

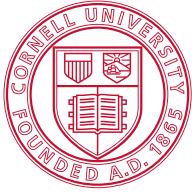


**Clinical Investigators'
Day**

October 5, 2018

Lecture Hall III





Cornell University College of Veterinary Medicine

Welcome to the 2018 Clinical Investigators' Day, sponsored by the Cornell University College of Veterinary Medicine. The primary goal of this forum is to provide an opportunity for residents and interns to showcase ongoing investigations carried out at Cornell University College of Veterinary Medicine. It is our hope that greater insights will be gained in the breadth and depth of clinical investigations conducted at the College and will serve as a catalyst to promote greater interactions among colleagues with clinical and basic science research interests.

Organizing Committee

Ms. Gail Babcock
Dr. Elizabeth Buckles, Co-Chair
Dr. Jonathan Cheetham
Dr. Erin Daugherty, Co-Chair
Mr. Kim Eaton
Mr. Doug Fink
Ms. Beline Falzon
Mr. Justin Limper
Dr. Mary Martin, Co-Chair
Ms. Suzette Moschetti
Dr. Santiago Peralta
Dr. Tracy Stokol, Co-Chair

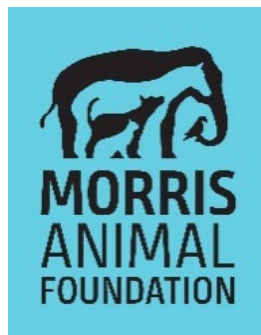
The organizing committee thanks the following individuals who contributed to the success of the Day:

Mr. Dave Frank
Mr. Drew Kirby
Mr. Chad Westmiller

Sponsors

We thank the following sponsors for their generous support and commitment to Clinical Investigators' Day:

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Feline Health Center

Office of the Dean

Office of Research and Graduate Education

University Programs

Center for Animal Resources and Education (CARE) at Cornell University



Current CVM Clinical Trials

Dogs

- Lymphoma tissue banking
- Metabolomics investigation of Canine GI disease
- Improving the diagnosis of degenerative myelopathy with imaging
- Biomarker guided antimicrobial therapy for septic peritonitis
- Flow cytometric analysis of platelets from thrombocytopenic dogs
- Evaluation of StablePlate Rx™ in Thrombocytopenic Patients
- Effects of spironolactone on arrhythmia burden and heart rate variability parameters in dogs with clinical dilated cardiomyopathy
- Targeted therapies for treating Canine Lymphoma
- Determine the transcriptome of canine soft tissue sarcoma
- Indirect computed tomographic lymphography for sentinel lymph node mapping
- Drug repurposing to aid tx of canine lymphoma
- Uncovering mechanisms of post-procedural hypocalcemia in dogs with hyperthyroidism
- Assessment of dietary intervention in Canine Inflammatory Bowel Disease and Canine Kidney Disease
- Evaluation of the effect of antibiotic use on the fecal flora: Dynamics of antibiotic resistance over time
- Evaluation of recombinant, attenuated *Listeria monocytogenes* expressing a chimeric human HER2/neu protein in dogs with osteosarcoma – COTC026
- Radiofrequency therapy for dogs with chronic osteoarthritis hind limb pain

More trials coming!

Cats

- Carboplatin in injection site sarcomas
- Characterization of subgingival micro-environment
- Senior feline common disorders
- Feline sepsis response
- Effect of phenobarbital on thyroid tests

Rabbits

- Diagnosing gastric outflow obstruction
- Characterization of normal ear canal cytology and microbiology (in ferrets too!)

Horses

- Relationships between body mass index (BMI) and surgical site infection (SSI) in horses
- Improving recovery from anesthesia for horses: Draining the bladder

Sloths

- Assessment of vitamin D metabolism and calcium homeostasis in indoor-housed Hoffmann's two-toed sloths

For more information or to participate contact:

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or call

607.253.3279

Program Schedule

Friday, October 5, 2018
Lecture Hall 3, Veterinary Research Tower

- 8:25 am – 8:30 am** Welcome & Introductions – **Robert Weiss, PhD**; Associate Dean for Research and Graduate Education. The Clinical Investigator’s Day Organizing Committee
- 8:30 am – 9:00 am** **Guest Presentation**
- Being a Mom Is Hard: Calcium Demands of Early Lactation Dairy Cows*
- Jessica McArt, DVM, PhD**; Assistant Professor. Cornell University, Department of Population Medicine and Diagnostic Sciences
- 9:00 am – 10:30 am** **Resident Presentations** – Moderated by **Sabine Mann, VMD, PhD**
- *Use of Novel DNA Damage Response Inhibitors to Overcome Chemoresistance in Feline Solid Tumors*
Yike Bing, DVM – Medical Oncology Resident **Pg. 1**
 - *The Role of High-Density Lipoproteins (HDL) in Modulating Neutrophil Activation During the Transition Period in Cows*
José Daniel Cruz Otero, DVM – Clinical Pathology Resident **Pg. 2**
 - *Anticancer Effects of Cannabidiol (CBD) – in Vitro Results of CBD on Proliferation and Death of Canine Neoplastic Cell Lines*
Joshua Henry, DVM – Medical Oncology Resident **Pg. 3**
 - *Assessment of Vitamin D Metabolites and Serum Cytokines in Dogs with Immune Mediated Disease*
Philippe Mick, DVM – Small Animal Internal Medicine Resident **Pg. 4**
 - *Evaluation of Arsenic, Cadmium, Lead and Mercury Contamination in Over-The-Counter Available Dry Dog Foods with Different Ingredients (Red Meat, Poultry and Fish)*
Hunter Kim, DVM, MS – Clinical Nutrition Resident **Pg. 5**
 - *Biological Variation of Symmetric Dimethylarginine and Other Biochemical Analytes in Clinically Healthy Cats*
Jennifer Prieto, DVM, MS – Small Animal Internal Medicine Resident **Pg. 6**
- 10:30 am – 10:45 am** **Break**

Schedule (cont.)

10:45 am – 12:00 pm

Resident Presentations – Moderated by Elizabeth Moore, DVM

- *Diagnosis of Septic Peritonitis Using Effusion-Blood Gradients of Novel Biomarkers in Dogs*
Pia Martiny, DVM – Emergency and Critical Care Resident **Pg. 7**
- *Clinical, Clinicopathologic, and Hepatic Histologic Features Associated with Suspected Ketoconazole Hepatotoxicity in 9 Dogs*
Luis Macho, DVM – Small Animal Medicine Resident **Pg. 8**
- *Validating the Use of a Smartphone-Based Noninvasive Electrocardiogram in Mice*
Rachael N. Labitt, DVM – Laboratory Animal Medicine Resident **Pg. 9**
- *Agreement of Equine Stall-Side and Laboratory Major Cross Match Test in Healthy Horses*
Melissa Fenn, DVM – Large Animal Internal Medicine Resident **Pg. 10**
- *Bile Acids as Prognostic Indicator for Horses with Liver Disease: A Retrospective Study*
Barbara Delvescovo, DVM, MRCVS – Large Animal Medicine Resident **Pg. 11**

12:00 pm – 12:45 pm

Lunch

12:45 pm – 3:00 pm

Resident Presentations – Moderated by April Choi, DVM, PhD, DAVCP

- *Ethanol Injected Intracoelomically as a Novel Method of Euthanasia in Zebra Finches (*Taeniopygia Guttata*) and Chickens (*Gallus Gallus Domesticus*)*
Nathaniel S. Kollias, DVM, MPH – Lab. Animal Medicine Resident **Pg. 12**
- *Dens Invaginatus in Dogs - a Case of Mistaken Identity?*
Kevin Ng, BSc, BVMS (Hons) – Dentistry and Oral Surgery Resident **Pg. 13**
- *Evaluation of On-Farm Microbiology Techniques for Detection of Pathogens in Milk*
Renato Rossi, BVSc – Ambulatory and Production Medicine Resident **Pg. 14**
- *Evaluation of Antimicrobial Administration in Critically Ill Dogs on the Fecal Flora: Dynamics of Antimicrobial Resistance over Time*
Sarah Robbins, MS, DVM – Emergency and Critical Care Resident **Pg. 15**
- *Epidemiological Investigation of Orofacial Clefts in Purebred Dogs*
Nicholas Roman – Dual DVM / MPH Student **Pg. 16**

