Pharmacologic Basis of Adverse Drug Reactions

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The increasingly large number of potent compounds available to treat patients makes it imperative that veterinarians renew and keep up-to-date information about drugs. Until fairly recently, a veterinarian used all of his clinical skills in making a correct diagnosis, but paid little attention to therapy since it was believed that anyone could administer medications based on a memorized schedule of dosage and side effects. With the increasingly high incidence of adverse reactions to drugs and their potential detriment to the patient, this position is no longer tenable.

After making the correct diagnosis, the veterinarian has four major choices open to him: (1) surgery, (2) rational pharmacotherapy, (3) do nothing (sometimes a wise decision), or (4) administer a wide variety of potent chemicals about which he has had little opportunity to learn anything. The latter is of practical significance especially in today's era of "polypharmacy" for it is the exception rather than the rule for patients to receive only one drug during the course of treatment. Drug interactions are complex and have important therapeutic implications.

Since World War II we have been in the midst of a "drug explosion." Currently, there are over 7,-200 prescription drugs and drug combinations available, 70% of which were unknown or unavailable fifteen years ago. This situation poses a serious challenge to the practitioner, universities, pharmaceutical industry and government.

The therapist must keep in mind that there is no completely "safe" drug unless the compound is pharmacologically inert. Thus, the art of therapeutics requires a consideration of the ratio between potential benefits and risks to the patient. Considerable risk may be tolerated when treating a life-threatening disease. However, even a small risk associated with drug therapy would be unacceptable in the management of a self-limiting disease.

Adverse drug reactions may be defined, for the purposes of this paper, as direct harmful effects on the patient, or lack of therapeutic effect.

The purpose of this paper is to provide a foundation of pharmacologic principles necessary for understanding adverse drug effects as they may occur in the bovine patient.

Dose-Related Effects

The disposition of a drug in the body is illustrated schematically in Figure 1. Following administration of the dosage form, the drug molecules must cross a series of biologic membranes to reach their site of action. After absorption the drug enters the central compartment (plasma) where a portion may be bound to plasma proteins. The unbound drug in the plasma is free to distribute to body tissues, to be metabolized or excreted, or to combine with receptors at the site of action.

Drugs usually induce more than one biological effect when given to an animal. The effects are related to the dose administered and to the resultant concentration of drug produced at the receptor site. A dose-response relationship is shown (Figure 2). Individual differences among a population are evident and the doses producing a response in 50% of the population are the most sensitive indices for characterizing a given drug. The rato LD_{50} : ED_{50} is commonly employed to express the "therapeutic index" which has the connotation of relative safety.

The veterinarian possesses drugs in his therapeutic armamentarium which vary widely in their dose-response relationships. Penicillin has an extremely large therapeutic index whereas intravenous digoxin has a comparatively small index. These considerations may be translated to concentrations of the drug in body fluids. Figure 3 illustrates hypothetical plasma drug concentration versus time curves following intramuscular administration of a drug. The objective of the dosage regimen is to provide enough drug at the appropriate dosage intervals to maintain concentrations greater than the minimal effect concentration but less than those which will produce toxic effects as shown in graph A. A number of adverse effects result when drug accumulates until toxic concentrations occur. This may take place when the drug is given in excessive doses or too frequently. Graph B illustrates the effect of giving the drug too frequently and graph C shows the plasma concentrations resulting from doses repeated at too long an interval.

Pharmacokinetics: Pharmacokinetics is concerned with the time course of a drug within the body. There are several concepts from this discipline which are pertinent to this discussion. These are rate constants, apparent volume of distribution and the plateau principle.

Most drugs when administered intravenously will disappear from the body by first order kinetics. This means that the rate of elimination at any time is proportional to the concentration of drug present. This is illustrated in Figure 4a. It can be seen that the drug concentration at 1 hour is 10 μg/ml, at 2 hours is 8.3 μg/ml, at 3 hours is 7 μg/ml, at 4 hours is 5.9 μg/ml, etc. This indicates that during each hour, the amount eliminated is 17% of the amount present at the beginning of that hour. This is an exponential process. If these same data are plotted on semi-logarithmic paper the elimination of drug plots as a straight line (Figure 4b). The significance of this phenomenon is that constants can be determined which are employed to establish dosage regimens for a given drug in a given species.

