MASTER CLASS

REPTILIAN THYROID ANATOMY, PHYSIOLOGY AND DISEASE

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ABSTRACT: The purpose of this lecture is to review thyroid anatomy, physiology and disease in reptiles to enhance veterinary appreciation. Thyroid disease is often under assessed in reptiles because thyroid physiology of reptiles is least known among vertebrates, few normal values, few scattered reports of disease and lack of veterinary pursuit. The old adage you cannot diagnose what you do not know applies. The practical application will be to encourage veterinarians to pursue diagnosis of thyroid disease.

KEY WORDS: thyroid, disease, reptiles, goiter, hypothyroidism, hyperthyroidism, T4, T3

THYROID ANATOMY

The basic unit of the thyroid gland is the follicle, which ranges in size from 50 to 300 µm (Lynn, 1970) but can be larger. Follicles are surrounded by a single layer of epithelial cells (follicular cells or thyrocytes) which vary from squamous to cuboidal to columnar with increasing activity. For example in the summer the follicular cells of *Graptemys geographica* were columnar with reduced colloid and in the winter hibernation the follicular cells were cuboidal with much stored colloid (Semple, 1975). However there is a lack of correlation between histologic parameters and hormone levels (John-Alder, 1983, Hulbert and Williams, 1988, Buehler, 2006). The follicular cells concentrate iodides from the thyroid's exceedingly rich blood supply. Given its size, the thyroid gland receives one of the largest blood supplies of any organ (Oldham and Smith, Rivera and Locke, 2008). The follicular cells convert iodide to iodine, one of which then attached to the amino acid tyrosine, to form monoiodotyrosine (MIT), or two of which make diiodotyrosine (DIT). MIT and DIT can be coupled to form triiodothyronine (T-3) or two DIT's can couple to form tetraiodothyronine (thyroxine or T4). These reactions depend on a glycoprotein the follicles produce called thyroglobulin. As the thyroglobulin is secreted into the follicular lumen iodination and coupling occurs and thyroglobulin stores all these molecules as eosinophillic colloid. There are various amounts of scant connective tissue between follicles and a capsule surround the entire gland. The capsule is composed of collagen, few elastic fibers and scattered melanophores (Buehler, 2006).

Any discussion of thyroid disease would be incomplete without appreciation of the hypothalamic/pituitary/thyroid axis. In reptiles, as in other vertebrates, the hypothalamus controls the pituitary gland, or hypophysis, through nerve impulses and secretion of hormones. The hypothalamus is the ventral part of the anterior brainstem or diencephalon. On the ventral surface of the hypothalamus is the optic chiasma, and just caudal to this the pituitary stalk emerges. The hypothalamus secretes thyrotropin- releasing hormone (TRH) which stimulates production of thyroid stimulating hormone (TSH) in the pituitary (Sawin, et al, 1981, Reiner, 1992). TSH controls the synthesis and release of T3 and T4 in the thyroid gland. When thyroid hormone is needed thyroglobulin molecules endocytosed from the colloid into the follicle and broken down into MIT, DIT, T3 and T4. MIT and DIT are deiodinated and the iodine is recycled. T3 and T4 are protein bound and distributed in the bloodstream to the peripheral tissues. T4 it is converted to the more active form, T-3, via de-iodinases. (Rivera and Locke, 2008) but in reptiles T4 predominates.

Two species (*Naja naja*, *Elaphe taeniuria*) are known to circulate large amounts of MIT and DIT with much less T4 (Wong and Chiu, 1974).

Several aquatic turtle genera (*Chrysemys*, *Pseudemys*, and *Trachemys*) have much higher thyroid values than other reptiles (Table 1), perhaps because of a thyroxine binding protein (TBP), which will be discussed later (Licht, Denver, Pavgi, 1991, Licht, Denver, Herrera, 1991).

Thyroid morphology varies tremendously among reptiles. In chelonians and snakes the thyroid is unpaired, roughly spherical, and lies ventral to the tracheal, cranial to the heart (Lynn, 1960, 1970). In chelonians the thyroid is near the bifurcation of the common carotid artery just cranial to the heart and caudal to the thymus. Bragdon (1953) described the thyroid gland in *Natrix sipedon sipedon* as light reddish brown and easily identified by its gelatinous translucent appearance. He found it to be 3x4 mm in large females and 1.5x2.5 mm in adult males and was easily identified between ventral scutes 21 to 25. McCracken (1991) found the thyroid gland to be immediately cranial to the heart in snakes. The anterior heart lay on the right side 20% of the distance between the snout and cloaca in colubrids, 22 % in elapids, 25% in boids, and 33% in viperids.