- *An Analysis of Medical Error Type and Severity in Veterinary Hospitals Through the Use of an Incident Reporting System*

Jessica Wallis, BVSc (Hons) – Emergency and Critical Care Resident **Pg. 17**

2:30 pm – 2:45 pm

Break

2:45 pm – 4:00 pm

Resident Presentations – Moderated by **Bryant Blank, DVM, MS, DACLAM**

- *QT Restitution in Boxers with ARVC: Relationship to Arrhythmia Vulnerability and Treatment Response*

Christophe Bourguignon, DVM – Cardiology Resident **Pg. 18**

- *Assessing the Effects of Cisapride and Buprenorphine on Gastrointestinal Transit Time in Rabbits*

Erica Feldman, DVM – Laboratory Animal Medicine Resident **Pg. 19**

- *Proximal Sesamoid Bone Microdamage and Fracture Toughness in Thoroughbred Racehorses*

Lauren Luedke, DVM – Large Animal Surgery Resident **Pg. 20**

- *Indirect Computed Tomographic Lymphography (IctL) for Sentinel Lymph Node Mapping in a Cohort of Dogs with Cutaneous Mast Cell Tumor – Technique Development and Effect on Peri-Operative Decision Making and Post-Operative Treatment / Monitoring Recommendations*

Janis Lapsley, DVM – Small Animal Surgery Resident **Pg. 21**

- *SOX2 Expression in Canine Malignancies*

Ileana Miranda, DVM, MS – Anatomic Pathology Resident **Pg. 22**

4:05 pm – 4:45 pm

Keynote Address

Equine Mesenchymal Stem Cells in Veterinary Medicine: Prospects and Challenges

Gerlinde Van de Walle, DVCM, PhD; Professor in Equine Health, Department of Microbiology and Immunology

5:00 pm

Award Presentations

Lorin Warnick, DVM, PhD; Dean, College of Veterinary Medicine

Following Awards

Reception (All Welcome!)

Keynote Speaker



Gerlinde Van DeWalle, DVM, PhD; Harry M. Zweig Assistant Professor in Equine Health, Cornell University

Dr. Gerlinde Van de Walle earned her DVM and PhD from Ghent University in Belgium, where she stayed on as a Postdoctoral Research Fellow and then as an Assistant Professor in the Department of Comparative Physiology and Biometrics. She is currently Assistant Professor at the Baker Institute for Animal Health at Cornell University where her research focuses on new avenues of therapeutic intervention by better understanding the pathogenesis of diseases important to veterinary and human medicine.

Guest Speaker



Dr. Jessica McArt, DVM, PhD; Section Chief, Ambulatory and Production Medicine Clinic, Cornell University Hospital for Animals

Dr. Jessica McArt is an Assistant Professor in the Department of Population Medicine and Diagnostic Sciences at Cornell University. She is Section Chief for the Ambulatory and Production Medicine Clinic, teaches veterinary students both in the classroom and on farms, and conducts applied research on periparturient diseases in dairy cattle.

Moderators



Bryant Blank, DVM, MS, DACLAM; Assistant Director, Agriculture Animals, Center for Animal Resources and Education (CARE) at Cornell University

Dr. Blank is a clinical veterinarian at the Center for Animal Resources and Education (CARE). He received his DVM from Kansas State University in 2009. He then completed a three-year veterinary residency in laboratory animal medicine at Cornell University. During this period he received his MS in Comparative Biomedical Sciences working on the pathogenesis of *Listeria monocytogenes*. Bryant is a Diplomate of the American College of Laboratory Animal Medicine.

He currently provides clinical care for a variety of species, oversees multiple rodent vivaria, maintains regulatory oversight of large agricultural facilities, and assists in CARE's residency training program and veterinary student rotations. He is involved in multiple research collaborations involving a diversity of species and fields, including reproductive physiology of the Giant Pouched Rat, safety assessment of a synthetic joint lubricant, patient derived tumor xenotransplantation novel treatment studies and welfare parameters associated with trio-breeding of mice.

Moderators (cont.)



April Choi, DVM, PhD, DAVCP; Clinical Instructor, Cornell University Department of Biomedical Sciences

Dr. April Choi is a clinical instructor in the Department of Biomedical Sciences, Section of Anatomic Pathology at Cornell University College of Veterinary Medicine. She earned her DVM degree from South Korea and her PhD from the University of Queensland, Brisbane, Australia where she worked on diagnostic glycoprotein biomarkers for canine hemangiosarcoma.

Prior to her current position, she completed her residency training at Cornell University and she is board certified by the American College of Veterinary Pathologists (ACVP). Dr. Choi's research interests focus on diagnostic pathology with special emphasis on tumor immunodiagnosics and small animal hepatobiliary disease.



Sabine Mann, VMD, PhD, Assistant Professor of Ambulatory and Production Medicine Clinic, Cornell University Department of Population Medicine and Diagnostic Sciences

Dr. Sabine Mann is an Assistant Professor in the Ambulatory and Production Medicine Clinic, Department of Population Medicine and Diagnostic Sciences. She graduated with her veterinary degree from Hannover University of Veterinary Medicine in 2007 and is board certified in the European College of Bovine Health Management, the American College of Veterinary Preventive Medicine, and is member of the Epidemiology Specialty. She received her German doctoral degree from the Ludwig-Maximilian-University in Munich in 2011. From

2007-2012 Dr. Mann completed an internship and residency both in Ambulatory and in a referral clinic, and worked as a lecturer.

She received her PhD through the BBS Comparative Biomedical Sciences program here at Cornell in 2016. Dr. Mann has a clinical appointment in the Ambulatory Clinic where she performs large animal farm visits with students. In addition, Dr. Mann's research interests in large animals focus on the interplay of metabolism, nutrition, and the immune system in times of stress.



Elizabeth Moore, DVM; Assistant Professor and the Anne Groot Sesquicentennial Fellow, Department of Biomedical Sciences, Section of Anatomic Pathology, Cornell University College of Veterinary Medicine

Dr. Moore graduated with her DVM from Cornell in 2012, and completed the laboratory animal medicine residency with the Center for Animal Resources and Education (CARE) in 2015. She began her PhD training in the field of Comparative Biomedical Sciences in the laboratory of Dr. Robert Weiss during her residency, and will be completing her graduate degree at the end of this year.

Her Ph.D. work focuses on understanding the mechanisms that maintain genomic integrity. Her projects investigate the role of the Rad9-Hus1-Rad1 DNA repair clamp in double stranded DNA break repair, probe the mechanisms behind the unique chemosensitivity of testicular germ cell tumors, and explore the role of the Fanconi Anemia DNA repair pathway in cellular and hepatic metabolism.

Judges



Dorothy P. Debbie, PhD; Senior Lecturer, Cornell University Department of Microbiology and Immunology

Dr. Debbie is a senior lecturer in the Department of Microbiology and Immunology at the Cornell University College of Veterinary Medicine where she teaches bacterial pathogenesis to undergraduate, graduate, and veterinary students.

She received her PhD at Stanford University studying bacterial genetics, then trained in bacterial pathogenesis with Stanley Falkow at the Stanford University School of Medicine. Prior to coming to Cornell, she was an Assistant Professor at the University of Colorado

Health Sciences Center studying pathogenic mechanisms of *Yersinia enterocolitica*.



Laura Goodman, PhD; Assistant Research Professor, Cornell University Department of Population Medicine and Diagnostic Sciences

Dr. Goodman is an emerging infectious disease researcher at the Cornell College of Veterinary Medicine who trained at the University of Michigan, Cornell, and Harvard. Her laboratory works on pathogen discovery, surveillance, and bridging the gap between research and diagnostics.

Her work has investigated mechanisms of pathogen emergence and development of novel high-throughput testing methods. She leads the development efforts in the Molecular Diagnostics section of the Cornell Animal Health Diagnostic Center /NY State Veterinary Diagnostic Lab and currently serves on the New York State task forces for tick-borne diseases and antimicrobial resistance, which are focus areas in her laboratory.



