamental concepts that a veterinary medical student needs as a foundation to build upon: in other courses; in clinics while in school; to prepare them to participate in their chosen professional endeavors after graduation; and to prepare them for a lifetime of learning. I hope to emphasize how these concepts mesh with problem solving. There is a common thread that will weave it's way throughout this presentation. That thread is reality and relevance. Students expect and deserve that their learning experiences to be relevant and to prepare them for the "real world" of veterinary medicine. These concepts of teaching and of clinical pharmacology will be presented in 3 parts.

Part 1. Teaching and Course Content Concepts

I'd first like to present my 7 C's of instructional objectives. They are communication for comprehension of current concepts for clinical applications with common sense and to be prepared for continued learning. One should have firmly in mind and follow a course philosophy and plan. This plan must be aimed directly at the student needs. The course plan that is needed for veterinary students who will apply their knowledge to the science and art of medicine will be different than the plan for graduate students who will add to the new knowledge. For veterinary students we must make certain that the course plan and objectives are aimed at the former. The course objectives which follow are given to each student on the first day of class and are referred to throughout the course.

Course Objectives for Pharmacology

- A. To gain a general understanding of all aspects of the basic science of pharmacology.
- B. To learn the vocabulary related to pharmacology.
- C. To understand the interactions of chemical compounds and living systems, which includes all of the following:
 1. The action(s) of drug(s) on an animal's system and the mechanism of this action, which may be either:
 - a. Therapeutic and of medical value; or
 - b. Possibly bring about adverse reactions.
 2. The action of the animal's body upon the drug.

3. Actions that might have a bearing on human health via the use of these drugs on, in or around animals.
- D. To gain an understanding of how drug actions and interactions relate to physiological principles. Pharmacology is simply: **PHYSIOLOGY OR PATHO-PHYSIOLOGY BEING INFLUENCED BY AN EXOGENOUS CHEMICAL COMPOUND(S)**.
 - E. To learn to relate the **ALTERED PHYSIOLOGY** of the system(s) involved in a given disease condition(s) to setting forth the **OBJECTIVES** of therapy.
 - F. To learn to summarize the different therapeutic means, based upon drug **MECHANISMS OF ACTIONS**, to accomplish the objectives of therapy.
 - G. To understand how to properly set up a **DRUG REGIMEN** based upon all of the above, to include.
 1. Drug or Drug Combinations
 2. Dosage and Route of Administration
 3. Frequency and Duration of Dosing
 4. Proper withdrawal times in food producing animals
 5. Consideration of all Precautions, Side Effects, **ADVERSE EFFECTS** and Possible Drug Interactions of drugs being used. Consider **BENEFIT** vs. **RISK**.
 - H. To learn the names, generic and trade, of selected common drugs from each of the drug groups and to associate the names with the general actions of that group.
 - I. To gain an appreciation for, and a clear understanding of, the **PRIVILEGES** and **RESPONSIBILITIES** that a Veterinarian has to themselves, to the animals, to the client, and to society; when drugs are used, dispensed or prescribed for Rational and Safe Therapy.

Encouragement for learning in this mode needs to be presented early and continuously reinforced. The following are examples to emphasize the application of learning to The Science and Art of Medicine (Appendix A). The basis of success of a professional career in Veterinary Medicine sets the tone. The student who attempts merely to memorize

the pharmacodynamic properties of drugs is foregoing one of the best opportunities for correlating the entire field of pre-clinical medicine. "Above all, do no harm." "All substances are poisons, there is none which is not a poison, the right dose differentiates a poison and a remedy." "Don't just do something, stand there." "A person's judgement is no better than their information." "Wisdom is the prime thing. Acquire wisdom and with all that you acquire, acquire understanding." We must prepare our students to apply the science of medicine to the art of medicine.

Part 2. Basic Concepts in Pharmacology

The principles and concepts that I will use as examples are well known to this group. I will use them to illustrate how they may be presented and related to patient care.

Clinical pharmacology is simply pharmacology applied to an animal patient. It involves all of the following:

- A. The interrelationship between physiology and pharmacology,
- B. The interrelationship between pathophysiology and pharmacotherapy, and
- C. It involves the interaction of foreign substances upon physiological and pathophysiological systems.