In the tuatara the thyroid is anterior to the heart and single but more elongate as it lies transversely across the trachea (Lynn, 1970) much like lizards. In some crocodilians the thyroid has well-defined lobes on either side of the trachea with the narrow isthmus connecting them (Lynn, 1970), in others (*Crocodylus niloticus*) they have two separate asymmetric lobes found not on the trachea but attached to the lateral side of each bronchi, the right closer to the to the right bronchus where it enters the lung and the left closer to the bifurcation of the trachea (Huchzermeyer, 2003).

Lizards have the greatest thyroid morphologic diversity (Lynn, 1960, 1970) having either a single broad, round or long gland, bi-lobed or paired. Variation is even extensive within families but consistent within genera. The most common forms (Lynn, 1960, 1970) are bi-lobed with a connecting isthmus between the trachea, such as in the green iguana, *Iguana iguana*, (Hernandez-Divers, et al, 2001), and a single broad thyroid stretching across trachea, such as in the *Lacerta, Xantusia* (Adams, 1939, Miller, 1955). See Lynn, 1970, for a chart of lizard thyroid morphology by family. In *Xantusia* the thyroid is found at the level of the cranial ventral shoulder girdle (Miller, 1955).

Amphisbaenids have unusual thyroids in that they are more cranial, either midway along the trachea or near the anterior trachea, away from the heart (Lynn, 1970). Paired glands are most common but they can either be spherical, oval or elongated, attenuated, threadlike paired organs (several centimeters long but only 1 mm wide; Lynn, 1970).

The thyroid gland of the iguana is dorsal to several ventral muscles layers (constrictor colli, omohyoideus, episternocleidomastoideus) and is easily exposed (Oldham and Smith, 1975, Hernandez-Divers, 2001). The thyroid gland has dual arterial supplies on both sides. In *Lacerta* and *Xantusia* the superior thyroid arteries (or right and left thyroid arteries), branch off the external or internal carotid's (respectively) and attach to the lateral thyroids(s). The inferior thyroid arteries (or right and left laryngotracheal arteries) are short large vessels that attach to the dorsal thyroid body(s). The thyroid glands are drained by one or two medial thyroid veins into the right tracheal, or right internal jugular, veins. The thyroid gland itself is contained in a large lymphatic sac (Miller, 1955). Innervation of the thyroid gland is from the laryngeal branches of vagus nerve and fine branches of the cervical sympathetics (Lynn, 1970, Adams, 1939, Oldham and Smith).

Unlike mammals reptilian thyroids are anatomically distinct from the parathyroid glands. The ultimobrachial (which secrete calcitonin) are also found nearby but separate. Thyroid glands are capable of regeneration if damaged or removed (Denver and Licht,1991).

THYROID PHYSIOLOGY

In reptiles thyroid physiology influences many processes such as shedding (Lynn, 1970), growth, development (Denver and Licht, 1991), reproduction, metabolic rate, nutrient assimilation and activity. Many factors also influence thyroid values including age, sex, diurnal changes, seasonal changes, day length, shedding, illness, stress and breeding (Licht, et al, 1985, Greenacre, 2001). In general reptiles have plasma concentrations of thyroid hormones that are far less than mammals (Hulbert and Williams, 1988) which has complicated thyroid hormone detection with assays designed for the higher levels of mammals. T4 and T3 values in reptiles are roughly 20 and 25%, respectively, of the average values in mammals (Hulbert and Williams, 1988). T4 has the highest concentration (except apparently in Naja and Elaphe, previously discussed), followed by T3, free T3 (fT3), and free T4 (fT4). In *Testudo* spp. fT4 is often below the limits of detection (< 0.45 pmol/L) of mammalian thyroid assays (Buhler, 2006). It is believed T4 plays a more central role in thyroid metabolism as Kohel et al, 2001, were unable to measure any T3 over a two-year period in desert tortoises (Macarthur, et al, 2004) or perhaps this simply reflects assay sensitivity. In experimental studies T4 accelerated shedding more than T3. Table 1 list thyroid values for reptiles, the bulk of which are from turtles, followed by lizards, with few values from snakes and crocodilians. Most of these values have not been validated for reptiles but in some cases they were (Etheridge, 1993, Greenacre, 2001).

