VETSULIN® ISSUES AND CHANGING INSULIN TYPES

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UPCOMING EVENTS
Hi Everyone:

I hope you are all having a very prosperous summer. With Padres euphoria hanging over us, we have a few announcements here at VSH. First, many of you have already met Ann Ong. Since March she has been working as our Events Coordinator. Although new to this role, Ann originally started as a tech several years ago at our first hospital. She left for awhile to be a full-time mother and we are delighted to have her back. In addition, Caren Folbre joined our staff in April as our Marketing Manager. She has extensive marketing and medical education experience on the human side of pharma. Together they will be bringing a revitalized CE program to you and they welcome your feedback. Several of our doctors just attended the ACVIM Forum, recently held in Anaheim. As is common at this meeting each year, we are proud that VSH had a strong presence with our doctors lecturing, presenting at evening meetings, and active in various committees.

I also just got back from New Orleans where I attended the Digestive Disease Week (DDW) Conference. This is the largest conference for human gastroenterologists. The technological advances in endoscopy and laparoscopy are amazing! One interesting new development is NOTES (Natural Orifice Transluminal Endoscopic Surgery). This technique involves the intentional perforation of a natural orifice with a flexible scope (for example perforation of the stomach, colon, or vagina). This allows entry into the abdominal cavity so similar procedures can be accomplished as would be performed with conventional operative laparoscopy. Examples include gallbladder removal, appendectomy, and colon resection. The main advantage is that there is much less pain and it is more cosmetic (for those who care about that kind of thing). I look forward to the day we can apply these techniques in our patients. As I interacted with physicians and vendors, I was amazed how they were amazed ("You do endoscopy on dogs?" "You do laparoscopy on cats?" "Dogs get inflammatory bowel disease, and you use cyclosporine?" etc, etc)! It reminds me again how advanced we are in veterinary medicine, but we just take it for granted because we do this stuff day in and day out.

Well, that’s all for now...

Keith Richter, DVM
Diplomate ACVIM
HEMATOPOIETIC CELL TRANSPLANTATION FOR CANINE LYMPHOMA NOW AT VSH
by BRENDA PHILLIPS, DVM, DACVIM (MEDICAL ONCOLOGY)

The problem:
Treatment outcome for canine multicentric lymphoma has changed minimally for the past several decades. Use of aggressive chemotherapy protocols similar to those used in humans violates the principles of maintenance of a good quality of life that veterinary professionals and the public demands for veterinary cancer patients.

Recent developments in treatment of canine multicentric lymphoma:
The most significant changes in treatment protocol have been to identify the least amount of therapy to achieve the best survival outcome, while maintaining a good quality of life. The 6-month UW-Madison multi-drug (CHOP) protocol, abbreviated chemotherapy protocols + ½ body radiation therapy, and abbreviated chemotherapy protocols followed by "consolidation" with high-dose cyclophosphamide are examples of such approaches. However, they have not significantly improved survival outcome for our patients.

Human bone marrow transplant history:
Bone marrow transplant therapy was initially explored as therapy for non-Hodgkin's lymphoma (the human type of lymphoma that is most similar to canine multicentric lymphoma) to improve survival outcomes compared to high-dose chemotherapy protocols. In general, survivals were only similar to high-dose chemotherapy and the therapy was much more complicated compared to chemotherapy protocols alone. Therefore, for most patients with B-cell lymphoma, bone marrow transplant has been replaced by chemotherapy in combination with anti-CD20 immunotherapy (Rituxan®). Bone marrow transplant is still considered a useful therapy for human patients with leukemia, Rituxan®-resistant B-cell lymphoma and myeloma.

Comparison of canine multicentric lymphoma and non-Hodgkin's lymphoma treatment options:
High-dose chemotherapy associated morbidity violates principles of good quality of life for veterinary oncology patients and Rituxan®-like immunotherapy is not yet available for our patients. Therefore, neither represents solutions for our canine lymphoma patients.

The solution:
"Bone marrow transplant" therapy is accomplished via hematopoietic cell collection from the peripheral blood prior to total body irradiation, and re-administration following total body irradiation is expected to improve survival outcome for canine multicentric lymphoma patients. This is a treatment method now available for canine multicentric lymphoma patients at Veterinary Specialty Hospital, one of 7 centers in the world able to offer this therapy.

