Newsletter September 2014

QML Pathology | Vetnostics

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MedWay

CANINE CUTANEOUS MAST CELL TUMOURS: QML VETNOSTICS OFFERS THE COMPLETE DIAGNOSTIC PACKAGE.

1. Grade: via both Patnaik (Grades I, II or III) and Kiupel (High or Low) grading schemes.

2. Mitotic index: an evaluation of cellular proliferation.

3. KIT IHC: Immunohistochemical evaluation of KIT protein expression pattern.

4. *c-KIT* mutation status: PCR based detection of internal tandem duplications in exon 11 and/or exon 8 of the *c-KIT* gene.

Mast cell tumours (MCTs) are one of the most common canine cutaneous neoplasms and they have a highly variable biological behaviour. In previous newsletters we have discussed how determination of mitotic index can help to better predict clinical outcome (May 2008 NL) and that aberrant expression of KIT protein by neoplastic mast cells is a negative prognostic indicator being associated with increased incidence of local or distal recurrence, shorter disease free interval, and decreased survival times (August 2011 NL). Research indicates that together with histopathological grading and specific determinants of tumour cell proliferation, KIT protein expression, and *c-KIT* gene mutation status provide important prognostic information in canine cutaneous MCTs and they may also be useful in determination of therapy.

QML vetnostics also now offers canine MCT *c-KIT* mutational analysis (via Colorado State University, USA) to detect the presence/absence of internal tandem duplications (ITD) of exons 8 and 11 of the *c-KIT* gene. There is a significant association between *c-KIT* ITD mutations, an increased rate of recurrent disease and mortality in dogs with canine cutaneous MCTs. ITD mutations in exons 8 or 11 of *c-KIT* have been detected in about 20 to 30 percent of canine cutaneous MCTs. MCTs with such mutations are highly aggressive, but may respond well to tyrosine kinase inhibiting (TKI) therapies. Since tyrosine kinase inhibiting compounds are now available for the treatment of dogs, the detection of *c-KIT* mutations has therapeutic as well as prognostic implications. ***c-KIT* mutational analysis can be subsequently performed on both cytologically- and histopathologically-diagnosed canine cutaneous mast cell tumours at an additional cost of $200 (ex. GST); 10-14 day TAT.**

1. Grade: Histopathology is the diagnostic method of choice for grading tumours and there are several potential grading systems for use. The most widely used is the Patnaik system where lower grade lesions are grade 1 and more malignant lesions are grade 3. A predominance of intermediate grade tumours, and variation amongst pathologists in designation of grades, are commonly mentioned weaknesses of the Patnaik histological grading system. The historical dilemma has often been associated with how to interpret the diagnosis of intermediate grade (Patnaik Grade II) tumours which comprise the majority of MCTs. Kiupel and colleagues have proposed a 2-tiered classification of either high grade or low-grade with the criteria for diagnosis of a high grade MCT based on the presence of any one of the following criteria;

- 7 or more mitotic figures per 10 high power fields (HPF).
- 3 or more multinucleated cells (3 or more nuclei) per 10 HPF.
- 3 or more bizarre nuclei per 10 HPF.
- Karyomegaly (10% of nuclei vary by 2 fold or more).

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Please note: A Canine Thyroid Profile + Total T4 will cost $117.90 (exc. GST). Free T4 measurement by Equilibrium Dialysis is still available ($115.50 exc. GST); please specify on the request form if Equilibrium Dialysis methodology is required.

- Electrolytes are now included in the following profiles:
  - Canine Geriatric
  - Feline Geriatric/Thyroid
  - Pre-anaesthetic Biochemistry
  - Pre-anaesthetic/Wellness, and
  - Kidney.
- The Liver Profile (Small Animal) now includes urea.

This group reported a 96.8% consistency rate between pathologists when comparing on a 2-tiered system and high-grade MCTs were associated with significantly shorter time to metastasis or new tumour development, and with shorter survival times (median survival times of < 4 months for high-grade MCTs and > 2 years for low-grade MCTs).

Both the Patnaik and Kiupel histological classification schemes are associated with clinical prognosis. **QML vetnostics reports canine cutaneous MCTs via both the Patnaik (Grade I, II or III) and Kiupel (High or Low Grade) classification schemes.**

2. Mitotic index: (Also refer to the May 2008 Newsletter) Mitotic index (MI) is a measure of cell proliferation and MI is a strong predictor of overall survival for dogs with cutaneous MCTs.