Scott Palmer, DVM; Adjunct Professor, Cornell University Department of Population Medicine and Diagnostic Sciences

Dr. Palmer received his veterinary degree from the University of Pennsylvania School of Veterinary Medicine in 1976 and is certified in equine practice by the American Board of Veterinary Practitioners. He worked in clinical practice as a staff surgeon and hospital director of the New Jersey Equine Clinic for 38 years prior to chairing the New York Task Force on Racehorse Health and Safety to investigate equine fatalities that occurred during Aqueduct's 2011-12 Winter Meet.

Dr. Palmer currently serves as the Equine Medical Director for the New York State Gaming Commission and is an adjunct professor in the department of Population Medicine and Diagnostic Sciences at Cornell University College of Veterinary Medicine. His research focus is the identification of horses at increased risk for fatal musculoskeletal injury and development of intervention strategies to prevent fatal musculoskeletal injuries.

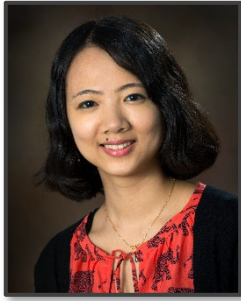
Judges (cont.)



Heidi Reesink, VMD, PhD, DACVS-LA; Assistant Professor, Cornell University Large Animal Surgery

Dr. Heidi Reesink is a board-certified large animal surgeon with clinical interests in orthopedic surgery and sports medicine. She received her veterinary degree from the University of Pennsylvania, followed by residency and PhD training at Cornell University.

Dr. Reesink's laboratory aims to unravel basic mechanisms underlying the development of orthopedic disease and to pioneer innovative therapies for the treatment of arthritis in equine, canine and human athletes. A major focus of the laboratory is understanding how glycans and glycoproteins, such as lubricin and hyaluronic acid, enable effective joint lubrication, mitigate inflammation and maintain cartilage homeostasis. The lab employs molecular biology, biochemistry, glycobiology and engineering techniques to investigate the role of glycans in osteoarthritis. A second major focus is deciphering how bone morphology and bone quality relate to catastrophic fracture in racehorses. Ongoing efforts include identifying quantitative CT parameters that can be used to estimate fracture risk. The lab uses epidemiology, advanced imaging, and fracture testing techniques to investigate these questions about racehorse fractures.



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Institution and Location

Cornell University, Ithaca, New York
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Cornell University, Ithaca, New York

Degree

DVM
Internship
Residency

Year

2016
2017
2017-Present

Current Position

Resident, Medical Oncology, 2nd Year

Abstract Title:

Use of Novel DNA Damage Response Inhibitors to Overcome Chemoresistance in Feline Solid Tumors

Authors Names:

Yike Bing, Abdo Dergham, Kelly R. Hume; Departments of Clinical Sciences, Cornell University, NY, 14853.

Project Mentor:

Kelly R. Hume, DVM, DACVIM, DVM; Department of Clinical Sciences

Abstract:

Introduction

Chemoresistance is an obstacle in the treatment of feline solid tumors. We have previously found that DNA damage exists in varying degrees in untreated feline injection site sarcomas (FISS), and high levels of DNA damage reflected by high baseline expression of γ H2AX was associated with resistance to carboplatin *in vitro*. Inhibiting cellular DNA repair mechanisms may help overcome chemoresistance.

Objective

To evaluate whether DNA damage response (DDR) inhibitors can enhance cytotoxicity of chemotherapeutics in feline solid tumor cells *in vitro*.

Methods

Using MTT (3-(4,5 dimethylthiazol-2-yl)-2,5-diphenyltetrazoliumbromide) cell viability assay, 2 FISS cell lines and 1 feline oral squamous cell carcinoma (SCC) cell line were treated with serial dilutions of the following drugs: doxorubicin, carboplatin, NU7026 (DNA-PKcs inhibitor) and MK1775 (WEE1 inhibitor). These results were used to determine the drug concentration needed to decrease cell viability by 50% (IC50). These same cells were then treated with a combination of chemotherapeutic and low dose DDR inhibitor (NU7026, 2 and 5 μ M; MK1775, 0.5 and 0.75 μ M) to determine their chemosensitizing effect. Significance was analyzed using Student's *t*-test to compare individual treatment to combination therapy. Degree of synergy was determined by calculating a combination index (CI) from IC50 values.

Results/Discussion

A synergistic effect was observed when SCC cells were treated with combination therapy with MK1775 (CI=0.47 for carboplatin, CI=0.79 for doxorubicin). This effect was not observed in combination therapy with NU7026, nor in FISS cells. MK1775 as a potential therapeutic agent for feline squamous cell carcinoma may be explored in future *in vivo* studies.



José Daniel Cruz Otero, DVM

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Institution and Location

Tuskegee University, Tuskegee, Alabama
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Degree

DVM
Residency

Year

2014
2016-Present

Current Position

Resident, Clinical Pathology, 3rd Year

Abstract Title:

The Role of High-Density Lipoproteins (HDL) in Modulating Neutrophil Activation During the Transition Period in Cows

Authors Names:

José Daniel Cruz Otero, Cheryl Wong, Erica Behling-Kelly; Department of Population Medicine and Diagnostic Sciences, Cornell University, Ithaca, New York

Project Mentor(s):

Erica Behling-Kelly, DVM, PhD, Dipl. ACVP; Department of Population Medicine and Diagnostic Sciences

Abstract:

Background

The 3 weeks before and after calving, the transition period (TrPe), is a high-risk period for the development of costly production-related diseases in dairy cows. During the TrPe, changes in lipid metabolism are thought to contribute to disease risk. High-density lipoprotein (HDL) has anti-inflammatory activity in a number of species. We hypothesized that bovine HDL has immunomodulatory activity that is negatively impacted by the metabolic demands of the TrPe.

Objective

Test the biological impact of bovine HDL isolated throughout TrPe on neutrophil activation.

Methods

HDL was isolated from EDTA-anticoagulated blood collected weekly throughout the TrPe from 12 adult multiparous Holsteins using density gradient ultracentrifugation. Heparinized blood from mid-lactation cows was treated for 4 hours with 50ng/ml LPS alone and in combination with 300mg/ml of isolated HDL. Dialysis buffer was the vehicle control. Neutrophil activation was determined by measuring changes in CD11b expression using flow cytometry.

Results

HDL decreased LPS-induced CD11b expression by 23% (SD \pm 14.6) before calving. HDL from near-calving was less efficacious against neutrophil activation allowing over activation of neutrophils by 45% (SD \pm 233.9). HDL did not regain immunomodulatory activity post-calving in 6/12 cows.

Conclusion

Bovine HDL decreases LPS-induced neutrophil activation in a manner that is dependent on the time relative to calving. The loss of HDL function near calving may contribute to the dysregulated inflammation that occurs during the TrPe *in-vivo*. Future studies are required to determine the HDL motif(s) involved in blunting LPS activity and identify interventions to help retain HDL's effective immunomodulatory activity through the TrPe.



Joshua G. Henry, DVM

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Institution and Location

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Cornell University, Ithaca, New York

Degree

DVM
Internship
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2013-2014
2016-Present

Current Position

Resident, Medical Oncology, 3rd Year

Abstract Title:

Anticancer Effects of Cannabidiol (CBD) – *in vitro* Results of CBD on Proliferation and Death of Canine Neoplastic Cell Lines

Authors Names:

Joshua G. Henry, Joseph J. Wakshlag, Cheryl E. Balkman
Department of Clinical Sciences, Cornell University, Ithaca, New York

Project Mentor(s):

Joseph J. Wakshlag DVM, PhD, DACVN, DACVSMR, Department of Clinical Sciences (Co-mentor)
Cheryl E. Balkman, DVM, DACVIM (SAIM /Oncology), Department of Clinical Sciences (Co-mentor)

Abstract:

Introduction

Cannabidiol (CBD) has gained popularity both in the medical and mainstream communities for its medicinal properties while lacking the psychotropic aspect of other phytocannabinoids. Nutraceutical use by clients for their companion animals is common. However, evidence-based resources for informed client education are lacking. Phytocannabinoid studies in companion animal species are limited and no studies to date have evaluated the effects of CBD on canine neoplastic cell lines.

Objective

The objective of this study was to investigate the impact of CBD on the viability of 5 canine neoplastic cell lines (HMPOS, D17, Abrams, CMT-12, 17-71) treated with CBD alone and in combination with doxorubicin at various concentrations.