Canine bone marrow transplant history:
Dogs have been treated with bone marrow transplant procedures in the research setting for several decades and in clinical patients over the past decade. The protocols for hematopoietic cell transplant have evolved to provide a well-tolerated treatment approach for our canine lymphoma patients.

The general procedure:
The procedure consists of 5 steps:
1) Extensive client education and appropriate patient selection. Patient selection consists of determination of post-induction chemotherapy remission status and general health status.
2) High-dose cyclophosphamide following initial 8-week CHOP induction therapy.
3) Apheresis to collect hematopoietic cells circulating in the peripheral blood [this is done to replace the old protocol of collection of cells directly from the bone marrow].
4) Total body irradiation (TBI) followed by administration of the collected hematopoietic cells to replenish the patient bone marrow.
5) Post-TBI recovery in an isolation room.

Practical considerations:
While the cost of hematopoietic cell therapy is moderately high, it compares similarly to costs of traditional induction chemotherapy followed by several rescue therapy protocols, typically necessary for most canine lymphoma patients to achieve > 1 year survival. While the protocol can be associated with morbidity and mortality, morbidity consisting of diarrhea, lethargy, fever and/or anemia is transient and mortality secondary to infection and/or hemorrhage is uncommon.

Please contact Dr. Brenda Phillips if you have a newly diagnosed canine multicentric lymphoma patient owned by a family who wishes to have the most advanced therapeutic options made available to their special 4-legged family member. Veterinary Specialty Hospital; (858) 875-7500, x2713
Vetsulin® is a porcine insulin zinc suspension (Lente) made by Inervet/Schering-Plough that is FDA approved for use in the dog and cat. Recently, the product has been found to be out of specification in regards to the long term stability of the crystalline, or long acting, component. This could mean that diabetic patients on Vetsulin® may experience a delay in onset of action, a delay in peak activity or an overall extension of the duration of activity. It is the company’s assessment that these issues should not adversely affect either the efficacy or the safety of Vetsulin®.

Due to its limited supply, veterinarians should transition their diabetic patients to other insulin products and should not be starting any newly diagnosed diabetic patients on Vetsulin®.

Types of Insulin:
Insulin products differ based on species of origin and on alterations that change duration of effect and potency. Vetsulin® was the only porcine-based and Lente type product available. The majority of insulin manufactured at this time is recombinant human insulin that exactly matches native human insulin. An FDA approved human recombinant PZI (ProZinc®) is now available and approved for use in cats.

Insulin can also be classified as to duration of effect as described in the following table. Typically the longer their action the less potent the effect.

<table>
<thead>
<tr>
<th>INSULIN</th>
<th>TYPE</th>
<th>DURATION</th>
<th>PREPARATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular</td>
<td>Human</td>
<td>Short</td>
<td>U-100</td>
</tr>
<tr>
<td>Vetsulin® (Lente)</td>
<td>Porcine</td>
<td>Intermediate</td>
<td>U-40</td>
</tr>
<tr>
<td>NPH</td>
<td>Human</td>
<td>Intermediate</td>
<td>U-100</td>
</tr>
<tr>
<td>PZI</td>
<td>Human/Bovine</td>
<td>Long</td>
<td>U-40</td>
</tr>
<tr>
<td>Glargine</td>
<td>Recombinant</td>
<td>Very Long</td>
<td>U-100</td>
</tr>
<tr>
<td>Detemir</td>
<td>Recombinant</td>
<td>Very Long</td>
<td>U-100</td>
</tr>
</tbody>
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Insulin Alternatives for Cats:
Glargine (Lantus®): Glargine is a human insulin analogue produced by recombinant DNA technology. It is a clear aqueous solution in 100U/ml vials. The interaction of the acidic insulin and the neutral pH of the SQ form insulin micro-precipitates. The micro-precipitates are absorbed slowly over time resulting in a very long duration of action. The slow absorption is dependent on the acidity, so glargine cannot be mixed or diluted. Glargine (and detemir) are termed peakless insulins, due to their slow gradual absorption. Optimal results are generally obtained with BID dosing.

Protamine zinc insulin (PZI; ProZinc®): ProZinc® is a new FDA approved long acting human recombinant PZI product for cats. The product replaces PZI-Vet®, a bovine-based insulin that had been produced by Idexx but had recently been discontinued.

