VetCom a bi-monthly electronic newsletter for the veterinary community

Abaxis
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ABAXIS

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Welcome!

Welcome to the October issue of VetCom. In this month's issue we are pleased to share Dr. Betta Breuhaus' ACVIM 2003-presented review of thyroid function in horses. We hope you find it useful.

Guerilla's Marketing Golden Rule #42-*Proving You Care*

More companies will fail than succeed in business, and the ones that succeed will be the ones that prove they care.
Customer Care is different than Customer Attention!
Ways to prove to your clients that you care:

1. Have a written document outlining the principles of your client service and patient care
2. Develop a precise measurement system for ensuring client satisfaction and reward employees who practice it.
3. Stay in touch with your clients-postcards, newsletters, telephone calls.
4. Consider having open house events to get to know your client and prospective clients better.
5. Meet client needs and exceed their expectations!

from: Guerilla Marketing Excellence, JC Levinson, Houghton-Miflin

In the Trenches

Thyroid Function in Horses-Uncovering the Myths
ACVIM 2003
Dr. Babetta A. Breuhaus, DVM, PhD

REVIEW OF PHYSIOLOGY
Formation, Storage and Secretion of Thyroid Hormones
The thyroid gland traps iodide and concentrates it 30-250 times the blood concentration. Within epithelial cells of the thyroid gland, the endoplasmic reticulum and Golgi synthesize and secrete thyroglobulin (a glycoprotein that contains tyrosine) into the follicles. Iodide is oxidized and bound to tyrosine either as mono-iodotyrosine (MIT) or as di-iodotyrosine (DIT). Two DITs are combined to form thyroxine (T_4), whereas tri-iodothyroine (T_3) is formed from one MIT and one DIT. Thyroid hormones are stored within the gland bound to thyroglobulin. Each thyroglobulin molecule contains approximately 30 T_4 molecules and a few T_3 molecules. In humans there is enough thyroid hormone stored within the gland to last a couple of months. Control of thyroid hormone secretion occurs at 3 sites. Thyrotropin releasing hormone (TRH) from the median eminence of the hypothalamus stimulates release of thyrotropin or thyroid stimulating hormone (TSH) from the anterior pituitary. TRH release is enhanced by a cold environment and inhibited by stress. TSH release is enhanced by α-adrenergic agonists and inhibited by dopamine, somatostatin and glucocorticoids. At the thyroid gland, TSH increases the size and activity of the epithelial cells, stimulates proteolysis of thyroglobulin, increases iodide trapping, increases coupling of MIT and DIT, and stimulates re-uptake of colloid into the cells by pinocytosis. T_4 and T_3 are released into the circulation, where they bind to plasma binding proteins. Only free (unbound) thyroid hormones are metabolically active. While the thyroid gland secretes primarily T_4, T_4 is deiodinated to T_3 (or reverse T_3) in blood and tissues. T_3 is much more active than T_4, while reverse T_3 has very little activity.
Actions of Thyroid Hormones
Thyroid hormones play an important role in growth, maturation, and metabolism in many species, including the horse. Free T_3 binds to intracellular thyroid hormone receptors, stimulating the production of proteins. In a general sense, thyroid hormones increase mitochondrial number and size, increase activity of Na,K-ATPase, increase protein synthesis and catabolism, increase heat production, and stimulate basal metabolic rate. They increase growth and maturation of a number of organ systems, resulting in increased mental activity and neural development, lung maturation, increased gastrointestinal function (e.g.,. increased appetite and intake, increased GI secretion and motility), increased cardiovascular function (e.g., increased heart rate, cardiac output, blood volume, and pulse pressure), and growth and maturation of the skeletal system.