3. KIT IHC: (Also refer to the August 2011 newsletter). The immunohistochemical staining of KIT protein is a useful prognostic parameter in canine MCTs. There is correlation between aberrant KIT expression and increased cellular proliferation, higher histological grade, presence of *c-KIT* mutations, increased local tumour recurrence, and/or decreased clinical survival. The KIT staining pattern I ('normal' staining pattern) is associated with a good prognosis. An aberrant pattern of distribution of KIT protein may be present even without concurrent *c-KIT* mutations.

4. *c-KIT* mutation status: As discussed previously.

MCT grading, cell proliferation analysis, *c-KIT* PCR, and KIT IHC results are therefore all linked to canine cutaneous MCT-associated survival and metastasis. **QML Vetnostics is able to offer all of these analyses in an effort to determine the appropriate prognosis and treatment regimes for your patients.**

NEW PANEL AND PROFILE

Code	Name	Turnaround	Cost (exc. GST)
V4I	T4 (free, by immunoassay)	3-5D	$50.00
=VCTP	Thyroid Profile Canine (FT4 Immunoassay + TSH)	3-5D	$100.00

EXPANDED PANELS AND DISCOUNTED TESTS

As previously introduced, reduced prices apply to the following tests when accompanying a profile*:

Code	Test	Normal Price (exc. GST)	Reduced Price (exc. GST)
VSR	Urine Specific Gravity	$24.70	FREE
TT4	T4 (total)	$43.10	$17.90
VUX	Urinalysis	$35.20	$17.90
VUY	Urinalysis & Urine Culture	$70.40	$37.80
FVX	FIV/FeLV Serology	$78.20	$46.20
VPL	Pancreatic specific lipase, qualitative canine (SNAP CPL) or feline (SNAP FPL)	$31.50	$21.00
=VUCY	Urinalysis + Cytology	$69.30	$52.00

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What is a titre?

A common question we receive is whether a titre is positive or negative.

Antibody titres are confusing, not only because they are expressed as a dilution, but because the concept of a more diluted sample corresponding to a higher titre seems counter intuitive. But the key to interpreting a titre is to understand how the test is performed.

An antibody titre is determined using serial dilutions. For some tests the dilution begins at 1:2, but for other tests the first dilution is higher, e.g., 1:16. The diluted samples are tested for the presence of detectable antibody. The assigned titre is indicative of the **last dilution in which antibody is detected**. Therefore, the higher the titre, and therefore the dilution, the greater the amount of antibody in the original blood sample.

Get the Newsletter by Email!

If you would prefer to receive the newsletter and other updates via email rather than hard copy, please send your details to vetnostics@qml.com.au or phone 1300 838 765 – option 6.

Synacthen® (tetracosactrin) Supply shortage

This is likely to be of relevance to veterinarians as stocks dwindle with an ongoing requirement for ACTH stimulation testing.

Our recommendation therefore after reviewing the literature is the use of Synacthen® Depot and the following protocol:

1. Collect a basal (0 hour) blood sample into a serum tube
2. Inject 250ug of Synacthen® Depot IM
3. Collect a further blood sample into a serum tube 60 minutes later
4. Label sample times clearly on the tube
5. Clearly indicate on the submission form that Depot Synacthen formulation was utilised as well as indicating dosage and blood sampling times
6. Tick ACTH stim (code VAS) as normal on submission form

Reference
Ginel PJ, et al: Evaluation of serum concentrations of cortisol and sex hormones of adrenal gland origin after stimulation with two synthetic ACTH preparations in clinically normal dogs. AJVR 2012; 73: 237-241.

It is imperative that a thorough clinical history is provided with these submissions to allow accurate and useful interpretation and advice.

As Synacthen® is in short supply, use a low dose ACTH protocol, e.g., 5 µg/kg IV for small dogs and 1 µg/kg IV for large dogs and store the remaining sample for future monitoring. Both doses have been proven to produce maximal cortisol secretion in healthy dogs (Martin et al 2007). If using really low doses, close attention with regards to timing of the post-stimulation sample is required. Timing needs to be PRECISELY one hour post injection for doses of 1 µg/kg or less (Martin et al 2007).

Intramuscular dosing with 5 µg/kg has also been shown to cause maximal cortisol secretion (Behrend et al 2006). In the author's opinion, IV dosing is preferable unless patient difficulties preclude it's use, as it ensures that the required dose does reach circulation.

Only a small amount of Synacthen® is administered when using a 1 - 5 µg/kg dose so freeze any remaining sample. Draw up the left-over Synacthen® in a 1 ml syringe (or draw up accurate doses into multiple 1 ml syringes), leaving a small air space at the end of the syringe. Cap each syringe, label it with dog name and date (frozen Synacthen® is stable for 6 months; Frank and Oliver 1998) and place it in the freezer. When that dog needs another ACTH stimulation test, thaw it, draw up the required dose and re-freeze the remainder.

