

The Veterinary Antimicrobial Decision System: Progress of a Project Supported in Part by the AABP

Michael D. Apley, DVM, PhD, DACVCP

Virginia R. Fajt, DVM

*Department of Veterinary Diagnostic and Production Animal Medicine
Iowa State University
Ames, Iowa*

Information on reasonable antimicrobial regimen design, particularly for extralabel use, is not currently available in a single easily-accessible source. Sources of information are scattered and may be difficult for the practitioner to locate in a timely manner. Even if the data are located, the interpretation may not be evident to the practitioner, particularly interpretation of pharmacokinetic and pharmacodynamic data.

The need for a system designed for the food animal veterinary practitioner is also apparent as the discussion in the public health venue focuses on the appearance of antimicrobial-resistant human pathogens. The correlation between antimicrobial use in food animals and the appearance of resistant pathogens in the human population may not be unequivocally established. However, there is little doubt that antimicrobial use, whether in human or veterinary patients, may affect microbial populations by selecting for resistant organisms. Therefore, a need exists for the prudent use of antimicrobials such that efficacy is maximized while selection for resistant pathogens is minimized. Prudent use also contributes to longevity of the clinical utility of antimicrobials we currently have. These statements are made realizing that we know a lot more about maximizing efficacy than minimizing resistance development.

With these needs in mind, the AABP, along with the Academy of Veterinary Consultants (the first to financially support the effort), the National Cattlemen's Beef Association, the American Association of Swine Practitioners, and the American Veterinary Medical Association have contributed a total of \$189,000 as startup money over a 3 year period. Supporting funds started to arrive in March of 1999.

Project Personnel

Beth Monroe started as project secretary on April 26 and has been busy setting up and organizing our offices as well as establishing protocols for management

of funds and communication between cooperators in the project. Sarah Bashaw, a second year veterinary student has worked on the project part time in the spring semester of this year and full time over the summer. She will continue part time during the school year and will hopefully be back next summer as well. This summer Sarah increased our reference base to over 5000 articles as we searched the world literature for pharmacokinetic articles in both cattle and swine. These articles are organized using reference manager. The procedure involves Sarah and Dr. Fajt going through initial search lists to remove obvious inappropriate articles. A list of articles is then reviewed by the author to select articles to retrieve for review and archiving. This summer we completed our pharmacokinetic search in cattle and swine, as well as recording and collecting abstracts on small ruminant pharmacokinetic articles to allow expansion as funding allows.

Pivotal to the progress of the Decision System was a meeting of the principal cooperators at Iowa State University on April 25-27 of this year. Jeff Wilcke, DVM, MS, (Virginia-Maryland Regional College of Veterinary Medicine) and Cory Langston, DVM, PhD, (Mississippi State University College of Veterinary Medicine) both participated in the meeting. Drs. Wilcke and Langston are both diplomates of the American College of Veterinary Clinical Pharmacology. Dr. Wilcke brings a wealth of informatics expertise to the project and is leading the efforts in setting up the website. Dr. Langston is proficient in pharmacokinetic modeling and will be instrumental in the regimen determination component of the project. Drs. Langston and Wilcke are currently contributing time to the project. We hope to secure funding to support their efforts in the future.

In conjunction with this project, Dr. Fajt was awarded one of the first two veterinary fellowships ever presented by the United State Pharmacopeia. The \$15,000 fellowship is divided between a stipend and support for research on the best format of the Decision System to facilitate use by practitioners.

Board of Directors

The board of directors for the VADS is charged with the following responsibilities:

1. serving to preserve continuity of the effort when/if the project director resigns or is unable to perform his/her duties
2. acting as liaisons for the board member's respective organizations
3. finalizing a mission statement for the database
4. guiding development of a publication process and determining the financial arrangements which will allow publication on a continuous basis
5. developing a plan for supporting continuous review and updating of the database followed by developing a budget and identifying the financial support for this effort.

The Board has been selected by the supporting veterinary organizations. They are Dr. Mark Kirkpatrick (AABP), Dr. Dan Upson (AVC), Dr. David Reeves (AASP), and Dr. Leonard Seda (AVMA). An initial teleconference is planned this fall for presentation of a progress report and initiation of the board's duties.

Review Panels

A review panel for bovine diseases will be formed this fall to work with the initial template on bovine neonatal diarrhea. Each review panel will consist of a clinical pharmacologist, a microbiologist, a regulatory official with pharmacokinetic or toxicology training, a Food Animal Residue Avoidance Databank representative, and 6 other veterinarians with clinical expertise. For the bovine panel, four clinical veterinarians will be nominated by the AABP, and two by the AVC. For the swine panel, 6 members will be nominated by the AASP. Length of term on the review panels will be determined by the nominating organizations, but should be a minimum of 3 years to assure consistency during the startup phase. Different panels may be selected for different diseases within a species if a significant focus of expertise is warranted.