Adult turtles in the genera *Chrysemys*, *Pseudemys*, and *Trachemys* have much higher thyroid values than other reptiles (Table 1) and females in these genera have higher levels than males, perhaps because of a thyroxine binding protein (TBP) which also causes marked seasonal variation. TBP has been identified in all 8 species of *Pseudemys* studied and in 3 other genera (*Chrysemys*, *Deirochelys*, and *Emyoidea*) of the same family, Emydidae (Licht, Denver, Herrera, 1991). TBP was minimal upon emergence from hibernation and maximal in late summer (July–August), about a month after the peak in plasma T4 (Licht, Denver, Pavgi, 1991).

Hypophysectomy causes expected changes in the thyroid gland, flattening of the follicular epithelium, failure of the colloid release, and reduced uptake of radioiodine and decreased shedding in lizards. (Lynn, 1970, Chui, et al., 1970, Chui, et al., 1969). In lizards thyroidectomy causes either a cessation of shedding with a build up of the horny layer (Lynn 1970) in Lacerta species, or shedding less frequently (*Hemidactylus brookii, Gekko gecko*). For example in Tokay gecko's, *Gekko gecko*, shedding frequency is temperature dependent, at 28° C they shed every 20 to 29 days, at 32° C every 19 to 24 days, at 36° C every 17 to 19 days. With thyroidectomy at 28° C they shed every 33 to 55 days, at 32° C they shed every 27 to 32 days and at 36° C they shed every 22 to 39 days. In all cases the mean cycle length increases over time. Hypophysectomy also increases cycle length and combination thyroidectomy and hypophysectomy produced even longer cycle length (Chiu, et al, 1986). Administration of thyroid hormone causes lizards to shed more frequently.

The reverse appears true in snakes. Excess thyroid supplementation causes shedding to cease, and hypophysectomy or thyroidectomy increases shedding frequency (*Thamnophis*, *Python*, *Natrix*, *Ptyas*, *Chionactus*) (Lynn, 1970, Chui and Lynn, 1970). Thus we would expect hypothyroidism to result in lizards shedding less, snakes shedding more and hyperthyroidism should cause lizards to shed more and snakes to shed less. Further light was shed on the atypical thyroid physiology of snakes by a study on Rat snakes, *Ptyas korros*, by Chiu, et al, 1983. Thyroidectomized rat snakes stopped eating and died after about 20 days or 20% weight loss, unless supplemented with DIT, MIT and thyronine didn’t help.

Thyroidectomy also causes a decrease in growth in lizards and turtles (John-Alder, Denver and Light, 1988). Experimentally, in *Trachemys scripta,* hypothyroidism (goitrogen treatment or surgical thyroidectomy) resulted in a marked suppression of TBP, and T4 treatment prevented its decline or reinstated it. Thus, in these turtles, TBP may show a different relationship to thyroid activity than the analogous T4 binding globulin in mammals (Pavgi and Licht, 1992). Thyroidectomy of *Trachemys (Pseudemys) scripta* significantly reduced growth rate within 6–8 weeks; length-specific growth rate was affected sooner than mass-specific growth rate. These results demonstrate the thyroid gland is needed for normal growth of turtles. Thyroxine replacement therapy of treated turtles restored growth after 6 weeks (Denver, Licht, 1991).