The rate of elimination is described by k_e which is related to the slope of the curve in Figure 2b. This defines the rate of elimination of the drug from the plasma and in the example is equal to 0.17 $hr.^{-1}$. Half life is another parameter which is often employed to describe elimination rates of drugs. It is the time required for the concentration to be decreased by half and is related to the elimination rate constant by:

$$t_{1/2} = \frac{0.693}{k_e}$$

The apparent volume of distribution (Vd) is defined as the volume of fluid into which the dose appears to distribute with a concentration equal to that in plasma. It is given by:

$$Vd = \frac{\text{Amount of drug in body}}{\text{Concentration of drug in plasma}}$$

It is unique for a given drug in an individual or species and is useful in determining the blood concentration of a drug which will be obtained from a given dose.

If the veterinarian administers fixed doses of a drug at intervals, the amount in the body will increase until a plateau level is attained. This effect is illustrated in Figure 3 (graphs A and B). The plateau is achieved when the rate of drug added to the body is equal to the rate of elimination. The time required to achieve a plateau concentration is solely dependent on the half life of the drug. It will require about four half lives to reach a plateau concentration. This is significant clinically because drugs with a short half life will reach a plateau state in the body rapidly and are easily controlled. For example, the half life of potassium penicillin G is 30 minutes. If one infuses this drug at a constant rate, a plateau (constant plasma levels) will be reached in two hours. If we consider a drug such as digoxin ($t_{1/2}$ = 38 hours) it would require 152 hours or 6-1/3 days to reach a steady state. Thus it would require a week to assess the effects of your therapy.

Several factors will modify the pharmacokinetics of a drug. These include interactions with other drugs, age and modification of the functional state of the animal by diseases. A brief discussion of specific mechanisms related to drug disposition in the body follows.

Biotransformation: Drugs are converted by the body to more polar (water soluble) forms which are easily excreted. Depending on the chemical nature of the drug it may be oxidized, reduced, hydrolyzed, acetylated or conjugated with glucuronate, various amino acids or sulfate. Many of these reactions take place in the endoplasmic reticulum of hepatocytes. The activity of the enzymes responsible for biotransformation of a given drug may be increased (enzyme induction) or decreased (enzyme inhibition) by other drugs. This may result in increased or decreased pharmacologic activity of the primary drug by prolonging or shortening its half life.

Plasma Protein Binding: Most drugs are bound to some extent to serum albumin. The bound portion is inactive and non-diffusible. This tends to serve as a depot for the release of additional free drug (active) and to protect the bound drug from biotransformation and excretion. An important mechanism for drug interactions and adverse effects is for one drug to displace another from protein binding sites thus abruptly increasing the amount of free drug for diffusion to sites of action.

Renal Excretion: Drugs may be excreted by glomerular filtration or tubular secretion. Thus rate of excretion of a drug may be altered by other drugs or diseases which alter renal blood flow, protein binding, urinary pH or compete with transport processes involved in active secretion. Alterations of efficacy of a drug designed to act in the urinary tract may occur as a result of changes in urinary pH.

Incompatibilities

There are a number of drugs which are physically incompatible when mixed in solutions. Such mixtures can produce adverse reactions in bovine patients. Precipitated materials may produce emboliams if administered intravenously or active constituents may be inactivated due to chemical changes. Incompatibilities are of practical significance in bovine practice when one mixes medicaments in the same syringe, extemporaneously mixes solutions for intramammary or intrauterine administration, or dilutes drug solutions with intravenous solutions.

A number of factors are involved in the matter of incompatibilities. These include pH, chemical nature of the drugs, presence of divalent ions and miscellaneous factors.

pH Change: If the final pH of an admixture is significantly different from the additive alone, one might suspect an incompatibility. This may even occur between a single additive and the primary solution as in the case of aminophylline or sodium am-