Methods

Cells were plated in 96-well tissue culture plates and incubated for 48 hours with vehicle control (ethanol), CBD, doxorubicin, or CBD and doxorubicin at varying concentrations. 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assays were performed and optical density was analyzed by a spectrophotometric plate reader. Results between the different groups were compared to determine the anti-proliferative effect of CBD alone and in combination with doxorubicin.

Results

All cell lines exhibited anti-proliferative sensitivity to CBD at physiologically attainable concentrations. The combination of CBD and doxorubicin had variable combinatorial effects on cell viability and appears concentration dependent.

Conclusion

Further research of cannabidiol as an adjuvant therapy for canine neoplasms is warranted in the pre-clinical and clinical setting. Additional research is necessary to elucidate its combinatorial effects with standard chemotherapies and to understand its mechanism of action.



Phillip J. Mick, DVM

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Institution and Location

Washing State University, Pullman, Washington
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Cornell University, Ithaca, New York

Degree

DVM
Internship
Residency

Year

2017
2018
2018-Present

Current Position

Resident, Small Animal Internal Medicine, 1st Year

Abstract Title:

Assessment of Vitamin D Metabolites and Serum Cytokines in Dogs with Immune Mediated Disease

Authors Names:

Phillip J. Mick, John P. Loftus, Joseph J. Wakshlag; Cornell University, College of Veterinary Medicine, Ithaca, New York

Project Mentor(s):

John P. Loftus, DVM, PhD, DACVIM; Department of Clinical Sciences

Abstract:

Introduction

Reduced vitamin D levels may be associated with immune mediated disease (IMD) and a poorer prognosis. Vitamin D isoforms, particularly calcitriol, have immune modulatory effects and may alter immune pathways associated with autoimmunity.

Methods

Serum was collected from canine patients diagnosed with immune mediated disease (immune mediated hemolytic anemia, thrombocytopenia, polyarthritis, steroid responsive meningitis arteritis). Vitamin D metabolites were measured by LC-MS/MS at an accredited lab. IL-17 and IL-10 were measured with commercially available canine-specific enzyme-linked immunosorbent assay (ELISA) kits.

Results

Serum 25(OH)D3 and 1,25(OH)2D3 were significantly reduced in dogs with IMD compared to healthy controls. Serum IL-10 levels were not significant between controls and dogs IMD. All dogs had IL-17 levels below the standard curve. However, estimated IL-17 levels were significantly increased in dogs with IMD (P = 0.02), though all were below the standard curve. The median survival time (MST) for dogs with 25(OH)D3 concentrations \leq the median was 106 days, while dogs with concentrations of 25(OH)D3 $>$ the median did not achieve a MST at the conclusion of the study (77.14% survival at 871 days).

Conclusion

Decreased serum 25(OH)D3 and 1,25(OH)D3, but not 24,25(OH)D3 are associated with canine IMD. IL-17 levels appear to be higher in dogs with IMD, but more sensitive reagents for detection of canine serum IL-17 are needed. Vitamin D metabolites represent a prognostic marker as well as a future area for targeted therapy in canine IMD. Additional research is needed before vitamin D analogs or metabolites should be considered for therapeutic use.



Hunter (Hyun-tae) Kim, DVM, MS

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Institution and Location

Kangwon National University, ChunCheon, S. Korea
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Cornell University, Ithaca, New York

Degree

DVM
MS
Residency

Year

2011
2015
2016-Present

Current Position

Resident, Clinical Nutrition, 3rd Year

Abstract Title:

Evaluation of Arsenic, Cadmium, Lead and Mercury Contamination in Over-The-Counter Available Dry Dog Foods with Different Ingredients (Red Meat, Poultry and Fish)

Authors Names:

Hyun-tae Kim, John P Loftus, Sabine Mann, Joseph J. Wakshlag; Cornell University, College of Veterinary Medicine, Ithaca, New York

Project Mentor(s):

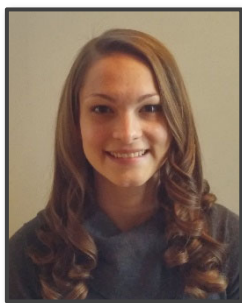
Joseph J. Wakshlag, DVM, PhD, ACVN, ACVSMR; Department of Clinical Sciences

Abstract:

There are few reports of heavy metal contamination of commercial dog foods and an increasing awareness of this issue by consumers. In an effort to understand toxic heavy metal content in commercial dog foods, arsenic, cadmium, lead and mercury of 51 over-the-counter maintenance or all-life-stage dry dog foods were examined by inductively coupled plasma mass spectrometry, that were classified as poultry-, red meat- or fish-based. Variables examined in this dataset were differences based on major protein source in the diet (poultry vs. red meat vs. fish). A non-Gaussian data distribution led to non-parametric statistical testing (Wilcoxon rank sum/Kruskal Wallis tests) and median (range) descriptive statistics. Comparison to average human consumption based on mg/Mcal was also examined. On average, total heavy metal consumption is higher in dogs than in humans. However, chronic toxic exposure levels are highly unlikely based on canine toxicity studies. Fish-based diets had significantly higher arsenic, cadmium and mercury content than the other poultry or red meat-based diets ($p < 0.004$). Red meat-based diets (beef, venison and bison) had higher lead concentration than poultry and fish-based diets ($p < 0.03$). Based on these findings, commercial dog foods appear to be safe for chronic consumption and concentrations of the heavy metals were dependent on primary protein sources. Overall, poultry-based diets had relatively lower heavy metal content than red meat and fish-based diets. These findings may be useful for establishing safe upper limits of heavy metals in pet foods although it is necessary to further investigate the bioavailability of these elements in dogs.

Learning Objective

Measure and understand heavy metal concentrations in commercial dog foods



Jennifer Prieto, DVM, MS

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Institution and Location

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Veterinary Medical Center of CNY, Syracuse, New York
Cornell University, Ithaca, New York

Degree

DVM
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Internship
Residency

Year

2013
2015
2016
2016-Present

Current Position

Resident, Small Animal Internal Medicine, 3rd Year

Abstract Title:

Biological Variation of Symmetric Dimethylarginine and Other Biochemical Analytes in Clinically Healthy Cats

Authors Names:

J.M. Prieto¹, P.C. Carney¹, M.L. Miller¹, M. Rishniw¹, J.F. Randolph¹, G. Farace², G. Bilbrough², M. Yerramilli², M.E. Peterson^{1,3}

¹Cornell University, College of Veterinary Medicine, Department of Clinical Sciences Ithaca, New York

²IDEXX Laboratories Inc., Westbrook, Maine

³Animal Endocrine Clinic, New York, New York

Project Mentor(s):

Patrick C. Carney, DVM, PhD, Department of Clinical Sciences (Co-Mentor)

Meredith L. Miller, DVM, Department of Clinical Sciences (Co-Mentor)

John F. Randolph, DVM, Department of Clinical Sciences (Co-Mentor)

Mark Rishniw, BVSc, MS, PhD, Department of Clinical Sciences (Co-Mentor)

Mark E. Peterson, DVM, PhD, Department of Clinical Sciences (Co-Mentor)

Abstract:

Background

Symmetric dimethylarginine (SDMA) is a marker of kidney function increasing earlier than creatinine in cats with chronic kidney disease. Biological variation of biochemical analytes, including SDMA, determines whether population-based reference intervals are appropriate when interpreting whether a particular change is clinically relevant for a specific individual.

Hypothesis/Objectives

To evaluate the biological variation of SDMA and other serum biochemical analytes in ten clinically healthy cats.

Methods

Prospective, observational study in which cats were sampled for serum biochemical analyses once weekly for six weeks. Samples were frozen and then single-batch analyzed. Outliers were identified, and restricted maximum likelihood estimation used to determine the coefficients of variation (CV) describing variation within each cat and between cats. The CV determined the individuality indices and reference change values (RCV).

Results

Seven analytes (alkaline phosphatase, cholesterol, albumin, creatinine, blood urea nitrogen, phosphorus, total protein) had high individuality indices, best evaluated based by RCV. One analyte (aspartate aminotransferase) had a low index of individuality, best evaluated by a population-based reference interval. Seven analytes (SDMA, creatine kinase, potassium, glucose, total bilirubin, calcium, alanine aminotransferase) had intermediate indices of individuality, best evaluated by combination of RCV and population-based reference intervals.