Neutral protamin Hagedorn (NPH; Humulin N®, Novolin®, others): with NPH, protamine and zinc are added to the insulin in a neutral solution that results in an intermediate duration of action. It has been used in cats with questionable results due to the short duration of effect (<8-hours) making NPH a poor choice.

Detemir (Levemir®): Detemir is a newer recombinant DNA technology synthetic insulin analogue with a very long duration of action. Detemir is also a peakless insulin. Anecdotally, detemir results in similar control and remission rates when compared to glargine, but no specific studies have been published.

Making the Change in the Cat:
Type: Based on current studies, it is most appropriate to switch to either glargine or ProZinc® for most cats. With either, due to the marked difference in kinetics, you cannot use the previous dose of Vetsulin®; instead you will need to begin with a new starting dose. Careful discussion with the owner regarding the clinical signs of hypoglycemia should be pursued when switching insulin types or when increasing the dose.

Differences in Glargine vs ProZinc®: Glargine is U100, less potent, and longer acting insulin compared to ProZinc® which is a U-40 preparation. Using the correct syringe type is very important. ProZinc® will usually result in the more typical glucose curve with a higher peak just before the next dose, usually having a glucose nadir anywhere from 6-9 hours. In contrast glucose concentrations are typically lower just before the next insulin dose with glargine and vary only slightly throughout the day (peakless).

Dose: The starting dose is 0.25 u/kg for both ProZinc® and glargine, or typically 1 unit per cat SQ BID. The insulin can be substituted for Vetsulin® the very next dose.

Insulin Alternatives for Dogs:
NPH: This intermediate acting insulin has been used in dogs for years with good effect in many dogs. Detemir and glargine: There are only limited studies evaluating these insulin preparations in the dog.

PZI: The efficacy of ProZinc® or other PZI insulin products has not been evaluated thoroughly in dogs.

Making the Change in the Dog:
Type: NPH is the initial insulin of choice to replace Vetsulin®.

NPH vs Vetsulin®: The two types are both intermediate acting insulin, moderate in potency, and typically require twice daily administration for adequate control. They both require careful monitoring for hypoglycemia or a Somogyi effect. NPH can be substituted for Vetsulin the very next dose.

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IN OUR COMMUNITY

Blood Donor Program – Save a Friend, Save a Life!
Veterinary Specialty Hospital has continuous need for canine and feline blood. Because of this need we have developed a community blood donation program. Please let your staff and patients know of this vital life-saving program. Participants receive an initial free screening blood panel and infectious disease testing. If accepted in the program, all followup screenings and examinations are also provided at no cost. Owners receive a50 gift card for every donation their pet makes. Canines: Must be 1–10 years of age, over 50 pounds and in good health. Felines: Indoor cats only, 1–12 years of age, over 10 pounds and in good health. For more information or to receive some brochures for your office, please contact Kathy Welte at 858.875-7500 or via email kathy.welte@vshsd.com.

TAKE NOTE ANNOUNCEMENTS

Dr. Sarena Sunico will join VSH July 20 to provide in-house radiology services. She pursued both her undergraduate and veterinary degrees at UC Davis. She then completed a 6-month internship at the Pet Emergency & Specialty Center in La Mesa, CA, followed by a rotating internship at Cornell University in Ithaca, NY. Dr. Sunico completed her radiology residency at the North Carolina State University. She has a particular interest in CT and MR imaging, but is well rounded in all areas of radiology.

In June, several of our doctors attended the American College of Veterinary Internal Medicine (ACVIM) Forum held in Anaheim, CA. Dr. Keith Richter presented “Highlights from the 2010 Digestive Disease Week: Human and Veterinary Correlates with Minimally Invasive Endoscopic Procedures”. Also, while at ACVIM, Dr. Steve Hill and Dr. Keith Richter attended the Comparative Gastroenterology Society (CGS) annual board meeting and membership business meeting/luncheon. Dr. Hill is the president-elect of the organization. In addition, three of our cases were presented at Animal Survivors. This was a media event that showcased amazing stories of animal survival that were managed by internal medicine specialists. This event included the pets, the owner and the veterinarians. Animal Survivors promotes veterinary specialty medicine by increasing public awareness of the profession’s capabilities. Dr. Hill, Dr. Phillips, and Dr. Stevenson each presented a case with VSH representing three of the five cases presented.