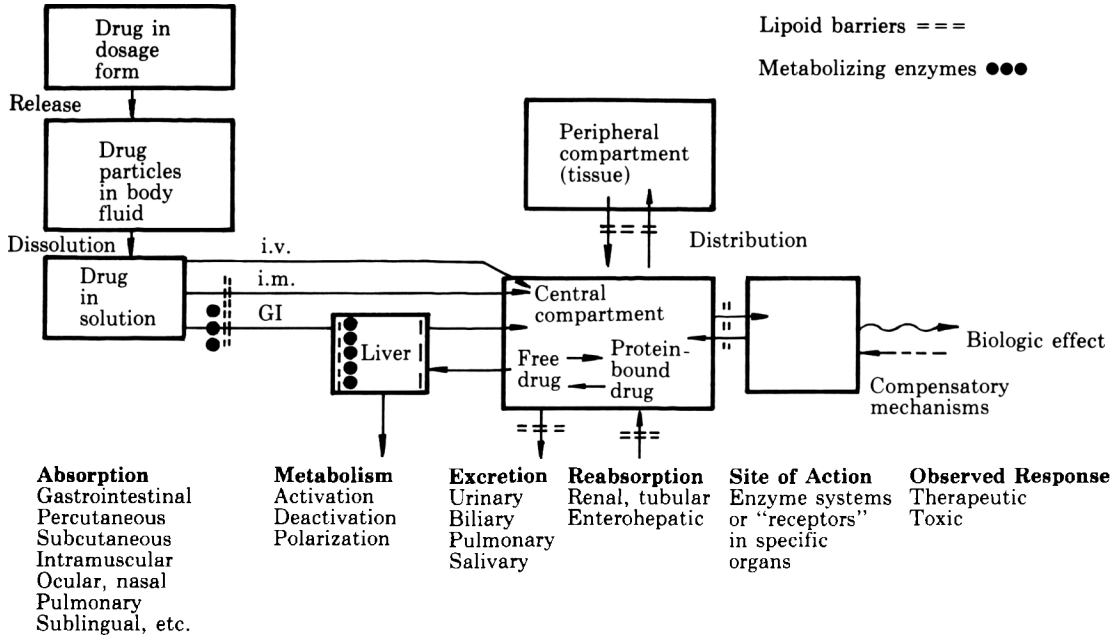

Figure 1. Factors that influence the onset, duration and intensity of drug effects. (From Barr, W.H.: Principles of Biopharmaceutics. Am. J. Pharm. Educ., 52:958-81, 1968.)

picillin in dextrose 5%. Change in pH may either affect the solubility of the drug resulting in its precipitation or it may inactivate the active constituent without visual manifestations. The pH values of common intravenous solutions are listed (Table 1).

Drugs Existing in Solution as Large Cations or Anions: Most commercial additives contain drugs which are in their salt forms. One naturally would not expect the salt of a weak acid to be compatible with the salt of a weak base. Oppositely charged large ions would most probably unite and precipitate. Generally speaking, salts of weak acids are compatible together as are salts of weak bases. However, other factors may be involved so we cannot generalize.

Divalent Ions: Divalent cations such as Mg^{++} or Ca^{++} have the potential of forming complexes with drugs such as tetracycline. Divalent anions such as $CO_3^{=}$ or $SO_4^{=}$ may form insoluble salts with any calcium that might be present in the admixture. Other considerations influencing compatibility of drugs include concentration of active substances; preservatives; buffers; stabilizers; antioxidants; time and order of mixing; effects of light, heat or air; and properties of the container.

Specific Additives: Definite statements are hard to make about the compatibility of drugs because of a wide variety of factors involved. Buffering systems, preservatives and vehicles for each additive must be considered because of their possible influence. In addition, some drugs compatible at one concentration may not be at another. Comments made on additives listed in Table 2 are observations on potential incompatibilities that have been made on certain preparations in a range of concentrations. To accept these statements as absolute truth for each product or for all concentrations that might be prepared would be in error. These are only to be used as guidelines to assist those involved in preparation of I.V. additives.

Allergic Drug Reactions

Hypersensitivity reactions, or allergic drug reactions, are those based on immunological responses, and are the result of antigen-antibody combination. Other types of adverse effects such as direct toxicity, overdosages, side effects, or interaction between drugs, are not caused by immune mechanisms.

Antibody Formation: Most drugs have a molecular weight less than 10,000 and are too small in size to be capable of stimulating antibody formation. These agents do produce allergy by virtue of their ability to covalently bind to endogenous protein, and to a lesser extent polysaccharides and polynucleotides. Most drugs do not have intrinsic protein reactivity, but must first undergo metabolic degradation. The incomplete antigen is termed a haptene, and following conjugation with endogenous protein it is capable of eliciting an immune response.

Generally a small chemical portion of the complex molecule is responsible for stimulating antibody formation; it is this same reactive site that combines with the antibody to precipitate the allergic response. Different drugs with similar reactive chemical sites may demonstrate cross sensitivity.

The complete antigen is phagocytized by macrophages and degraded into immunological fragments of RNA. This may be transferred to receptor sites on the surface of lymphocytes associated