Conclusions

Clinicians should consider biological variation when selecting the best method for interpreting changes in biochemical analytes. Specifically, establishing each cat’s baseline values and applying RCV to subsequent measurements of analytes with high indices of individuality may improve recognition of meaningful biological changes. In most situations, SDMA concentrations can be evaluated against population-based reference intervals.



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Resident, Emergency and Critical Care, 2nd Year

Abstract Title:

Diagnosis of Septic Peritonitis Using Effusion-Blood Gradients of Novel Biomarkers in Dogs

Authors Names:

Pia M. Martiny, Cornell University, College of Veterinary Medicine, Ithaca , New York
Robert Goggs, Cornell University, College of Veterinary Medicine, Ithaca , New York

Project Mentor(s):

Robert Goggs, Cornell University, College of Veterinary Medicine, Ithaca , New York

Abstract:

Septic peritonitis (SP), defined as the presence of bacteria within the abdominal cavity, is common in dogs and is associated with high mortality. Early recognition and aggressive management are essential to maximizing survival. Few biomarkers for diagnosis of SP have been evaluated in dogs to date. This study aimed to evaluate the utility of novel biomarkers for the diagnosis of SP in dogs.

Objective

To evaluate the hemodynamic effects of two doses of atipamezole administered intramuscularly (IM) to anesthetized cats receiving dexmedetomidine.

Methods

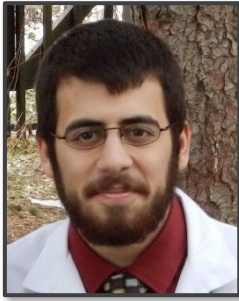
Eighteen dogs with SP and 19 age-matched controls with evidence of systemic inflammation but non-septic abdominal effusion (NSP) were prospectively enrolled. Blood and effusion were obtained at presentation, and concentrations of cfDNA, glucose, HMGB-1, inflammatory cytokines, lactate, NT-proCNP, NGAL, nucleosomes, and procalcitonin measured. Effusion-blood gradients were compared between dogs with SP and with NSP by Mann-Whitney U test. ROC curve analysis and calculation of AUROC was used to determine the gradients most discriminating for SP. Bonferroni corrections were used to adjust for multiple comparisons.

Results

Compared to NSP, dogs with SP had significantly greater effusion-blood gradients of CCL2, IL-6, IL-10, and lactate (all $P \leq 0.0255$), and significantly smaller effusion-blood gradients of glucose ($P = 0.0135$). ROC curve analysis indicated that these 5 biomarkers were discriminant for the differentiation of SP from NSP. The most discriminating was IL-10 (AUROC 0.8216, $P = 0.012$).

Conclusion

This study suggests that effusion-blood gradients of IL-10, CCL2, glucose, lactate and IL-6 discriminate SP from NSP in dogs. Considering ease of measurement and good discriminating performance, this study supports the measurement of effusion-blood gradients of glucose and lactate for identification of SP in dogs.



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Resident, Small Animal Internal Medicine, 3rd year

Abstract Title:

Clinical, Clinicopathologic, and Hepatic Histologic Features Associated with Suspected Ketoconazole Hepatotoxicity in 9 Dogs

Authors Names:

Macho, Luis; Center, Sharon; Randolph, John; Dumars, LeeAnn; Rogers, Mira; Rush, Susan; Lucy, John; Hall-Fonte, Deb; McDonough, Sean; Peters-Kennedy, Jeanine

Project Mentor(s):

Sharon A. Center, DVM, Department of Clinical Sciences (Co-Mentor)
John F. Randolph, DVM, Department of Clinical Sciences (Co-Mentor)

Abstract:

Background

Ketoconazole hepatotoxicity is anecdotally described in dogs.

Animals

9 client-owned dogs

Methods

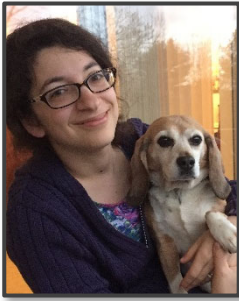
Review of liver biopsies spanning 3 years identified a unique pattern of lipofuscin-engorged macrophages and liver injury coordinating with oral ketoconazole administration in 9 dogs. Signalment, clinical signs, clinicopathologic and abdominal ultrasound findings, hepatic histopathologic features, ketoconazole dosage and duration, concurrent treatments, antecedent illnesses, and survival of these 9 dogs were recorded. Hepatic histopathologic features were scored semi-quantitatively (Mild, moderate severe), by a pathologist and internist with special interest in hepatic pathology, and summated. Hepatic copper concentration was quantified with a colorimetric algorithm previously developed at Cornell.

Results

Dogs of 7 breeds, median age 8.4 (6-15) years, had received ketoconazole for atopy complicated by Malassezia; dose and duration ranged between 5-26 mg/kg/day administered for 3-156 weeks. Concurrent medications included macrocyclic lactones (6), antibiotics (3), antihistamines (3), glucocorticoids (2), cyclosporin (2), oclacitinib (2) and IL-31 monoclonal antibody (2). Clinical signs included lethargy (9), inappetence (9), and vomiting (7). All dogs had increased liver enzymes without jaundice with 3-fold increases in ALT (67%), AST (63%), ALP (33%), and GGT (33%). Histopathologic features included glycogen-type hepatocyte vacuolation (6), variable mixed portal and/or centrilobular inflammation, fibrosis or bridging (6), pyogranulomatous hepatitis (2), increased hepatocyte copper (5), and aggregates of lipofuscin-engorged macrophages (9). With ketoconazole discontinuation, 4 dogs remain alive (12-42 months) and 5 dogs were euthanized (6-12 months). Death was attributed to continued liver injury in 3 dogs (including 2 dogs with pyogranulomatous hepatitis).

Conclusions and Clinical Importance

Ketoconazole-associated hepatotoxicity has a necroinflammatory pattern and remnant lipofuscin-engorged macrophages reflecting oxidative damage. Awareness of potential drug-induced injury advises proactive monitoring of liver enzymes.



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Abstract Title:

Validating the Use of a Smartphone-Based Noninvasive Electrocardiogram in Mice

Authors Names:

Rachael N. Labitt¹, Eva M. Oxford², Scott D. Butler³, Frances L. Chen², Erin K. Daugherty¹

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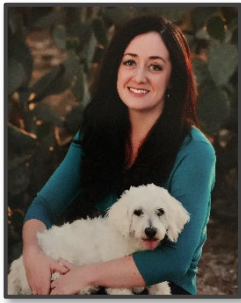
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Project Mentor(s):

Erin K. Daugherty, DVM, MS, DACLAM; Center for Animal Resources and Education, Cornell University, Ithaca, New York

Abstract:

Noninvasive electrocardiogram (ECG) devices are not often used in mice. They require restraint or anesthesia, expensive equipment, and are reported to produce ECGs of questionable quality. The gold standard for obtaining ECGs in mice is the invasive surgical implantation of telemetry devices. Telemeters allow for continuous ECG recording of unrestrained, unanesthetized mice. However, telemeter implantation requires invasive surgery and can be prohibitively expensive, and is therefore not practical to use as a screening tool. We validated the use of a smartphone-based, noninvasive, single lead ECG system in mice. The smartphone ECG transmits an ECG recording to a smartphone if placed in contact with the ventrum of a restrained, conscious mouse. The smartphone ECG is inexpensive, does not require surgery, and can be used to quickly screen animals for cardiac rhythm disturbances. We surgically implanted FVB mice and mice with known cardiac arrhythmias with telemeters and obtained simultaneous ECG recordings by telemetry and smartphone system. Recordings were obtained in restrained, conscious mice and in unrestrained, anesthetized mice. Results were evaluated blinded to genotype, but not recording method, due to differing formats. Rhythm was assessed by a veterinary cardiologist. The smartphone ECG produced good quality recordings in conscious mice and adequate quality recordings in anesthetized mice in ventral recumbency. Both methodologies produced ECGs of similar heart rate and rhythm, with lower resolution in the smartphone recordings. The use of a smartphone-based, noninvasive ECG in mice appears to be a cost effective, valuable screening tool for assessing mice for cardiac rhythm disturbances.