By doing this, multiple doses can be obtained out of one vial. This significantly decreases the cost of monitoring treatment: the owner can be billed for the whole vial initially but thereafter, until another vial is required, there is no more cost for Synacthen®, just fees for cortisol measurement and procedure.

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Australian Veterinary Association
VetEd
Professional development for Australia's veterinarians

AVA APPROVED
AVA members automatically accumulate Vet Ed points when they provide their AVA number.

HOW DO I PARTICIPATE IN THE QML VETNOSTICS CPD PROGRAM?

- Perform in-house cytology.
- Complete the QML Vetnostics CPD Program request form ensuring that you provide a detailed gross pathological and in-house cytological description together with a preferred diagnosis +/- a list of differential diagnoses (if appropriate).
- Submit cytology or histology specimen to QML Vetnostics.

For further information about QML Pathology's Vetnostics Service

Phone: 1300 VET QML

Earn CPD points by submitting cytology and histopathology specimens to QML Vetnostics

QML Pathology Vetnostics now offers an innovative continuing professional development service, exclusive to its veterinarian clients.

The program enables veterinarians to systematically assess their diagnostic accuracy in the clinical setting, with the ultimate goal of improving both their pathology skills and the quality of patient care.

EARN CPD POINTS

Earn **one** structured CPD point for every **four** specimens submitted, where a clinical workup has been sufficiently documented and clinical diagnoses are accurate.

NO NEED TO REGISTER

Participants simply need to submit samples together with a completed **QML Vetnostics Pathology CPD Program request form** to participate and automatically receive program reports and CPD points.

RECEIVE REPORTS ANNUALLY

A CPD points certificate, and report will be provided to participants annually, detailing:

- total number of examined specimens
- prevalence of lesion types observed
- diagnostic accuracy for each lesion type
- margin clearance (Histo only).

To order QML Vetnostics Pathology CPD request forms, please email vetnostics@qml.com.au or call 1300 VET QML (1300 838 765) and select option 6 (All other enquiries).

QML Pathology Vetnostics Service

Find out why we are Queensland's premium veterinary pathology provider.

- Cases are reported by a team of dedicated Veterinary Pathologists, providing a personalised service.
- Medical Consultants are available to discuss treatment and complicated cases.
- We offer a wide range of veterinary testing, including blood biochemistry and haematology, microbiology, endocrinology, serology, histopathology and cytology.
- Our comprehensive lab network ensures the fastest turnaround times in QLD.
- Low cost non-interpreted profiles.
- Simple histopathology charges - no hidden costs.

For any further information, please contact the Vetnostics Department at QML Pathology on **1300 VET QML** (1300 838 765) or visit the QML Pathology Vetnostics website **www.qml.com.au/vetnostics.aspx**

Available Now

Vet diagnostic test kits

QML Pathology is a leading supplier of vaccines to the medical and veterinary community.

In conjunction with veterinary vaccines and consumables, QML Pathology has expanded its vaccinations catalogue to include the Witness range of in-house diagnostic kits available to our veterinary customers.

QML PATHOLOGY IN-HOUSE VETERINARY DIAGNOSTIC TEST KITS

QML Pathology now offer the below Witness in-house diagnostic veterinary test kits as part of Pfizer's Animal Health range, Zoetis. These kits are available for sale in conjunction with our extensive range of veterinary vaccines and consumables.

WITNESS® FIV
WITNESS® FeLV/FIV

WITNESS® FeLV detects the feline leukaemia virus antigen. WITNESS® FIV detects Feline Immunodeficiency Virus antibodies.

WITNESS® Parvo Antigen

WITNESS® Parvo Antigen is a Rapid Immuno-Migration Assay for detection of Parvovirus antigen in the faeces of dogs.

WITNESS® HW

WITNESS® HW is an in-clinic test that detects the presence of adult Dirofilaria immitis antigens in dogs and cats.

WITNESS® Relaxin

WITNESS® Relaxin is a convenient in-house pregnancy test for cats and dogs.

FUNGASSAY®

FUNGASSAY® provides a simple, rapid, and practical method for confirming diagnosis of dermatophyte infections.

OVASSAY® Plus Kit

OVASSAY® Plus Kit an easy and accurate in-clinic faecal flotation method for identifying gastrointestinal parasites.

QML Pathology. | Veterinary Vaccines

Orders: Email **VaccCustServ@qml.com.au** or phone **(07) 3121 4523**.

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