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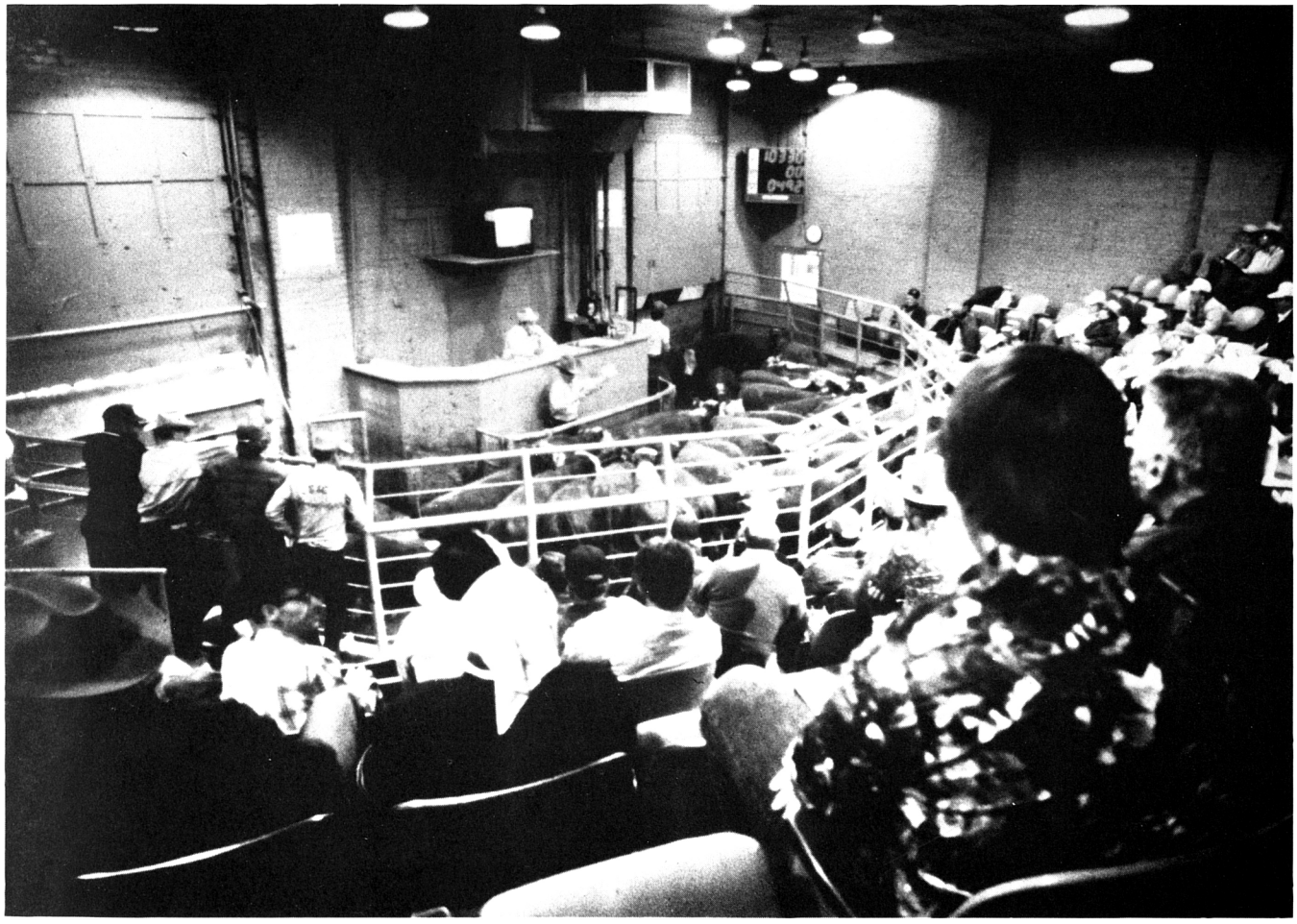

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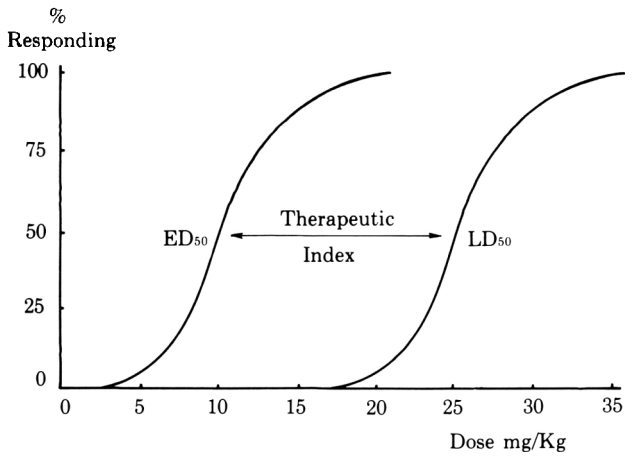

Figure 2. Dose-Response Relationship of a Hypothetical Drug.