Temperature, light and reproduction have big effects on thyroid physiology. TSH is unresponsive to TRH at 20° C or below (Licht, et al, 1989) in *Pseudemys scripta*. Continuous exposure to light in *Testudo horsfieldi* caused thyroid production to peak at five days with a gradual decline to inactivity by 35 days (Lynn, 1970). *Pseudemys scripta* kept under continuous light and constant temperature (28°C) for 4.5 months showed a pronounced depression of plasma T4 (2.6 +/- 1.1 ng/ml) compared to animals raised under variable conditions (T4 = 69.6 +/- 22 ng/ml) for the last 2 months (Licht, et al, 1990). In soft-shelled turtles, *Lissemys punctata punctata,* thirty days exposure of short photoperiod (2 hours light, 22 hours dark) stimulated thyroid activity and long photoperiod (22 hours dark, 2 hours light) inhibited thyroid activity (Sarkar, 2007). Plasma T4 levels in captive green sea turtles, *Chelonia mydas*, with little environmental annual and seasonal temperature variation (Cayman Turtle Farm, Grand Cayman Islands) remained uniform (Licht, Wood, Wood, 1984). Gravid reptiles (*Lacerta*) may have higher thyroid values because they are basking more which raises body temperature (Lynn, 1970).

At the risk of overgeneralization, several seasonal patterns are typical. In a wide variety of temperate reptiles (*Sceloporus*, *Lacerta*, *Dipsosaurus*, *Natrix*, *Vipera*, *Gopherus*, *Chrysemys*, *Trachemys*, *Pseudemys*) thyroid activity is high during summer higher temperatures and low during winter lower temperatures (Sengupta, et al, 2003, Miller 1955, Gartner, et al. 1965, Chui, et al. 1969, Kohel,2001) even in some non-hibernating species (Xantusia, Leilopisma). But the picture is generally never so simple. For example, in Sceloporus thyroid levels peak with female folliculogenesis and ovulation then decrease from July through September during some of the hottest months when the lizards aestivate (Lynn, 1970). In many species reproductive activity can cause spikes in thyroid values. T4 levels in *Gopherus agassizii* were lowest just before and during hibernation, rose during early emergence and peaked in early spring in females then declined from May through August. Males showed a second peak in July and August coincident with male-male combat and spermatogenesis (Kohel, 2001). Some reptiles (*Natrix*, *Naja*, *Vipera*) don't conform to this pattern having lower thyroid activity in the summer and peaks associated with mating or forging behavior (Chui, et al, 1969). The highest seasonal values in *Cnemidophorus* were found during hibernation (Sellers, et al, 1982), these were significantly higher than during warmer summer months. Tropical species, such as *Anolis*, may have higher thyroid values in the cooler months and decreased values in the warmer months when they are often less active (Lynn, 1970).

Nutrition can also influence thyroid levels. Withholding food for 14 days significantly decreased T4 levels in *Gopherus agassizii*, once fed T4 levels rose within 36 hours (Kohel, 2001).

Several drugs can also affect thyroid levels. Melatonin suppressed thyroid activity (Sarkar, et al, 1997), as did propofol (Laforgia, et al, 1992).

Recently Buhler, 2006, found no correlation between ultrasonic thyroid size and blood levels of thyroid hormones. Buhler also found juvenile tortoises had significantly higher T3 values than adult tortoises. Male tortoises had higher fT3 and T3 values than females but it was deemed not clinically significant. Profoundly ill tortoises that often went on to die had significant elevations of fT3 (Buhler, 2006).

THYROID AND PITUITARY DISEASES

Goiter

Goiter is the enlargement of the thyroid gland in an attempt to compensate for a deficiency in iodine. Goiter is now being classified as toxic or nontoxic. Toxic goiter refers to thyroid enlargement associated with alteration in thyroid function, whereas nontoxic goiter represents thyroid enlargement that does not result from an inflammatory or neoplastic process and is not associated with abnormal thyroid function (Gyimesi, et al, 2008).

The most common causes of nontoxic goiter are the result of a dietary deficiency in iodine, or the result of feeding foods high in iodine-binding goitrogens, which are found in, cabbage, kale, broccoli, rapeseed, turnips, mustard seed, cauliflower, Brussels sprouts, and bok choy (Donoghue, 2006; Frye, and Dutra, 1974). Excess dietary nitrates, the result of ingestion of fertilized grasses and hays, vegetables grown hydroponically, and iodine intoxication, the result of over-supplementation, have also been noted to predispose animals to goiter (Gyimesi, et al, 2008; Donoghue, 2006).

