THE INTERIM REPORT OF THE WORKSHOP

ON

EQUINE PROTOZOAL MYELOENCEPHALITIS: TESTING & TREATMENT

EDITORS: T. Tobin, W. Saville, & W. Carter

WORKSHOP SUMMARIES: N. Cohen, T. Divers

ORGANIZING COMMITTEE

Dr. Thomas Tobin
Dr. Steve Reed
Ms. Wyndee Carter
Dr. William Saville
Dr. Bradford Bentz
Dr. Levent Dirikolu

AT
THE MAXWELL H. GLUCK EQUINE RESEARCH CENTER
UNIVERSITY OF KENTUCKY
1:00-5:30 P.M.
NOVEMBER 20TH, 1997

SPONSORS

The Maxwell H. Gluck Equine Research Center
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108 Gluck Equine Research Center
Lexington, KY 40546-0099

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Lexington, KY 40505

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9009 West 67th Street
Merriam, KS 66202

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University of Kentucky
A165 ASTeCC Building
Lexington, KY 40506-0286

RESEARCH SUPPORT

The research on new therapeutic approaches to EPM at the University of Kentucky was supported by the United States Trotting Association, Claiborne Farms, American Live Stock Insurance, Three Chimneys Farm Syndicates, Juddmonte Farms, the Kentucky Thoroughbred Farm Managers Club, Castleton Farm, the Deputy Minister Syndicate, the Forest Wildcat Syndicate, Rood & Riddle Equine Hospital, Hagyard-Davidson-McGee Veterinary Practice, Walnut Hall Limited, W. Bruce Lunsford, Mrs. Adele B. Dilschneider, Darley Stud Management Inc., Ogden Mills Phipps, Ogden Phipps, Edward A. Cox, and Cherry Valley Farm.

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CONTENTS

OVERVIEW OF THE WORKSHOP

PURPOSE:
This workshop was called to address two critical question in the area of diagnosis and treatment of Equine Protozoal Myeloencephalitis.

STRUCTURE:
About forty invited participants attended the workshop. From these participants a small number of discussion leaders were selected. Each leader made a ten minute presentation in his or her assigned area, after which the floor was opened for discussion. At the end of each session a draft summary statement was presented by the participant assigned to summarize each session.

SUMMARIES:
Following the workshop, these summaries were then worked over by the draftees and circulated to each workshop participant for review. The final draft summaries are attached, followed by a copy of the workshop agenda and a list of the workshop participants / attendees.

RECORDING PUBLICATION:
This workshop was taped, and a complete transcript of the proceedings is being generated. Each participant will be provided with the transcripts of their presentations and comments and will have ample opportunity to edit their presentation/comments as they see fit. Participants are encouraged to rework their presentations to make for a coherent final manuscript.

THANKS:
Many individuals contributed to the development and implementation of this workshop. Our thanks go to Dr. Peter Timoney for making the facilities at the Maxwell H. Gluck Equine Research Center available to us for this workshop and for his support throughout this entire project. Special thanks must go to Ms. Deborah Taylor for critical assistance with fund raising for this project and to our sponsors, namely Neogen Corp, Equine Biodiagnostics Inc. and Bayer Animal Health, without whom it would not have been possible to implement this workshop. Finally, as always, we must thank Ms. Wyndee Carter, Mr. Jeff Boyles, Dr. Dan Harkins, Dr. Fritz Lehner, Mr. Ed Woods, Ms. Leslie Ayers and the faculty and staff of the Maxwell H. Gluck Equine Research Center for their enthusiastic support of this endeavor.

WORKSHOP SUMMARIES:

1) Diagnostic Questions: Dr. Noah Cohen

The following questions were addressed by a panel of discussants in an effort to diminish confusion associated with immunoblot testing of equine CSF for antibodies to *S. neurona*, the causative agent of equine protozoal myeloencephalitis (EPM):

Question 1: Should clinically normal horses be CSF- tested for EPM by immunoblot?

Question 2: What is the diagnostic significance of a CSF- positive test result in a clinically normal horse?

Because the positive predictive value of a positive result (ie., probability that a positive result is from a horse with EPM) is very low in a clinically normal horse, testing clinically normal horses should be discouraged; a positive result in a clinically normal horse is much more likely to be a false positive than a true positive. In contrast, the negative predicative value of a negative test in a clinically normal horse is very high (very likely the horse does not have EPM).