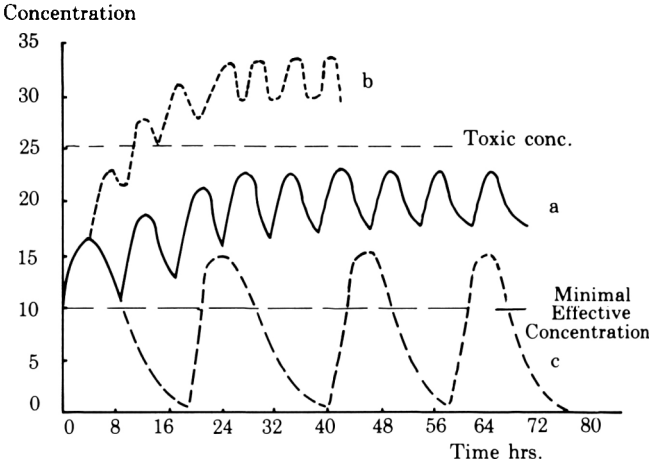

Figure 3. Relationship Between Blood Concentrations and Time Showing Results of Three Different Dosage Regimens.

with bone marrow, or B-lymphocytes. The result is the formation of plasma cells which are capable of producing specific immunoglobulins (humoral antibodies) or long term memory cells. If the processed antigen binds to T-lymphocytes, those cells associated with the thymus gland, specifically sensitized lymphocytes are produced which are responsible for cell mediated immunity. Long term memory cells may also be produced from T-lymphocytes.

Five basic types of immunoglobulins are produced by B-lymphocytes, IgM, IgG, IgA, IgD, and IgE; IgE, IgM, and IgG are involved in most cases of drug allergy. IgE is associated with anaphylaxis and cutaneous lesions. IgM and IgG are thought to be responsible for serum sickness, and the hemolytic anemias associated with penicillins and cephalosporins.

Upon contact with the processed antigen the T-lymphocyte is transformed into a specifically sensitized lymphocyte which produces cell mediated immunity. When this special lymphocyte is exposed to the specific antigen a characteristic allergic response occurs. Contact dermatitis is an example of cell mediated immunity.

Long term memory cells are formed from either B-lymphocytes or T-lymphocytes. Upon exposure to the original antigen these will rapidly differentiate into specifically sensitized lymphocytes or produce humoral antibodies. Long term memory cells retain this ability for months or years after sensitization.

The Allergic Response: In order to elicit signs of hypersensitivity the antigen must have multiple combining sites, permitting it to form a bridge between antibody molecules. Following conjugation, soluble humoral antibodies may react with complement and release cytoactive peptides. Bridging between cell bound antibody (IgE) or antigen receptors on specifically sensitized lymphocytes produces conformational changes necessary for activation of mediator release or lymphocyte transformation. Univalent haptens, either as free drug or unconjugated metabolites, not only fail to elicit allergic responses but compete with multivalent antigens for antibody, thus inhibiting the response.

Anaphylaxis and serum sickness are examples of generalized systemic allergic reactions, but individual organs may also be affected. If the haptene reacts chemically with a tissue introducing antigenic groups on the cell surface, the tissue may become susceptible to antibody or lymphocyte-mediated cytotoxicity. Soluble antigen-antibody complexes may localize on the cell surface, damaging the cell as an innocent bystander. It is also possible for organ specific proteins to be replaced by haptene, resulting in organ directed autoimmunity.

Timing of Allergic Reactions: A time relationship may usually be established for allergic manifestations, and correlates with the formation or existence of antibodies. Allergic reactions may be classified according to their clinical appearance as immediate, delayed, or accelerated delayed reactions. Immediate reactions occur anytime within the first twenty-four hours after therapy is initiated. An immediate reaction requires prior sensitization to the antigen since preformed antibodies are responsible for the response. A delayed reaction occurs typically after two or three weeks of therapy, but may appear within seven to ten days. The appearance is dependent on the formation of sufficient amounts of antibody to precipitate an allergic response. Prior sensitization is not required for the appearance of a delayed allergic reaction. Accelerated delayed reactions occur within two to three days to one week after the start of therapy. There is usually a history of prior exposure to the offending agent since long term memory cells are thought to be responsible for this reaction.

Characteristics of Allergic Responses: Allergic reactions are not dose related. In many cases microgram amounts of antigen are sufficient to precipitate the allergic response. A few exceptions exist, such as drug induced hemolytic anemias. Circulating or cellular