Clinical pharmacology involves problem solving with the ultimate goal of setting up the treatment. Other treatments may be appropriate, such as: nutrition and/or management changes; a need for surgery and accompanying anesthesia; and may involve the need for pharmacotherapy.

The following are decisions that need to be made relative to whether to use pharmacotherapy or not. These are judgement decisions. Will it work? Is it safe for target animal and for man? Is it needed? Is it economically feasible? You must weigh benefit versus risk. Is it ethically and legally proper? Will it adversely effect the environment?

The following is an outline of the basic philosophy of proper therapy.

- A. Evaluate the patient
 1. Assess the altered physiology, and
 2. Establish the physiological needs of the patient.
- B. Set forth the objectives of therapy.
- C. Decide the therapeutic means to accomplish these objectives. This is based upon:

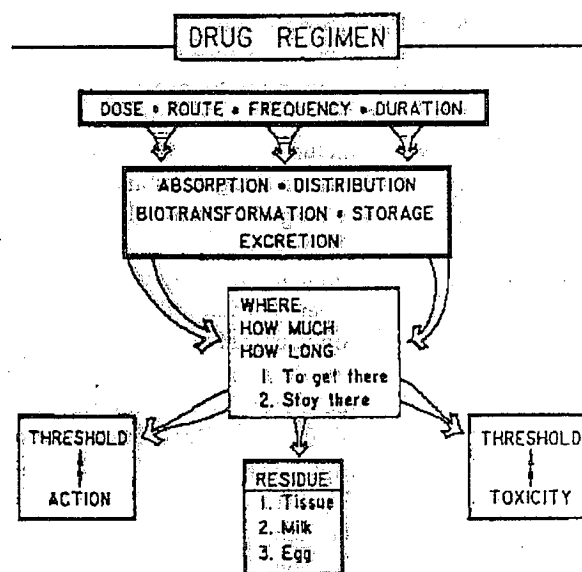
1. Kinetics, actions, and mechanism(s) of action of the drug; and/or
 2. Empirical systematic and controlled observations.
- D. Consider possible adverse reactions and interactions.
1. Know the signs of intoxication, and
 2. Know how to treat the problem.
- E. Set up the proper treatment regimen.
- F. Establish how to evaluate the results of the treatment.

Pharmacotherapy REVOLVES AROUND THE REGIMEN. The regimen is impacted by and/or influenced by all of the following: pharmacokinetics; pharmacodynamics; ethics and jurisprudence; and economics. Pharmacology is simply the interaction between pharmacokinetics and pharmacodynamics. Pharmacokinetics provides information beginning with the regimen leading to plasma concentration and concentrations of drug at infection site or receptor site, while pharmacodynamics speaks to the resulting pharmacological actions and thus the clinical response or therapeutic outcome.

The following is an outline of practical pharmacokinetics.

- A. Where does the drug go?
- B. How much of it goes there? (concentrations). This includes:
 1. Plasma levels; and
 2. Specific tissue levels; and
 3. The relationship between plasma and tissue levels which may be estimated by the volume of distribution.
- C. How long does it take for the drug to get there and how long will it stay there? (rates)
 1. Time to reach the site of action which may be estimated by:
 - a. Peak plasma levels; or
 - b. The alpha half-time of the plasma disappearance curve.
 2. Time of stay:
 - a. At the site of action; and in the animal's body.
 - b. This time course may be estimated by: the beta half-time of the plasma disappearance curve; and/or tissue depletion times.

Tissue depletion times are important because they may establish the duration of therapeutic concentrations, or the time for tissue concentrations to go below tolerance or the time for tissue concentrations to reach zero (less than 1 part per trillion). Pharmacokinetics may be influenced by several variables that are important as one sets up the regimen: the dose; the form of the drug and its vehicle; the route of administration; and the volume per injection site. The following is a schematic that attempts to tie together the fundamental concepts of proper therapy which include the desired action and also the potential for problems such as adverse reactions and violative residues.