Question 3: What is the diagnostic significance of a CSF-positive test result in a horse with neurological disease?

The predictive value of a positive test result will be higher (but still undefined) in a horse with neurological disease than in a horse without neurological disease. The diagnostic weight to be applied to the test depends to some extent on the neurological disease of the horse. A positive test result in a horse with neurological disease will more likely be a true positive in certain situations (e.g., a horse with classical clinical signs of EPM) than in others (e.g., a horse without classic EPM signs).

Question 4: What is the diagnostic significance of a CSF-positive test result in a horse that has been successfully treated for EPM?

The predictive value of a positive test result will be higher (test result is more likely to be a true positive in a horse that has been successfully treated for EPM than in horses less likely to have EPM. It should be considered that some horses that do not have EPM may appear to respond to treatment (placebo affect, or response to non-specific therapies) and that some horses with EPM will not respond to treatment.

We lack much more important information regarding the biology and natural history of infection with *Sarcocystis neurona* needed to more fully understand the meaning of detecting antibody to this organism in CSF collected from horses. As new information emerges, the preceding questions will need to be revisited to provide more accurate answers. Establishing a standardized case definition of EPM (a thorny proposition!) would facilitate diagnosis and interpretation of diagnostic tests. Because it is improbable that a test will be developed that will perfectly differentiate between horses with active infection of the CNS with *S. neurona* and those without such infection, some amount of uncertainty and inaccuracy will be inherent in the diagnostic process.

2) Treatment Questions: Dr. Tom Divers

A) Information provided at this workshop on EPM suggests that our ability to treat the disease may be more advanced than our ability to accurately diagnose EPM.

B) Currently the most commonly used treatment is a combination of pyrimethamine (1mg/kg PO of 21 hours) and a sulfonamide (20-30 mg/kg PO of 24 hours). The medications are preferably given as distant as possible from feedings.

C) The pyrimethamine with sulfonamide-trimethoprim product is still used by a substantial number of veterinarians: however, there is no work to establish which treatment protocol is more efficacious (pyrimethamine-sulfadiazine vs. pyrimethamine-trimethoprim/sulfa).

D) The general feeling seems to be that approximately 70% of EPM cases show improvement in their clinical signs with either treatment protocol. There is a justifiable concern of enhanced toxicity when both pyrimethamine and trimethoprim are used, but it appears that the incidence of severe toxicity is low.

E) The risk of toxicity with either protocol might be of more concern in pregnant mares and confidence in accuracy of the diagnosis and/or severity and/or progression of the disease should all be considered prior to treating pregnant mares. Historical experience suggests that treatment of pregnant mares can generally be accomplished without toxicity to the mare or the foal.

F) Folic acid supplementation cannot be recommended at this time because of recent reports in the horse and other species of enhanced toxicity from pyrimethamine when folic acid is given.

G) In some severe per-acute EPM cases pyrimethamine has been given at a "double" loading dose (2 mg/kg) for the initial 1-2 weeks of treatment. Enhanced efficacy has not been proven with the increased dose although it would be reasonable to expect as much...

H) Conversely, the incidence of toxicity might be increased by this approach, although this has not been reported.

I) The proper duration of treatment with pyrimethamine-sulfonamides is unknown and would likely vary between affected horses. Most horses believed to have EPM are treated for a minimum of 3 months. If the CSF becomes negative for *S. neurona* antibody, treatment can be safely discontinued. It would be ideal if all horses had a "negative" CSF prior to discontinuation of treatment; this is difficult to recommend for all horses because of the suspicion that some of the antibody in CSF samples submitted to laboratories may be serum derived. There is a substantial number of observations that the great majority of treated cases are still positive in CSF after 90 days of treatment.

J) A potentially exciting new development has been the experimental use of Diclazuril in horses with EPM. The clinical response is reported to be at least equal to the current pyrimethamine / sulfonamide treatment. There are no reports of serious side effects and the duration of treatment (21-28 days) and cost have been much less than the pyrimethamine / sulfonamide treatment. More long term studies on diclazuril are necessary in order to gain confidence in its efficacy and safety.

November 20th, 1997

1:00PM – 5:30 PM

Welcome to Kentucky: .....Dr. Thomas Tobin **1:00 p.m.**
Opening Remarks:.....Dr. Steve Conboy **1:05 p.m.**

A) PERSPECTIVES OF OWNERS/VETERINARIANS: 1:10 p.m.