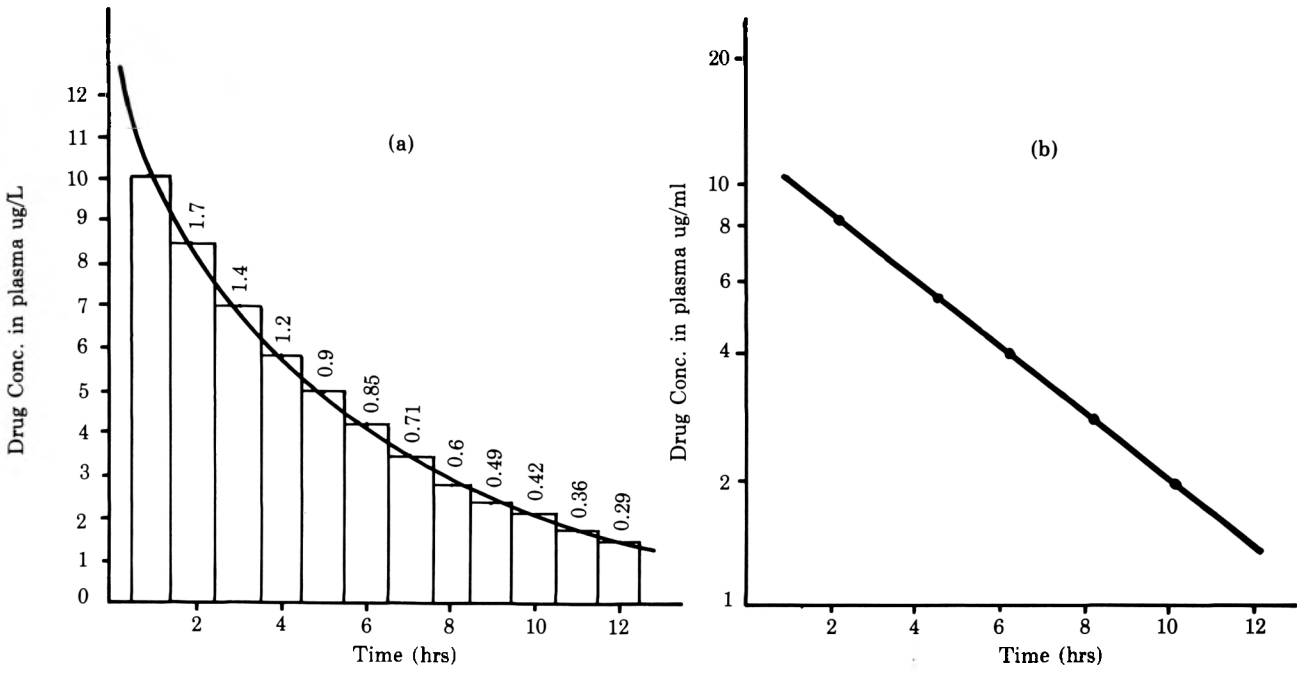

Figure 4. (a) Graph depicting elimination of a hypothetical drug from blood plasma. The numbers on the graph indicate decrease in concentration each hour. (b) Semi-log plot of the same data shown in (a).

antibodies may be demonstrated. Mast cell degranulation may occur. The same reaction will occur in the original form when a test dose is given. It is also possible for a more severe reaction to appear upon challenge with the drug. The reaction usually subsides when the drug is eliminated from the body. Supportive medication may be required in the interim. Eosinophilia is common. This may occur, however, before, during, or after the allergic manifestation. The clinical picture conforms to a known allergic pattern.

Lack of Effect

The failure of a drug to exert its expected pharmacologic effect in a patient needing therapy constitutes an adverse response. Several of the principles described previously apply here.

Dosage Regimens Inappropriate to the Species: Many drugs are rapidly eliminated from the body of ruminant animals due to rapid biotransformation (e.g., salicylates, chloramphenicol) or to diffusion and "ion-trapping" within the rumen (e.g., amphetamine, ephedrine, quinidine). Because of these features many drugs must be given more frequently to cattle than to other species to produce a comparable clinical effect. Some drugs diffuse into the rumen from the blood so rapidly that negligible effects are observed (e.g., opiates, amphetamine), even with rather large doses. Due to the nature of the digestive tract of the ruminant, many drugs are either poorly absorbed or destroyed within the ruminal environment.

Drug Interactions: One drug may interact with another or with various nutrients to negate its therapeutic effects. Tetracyclines administered with milk replacers or with milk are poorly absorbed from the digestive tract of calves. The calcium is chelated by tetracyclines to form a non-absorbable complex. Adsorbents such as kaolin or pectin will combine with macrolide antibiotics and prevent absorption of the antibacterial drug.

Administration of pharmacologic antagonists will produce a failure of response. If pilocarpine were given to an animal which had been treated previously with atropine, one would not expect to observe signs of cholinergic stimulation. If epinephrine were given to a patient suffering from a hypotensive reaction to a phenothiazine tranquilizer the situation may worsen because the alpha receptors are blocked.