It is well at this point to list the adverse drug effects, which I have divided into two categories.

- A. Welfare of the patient, which includes:
 1. Cellular or organ system toxicity;
 2. Alteration of their production capability;
 3. Alteration of their athletic or performing ability;
 4. Alteration of their companionship value to man; and/or
 5. Inhibition of the animal's ability to survive.
- B. The lack of efficacy which is indeed an adverse drug effect.

It follows then that one must also understand the principles involved in the treatment of drug intoxication. I firmly support the concept that the improper dosage regimen of the proper drug is probably as common a cause of therapy failure for toxicity as the use of an improper drug.

Another means to emphasize the understanding of concepts versus rote memorization is to ask the question, WHAT IS THE DOSE? Doses cannot simply be memorized, they must be carefully thought out and based upon all of the following. 1. Relative to the animal, one needs to be aware of the species; the age of the animal; and whether there is any existing pathophysiology that would influence the activity of the drug. 2. One needs to be totally aware of the disease or condition to be treated. If it is infectious, one needs to know what tissues are involved and/or is it a septicemia. One needs to know what organisms are involved and the susceptibility of these organisms to antimicrobial drugs. One needs to ascertain the duration of the infection as to whether it is acute or chronic. If the disease is non-infectious, one needs to understand the nature of the altered physiology, what the needs of the animal are, and what then are the objectives of the therapy. 3. One needs to be totally knowledgeable of the drug itself. What is its pharmaceutical form. Is it in its base form or is it a salt; and if it is a salt, which salt is it? One needs to know if it is a conventional or a slow release product. What vehicle[s] is the drug in? What are the kinetics of the drug? Does it have any unique tissue affinities in the body? Of prime consideration is the route by which the drug will be administered.

I also strongly feel that veterinary students must be made aware of the concepts of ethics and jurisprudence. Ethics is simply the total of the values and guidelines that should govern decisions in veterinary medicine. Jurisprudence is the knowledge of the laws of the land and the application of the principles of law and justice as they relate to the practice of Veterinary Medicine. Jurisprudence also involves relationships of veterinarians to each other and to society in general. Veterinary students must be made very much aware of their responsibilities in the area of the ethics of pharmacotherapy. I have outlined the ethics of pharmacotherapy (Appendix B) that incorporate ideals from the Veterinarian's Oath, and from the Principles of Veterinary Medical Ethics of the American Veterinary Medical Association.

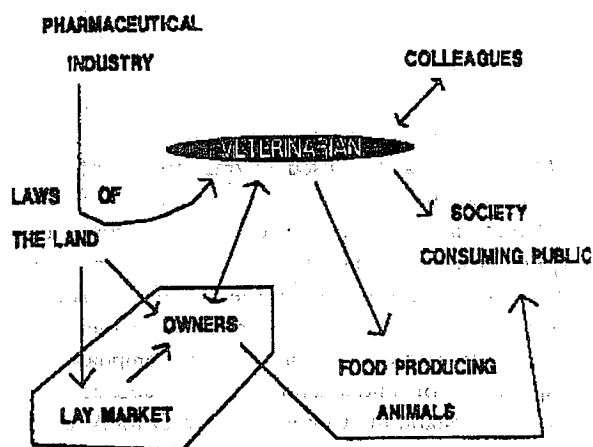
Part 3. Clinical Examples Used to Illustrate Pharmacological Concepts

Setting up a proper regimen for antimicrobial therapy of infectious disease is a very good way to emphasize the basics of pharmacokinetics. The regimen must match the concentration at the site of infection with the susceptibility of the organism. The relationship between plasma levels and tissue levels is extremely important as is whether we are treating a pneumonia, for example, or a septicemia. Penicillin G is an excellent example to use here in that its label dose is based upon using the sodium salt intravenously to treat a septicemia while in clinical situations the procaine salt is usually used I.M. or S.C. and is used to treat tissue infections. Since penicillin G has a rather low volume of distribution, this is also an excellent example to use to emphasize the importance of kinetics and can be followed by a discussion on the use of plasma assays for monitoring drug therapy in clinical patients.

