A New Tool for Diagnosing Challenging Liver Cases: Premium Liver Biopsy Panel Added to Test Catalog

By: Rebecca C. Smedley, DVM, MS, DACVP

Interpretation of liver biopsies can be challenging and often involves additional time and discussion among pathologists as well as communication with the submitting clinician. In order to provide our clients with the most accurate interpretation of these cases, additional testing such as evaluation of special stains, immunohistochemical markers, and/or heavy metal analysis, is often required. Therefore, to better serve our clients, we now offer a Premium liver biopsy panel (test code 40090) which will be available in our test catalog Thursday, September 1.

The premium liver biopsy panel includes histologic evaluation of the biopsy by at least one pathologist who specializes in liver disease who will automatically order specialized stains and/or immunohistochemical markers and/or heavy metal analysis as needed for an accurate diagnosis. This panel can be performed on any liver biopsy, but is especially recommended for challenging internal medicine cases, suspected vascular anomaly cases, intrahepatic neoplasms, and suspected cases of copper-associated hepatitis (CAH), including any liver biopsy from a dog breed that is prone to CAH (e.g. Bedlington Terriers, West Highland White Terriers, Labrador Retrievers, Doberman Pinschers, Dalmatians, etc.).

How Does It Work?
The liver biopsy is first reviewed histologically by one or more liver pathology specialists who then decides if up to three special stains (Trichrome for fibrosis, Rhodanine for copper, and Reticulin for lobular architecture) or up to two immunohistochemical markers (for vascular anomalies or neoplasms), and/or heavy metal analysis (quantitative evaluation for copper, iron, lead, selenium, and zinc) are required. When whole lobes with intrahepatic neoplasms are submitted, the surgical margins will be evaluated and sectioning of these margins will be documented via images that are available on our website. These tests are included in the price of the panel and are ordered automatically if enough tissue is available and if deemed necessary by the pathologist. This Premium liver biopsy panel can be performed on any standard formalin-fixed liver biopsy sample. If an infectious cause is suspected, submission of a fresh frozen sample of liver is also strongly recommended. If needed, bacteriology and/or virology testing can be performed on fresh samples for additional fees. Additional immunohistochemistry and in-situ hybridization testing is also available for other infectious agents.

When requesting this panel we require a complete and detailed history that includes signalment, clinical signs, clinicopathologic findings, imaging results, gross findings, and results of any other tests. Ideally, multiple liver biopsies that represent multiple liver lobes should be submitted for every case. For certain disease processes, such as vascular anomalies, the histologic features can vary greatly between liver lobes and some lobes may appear normal histologically. Thus, vascular anomalies can be missed if only a single liver biopsy is submitted. Other diseases, such as copper associated hepatitis, can be masked by secondary chronic changes such as fibrosis and nodular regeneration. Submission of multiple biopsies can increase the likelihood of identifying less chronically affected areas that still contain large amounts of copper.

Samples from different lobes, or those representing different gross appearances in the same lobe, should be submitted in separate properly labeled containers or otherwise identified in order to ensure the most accurate evaluation. If the samples are small, such as those obtained via needle
biopsy, samples from different lobes can be submitted in separate tissue cassettes or rubber-free tubes such as microcentrifuge tubes filled with formalin and properly labeled. Larger samples, such as whole lobes, could be identified with different colors or numbers of sutures or different colors of ink.

**Noting the location of samples and gross findings on the submission form is extremely helpful to the pathologist.** Please also indicate if samples are taken from nodular lesions or any other masses. For example, if the pathologist is not aware that a sample is taken from the center of a hyperplastic nodule, and there are no bordering normal hepatocytes in the sample, a misdiagnosis of steroid hepatopathy may be made, as hyperplastic nodules often contain glycogen-laden hepatocytes.

**Why Test for Minerals?**

In recent years, we have diagnosed increased numbers of cases of canine CAH, especially in Labrador Retrievers, but we have also seen sporadic cases of CAH in a number of different dog breeds as well. Suspected CAH has also been reported in the literature in small numbers of cats and in two ferrets. In addition, we have found that liver copper values have been increasing in dogs since the 1980s. A combination of environmental and genetic effects is likely responsible for this increase.

To our knowledge, the DCPAH toxicology laboratory is the only veterinary diagnostic laboratory that offers validated quantitative analysis of hepatic copper, iron, lead, selenium, and zinc in formalin-fixed paraffin-embedded tissues. Thus, we can accurately determine the amount of these elements in small liver samples after they have been completely embedded and reviewed histologically. This allows the pathologist to directly correlate what is seen histologically in Rhodanine (copper stain) stained sections with a quantitative value from the same section, as opposed to a separate liver sample that may exhibit different findings. Quantitative analysis can even often be performed on needle biopsy samples if several samples are taken and combined. Ideally, the total amount of liver submitted for element testing should weigh more than 50mg.

For more information on price, specimens, collection protocol, shipping requirements, and other additional information, please see our catalog of available tests on our website or call us at (517) 353-1683.

**The Buzz on Zika Virus**

To date, Zika virus does not appear to pose any risk to animal health. There is also no evidence that animals are involved in the spread of the virus. Nonhuman primates have been known to become infected from the virus, but, like humans, these infections are generally very mild and often cause no clinical signs. Thus far, there have been no reports of livestock or pets showing signs of illness from exposure to Zika. Studies and research on animal populations and Zika virus have not yet been completed or published.

While it has been reported that Zika is in the same family as viruses known to cause illness in animals—such as Japanese encephalitis, West Nile, Bovine Viral Diarrhea (BVD), and Classical Swine Fever (CSF)—it is important to note that the viruses are genetically distinct and biologically quite different.