Moderator: Dr. Bill Saville

Dr. Bill Saville.....10 minute overview
Dr. Steve Reed.....10 minute overview

Discussion from the floor.....20 minutes

B) TESTING THEN & NOW : AN EPIDEMIOLOGICAL ANALYSIS 1:40 p.m.

Dr. David Granstrom.....10 minute overview
Dr. Frank Andrews; CSF indices & test.....10 minute overview
Dr. Clara Fenger.....10 minute overview
Dr. Paul Morley .....10 minute overview
Dr. Linda Mansfield.....10 minute overview
Discussion from the floor.....20 minutes

REVIEW OF DIAGNOSTIC QUESTIONS: 2:50 p.m.

Based on our current knowledge, what are the appropriate uses and interpretations of the EPM test?

1.1/ Should clinically normal horses be CSF tested?

1.2/ What is the diagnostic significance of a CSF positive in a clinically normal horse?

1.3/ What is the diagnostic significance of a CSF positive in a neurological horse?

1.4/ What is the clinical significance of a CSF positive in a horse that has been successfully treated?

Dr. Noah Cohen.....Drafting Summary Statement.

BREAK
3:10-3:30 p.m.

C) CURRENT TREATMENT; ADVANTAGES & DISADVANTAGES: **3:30 p.m.**

Moderator: Dr. Tom Divers

Dr. Rob MacKay.....10 minute overview
Discussion.....10 minutes

EXPERIMENTAL TREATMENTS : POTENTIAL ADVANTAGES & DISADVANTAGES: **3:50 p.m.**

Dr. Levent Dirikolu/ Tobin .....10 minute overview
Dr. Bradford Bentz/ Tobin .....10 minute overview
Dr. Philip Johnson.....10 minute overview
Dr. Martin Furr.....10 minute overview

Discussion from the floor.....20 minutes

2/ TREATMENT QUESTIONS: **4:50 p.m.**

2.1/ Based on what we know today, what is the relative efficacy / toxicity of pyrimethamine / sulfonamide combinations?

2.2/ Based on what we know today, what is the relative efficacy / toxicity of pyrimethamine / sulfonamide trimethoprim combinations?

2.3/ Based on what we know today, what is the relative efficacy / toxicity of experimental therapies

Dr. Tom Divers .....Round Table Discussion & Summary **5:30 p.m.**

PARTICIPANTS

Dr. Frank Andrews University of Tennessee	Ms. Jan McKinney University of Kentucky
Dr. Fairfield Bain Hagyard-Davidson-McGee	Dr. David Miller Lake Equine Associates, Inc.
Dr. Bradford Bentz University of Kentucky	Dr. Meg Miller University of Pennsylvania
Dr. Bill Bernard Rood & Riddle Equine Hospital	Dr. Paul Morley Ohio State University
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Dr. Doug Byers Hagyard-Davidson-McGee	Dr. Steve Reed Ohio State University
Mr. Ed Carter Equine Biodiagnostics, Inc.	Dr. Bill Saville Ohio State University
Ms. Wyndee Carter University of Kentucky	Dr. Hal Schott Michigan State University
Dr. Noah Cohen Texas A & M University	Mr. Steve Schneider University of Kentucky
Dr. Steve Conboy Private Practitioner	Mr. Dwight Schroedter Neogen Corporation
Dr. Levent Dirikolu University of Kentucky	Dr. Michael Sheets Equine Biodiagnostics, Inc.
Dr. Clara Fenger University of Kentucky	Ms. Mary Smith Neogen Corporation
Dr. Martin Furr Marion du Pont Scott Equine Med. Center	Mr. Shelby Stamper University of Kentucky
Dr. David Granstrom AVMA	Dr. Corrinne Sweeney University of Pennsylvania
Dr. Dan Harkins University of Kentucky	Dr. John Timoney University of Kentucky
Mr. Broussard Hundley Saxony Farm	Dr. Peter Timoney University of Kentucky
Dr. Louis Johnson Saxony Farm	Dr. Thomas Tobin University of Kentucky
Dr. Philip Johnson University of Missouri-Columbia	Dr. Wendy Vaala Mid-Atlantic Equine medical Center
Ms. Terri Juricic Vice President	Dr. Neil Williams University of Kentucky
Dr. Tom Kennedy Bayer Animal Health	Mr. Mark Wold Neogen Corporation
Dr. Linda Mansfield Michigan State University	