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Resident, Large Animal internal Medicine, 3rd Year

Abstract Title:

Agreement of Equine Stall-Side and Laboratory Major Cross Match Test in Healthy Horses

Authors Names:

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Project Mentor(s):

Gillian Perkins, Cornell University, Department of Clinical Sciences, Ithaca, NY (Mentor)

Tracy Stokol, Cornell University, Department of Population Medicine and Diagnostic Sciences, Ithaca, NY (Co-mentor)

Abstract:

Blood transfusions are often needed to treat anemic horses. Horses have 8 blood groups, with >30 factors, yielding >400,000 potential blood types. Incompatible transfusions can cause life-threatening reactions. To avoid such reactions, crossmatches are usually performed in diagnostic laboratories but are technically difficult, labor-intensive, protracted and costly. An accurate point-of-care kit would overcome these limitations in emergencies or private practices. Our goal was to evaluate the performance of a rapid stall-side gel-based equine crossmatch kit (Alvedia; KIT) with the laboratory procedure (LAB) in horses of known and unknown blood types. Expected positive (n=34) and negative (n=35) crossmatches were established using 21 blood typed and antibody screened horses and known antisera. The sensitivity and specificity (95% confidence intervals) for expected reactions were 88 (73-97)% and 71 (54-85)% for KIT and 76 (59-89)% and 74 (57-88)% for LAB. Agreement was 65 and 63% for expected positive and negative reactions, respectively. The lowest agreement was found with anti-Aa (KIT positive, LAB negative in 8/12, 33% agreement), then anti-Qa (KIT negative, LAB positive in 4/10, 60% agreement) crossmatches, with 100% agreement for anti-Ca (KIT and LAB positive in 12/12) crossmatches. To mimic field situations when unscreened horses may be transfused with untyped blood, reciprocal crossmatches were performed in 69 untyped/unscreened horses. Test results agreed in 89/138 (68%) (Cohen's $\kappa = 0.21$ [0.04 to 0.38]) crossmatches. Our data showed that performance of both tests with expected positive reactions was blood type dependent. Agreement between the tests was fair for both expected and unknown reactions.



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Abstract Title:

Bile Acids as Prognostic Indicator for Horses with Liver Disease: A Retrospective Study

Authors Names:

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²Department of Clinical Sciences, Cornell University, Ithaca, New York

Project Mentor(s):

Thomas J. Divers DVM, DACVIM, DACVECC, Cornell University, College of Veterinary Medicine, Ithaca, New York

Abstract:

Introduction

Measurement of serum Bile Acids (BA) is used in horses to establish severity of liver disease and monitor response to treatment. Recent published data from Europe supports the use of serum BA as a prognostic indicator of short and long-term outcome in horses. However, the etiopathology of hepatic disease in northeastern U.S. horses might differ from horses in the European study causing predictive outcome value of SBA to differ. Determining the prognostic value of SBA in Northeastern U.S. horses with liver dysfunction might therefore provide more accurate prognostic information on horses in this region. The prognostic value of serum gamma-glutamyltransferase (GGT) activity, the most commonly used biomarker for liver disease in horses was also evaluated in the study horses.

Objective

To retrospectively evaluate the predictive value of SBA and serum GGT activity on outcome in the population of horses presented to Cornell University, with both primary and secondary liver disease causing abnormally high serum BA.

Results

45 horses presented with liver disease and BA values above 30 $\mu\text{mol/L}$ and were included in the study. 80% of the horses survived long term (>6 months).

Logistic regressions for primary and secondary diseases showed no correlation between SBA values and long-term outcome ($P=0.98$) or GGT activity and outcome ($P=0.52$).

Conclusions

Serum BA concentration and GGT activity did not differ among survivors and non-survivors. According to these results, SBA do not seem to represent a good long-term prognostic indicator in this population of Northeastern U.S. horses with liver dysfunction.



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Abstract Title:

Ethanol Injected Intracoelomically as a Novel Method of Euthanasia in Zebra Finches (*Taeniopygia Guttata*) and Chickens (*Gallus Gallus Domesticus*)

Authors Names:

[Nathaniel S. Kollias](#)¹, [Andre Escobar](#)², [Elizabeth Buckles](#)³, [Elizabeth Moore](#)³, [Ava Oxford](#)³, [Wendy O. Williams](#)¹, [Erin K. Daugherty](#)¹

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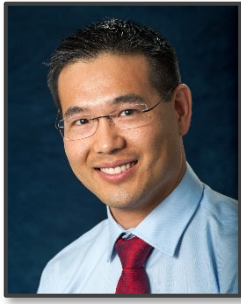
Project Mentor(s):

Erin K. Daugherty, DVM, MS, DACLAM; Center for Animal Resources and Education (Mentor)

Wendy O. Williams, DVM, DACLAM, Center for Animal Resources and Education (Co-mentor)

Abstract:

According to the [AVMA Guidelines for Euthanasia of Animals 2013](#), injectable pentobarbital and inhalant CO₂ are “acceptable” and “accepted with conditions” methods of euthanasia for avian species. However, barbiturates are controlled substances and challenging to use in the field and laboratory setting. Additionally, there is limited literature on the use of CO₂ in avian species and flow rates are extrapolated from mammalian studies. Most importantly, CO₂ has been reported to induce euthanasia inconsistently and is cited by users to be distressful. Recent studies have investigated intraperitoneal (IP) ethanol as an alternative to CO₂ due to its unique pharmacological properties with results suggesting IP ethanol overdose is a humane euthanasia agent in mice, but is inconsistent in rats. Thus, we sought to determine if intracoelomic (IPc) 100% ethanol could be used as an alternative euthanasia agent in chickens. Chickens were fitted with ECG, capnography, doppler, and randomized into three groups: 20ml of 100% ethanol, 20ml saline, or 0.5ml of pentobarbital IPc. Chickens receiving either pentobarbital or ethanol exhibited a smooth transition into anesthesia, with 5/7 birds in the ethanol group declared euthanized at approximately 10 minutes post injection and 5/7 pentobarbital birds declared euthanized at approximately 7 minutes. Post mortem examination revealed no significant degradative tissue effects (histological examination and RNA extraction) with using ethanol as a euthanasia method. There were no significant aberrations appreciated on ECG recordings. We conclude that IPc ethanol overdose induces euthanasia inconsistently, which currently prevents it from being used as a euthanasia method.



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Intern. Companion Exotics, Wildlife and Zoo Medicine

Abstract Title:

Dens Invaginatus in Dogs - a Case of Mistaken Identity?

Authors Names:

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²Department of Biomedical Sciences, College of Veterinary Medicine, Cornell University, Ithaca, New York

Project Mentor(s):

Santiago Peralta, DVM, Dipl. AVDC, Department of Clinical Sciences

Abstract:

Introduction

Dens invaginatus is a rare developmental malformation of the tooth arising from the invagination of the enamel organ, resulting in additional layers of dental tissue. This malformation has been associated with early-onset periodontitis and pulp necrosis in dogs. The existing veterinary literature is limited to case reports and the internal structure of affected teeth has not been well described. The purpose of this study was to describe the radiographic and histological characteristics of teeth with suspected dens invaginatus using a variety of radiographic and histological methods.

Materials Methods

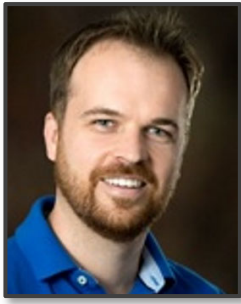
Four teeth from 3 dogs with suspected dens invaginatus were surgically extracted and stored in formalin. Full-mouth radiographs were performed for each dog. Radiographic analysis consisted of *in vivo* and *ex vivo* radiographs with an intraoral phosphor plate system, as well as high-resolution micro-computed tomography. Histologic examination of each tooth was performed with demineralized and non-demineralized methods, and immunohistochemistry.

Results

An area of abnormal mineralized tissue surrounded by disorganized dentin was identified within each tooth. In 3 teeth, the abnormal tissue extended to the external surface of the tooth, while in 1 tooth, the abnormal tissue was wholly contained within dentin. Small channels traversed the abnormal tissue, communicating with the pulp cavity and the external surface of the tooth. Invaginated enamel layers could not be confirmed in any of the affected teeth.

Conclusions

Radiographically, the findings reported here were dissimilar to previously described forms of dens invaginatus, but bore a close resemblance to a recently described developmental abnormality in humans known as molar-incisor malformation.