For more on the role laboratories like DCPAH play in fighting emerging diseases, and for links to additional information, please see our website at animalhealth.msu.edu.
## Upcoming CE Opportunity: Join Us for a Free Endocrinology Seminar

### Thyroid Disease in Dogs: From Clinical Signs to Test Results

**Friday | September 23, 2016 | 1:00 – 5:30 p.m. EDT**  
(4 hours CE)

Room 101, Michigan State University Diagnostic Center for Population and Animal Health (DCPAH)

This seminar is free but registration is required. Register online: [http://bit.ly/MSUcaninethyroid](http://bit.ly/MSUcaninethyroid). A link to the registration is also available at [animalhealth.msu.edu](http://animalhealth.msu.edu).

**Presenters**

**Brian Petroff, DVM, PhD** - Section Chief, Endocrinology, Michigan State University DCPAH  
**Kent Refsal, DVM, PhD** - Endocrinologist, Michigan State University DCPAH

**Description**

Small animal practitioners often have questions about their canine patients with thyroid disease. Is this dog just overweight? Is there a breed predisposition? What test do I order? Do these results make sense? Is this therapy working?

This session will provide a review of the pathophysiology, clinical signs, and other factors that lead to a differential diagnosis. The range of available tests and how to decide which to use will be covered along with review and discussion of case results, including how to interpret equivocal results. Monitoring treatment therapies will also be discussed. We encourage attendees to bring questions with them. There will be opportunities to ask questions throughout the seminar, and attendees can ask questions in a more personal setting during the mixer at the end of the day.

### Agenda

<table>
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<tr>
<th>Time</th>
<th>Event</th>
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<tbody>
<tr>
<td>11:00 – 11:45 a.m.</td>
<td>Optional Tour of the Laboratory</td>
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<tr>
<td>11:45 a.m. – 1:00 p.m.</td>
<td>Lunch on your own</td>
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<tr>
<td>12:45 – 1:10 p.m.</td>
<td>Registration</td>
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<td>1:10 – 2:00 p.m.</td>
<td>Pathophysiology, Adult-Onset and Congenital Hypothyroidism (B. Petroff)</td>
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<td>2:10 – 3:00 p.m.</td>
<td>Clinical Signs, Breed Predisposition (K. Refsal)</td>
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<td>3:10 – 4:50 p.m.</td>
<td>Available Diagnostic Tests, Interpreting Case Results, Diagnosis and Monitoring Treatment, Emerging Topics (K. Refsal)</td>
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<tr>
<td>4:50 – 5:30 p.m.</td>
<td>Meet the Endocrinologists Mixer: Ask questions, chat with the presenters, other endocrinologists and guests, and visit with fellow attendees</td>
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**Also in attendance:**

**MaryDee Sist, DVM** - Specialist, Endocrinology, MSU Diagnostic Center for Population and Animal Health  
**Daniel Langlois, DVM, DACVIM** - Assistant Professor, Small Animal Sciences, MSU College of Veterinary Medicine

**Objectives**

Participants will leave the session with an increased understanding of:

- Pathophysiology of thyroid dysfunction  
- Rationale for testing  
- Effective case management utilizing test results

Please submit any questions to: chapinco@dcpah.msu.edu

**NOTE:** This program 1067-27500 is approved by the AAVSB RACE to offer a total of 4.00 CE Credits (4.00 max) being available to any one veterinarian: and/or 4.00 Veterinary Technician CE Credits (4.00 max). This RACE approval is for the subject matter categorie(s) of:

- Category One: Scientific  
- Category Two: Non-Scientific-Clinical

using the delivery method(s) of: Seminar/Lecture. This approval is valid in jurisdictions which recognize AAVSB RACE; however, participants are responsible for ascertaining each board’s CE requirements.

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A Message from the Director

The fall semester is almost ready to kick off and already the campus is humming as students return to the area and the quiet of summer wanes. We are looking forward to this year’s senior class as they rotate through the Laboratory as part of their training, and we are also excited to welcome four new residents in Anatomic Pathology. The diverse caseload at DCPAH provides training opportunities across multiple species, and exposes both students and residents to the use of traditional as well as advanced, molecular diagnostic methods and tools. We have also been pleased to expand on our education mission by offering CE webinars and our upcoming on-site workshop on canine thyroid disease. More details on this workshop can be found on page 3.

The laboratory continues to play a role in disease surveillance. In the last fiscal year, the laboratory performed over 13,000 tests to screen for Avian Influenza, tested nearly 8,000 samples for Chronic Wasting Disease, performed more than 1,700 necropsies, and tested approximately 2,000 samples for Bovine Tuberculosis. Although some “traditional” seasonal disease patterns remain (e.g. detection of clinically affected animals with arbovirus infections in late summer, early fall), the changing climate, global travel/importation, and other factors, mean that we must continue to watch for potential emerging or changing disease patterns. For example, so far this summer the laboratory has confirmed Rocky Mountain Spotted Fever in a Michigan dog, and the U.S. is now facing challenges to human health with Zika virus.

More than ever, establishing international collaborations will be critical to develop a global network of researchers and educators focused on animal health. DCPAH is excited to be part of a USDA-supported Faculty Exchange program this year, hosting two visiting scholars from Africa who are focused on veterinary microbiology and pathology. Faculty mentors for these visiting scholars will have the opportunity to travel to the visiting scholar’s home institution after their return, to provide onsite advice, lectures and seminars as necessary, and to explore opportunities for future collaboration. Look for highlights from this partnership in an upcoming newsletter.

As many of you may have also done, I marveled at the performances at the Summer Olympic Games—excellence built on countless hours of training, the desire to excel, and the love of the sport itself. There are clear parallels to the art and practice of veterinary medicine and diagnostics. As always, DCPAH is here to serve your needs.

Cordially,

[Signature]