Latin Comparative Pathology Group Session at the 2022 ACVP/ASVCP meeting

(Latin American Division of the Davis/Thompson Foundation)

Date: Monday, November 14th, 2022
Time: 12:15-3:00 pm EDT
Location: Westin Boston Seaport District (Boston, Massachusetts)

Session Chairs

Ana Alcaraz DVM, PhD, DACVP
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College of Veterinary Medicine
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Angela Arenas DVM, PhD, DACVP
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College of Veterinary Medicine and Biomedical Sciences
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College Station, TX

Ileana Miranda DVM, MSc, DACVP
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Laboratory of Comparative Pathology
Memorial Sloan Kettering Cancer Center
New York, NY

Program

12:15-12:30 pm

Welcome and Introduction of LCPG activities
Paola Barato, DVM, Esp. PhD, President LCPG
paola.barato@corpavet.com
Corpavet
Bogota, Colombia

12:30-1:00 pm

Mouse Kidney Parvovirus: Discovery of a Pathogen of Laboratory Mice and Assessment of its Impact on Research
Dr. Sébastien Monette, DMV, MVSc, DACVP
monettes@mskcc.org
Laboratory of Comparative Pathology
Memorial Sloan Kettering Cancer Center
Weill Cornell Medical College
The Rockefeller University
New York, NY

1:00-1:30 pm

Behind the scenes: BSL-4 Non-Human Primate Filovirus Research from the Veterinary Pathologist Perspective
Dr. Olga Gonzalez, DVM, DACVP
ogonzalez@txbiomed.org
Professor, Disease Intervention & Prevention
Southwest National Primate Research Center
Texas Biomedical Research Institute

1:30-1:50 pm

Frequency of detection and load of amastigotes in the pancreas of Leishmania infantum-seropositive dogs: clinical signs and histological changes
Dr. Rodrigo Caldas Menezes, DVM, PhD
rodrigo.menezes@ini.fiocruz.br
Instituto Nacional de Infectologia Evandro Chagas
Fundação Oswaldo Cruz
Rio de Janeiro, Brazil

2:00-3:00 pm

Executive meeting (everyone is welcome)

Dr. Sébastien Monette, DMV, MVSc, DACVP

Mouse Kidney Parvovirus: Discovery of a Pathogen of Laboratory Mice and Assessment of its Impact on Research

Learning Objectives:

During this presentation attendees will learn about the anatomic and clinical pathologic findings observed in mice infected with mouse kidney parvovirus, diagnostic methods used to detect this virus in mouse colonies, and the potential effects of this pathogen on research performed in mouse models.

Abstract:

In 2018 Mouse kidney parvovirus (MKPV) was discovered and determined to be the etiology of murine inclusion body nephropathy (IBN). The virus was subsequently found globally in laboratory mouse colonies with a prevalence of 5.1%. MKPV causes a chronic infection with viral replication predominantly occurring in renal tubules and shedding in urine. In highly immunocompromised mice, IBN can progress to marked renal lesions, renal failure and mortality, whereas in immunocompetent mice the infection causes mild lesions and remains subclinical. Experimental infection studies have shown strain differences in shedding kinetics between immunocompetent inbred C57BL/6NCrl (B6) and outbred Crl:CD1(ICR) mice, and highly immunocompromised NOD.Cg-PrkdcscidIl2rgtm1Wjl/SzJ (NSG) mice. To study the impact of MKPV infection on research outcomes, experimentally infected and naive B6 and NSG mice we used in pharmacokinetic (PK) studies of two renally excreted drugs, and infected and naive B6 mice were used to model chronic kidney disease (CKD) with the adenine diet model, followed by evaluation of anatomic and clinical pathology endpoints of renal structure and function. MKPV infection did not result in significant alterations of PK parameters. In the CKD model, infection significantly altered the severity of interstitial lymphoplasmacytic infiltrates and fibrosis. MKPV should be excluded from immunodeficient mouse colonies because of its potential to induce morbidity and mortality. In light of recent findings on its effects on the research outcome of a model of CKD, MKPV infection may confound results of kidney disease research performed in mice, and MKPV status should be reported in these studies.

Bio:

Sébastien Monette is the Head of Anatomic Pathology at the Laboratory of Comparative Pathology (LCP) and Genetically Modified Animal Phenotyping Service of Memorial Sloan Kettering Cancer Center, Weill Cornell Medicine, The Rockefeller University, and Hospital for Special Surgery in New York, and a Laboratory Member in Sloan Kettering Institute's Cancer Biology and Genetics Program. He received his veterinary degree from the Université de Montréal, completed residency training in anatomic pathology at the University of Saskatchewan, and has been a diplomate of the ACVP since 2003. Prior to joining the LCP in 2008, Dr. Monette worked as a diagnostic pathologist at The Animal Medical Center in New York. At the LCP, Dr. Monette collaborates with investigators on a wide variety of research projects, with a focus on the characterization of novel cancer models and the pre-clinical development of therapeutic and imaging modalities, including cell therapies, monoclonal antibodies, nanoparticles, and devices used in interventional radiology. His research program has focused on the discovery and characterization of naturally occurring pathogens in laboratory mice, and the assessment of their impact on research, with a main focus on Mouse Kidney Parvovirus.

Dr. Olga Gonzalez, DVM, DACVP

Behind the scenes: BSL-4 Non-Human Primate Filovirus Research from the Veterinary Pathologist Perspective

Learning Objectives:

- Review and discuss the challenges of performing necropsies in maximum containment setting.
- Recognize the importance of NHP animal models for FDA Animal Rule.
- Identify the gross and histopathologic features of experimental filovirus infection in non-human primates.