ASSESSMENT OF THYROID FUNCTION IN HORSES
Clinical Laboratory Tests
Diagnosis of thyroid disease in the horse traditionally has been difficult. Documented cases of thyroid disease in adult horses are rare, despite the fact that assays for T_4 and T_3 have long been available for use in this species and normal values, including a circadian rhythm, have been reported. Single measurements of T_4 and T_3 are difficult to interpret, especially if free fractions are not included, because thyroid hormone metabolism or transport can be affected by a variety of drugs and physiologic or pathophysiologic states (see below). Commercial laboratories often do not offer measurement of free fractions, or clinicians do not know to order them. In addition, the validity or usefulness of measurement of free T_4 by equilibrium dialysis (fT_4D) has not been studied in the horse. In humans, dogs and cats, fT_4D is generally believed to better reflect true thyroid status in ill animals, compared to other methods of measurement of free T_4. Because of problems interpreting results of single point-in-time serum thyroid hormone measurements, measurement of thyroid hormone responses to administration of either TRH or TSH has been advocated as a more accurate measurement of thyroid function in the horse. However, these tests are often not practical for use by ambulatory clinicians, due to the time required to conduct them and the fact that medical preparations of TRH and TSH for client owned animals are often either unavailable or prohibitively expensive. Assays for measurement of serum TSH are well developed in humans, and serum TSH measurement is a very sensitive and accurate tool for diagnosis of thyroid dysfunction in people. Although a commercial assay for measurement of serum TSH in dogs has been available for several years, overlap exists in naturally occurring canine thyroid disease such that approximately 20-40% of hypothyroid dogs do not have elevated serum TSH concentrations, and TSH has been found to be increased in as many as 14% of euthyroid dogs. TSH measurement in euthyroid horses and horses made hypothyroid by administration of propylthiouracil has been described. Hypothyroid horses had significantly increased serum TSH concentrations and the TSH response to TRH was exaggerated. However, a commercially available TSH assay is not currently available for use in the horse, and it

In this Issue

Welcome	1
In the Trenches	1
Thyroid Function in Horses	
Coming Conferences	2
Events of Note	2
VetScan News & Offers	3
In Your Opinion	3
Abaxis Contact Info	3
VetScan Authorized Distributors	4

remains to be seen whether serum TSH measurement will be useful in the diagnosis of naturally occurring thyroid disease in this species.

Physiologic, Pathophysiologic and Pharmacologic Alterations of Thyroid Function

Thyroid hormone metabolism or transport has been shown to be affected by certain drugs, as well as by starvation in the horse. Phenylbutazone decreases serum concentrations of T_4 and T_3, primarily by competition for binding to carrier proteins, but phenylbutazone also may decrease T_4 production by the thyroid gland. Although glucocorticoids can cause secondary hypothyroidism in humans and dogs, dexamethasone administration for 5 days did not result in decreased serum concentrations of T_4 or T_3 in clinically normal horses. Food deprivation has been reported to cause decreases in both T_4 and T_3 in the horse, although the decreases in T_3 appear to be more consistent. The mechanism for this decrease is thought to be inhibition of 5'-deiodinase, resulting in decreased conversion of T_4 to T_3. In humans, dogs and cats suffering from systemic illnesses, non-thyroidal illness syndrome is characterized by low serum concentrations of T_3 with or without concomitant decreases in T_4 and low or normal TSH. The degree of thyroid hormone suppression has been correlated to severity of disease and to mortality. Although equine clinicians have assumed that non-thyroidal illness syndrome also occurs in horses, to date no actual studies have been performed to document it. Without consideration of the factors described above, measurement of low serum T_4 or T_3 in a horse that is off feed, suffering from systemic illness, or receiving certain drugs could easily lead to a misdiagnosis of hypothyroidism and subsequent unnecessary thyroid hormone supplementation.

"Although subject to some controversy, the existence of true hypo-thyroidism in adult horses is probably rare."

ABNORMALITIES OF THYROID FUNCTION IN HORSES

Hyperthyroidism

Hyperthyroidism has not been reported in the horse, despite numerous reports of tumors of the thyroid gland (including adenomas, adenocarcinomas, medullary thyroid carcinomas and C-cell tumors). In many of the case reports, thyroid hormones were not measured. However, where measured, most horses with thyroid tumors were euthyroid. Mildly decreased resting concentrations of total T_4 and T_3 have been reported in some cases of thyroid tumors, but some of these horses were also suffering from systemic illness. Isolated incidences of elevated serum concentrations of thyroid hormones have been seen by or reported to the author, but in all of these cases repeated measurements revealed normal values. It is thought that external sources of iodide, such as may be contained in dietary supplements or in blisters, could potentially cause transiently elevated serum concentrations of thyroid hormones.