Examples can be used to emphasize the importance of understanding jurisprudence. One must understand the Comprehensive Drug Abuse and Control Act as it relates to veterinarians using drugs for analgesia, chemical restraint and anesthesia. Some of these drugs may be used in a manner not consistent with their label and many times human label products are used. The extra label use of drugs is vital to the practice of Veterinary Medicine. A thorough understanding of the discretionary policy of the Center for Veterinary Medicine/Food and Drug Administration relative to extra label drug use is mandatory. Procaine Penicillin G again is an excellent example of extra label drug use because, in order to effectively treat tissue infections, the dose must be increased. This then creates a whole new ballgame relative to tissue kinetics and tissue depletion and slaughter and milk withdrawal times. Many times owners want to give Procaine Penicillin G in excessively large volumes per injection site, which creates real problems relative to a slaughter withdrawal time. The use of neomycin in food animals is another example that can be used, not only to emphasize kinetic principles, but also to emphasize proper extra label drug use. Oral neomycin is approved for food animals and parenteral neomycin is not approved for use in food animals. If used orally, very little neomycin will become systemic and therefore toxicity and tissue residues are predictable. However, when neomycin is injected to treat respiratory problems, it not only can initiate a vicious

circle leading to nephrotoxicity but also will create serious tissue residue problems, necessitating extremely long withdrawal times or not using this drug at all.

These examples clearly show the need to emphasize to the students that the veterinarian should be the hub of the use of drugs in all animals and should be totally in charge of all uses of these drugs.



An understanding of the autonomic nervous system is basic to understanding disease processes, and the compensatory mechanisms by which the animal attempts to correct pathophysiology. The autonomic nervous system also serves as a basis for many types of therapy. One example would be the way organophosphates intoxicate animals via an overabundance of acetylcholine. The use of atropine to treat organophosphate intoxication is a means to emphasize drug receptor interactions and the principles of affinity and efficacy at the receptor site. Another example would be the importance of understanding the adrenergic portion of the sympathetic nervous system. A proper understanding of the adrenergic agonists such as epinephrine, norepinephrine, isoproterenol, and dopamine can be plugged right into the treatment of cardiovascular shock. For example, early in cardiovascular shock, the agents with both alpha and beta adrenergic activity may be indicated. In long standing shock, alpha adrenergic agonists are contraindicated and beta adrenergic agonists should be used to increase the contractility of the heart and to increase perfusion of the viscera including the kidney. The effect of intravenous epinephrine on the kidney to produce anuria is a very good means to illustrate these

principles. The relationship between pain (of colic) and fear, and hypoxia resulting in decreased visceral perfusion can also be emphasized.

Another means of emphasizing concepts would be an understanding of the arachidonic acid cascade and its modification by therapeutic agents. A discussion of the prostaglandin synthesis inhibitors would involve not only their mechanism of action for therapeutic use, but the same principles need to be emphasized as a mechanism for their producing gastrointestinal and renal toxicity. The drug Banamine® can be used as an example to illustrate how a prostaglandin synthesis inhibitor may be used to treat the pain of equine colic. At this point one can also emphasize autonomic concepts such as; if an animal is in pain, the wall of the intestine will not be perfused due to excess alpha adrenergic activity. Furthermore, Banamine can be used to emphasize its action centrally in the pain perceiving area of the brain and its action peripherally as an anti-inflammatory agent at the site of the problem in the intestinal tract. It also fits quite well at this point to include an understanding of the glucocorticosteroids as they are used as anti-inflammatory agents. Although their mechanism is different, the end results can be similar. The use of glucocorticosteroids also lends itself very well to a discussion of a drug that if properly used can be very efficacious and if improperly used, can lead to all kinds of serious adverse effects. For example, glucocorticosteroids are contraindicated for chronic use in animals with infectious disease.