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Abstract Title:

Evaluation of On-Farm Microbiology Techniques for Detection of Pathogens in Milk

Authors Names:

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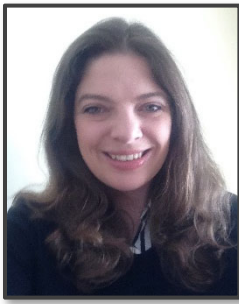
Project Mentor(s):

Daryl Nydam, DVM, PhD, Department of Population Medicine and Diagnostic Sciences (Mentor)

Anja S. Sipka, DVM, PhD, Department of Population Medicine and Diagnostic Sciences (Co-mentor)

Abstract:

On-farm culture systems are useful tools for pathogen based mastitis management in dairy cows which is advantageous for both economic reasons and to reduce antimicrobial use in livestock. We evaluated the use of 3 on-farm mastitis diagnostic assays: AccuMast[®] Mastitis Culture System (chromogenic media) and MN Easy[™] Culture System Bi-plates and Tri-plates (selective media). A total of 628 milk samples submitted to Quality Milk Production Services for routine diagnostics in 2017 were cultured simultaneously for 24h on test media and on blood agar for subsequent MALDI-TOF analysis (reference method). All on-farm culture plates were interpreted independently by trained and untrained readers based on the algorithm of the respective system. For the outcomes no growth, gram positive, gram negative, Staphylococcus aureus, Streptococcus species, Escherichia coli and Klebsiella we determined sensitivity, specificity, predictive values and strength of agreement between reader group and reference method. When interpreted by a trained reader all systems showed intermediate to high specificity (> 76%), negative predictive values (78.1 to 98.4%) and a moderate to good strength of agreement with the reference method for no growth, gram positive and gram negative. Untrained readers had lower test statistic values and only fair to moderate strength of agreement for these categories. Across all three systems and groups of pathogens trained readers showed moderate to good agreement with the reference method while none of the systems agreed well with the reference method when assessed by readers who only had access to the training materials provided by the three systems.



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Current Position

Resident, Emergency and Critical Care, 2nd Year

Abstract Title:

Evaluation of Antimicrobial Administration in Critically Ill Dogs on the Fecal Flora: Dynamics of Antimicrobial Resistance over Time

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Project Mentor(s):

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Robert Goggs, BVSc, DACVECC, DECVECC, PhD; Assistant Professor in ECC, DCS

Abstract:

Introduction

Extensive antibiotic usage has exerted selection pressure leading to development of bacterial antimicrobial resistance (AMR) in organisms at the infection site, and within the commensal bacterial population.

Objective

To assess the effect of antibiotic administration to dogs with sepsis on the antimicrobial resistance patterns of the gastrointestinal microflora over a 60-day period.

Methods

Sixteen dogs with septic peritonitis (n=6), pyometra (n=5) and pneumonia (n=5) were prospectively enrolled. Fecal samples were collected for culture at-presentation and again seven and 60 days later. *Escherichia coli* isolates from each time point were tested for resistance against a panel of antibiotics including amoxicillin-clavulanate, ampicillin, cefazolin, cefovecin, cefpodoxime, cephalexin, chloramphenicol, clindamycin, doxycycline, enrofloxacin, imipenem, marbofloxacin, metronidazole, and orbifloxacin. Resistant isolate frequencies were compared between timepoints using binomial tests with post-hoc multiple comparisons correction using a 5% false discovery rate per Benjamini-Hochberg.

Results

Between admission and day seven, there were significant increases in the frequency of resistance in *E. coli* isolates against the following antibiotics (percent resistance at admission, percent resistance day 7, P-value): ampicillin (36.8%, 100%, P=0.008); cefazolin (15.8%, 100%, P=0.004); cefovecin (21.1%, 91%, P=0.008); cefpodoxime (15.8%, 90%, P=0.008); cephalexin (15.8%, 91%, P=0.008); enrofloxacin (15.8%, 92%, P=0.002); marbofloxacin (15.8%, 100%, P=0.002); orbifloxacin (15.8%, 100%, P=0.002). There were no significant differences in resistance frequencies between admission and day 60.

Conclusions

In dogs with sepsis receiving antibiotics, fecal *E. coli* isolates developed antimicrobial resistance within seven days to multiple types of antimicrobials including drugs to which individuals were not exposed. This resistance diminished by day 60.



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Abstract Title:

Epidemiological Investigation of Orofacial Clefts in Purebred Dogs

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Project Mentor(s):

Patrick Carney, DVM, PhD, Department of Clinical Sciences

Santiago Peralta, DVM, Department of Clinical Sciences

Abstract:

Introduction

Congenital orofacial clefts occur when the tissue that forms the primary or secondary palate fails to fuse during embryonic development, resulting in an abnormal fissure in the upper lip or roof of the mouth. Etiopathogenesis is multifactorial, involving genetic and environmental factors. These malformations have been reported in dogs and other species, including humans. Anecdotally, brachycephalic breeds seem overrepresented. Improved understanding of the frequency with which clefts occur as well as possible causes, predictors, and risk factors may help improve diagnosis, treatment, and prevention and benefit breeding operation economics.

Objective

To investigate incidence and phenotype of congenital orofacial clefts among purebred dogs, examine potential risk factors, and estimate financial impact on breeding programs. Methods: Dog breeders were solicited to participate in an anonymous survey through invitations sent to various kennel clubs. Breeders having whelped a litter in the past 12 months were eligible to participate. Litters affected by other congenital abnormalities were excluded from analysis. Breed, genetic clade, skull conformation, litter size, sex, and geographic area were analyzed for associations with clefts.

Results

Among 7,429 puppies born in the 12 preceding months, 226 orofacial clefts (3%) were reported. Breeds in the mastiff-terrier genetic cluster were at increased odds of orofacial clefts of any type (OR, 2.72; 95% CI, 1.89 to 3.90; $P < 0.001$), cleft lips (OR, 1.77; 95% CI, 1.01 to 3.11; $P = 0.0455$), cleft palates (OR, 2.62; 95% CI, 1.70 to 4.03; $P < 0.001$), and both (OR, 4.75; 95% CI, 1.81 to 12.46; $P < 0.001$). Breeds in the ancient breed cluster were at increased odds of orofacial clefts of any type (OR, 2.91; 95% CI, 1.53 to 5.53; $P < 0.001$) and cleft palates (OR, 4.43; 95% CI, 2.13 to 9.22; $P < 0.001$). Brachycephalic breeds were at increased odds of orofacial clefts of any type (OR, 4.75; 95% CI, 3.57 to 6.31; $P < 0.001$), cleft lips (OR, 9.12; 95% CI, 4.88 to 17.03; $P < 0.001$), cleft palates (OR, 2.60; 95% CI, 1.81 to 3.73; $P < 0.001$), and both (OR, 20.47; 95% CI, 7.18 to 58.31; $P < 0.001$).

Conclusions

Results support our clinical impressions that certain breeds, especially brachycephalic breeds, are overrepresented among cases of orofacial clefts.



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Abstract Title:

An Analysis of Medical Error Type and Severity in Veterinary Hospitals Through the Use of an Incident Reporting System

Authors Names:

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Project Mentor(s):

Daniel J. Fletcher, PhD, DVM, DACVECC, Department of Clinical Sciences

Abstract:

Introduction

Medical errors are commonly regarded as a leading cause of mortality in human medicine. In contrast, errors in veterinary medicine are rarely discussed, and there is little knowledge regarding their nature and frequency.

Objective

To evaluate the type and severity of medical errors reported in three veterinary hospitals.

Methods

The voluntary online incident reporting systems of a small animal teaching hospital, large animal teaching hospital, and small animal private practice were reviewed. Reports were included if they were entered between February 2015 and March 2018, and involved an incident pertaining to patient safety. The reporting systems included classification of errors into the following categories: drug, iatrogenic, system, communication, lab, oversight, staff, or equipment errors. In addition, all incidents were classified as resulting in either a near miss, harmless hit, adverse incident or unsafe condition. Adverse incidents were further evaluated for error severity retrospectively.

Results

A total of 560 incident reports were included for analysis. Drug errors were the most frequently reported in all three hospitals, followed by failures of communication. Errors most commonly reached patients without causing harm (45%); however, 15% of all incidents resulted in patient harm. Eight percent of these patients suffered permanent harm or death.