Abstract:

Texas Biomedical Research Institute (TxBiomed) has the only privately-owned biosafety level 4 (BSL-4) laboratory focused on developing vaccines and therapeutics against high-consequence viral pathogens. The Maximum Containment Contract Research Program (MCCR) comprises a team of specialized staff with appropriate certifications and approvals to run a BSL-4 facility and develop select agent experimental models needed for animal rule studies. Researchers at TxBiomed study how hemorrhagic fever viruses (HFV) replicate and spread in vitro and in vivo using rodent and non-human primate models. TxBiomed veterinary pathologists support the MCCR program by performing necropsies and generating data detailing the pathology of HFV such as Ebola and Marburg virus. Necropsy procedures follow established protocols with whole body assessment and tissue collection lists similar to necropsies performed in a diagnostic setting. Necropsies are performed inside a bio-bubble within the BSL-4 laboratory with additional safety measures including a positive pressure suit and at least five layers of gloves, including cut-proof gloves. Cynomolgus and Rhesus macaques are experimentally infected with Ebola and Marburg virus via aerosol or intra-muscular injection. Systemic pathologic markers of Ebola and Marburg virus in the cynomolgus and rhesus macaque models are similar including the following observable features: dehydration, diarrhea, melena, epistaxis, rash, muscle necrosis at the site of inoculation, lymphadenitis, hepatic, splenic, and lymph node necrosis, and multiple organ hemorrhages. Necropsy findings are critical for validating the qualities of an NHP research model and assessing the effectiveness of interventional strategies (vaccines & therapeutics).

Bio:

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Dr. Rodrigo Caldas Menezes, DVM, PhD

Frequency of detection and load of amastigotes in the pancreas of Leishmania infantum-seropositive dogs: clinical signs and histological changes

Learning Objectives:

Learn about the frequency of detection and load of amastigotes in the pancreas of *Leishmania infantum*-seropositive dogs, identification of the clinical signs and histological changes associated with parasitism of this organ and diagnostic methods used to detect this protozoan in dogs.

Abstract:

Background: Zoonotic visceral leishmaniasis is caused by the protozoan *Leishmania infantum* and is highly lethal in humans and dogs if left untreated. The frequency of this parasite and associated histological changes in the pancreas of dogs are poorly studied. Therefore, the objectives of this study were to evaluate the frequency of detection and load of amastigotes in the pancreas of *L. infantum*-seropositive dogs and to identify the clinical signs and histological changes associated with parasitism of this organ. Methods: One hundred forty-three dogs from an endemic area in Brazil that tested seropositive for *L. infantum* were studied. The dogs were clinically examined, killed, and necropsied between 2013 and 2014. One fragment of the pancreas was randomly collected for histopathology and immunohistochemistry, and spleen and bone marrow were collected for culture. Results: Leishmania amastigotes were detected in the pancreas of 22 dogs (15.4%) by immunohistochemistry, all exhibiting *L. infantum* parasitism in the spleen and/or bone marrow. Poor body condition and cachexia were only associated with infection of the pancreas with *Leishmania* spp. ($p = 0.021$) and were found in 40.9% of dogs with pancreatic infection. Anorexia, vomiting, and/or diarrhea were observed in 9.2% of dogs with pancreatitis. The median parasite load in the pancreas was 1.4 infected macrophages/mm2. Pancreatic histological changes and their frequencies were: granulomatous pancreatitis (28.0%), lymphoplasmacytic pancreatitis (23.8%), acinar cell degeneration (6.3%), fibrosis (5.6%), hemorrhage (2.1%), eosinophilic pancreatitis (0.7%), suppurative pancreatitis (0.7%), and necrosis (0.7%). Conclusions: The present results demonstrate that *L. infantum* is one of the etiological agents of chronic pancreatitis in dogs; however, the frequency of detection and parasite load are low in this organ. The lack of an association of poor body condition and cachexia with pancreatitis and the low frequency of clinical signs commonly associated with pancreatitis suggest that a significant portion of the organ is not affected by this parasite. On the other hand, the association of poor body condition and cachexia with concomitant infection of the pancreas, spleen, and/or bone marrow with this parasite suggests that these manifestations are the result of a more advanced stage of canine visceral leishmaniasis.

Bio:

Dr. Rodrigo Caldas Menezes has a degree in Veterinary Medicine at the Fluminense Federal University (1997), a Master's degree in Veterinary Medicine (Veterinary Pathology) at the Fluminense Federal University (1999), a PhD in Parasitic Biology at the Oswaldo Cruz Foundation (2004) and a postdoctoral degree in Veterinary Pathology at Michigan State University (2012), USA. He is currently a senior technologist at Fundação Oswaldo Cruz, member of the Latin Comparative Pathology Group, Charles Davis Foundation (USA), member of the Brazilian Association of Veterinary Pathology, assistant coordinator of the Stricto Sensu Postgraduate Program in Clinical Research in Infectious Diseases (CAPES 5) and permanent member of the professional master's degree in Clinical Research, both from INI, Fiocruz. He is one of the project coordinators of the Institutional Internationalization Program of Fiocruz's Stricto Sensu Graduate Programs (PrInt Fiocruz-CAPES). Has experience in Veterinary Medicine, with emphasis on Zoonoses, Parasitic Diseases and Anatomical Pathology of Animals.