Hypothyroidism

Although subject to some controversy, the existence of true hypothyroidism in adult horses is probably rare. Certain clinical syndromes (including poor performance, recurrent rhabdomyolysis, infertility, laminitis, anhidrosis, obesity and cresty necks) have been associated with hypothyroidism, despite lack of convincing evidence, and despite the fact that these conditions have not been produced when the thyroid glands have been surgically removed from horses or when horses were made hypothyroid by administration of propylthiouracil. Unfortunately, it is not uncommon for equine clinicians to misdiagnose horses suffering from Equine Cushing's Disease or Equine Metabolic Syndrome with hypothyroidism. Perhaps this stems from an early study in which surgical removal of the thyroid glands of young growing horses resulted in dull coarse haircoats, delayed shedding of winter coats, and a coarse thickened appearance to the face. Other effects of thyroidectomy reported in growing horses included decreased feed consumption with associated decreases in body weight gain, delayed physeal closure, failure to grow in height, delayed tooth eruption, cold sensitivity, rear limb edema, lowered rectal temperature, lowered serum phosphorus concentration, increased serum cholesterol concentration, and a docile, lethargic temperament. In two more recent studies, surgical removal the thyroid glands from adult horses resulted in decreased basal heart rate, cardiac output, respiratory rate, and rectal temperature and increased blood volume, plasma volume, and serum concentrations of triglycerides, cholesterol and very low density lipoproteins.

With these discrepancies and controversies in mind and with serum TSH measurement and TRH stimulation tests in hand, the author has begun to attempt to systematically characterize thyroid function in response to various

Coming Conferences

We'll See You There!

Southwest Veterinary
Symposium
Forth Worth, TX
Oct 3-5

Wild West Veterinary
Conference
Reno, NV
Oct 9-11

WI VMA
Madison, WI
Oct 10-12

AALAS (Lab Animal)
Seattle, WA
Oct 12-15

Atlantic Coast Vet Conf
Atlantic City, NJ
Oct 14-16

HI VMA
Honolulu, HI
Nov 7-9

KSU-Midwestern Exotic Conf
Manhattan, KS
Nov 8-9

AAEP (Equine)
New Orleans, LA
Nov 22-24

Events of Note

Wild, Wild West

We will be sponsoring an Abaxis "Beer Bash" social in conjunction with the Wild West Veterinary Conference in Reno. Stop by our **booth #711** to play some golf and get your tickets to the Bash!

Looking for CE for your local VMA meeting?

Abaxis Representatives are available to present a one-hour, RACE accredited, presentation on the topic of in-clinic wellness programs and diagnostic testing .

More clinically-focused, DVM-presented programs are also available.

To request a speaker at your event, please contact your Abaxis area sales director, or:
jenniferambra@abaxis.com

VetScan® News & Special Offers

VetScan Externship

Abaxis is proud to be partnering with the Avian & Exotic Animal Medical Center of Miami, Florida (Don Harris, DVM) to sponsor a summer externship program in avian and exotic animal medicine.
DVMs interested in applying for the Jun-Aug 2004 course or for additional information contact:

pamconboy@abaxis.com

Win a TRIP to NAVC Orlando, FL-Jan 2004

All non-VetScan customers requesting product information or an in-clinic demonstration *(including on-site lab testing)* through December 2003 are entered to win a trip for two to the North American Veterinary Conference. (2 RT airfare, 3 nights dbl occ hotel room and a full DVM NAVC registration) Refer to Offer **VC10** when requesting information/ demonstration to be entered.

NEW Abaxis Website!

Be sure to visit our newly updated website!
Your suggestions and feedback are welcome and encouraged
www.abaxis.com

FREE CE!!