Discussion

This study demonstrates that medical errors have a substantial impact on veterinary patients. Establishing that drug and communication errors are most frequent in a variety of hospitals is the first step towards interventions to improve patient safety and outcomes in veterinary medicine.



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Abstract Title:

QT Restitution in Boxers with ARVC: Relationship to Arrhythmia Vulnerability and Treatment Response

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Abstract:

Introduction

Morbidity and mortality are high in Boxers diagnosed with Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC), which affects approximately 60% of all dogs in this breed. Ventricular arrhythmias (VA) are commonly present and have a high potential for degeneration to fatal ventricular fibrillation. Currently, sotalol, a potassium channel blocker and β -adrenergic blocker is the first line antiarrhythmic used to decrease the frequency and severity of VA. This response may be related to its effect on cardiac repolarization and heart rate, reflected by the QT and TQ interval duration on the electrocardiogram.

Objective and Methods

To understand the mechanism behind VA in Boxers with ARVC and the reason for a between-dog variability of response to sotalol. In this study, Boxers with more than 10,000 VA per 24 hours on Holter recordings and treated with sotalol are selected. An 85% reduction in VA number identifies response to treatment. ECG restitution techniques to evaluate the ratio between the working phase (QT interval) and the resting phase (TQ interval) of the ventricles are applied to digital electrocardiographic recordings. Furthermore, the association between restitution parameters and VA are studied.

Hypothesis

We hypothesize that ECG restitution parameters distinguish Boxers that respond to sotalol therapy from those that experience a smaller reduction in VA. Preliminary results indicate an impact of sotalol therapy on restitution parameters. It remains to be determined whether this effect is independent from heart rate changes after treatment, and if it is associated with VA reduction.



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Abstract Title:

Assessing the Effects of Cisapride and Buprenorphine on Gastrointestinal Transit Time in Rabbits

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Manuel Martin-Flores, MV, DACVAA, Department of Clinical Sciences

Abstract:

Background / Rationale for the Study

Buprenorphine is the first-line opioid used for analgesia in rabbits. Buprenorphine significantly reduces gastrointestinal (GI) motility, reduces fecal output, and delays GI transit time in rabbits. These deleterious effects may discourage the use of buprenorphine or other opioids in rabbits. Cisapride is a gastroprokinetic agent that promotes gastric emptying in a variety of species. Cisapride has been used anecdotally for GI stasis in rabbits, but its effectiveness at ameliorating opioid-induced GI stasis in this species has not been investigated. We hypothesize that cisapride decreases GI transit time if administered alone. We further hypothesize that the addition of cisapride when co-administered with buprenorphine will significantly reduce opioid-induced GI stasis in New Zealand White rabbits. In this study, we will first determine the most efficacious method of measuring GI transit time in rabbits. We will then administer 4 different treatments to rabbits in random order: buprenorphine, cisapride, buprenorphine+cisapride, and normal saline twice a day for 2 days. Fecal production will be measured every 6 hours, and water/food consumption, and body weight will be measured daily for 5 days after each treatment. We expect that cisapride will reduce GI transit time, and that when combined with buprenorphine, will reduce GI transit time compared to buprenorphine alone. This study will impact rabbit welfare by showing that some of the GI side effects of buprenorphine can be minimized, leading to less hesitation when using opioids for analgesia in this species.



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Abstract Title:

Proximal Sesamoid Bone Microdamage and Fracture Toughness in Thoroughbred Racehorses

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Abstract:

Proximal sesamoid bone (PSB) fractures are the most common cause of catastrophic injuries on Thoroughbred racetracks in North America and Hong Kong, yet PSB fracture etiology is poorly understood. It is unclear whether fractures occur as acute, traumatic monotonic fractures or are the result of chronic, cyclical bone stress with inadequate secondary bone remodeling. The goal of this research is to determine whether there are differences in the amount of microdamage accumulation in PSBs in horses sustaining fracture as compared to sex-age-matched controls (SAMC), to assess whether intact PSBs from the contralateral limb of fracture horses (FXCL) have reduced fracture toughness, and to investigate the amount of microfracture that occurs during fracture testing. Our first hypothesis is that PSBs undergoing catastrophic failure will have evidence of pre-existing microdamage. To test this hypothesis, microdamage will be assessed in SAMC and fractured PSBs using lead uranyl acetate (UA) staining and micro-CT for volumetric assessment and basic fuchsin staining for histologic assessment of microarchitecture. Second, fracture toughness is thought to be higher in more porous bone as it facilitates dissipation of fracture energy in the form of microfracture. Therefore, we postulate that PSBs from SAMC will have increased microfracture following three-point-bending fracture toughness testing, hence increased fracture toughness compared to FXCL. Following dissection, imaging, and morphometric measurements of PSBs, fracture toughness will be assessed using *in vitro* mechanical testing. Fracture toughness will be compared between FXCL and SAMC, and correlated with morphometric measurements, bone density, and microfracture volume as measured via micro-CT.



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Abstract Title:

Indirect Computed Tomographic Lymphography (ICTL) for Sentinel Lymph Node Mapping in a Cohort of Dogs with Cutaneous Mast Cell Tumor - Technique Development and Effect on Peri-Operative Decision Making and Post-Operative Treatment / Monitoring Recommendations

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Abstract:

Literature Review

Cutaneous mast cell tumor (MCT) is one of the commonest malignant cutaneous tumors in dogs. Current treatment standards include wide-margin surgical excision of the primary tumor with regional lymph node excision and chemotherapy if nodal metastasis is present. Removal of the draining lymph node in combination with surgical excision of the primary tumor has been shown to extend survival times in the context of multiple malignant tumor types in both humans and animals. Draining node removal appears to confer both a therapeutic advantage by reducing the cancer burden, as well as a diagnostic advantage by improving the accuracy of staging of disease for the individual, with associated alteration in recommended therapy and monitoring. The success of this approach relies on successful identification and removal of the correct draining lymph node(s), known as the sentinel lymph node(s) (SLN).

Rational for Study

The SNL is not necessarily the same as the regional node predicted by anatomic location of the tumor. Multiple techniques have been developed in human oncology to determine the sentinel node(s) and some of these techniques may be applicable to animals.

Scientific Design

Observational cohort study using ICTL with 4 quadrant peri-tumoral iopamidol injection in client owned dogs (n=20) with MCT >1cm undergoing surgical excision of the MCT and identified SLN.

Hypothesis and Expected Outcomes

ICTL is a useful technique for identification of sentinel lymph nodes in dogs with MCT which will facilitate removal of the SLN, and influence operative decision making and post-operative recommendations.



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SOX2 Expression in Canine Malignancies

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Abstract:

Background/Rationale

Background/Rationale: SOX2 is a major transcriptional regulator of embryonic stem cell pluripotency, and self-renewability. Its expression in cancer stem cells from at least 25 different tumors in humans and rodent models has directly implicated it in tumorigenicity, metastasis, drug resistance, recurrence, and poor survival. Thus far in veterinary medicine, the SOX2 gene is overexpressed in metastatic canine mammary tumors, and isolation of primary canine osteosarcoma cell cultures proved that SOX2-positive cells exhibit distinctive sensitivity to drugs with potential to inhibit proliferation, metastasis, and self-renewal. Recognizing alterations of SOX2 expression between normal and neoplastic tissues is an essential step for better understanding tumor biology and the roots of canine cancer.

Objective/Hypothesis

To investigate the expression of SOX2 in canine malignancies, hypothesizing that variations in SOX2 expression directly relate to tumorigenicity and tumor progression in different types of cancer.

Scientific Design

Immunohistochemistry for SOX2 will be performed on archived formalin-fixed paraffin-embedded canine biopsy tissues diagnosed with various epithelial, mesenchymal, neuroectodermal and hematopoietic tumors. Results will be compared with SOX2 immunoreactivity in normal canine tissues (via tissue microarray), and summarized using standard descriptive statistics.

Expected Outcomes

This study will provide new insights into the molecular pathways of canine malignancies, potentially representing a valuable comparative model for human cancer, and may offer novel clinical applications for SOX2 as a prognostic indicator. Screening methods based on cellular plasticity and pluripotency biomarkers will help provide avenues for the rational design of therapeutic strategies that target vulnerable signals upstream or downstream of SOX2 in different cancer types.

Notes