Factors in Failure of Antibiotic Therapy: If we assume that the drug, its route of administration and dosage are appropriate to the nature and location of the infection we may still observe therapeutic failures. Drug interactions or incompatibilities may compromise the effectiveness of the antibacterial agents. Variations of urinary pH may influence drug activity in urine. Aminoglycosides may be inactive in acidic urine whereas methenamine is inactive in alkaline urine. There may be a non-draining, deep abscess present. The infection will respond to therapy

Table 1
Common Primary Solutions

Solution	meq./L	U.S.P. pH range	Common pH
Dextrose 5% in Water		3.5 - 6.5	4.0
Dextrose 10% in Water		3.5 - 6.5	4.0
Sodium Chloride 0.9% in Water	Na 154 Cl 154	4.5 - 7.0	5.5
Ringer's Solution	Na 147.5 K_4 Ca 4.5 Cl 156	5.0 - 7.5	5.7
Lactated Ringer's Solution	Na 130 K_4 Ca 3 Cl 109 Lactate 28	6.0 - 7.5	6.5
Dextrose 5% in Lactated Ringer's Solution	Na 130 K_4 Ca 3 Cl 109 Lactate 28		5.0

Table 2
Common Drug Incompatibilities

Aminophylline (pH 8.0 to 9.0): Aminophylline is not stable if the pH is significantly below 8.0.

Calcium Chloride (pH 6.5 to 8.5): Reported physically compatible with the following in Dextrose 5%: Chloramphenicol Sod. Succinate; Penicillin G Potassium 2,000,000 u/1; Penicillin G Sodium 2,000,000 u/1; Pentobarbital Sodium. Incompatible with: Cephalothin sodium; Chlorpheniramine; Chlortetracycline, Oxytetracycline, Tetracycline (inactivation due to complex); Sodium bicarbonate (conc. dependent).

Chloramphenicol sodium succinate (pH 6.4 to 7.0): Will retain chloramphenicol potency for 24 hours when added to common primary solutions.* Incompatible with: Hydrocortisone sodium succinate, (Solu-Delta-Cortef® would be suspected), Oxytetracycline, Vit B Complex with C.

Digoxin: Should not be mixed with I.V. infusion fluids.

Epinephrine 1:1000 (pH 2.5 to 5.0): Compatible with common primary solutions.* Use all mixtures immediately.

Furosemide (pH 8.8 to 9.3): Incompatible with acidic solutions. The maintenance of an appropriate pH is essential for this drug to remain in solution. Therefore, it is recommended that no additive be mixed in the same bottle with it.

Gentamicin sulfate: Is not to be physically combined with other drugs, but is to be administered separately by the recommended route of administration and dosage schedule. The veterinary product is not approved for intravenous use whatsoever. The human product is said to be compatible with common primary solutions*, but one should be cautious of the sulfate in solutions with calcium such as Ringer's and lactated Ringer's solutions.

Isoproterenol - Isuprel®: Compatible with common primary solutions*.

Levarterenol bitartrate - Levophed® (pH 3.0 - 4.5): Levophed® should be administered in 5% dextrose in water or 5% dextrose in saline solutions. Fluids containing dextrose provide protection against significant loss of drug potency due to oxidation. Incompatible with most basic additive (e.g., pentobarbital sodium, phenobarbital sodium, sodium bicarbonate).

Magnesium sulfate: Compatible with dextrose 5% and isotonic saline. May be compatible in low concentration in Ringer's and lactated Ringer's solution although not recommended with those preparations containing calcium. Incompatible with sodium bicarbonate.

Oxytetracycline: Quite a sensitive solution. Should not be combined with basic substances because it can precipitate the free acids of barbituric acids and sulfanilamide derivatives. Calcium or magnesium containing preparations must be avoided because of the formation of an inactive complex.

Penicillin G, potassium or sodium (pH 5.0 to 7.5): Compatible in common primary solutions*. Incompatibility: Optimum pH range 6.0 to 7.0. Below pH 5.5 and above pH of 8 significant inactivation of penicillin activity results. Additives with low pH's are aramine, ascorbic acid (not sod. ascorbate), tetracycline, Vit. B with C. Those with high pH include aminophylline and sodium bicarbonate.

Sodium bicarbonate (pH 7.0 to 8.0): Compatible with saline and dextrose solution but not Ringer's or lactated Ringer's solution because of the calcium. Incompatible with the following: Calcium chloride, calcium gluconate, Levophed® magnesium sulfate, tetracyclines, penicillin G, sodium pentobarbital, thiopental sodium, streptomycin.

Sodium Iodide (pH 7.5 to 9): Compatible in common primary solutions.* Incompatible with levartenerol, Vit. B complex with C.