RACE accredited programs available correspondence:

Practitioners Perspectives on In-Clinic Wellness Programs-1 CEU

Canine Hypothyroidism
1 CEU

Basic Hematology
2 CEU
to order a CE program, or request a topic for a future program, email:
jenniferambra@abaxis.com

Need a Speaker at Your Local VMA Meeting?

contact your Abaxis regional area sales director to discuss the options

New VetScan Software

The delayed VetScan software update is now scheduled for October 2003.
Please be sure to update your VetScan and return your old software card in the provided post-paid envelope!

Colleague Referrals

Know some who would benefit from the VetScan system?
send us a referral!
We will gratefully send you a 10-rotor *Thank You* for any referral who ultimately becomes a VetScan customer!

send referrals to:
pamconboy@abaxis.com

Interested in sharing your opinion?

We are always looking for DVMs interested in sharing their opinion on new development projects, clinical applications of diagnostic tools and general trends in veterinary medicine.
If you would like to be included in future discussions, contact:

pamconboy@abaxis.com

user thoughts on VetScan

The (VetScan) analyzer truly expanded my service and I can offer comprehensive diagnostics, where I had to choose a few parameters in the past due to limited volume of blood available in small birds, reptiles and mammals.

Joerg Mayer, DVM

In Your Opinion

If a simple blood test were available for differential diagnosis and prognostic indications in canine and feline heart disease, do you feel it would be a useful tool?

If so, how frequently would you use such a test and what would be a reasonable cost?

For information and early study results of veterinary applications of a BNP assay for diagnosis and monitoring of canine and feline congestive heart failure, contact me via email or fax at: 510-217-6664.

Got a Question for the Lab? Send it in….

Email me with your replies and queries:

pamconboy@abaxis.com

Abaxis Contact Information

1-800-822-2947

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diets, drug administrations or disease conditions that have traditionally been associated with hypothyroidism. Rationale behind these investigations and preliminary results will form the remainder of these proceedings.

Fescue Ingestion

Tall fescue (*Festuca arundinaceae*) is a cool-season, seed-propagated perennial grass that is grown commonly in the Southeast because it is relatively easy to establish, has a long growing season, and has good disease and drought resistance that allow it to survive hot, humid summers. A variety of reproductive problems have been described in mares consuming fescue, and these have been shown to be caused by alkaloids produced by an endophytic fungus *(Neotyphodium coenophialum*) that lives symbiotically on the fescue plant and acts as a dopamine agonist. Since TSH release from the pituitary is inhibited by dopamine, it has been suggested that fescue consumption could lead to hypothyroidism and may have contributed to lower serum TSH concentrations in mares and foals consuming endophyte-infected fescue on a farm in central Kentucky, compared to mares and foals on a nearby farm grazing pastures that were mainly free of endophyte-infected fescue. In a recent study by the author, feeding endophyte-infected fescue seed to adult, non-pregnant horses resulted in no differences in baseline concentrations of thyroid hormones or TSH, or in their responses to administration of TRH.

Anhidrosis

Anhidrosis is a condition of adult horses characterized by a decreased ability or inability to sweat in response to appropriate stimuli. The cause is unknown. Hypothyroidism has long been associated with anhidrosis, perhaps because treatment with iodinated casein was reported to be helpful in the 1950's. In a recent study, the author found that baseline concentrations of thyroid hormones and TSH were normal in horses with anhidrosis. Thyroid hormone responses to TRH were also normal, but TSH responses to TRH were greater in anhidrotic horses than they were in horses with normal sweat production. These data suggest that anhidrotic horses either have altered thyroid gland TSH receptors or that increased TSH release compensates for decreased ability of the glands to secrete thyroid hormones. However, since serum thyroid hormone concentrations remain within normal limits, the usefulness of exogenous thyroid hormone administration must be questioned. It is possible that, if thyroid hormone supplementation does indeed facilitate sweating in anhidrotic or hypohydrotic horses, the effect may be pharmacologic rather than physiologic. Equine sweat glands are stimulated to secrete by activation of β_2-adrenergic receptors, and, although not demonstrated so far, it has been proposed that anhidrosis results from desensitization or downregulation of these receptors. Thyroid hormones modulate adrenergic receptor function, such that tissues from hypothyroid individuals are less responsive to β-adrenergic agonists. Both desensitization and downregulation of β-adrenergic receptors have been shown in hypothyroid animals. Thus, perhaps iatrogenically making horses mildly hyperthyroid restores β-adrenergic receptor numbers or sensitivity, or potentiates sweat responses to whatever neural stimulation remains.