The use of drugs to influence the cardiovascular system is another example that can be used. When discussing the use of cardiovascular drugs, one must have a thorough understanding of the concepts of cardiac output. This leads then to discussions of drug mechanisms that alter preload, or afterload, and includes the study of drugs that are positive inotropes. The angiotensin converting enzyme inhibitors, such as captopril, may be used to emphasize a drug whose action is directed towards inhibition of pathophysiological processes. While studying the cardiovascular drugs there is a great opportunity to emphasize the interaction between the cardiovascular system and the urinary system.

I furnish for the students a core drug list which contains some 200 drug names. The use of this list serves two purposes. One is to give them an idea of what drug names they will be responsible for on exams and secondly, to de-emphasize rote memorization of names and thereby emphasize

concepts. I do not require the memorization of any dosages.

In conclusion, it should be emphasized that proper pharmacotherapy is based on a thorough understanding of basic pharmacological concepts and revolves around the regimen.

Appendix A

The Science and Art of Medicine

- A. THE BASIS OF SUCCESS OF A PROFESSIONAL CAREER IN VETERINARY MEDICINE
1. Knowledge, correlation of knowledge, and the application of knowledge
 2. Scientific curiosity
 3. In depth observations
 4. Communication
 5. Positive attitude, concern, enthusiasm
- B. "The student who attempts merely to memorize the pharmacodynamic properties of drugs is foregoing one of the best opportunities for correlating the entire field of preclinical medicine."
- C. Differences of opinion are the inevitable accompaniment of education. In the medical sciences particularly, experimental and clinical observations lend themselves to diverse interpretation and the undergraduate veterinary medical student will be confronted with this dilemma throughout his/her period of training. Nor will this problem dissipate in practice, for biological phenomena rarely fit into a strict and conforming mold. The essence of a medical education is not merely the memorization of a vast amount of information, but the development of a method to integrate this material intelligently in order to understand and cope with the infinite variations in biology and medicine.
- D. Do not fall into the trap of believing present concepts to be so perfect that there is no longer a place for alternative premises, procedures, and points of view in evaluating the clinical utility of drugs.
- E. Do not assume that OLD drugs are not appropriate for use and/or NEW means better.
- F. Since every therapeutic measure, including

inaction, involves a certain risk, the mark of a competent practitioner is his capacity to place into balance a multitude of tangible and intangible factors so as to arrive at a course of therapeutic action with the best benefit-to-risk ratio for a particular patient and its owner.

- G. Hippocrates said: "To do nothing is sometimes a good remedy." "Above all, Do no harm." Hippocratic Oath: "I will prescribe regimen for the good of my patients according to my ability and my judgement."
- H. Paracelsus said: "All substances are poisons. There is none which is not a poison. The right dose differentiates a poison and a remedy."
- I. Sir William Osler said: "Remember how much you do not know. Do not pour strange medicines into your patient."
- J. Galileo said: "You cannot teach a person anything: you can only help them find it within themselves."
- K. Dr. Frick said: "A person's judgement is no better than their information."
- L. "Science is merely an extension of common sense" Einstein.
- M. "Don't just do something, stand there." Dr. Carl Osborne.
- N. Upson says: "LEARNING CAN BE FUN."

Appendix B

Ethics of Pharmacotherapy

- A. The principal objectives of the Veterinary Profession are:
1. to render service to society;
 2. to conserve our animal resources; and
 3. to prevent and relieve suffering of animals.
- B. The responsibilities of the Veterinary Profession extend not only to the patient but also to society.
- C. Veterinarians should conduct themselves in relation to the Public, their Colleagues, their Patients, Clients, and the allied professions, so as to merit their full confidence and respect.
- D. Determination of Therapy shall be based upon:

1. The needs of the patient;
 2. The welfare of the client; and
 3. Safety to the public.
- E. Veterinarians shall comply with the common law governing their obligations to their clients and shall obey the Laws of the Land governing their acts.
- F. In the choice of drugs (regimen), biologicals, or other treatments, Veterinarians are expected to use their professional judgement based upon:
1. the knowledge of the condition;
 2. the effects of the treatment; and
 3. the available scientific evidence which may affect these decisions.
- G. Veterinarians are fully responsible for their actions with respect to a patient from the time they accept the case until it is released from their care or in the case of food animals, until the meat, milk, or eggs are marketed.