System Goals

The Veterinary Antimicrobial Decision System will be a peer-reviewed system focused on therapeutic application rather than individual drugs that will allow practitioners to quickly reach a starting point for regimen design. It will be a compilation of available information along with a peer-reviewed interpretation of that information. The extent of data and the need for interactive links between these data are making it apparent that a web-based system is the most efficient way to

interact with practitioners. A CD-ROM is being considered as an ancillary form of publication, but has the drawbacks of not being constantly updated and providing for outdated copies being in use. It is important to recognize that the Decision System is only valuable as a "current state of the art" tool, requiring the practitioner to have the latest form in hand.

The goal is to bring to the local practitioner pharmacodynamic, pharmacokinetic, toxicological, and clinical efficacy data to support decisions for label and extralabel use of antimicrobials. Also included will be retrospective susceptibility profile information and interpretation of the National Committee on Clinical Laboratory Standards' breakpoints relating to label and extralabel use. Any available information on how antimicrobial selection and regimen design affects the development of resistance will be included in the database. We will also be coordinating withdrawal time information with the Food Animal Residue Avoidance Database (FARAD) as this is an important component of the human health impact of antimicrobial use in food animals. While the initial effort will focus on food animals, it is hoped that the template can be utilized for a similar effort for companion animals.

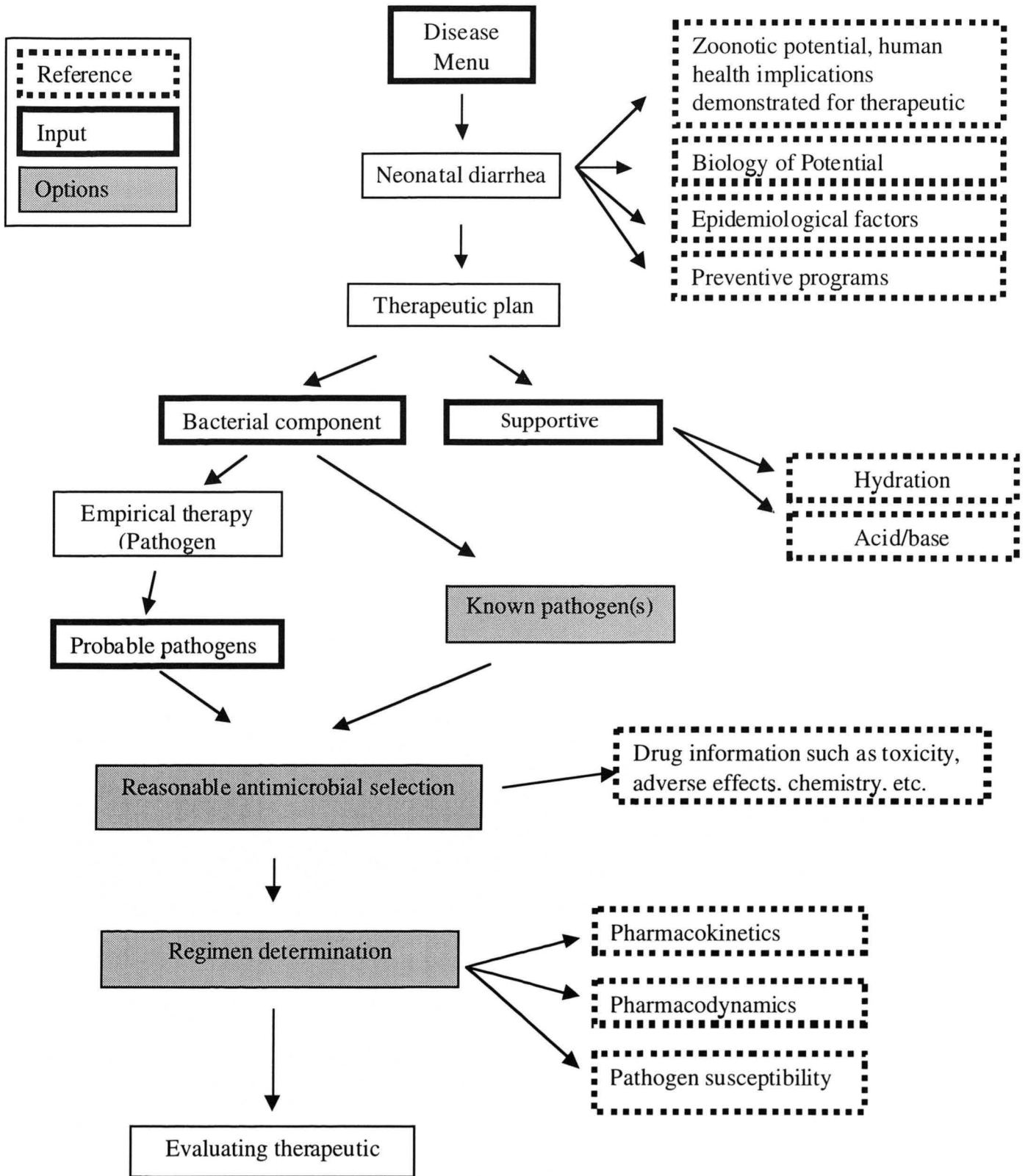
The system will include case-specific responses that will depend on the information available to the practitioner. Branching within the system, based on the practitioner's selection, will provide a moderate level of decision support. Pharmacokinetic data, graphs, mathematical calculations, and formulas will be available for viewing. Navigation through the system will be accomplished using standard HTML-based anchor tags. Every effort will be made to maintain a high degree of platform and browser version independence so that the system remains accessible to the widest possible audience. After accessing the information, the practitioner can use his or her judgment of the local conditions and pathogens to develop a starting point for the administration of an antimicrobial. A reasonable starting point for dose, route, frequency, and duration of therapy will be generated. The format will initially be developed for neonatal diarrhea in calves as outlined in the diagram.