Non-Thyroidal Illness Syndrome

Preliminary data from blood samples collected from horses admitted to the North Carolina State University Veterinary Teaching Hospital suffering from a variety of illnesses indicate that, not only are serum concentrations of thyroid hormones decreased, but the magnitude of these decreases are profound in many cases, especially in horses that ultimately died or were euthanized. The contribution of various drugs administered to treat these diseases remains to be determined. Also, since measurements of total thyroid hormones are influenced by alterations of serum binding capacity (which occur in non-thyroidal illness syndrome) and since free thyroid hormones are the metabolically active forms, measurements of free fractions of thyroid hormones are critical for accurate estimation of thyroid function. Many commercially available assays for free T_4 show significant biases related to protein binding, and thus are inaccurate when serum binding capacity is altered. Measurement of fT_4D is considered to be the most accurate measurement of free T_4 currently available. Comparison of fT_4 measured directly to fT_4 measured after equilibrium dialysis shows a good correlation between the two measurements in normal horses and in horses made hypothyroid by administration of propylthiouracil. In 291 samples collected from healthy horses in previous studies, median (range) serum fT_4 and fT_4D were 12 (0-50pmol/L) and 24 (0-8pmol/L), respectively. Further studies are ongoing to determine whether fT_4D more accurately predicts true thyroid function than does direct fT_4 in horses with systemic illnesses.

Laminitis

Laminitis is a significant clinical problem in horses, resulting in pain and decreased quality of life, decreased usefulness or athletic ability, and even loss of life itself. The pathophysiology of laminitis is incompletely understood, and its cause is probably multifactorial. A role for decreased thyroid function in the pathogenesis of laminitis is poorly documented and remains a controversial topic. While decreased serum thyroid hormones have been associated with some horses that experience acute laminitis, it is unlikely that decreased thyroid function alone causes laminitis. In three studies in which hypothyroidism was induced either by surgical removal of the thyroid glands or by administration of propylthiouracil, laminitis did not occur. Thus, any alterations in serum thyroid hormone concentrations in horses experiencing laminitis may be caused by factors associated with the episode of laminitis, rather than the cause of the laminitis itself. Such factors could include drugs used to treat laminitis (e.g., phenylbutazone), development of non-thyroidal illness syndrome, or a direct effect of factors such as endotoxin or one of the inflammatory cytokines that contribute to the onset of laminitis in some cases. In the author's experience, stimulation tests performed in horses that have suffered an episode of laminitis, or that have had bouts of recurrent laminitis, show normal thyroid hormone responses to TRH when these tests are performed once the horse is stabilized and has been off all medications for 4 weeks. Despite this, some veterinary clinicians think that treatment of horses with iodinated casein during an acute episode results in improvement. These horses often are treated without prior measurement of thyroid hormones. Some are treated even when measurement shows serum thyroid hormone concentrations to be within the normal range. These horses are then often kept on thyroid hormone supplementation indefinitely. To date, no controlled studies have been performed to determine whether or not administration of thyroid hormones during acute episodes of laminitis is beneficial. However, since β-adrenergic receptors on vasculature are vasodilatory, it is possible that thyroid hormone administration may increase circulation to the foot by its ability to potentiate β-adrenergic receptor numbers and sensitivity. Thus, as suggested for anhidrosis, any beneficial effect of thyroid hormone administration in horses suffering from laminitis may be pharmacologic rather than physiologic.

Our sincere thanks to Dr. Breuhaus of North Carolina State University Veterinary School for permission to reprint this comprehensive review.