CURRENT CLINICAL TRIALS

Dermatology – Medication to Control Pruritus
Dr. Laura Stokking is enrolling dogs for a new medication to control pruritus. Contact Christie Yamazaki at (858) 875-7500.

Internal Medicine – Canine IBD Study
In conjunction with the Texas A&M GI Lab, VSH is enrolling dogs with chronic gastrointestinal disease in a study to evaluate the usefulness of several new markers of inflammatory diseases in serum, urine, and feces. Dogs with chronic small bowel diarrhea, vomiting or weight loss are eligible. Contact Dr. Hill at (858) 875-7575 x702 or Jen Fulbright at (858) 875-7500 x729.

Internal Medicine– Mycophenolate IMHA study
Purpose: To evaluate the use of mycophenolate in addition to standard therapies (prednisone, low dose aspirin, transfusions) for the treatment of primary IMHA.

Inclusion: patients diagnosed with IMHA (positive slide agglutination and/or presence of spherocytes and/or positive Coombs’ test with a regenerative anemia) and no evidence of underlying disease as assessed by history (vaccination and drug history), infectious disease testing, thoracic radiographs, and abdominal ultrasound exam.

Exclusion: Patients with secondary IMHA or Evan’s syndrome; patients that have received prednisone for >36hr before admission; patients on immunosuppressive medications; patients <8kg

Client benefits: Study covers 100% of the cost of the mycophenolate for 2 months and reduced fee for infectious disease panel; additionally clients receive a 25% discount off CBC and chemistry panels done post-hospitalization for up to 2 months. Contact Dr. West at (858) 875-7500.

Internal Medicine – Spotted Fever Rickettsioses in So. California Dogs
Purpose: To determine if Spotted Fever Group Rickettsia infections are occurring in dogs with signs of tick-borne illness in Southern California. The study provides an extensive tickborne disease screening panel with both serology and PCR. The owner is required to return 10 days to 3 weeks after the acute sample for convalescent sample. Cost to the owner is a one time fee of $201.76.

Case Selection: Dogs with a variety of clinical signs suggestive of or consistent with a tick-borne illness can be included. Samples need to be drawn prior to administration of doxycycline, enrofloxacin or chloramphenicol (will cause PCR to be negative). If you have a case where a tick-borne illness is suspected you can contact any of the internal medicine specialists at VSHSD or VSHNC for further information.

Surgery – Micro Total Hip Replacement
VSH is enrolling 25 small dogs in a clinical study to compare the results of micro THR to those of femoral head and neck excision. If you know of a candidate for this procedure or would like to learn more about the benefits of participating, contact any VSH surgeon at (858) 875-7575.
Vetsulin® Issues and Changing Insulin Types  

continued from inside...

**Dose:** When switching from Lente to NPH, the current dose should be reduced by 20–25% and a Q2 hour glucose curve should be performed after 5–7 days. An "mini" glucose curve (Q3–4 hours) immediately after the first dose could be considered to rule out hypoglycemia, however the dose should not be increased if hyperglycemia is noted.

WE'RE LISTENING

We understand that it is more convenient for some of your clients to see a specialist on Saturdays. We are happy to announce that we are scheduling Saturday appointments for Dermatology, Internal Medicine, Neurology and Surgery in the San Diego and San Marcos facilities. We are always open 24/7, 365 days a year, for emergency and critical care.

SAVE THE DATE

**Summer CE Dinner and Lecture**  
(San Diego and North County Facilities, Webinar)
July 29, 6:00 pm – 9:15 pm

- Fun With External Fixators, Dr. Sean Aiken
- Neurology Highlights from ACVIM 2010, Dr. David Lipsitz
- Updates on the Treatment of IMHA, Dr. Kevin Mallery
- Great Impersonators in Dermatology, Dr. Laura Stokking

August, no events – Happy Summer!

**September Roundtable Discussion: Pancreatitis**  
September 16, 7:00 pm (San Diego Facility)

**Annual Conference of the Veterinary Cancer Society**  
October 29–November 1, 2010
Lowes Coronado Bay Resort, San Diego, CA
For more information, go to the Veterinary Cancer Society web site: www.vetcancersociety.org/ or call (619) 741-2210.

For more information on Continuing Education events, please contact Ann Ong at (858) 875-7544 or ann.ong@vshsd.com