The veterinary practitioner must play a role in the development of the system. During system development, the authors will seek assistance from practicing veterinarians concerning content and format. Once on-line, the system will include a mechanism to capture input from users, allowing for comments concerning content and usability. An on-line tutorial for use of therapeutic information and navigation through the website will be available.

Format of the System

The diagram/flow chart is an example of how the user will navigate through the system based on an indi-

System flowchart for neonatal diarrhea in calves



vidual therapeutic application. The presumption will be that the practitioner has reached the appropriate diagnosis; this system is not designed for assisting in diagnosis of disease, only in implementation of antimicrobial therapy when appropriate. The various portions of the system can be described as those which are decision-based, i.e., they allow for interaction and input, and those which provide support only.

Decision-Based Portions

Selection of therapeutic application from Disease Menu—This step requires a clinical diagnosis by the attending veterinarian.

“Empirical Therapy” or “Known Pathogen”—If empirical therapy is selected, there will be a list of reasonable choices for the presumed pathogen, based on the therapeutic application. In some cases with unpredictable pathogens or susceptibilities, the dangers of the empirical approach will be outlined. If culture and susceptibility data are available, therapeutic guidance will be based on these results.

“Reasonable antimicrobial selection”—The practitioner will select from a list of reasonable selections and will then be taken through regimen determination based on animal size, age, etc. The practitioner may examine the suggested regimens for several antimicrobial choices and then make his/her final decision based on practicality of administration and economics. Additional reference materials will also be available for the decision process.

Reference Materials

“Zoonotic potential”, “Biology of Potential pathogens”, “Epidemiological factors”, “Preventive programs”—These will be a set of linked monographs which detail “things to consider” before using antimicrobials as a management tool.

“Therapeutic plan”—This area will contain information on ancillary therapy. For example, in the case of *E. coli*, it will be emphasized that antimicrobial therapy without acid/base and fluid volume correction will be fruitless in many cases. The use of ancillary compounds such as antiinflammatories will also be discussed.

“Regimen Determination”—Published susceptibility summaries (or new ones created from diagnostic lab summaries) and the drug parameters will be used to

come up with a reasonable dose, or, if there is a labeled, effective compound, the labeled dose will be reported.

“Evaluation of therapy”—A critical point in the development of regimens is evaluating the response to therapy. Common pitfalls and general guidelines related to the specific application will be available to the practitioner. General advice as to when to reevaluate the antimicrobial selection will be given here.

Challenges

1. Develop a template from which to design all therapeutic applications. The template will include the best methods of initial development of content, review panel processing and organization, and website development. The first year of the project will be dedicated to developing this template.

2. Develop a system that is easy to use and that provides the information veterinarians want and need. The goal of this project is to create a system that veterinarians will use that will have the highest impact on their practice of medicine. Providing support to food animal veterinarians in the appropriate selection and regimen design will also help to protect public health. By creating this system, we will take a giant step toward prudent use by maximizing the efficacy of antimicrobials selected.

3. Maintain adequate support and funding to permit the efforts required to make this a truly useful system. Funding will be sought from other sources for partial salary replacement for the principal cooperators in the project to allow focusing on the project. Long-term funding for continued support of the project is the ultimate goal.

4. Computerize and automate as many processes as possible while recognizing the importance of the attending veterinarian in determining the final regimen. This system will not be a simple list of drugs and doses. Neither is the purpose of this system to tell practitioners which antimicrobials to use first, then next, and so on for a given application. The practitioner will remain the final decision-maker, and this system will support that decision with data and recommendations from clinical pharmacologists, other specialists, and practitioners selected for their expertise in clinical practice.