Succinylcholine chloride (pH 3.0 to 4.5): Stable in acid solution but unstable in alkaline solutions such as those containing short-acting barbiturates. Compatible in Dextrose 5% in water and normal saline.

Tetracycline: See oxytetracycline. Administer alone if at all possible to avoid potential incompatibilities.

Thiopental sodium (pH 10 to 11): A 3.4% concentration in sterile water for injection is isotonic. The most stable solutions are those prepared in normal saline and sterile water for injection. Discard solutions at 24 hours. Incompatible with a number of acidic solutions including succinylcholine chloride.

*Common primary solutions include: Dextrose 5%, Dextrose 10%, Ringer's, Lactated Ringer's and Normal Saline.

only with the provision of drainage. There may be obstruction to natural drainage of an infected area, e.g., bronchi, uterus, ureter. The infection will only respond with relief of the obstruction. A foreign body present at the site of infection will prevent cure of the infection until the object is removed.

Diseases impairing host defenses may result in little or no response of the infectious agent to the antimicrobial drug. Ultimate elimination of bacterial infections is dependent on active phagocytic activity and the immune response. Concomitant administration of corticosteroids may diminish the competence of host defenses.

A penicillin-susceptible pathogen may be protected

Table 3
Allergic Patterns

1. Anaphylactic shock is thought to be caused by the release of histamine and/or serotonin. It may appear as hypotension with any combination of the following: bronchospasm, angioneurotic edema, laryngeal edema, urticaria or other skin rash. This reaction is usually seen within 5 to 30 minutes after exposure to the offending agent.
2. Anaphylactoid Reaction: This reaction is very similar to anaphylactic shock but the patient does not develop hypotension. The other features of anaphylaxis are apparent.
3. Angioneurotic Edema: This is an acute circumscribed edema often occurring in association with urticaria. It may affect the eyelids, lips, ear lobes, external genitalia, or mucous membranes. The overlying skin may be unaltered, or erythematous and tender.
4. Drug Fever: This reaction appears as a sudden onset of fever which is characteristically high. This lyses within one to three days after the drug has been discontinued.
5. Eosinophilia.
6. Serum Sickness: This syndrome includes skin rash, fever, enlargement of lymph nodes, painful joints, and may be associated with allergic vasculitis.
7. Allergic Vasculitis.
8. Polyarthralgia.
9. Lupus Syndrome: This may be differentiated from spontaneous systemic lupus erythematosus by the infrequent appearance of CNS, cutaneous and renal involvement.
10. Pseudo-infectious Syndrome: This syndrome combines fever, leukopenia, and myalgia.
11. Vaccinia: This severe skin lesion resembles smallpox, and occurs when allergic patients are given a smallpox vaccination.
12. Cholestatic Jaundice (Hepatitis).
13. Allergic Hematological Disorders.

on mucosal surfaces by a penicillinase-producing member of the normal host flora. Thus, the antibiotic is inactivated before it can kill the pathogenic organism.

With high doses or broad spectrum antibiotics one may induce a superinfection by resistant organisms. An alternative effect might be the elimination of competing normal flora which serve to keep a potential pathogen in check.

Lastly, one must consider the possibility that his diagnosis was incorrect and he has been treating an untreatable disease such as a virus or fungal infection. Alternatively, some non-infectious diseases and drug reactions will mimic infections.

How Can You Minimize the Occurrence of Adverse Drug Effects In Your Practice?

1. Where possible, avoid multiple drug therapy. The knowledgeable use of a single drug in pharmacotherapy is superior to the blind administration of a series of drugs with no regard to how they may influence one another.
2. Avoid combination products. As a matter of policy, we do not include combination products in our Veterinary Medical Teaching Hospital Formulary.
3. Avoid simultaneous use of drugs which may be antagonistic.
4. Try to minimize your personal formulary to the point that you are thoroughly familiar with each drug. Today there is a greater danger from overtreatment than from undertreatment of most cases.
5. Limit intravenous infusion solutions to only one drug additive to avoid incompatibilities.
6. Always have on hand appropriate drugs with which to treat acute allergic reactions. If dispensing drugs for administration by the owner, explain how to recognize and treat an anaphylactic reaction. Penicillin allergy in cattle is being seen more commonly today.
7. **When in doubt consult your local pharmacist. By training he is an excellent source of information on drug incompatibilities, interactions and adverse effects.**

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President-Elect AVMA

Dr. Vernon L. Tharp (OSU, '40), Columbus, Ohio, was elected president-elect of the American Veterinary Medical Association for 1977-78 by the House of Delegates on July 10, 1977.

Dr. Tharp is a past-president of the American Association of Bovine Practitioners. Congratulations, Vernon.