Case reports of nontoxic goiter have been documented in giant tortoises (Frye, and Dutra, 1974), an eastern diamondback rattlesnake, *Crotalus adamanteus* (Topper, et al, 1994), a green iguana, *Iguana iguana* (Griffin, 2006), and Kirtland's snakes, *Clonophis kirtlandii* (Gyimesi, et al, 2008).

The most common presenting complaint is a swelling noted cranial to the heart. Note that thymic hyperplasia can also present as a ventral cervical neck swelling (much more distal than goiter) and also has presented in groups of Galapagos tortoises (Fleming, et al, 2004). Few other clinical signs appear to be attributed to nontoxic goiter consistently in the literature. Low T3 and T4 levels, along with a swelling in the neck were used to diagnose goiter in a giant tortoise (Donoghue, 2006), others were diagnosed on necropsy (Gyimesi, et al, 2008; Frye and Dutra, 1974, Griffin, 2006, and Topper, et al, 1994).

Cases in the literature showing a positive response to therapy involve giant tortoises. Unsuccessful attempts were made to appropriately supplement the diet of captive Kirtland's snakes diagnosed with goiter and all snakes died or were euthanized (Gyimesi, et al, 2008). Iodized salts and kelp can and have been used to supplement iodine deficient animals. An estimate of the required dietary iodine in a reptile has been made at one third to one quarter of that needed in humans, and can be calculated as 0.3g/Kg BW (Donoghue, 2006). Buehler (2006) described an adult male Greek tortoise, *Testudo hermanni*, making a whistling respiratory sound with a sonographically enlarged thyroid gland compressing both atria. Blood parameters and thyroid hormone concentrations were within established normal ranges. After one month of 1 mg/kg of potassium iodide orally daily the whistling sound ceased and the sonographic thyroid diameter had decreased from 34 mm to 23 mm and the atria were no longer compressed. Therapy was continued and three months later the ultrasonic thyroid diameter was 16.8 mm. Over the next few months the thyroid diameter remained 17.0 mm ± 0.2 mm and the potassium iodide was reduced to twice weekly doses and the thyroid size remained unchanged sonographically for six additional years.

Two cases of intranuclear coccidiosis had non-toxic goiter, a radiated tortoise, *Geochelone radiata* (unpublished data), and a Bowsprit tortoise, *Chersina angulata* (Garner, et al, 2006). In the radiated tortoise the T4 was 11.5 nmol/L eleven days prior to necropsy and the ventral neck, head and front legs were edematous. The thyroid interstitium was infiltrated by moderate numbers of lymphocytes and plasma cells, which is characteristic of intranuclear coccidiosis. Garner, et al, 2006, found intranuclear coccidiosis in the thyroid of two out of six tortoise cases in which the thyroid was examined. This did not include the Bowsprit with goiter.

Endemic goiter was reported by Zwart and Kok, 1978, in reptiles in the Netherlands. Nontoxic goiter should be suspected in reptiles presenting with an enlargement cranial to the heart, anterior edema and a history of a diet high in goitrogenic compounds, the patient being endemic to an area with soil deficient in iodine, or a history of excessive iodine supplementation.

Hypothyroidism

Hypothyroidism is an uncommonly reported disorder which is characterized by decreased production and release of thyroid hormones resulting in decreased metabolic activity (Rivera and Lock, 2008).

Primary hypothyroidism, the result of idiopathic thyroid atrophy or lymphocytic thyroiditis, and secondary hypothyroidism the result of iodine deficiency in the diet are most commonly implicated in disease (Norton, et al, 1989, Buhler, 2006). Regardless of the cause the cases present in a similar manner and will be discussed as one.

Primary hypothyroidism has been described in a Galapagos tortoise, *Geochelone nigra* (Norton, et al, 1989), and in an African spurred tortoise, *Centrochelys sulcata* (Franco, and Hoover, 2009). Secondary hypothyroidism has been described in the Galapagos tortoise and the Aldabra tortoise (Frye, and Dutra, 1974; Donoghue, 2006; DiGesualdo, et al, 2004). The most common presenting signs are anorexia, lethargy, goiter, myxedema of subcutaneous tissues generally involving the head, neck, and proximal forelimbs. Clinical signs may be suggestive of hypothyroidism, but proper diagnosis should be based on measurements of total T4. There is a growing body of normal values one can reference in the literature (Table 1). The hypothyroid Galapagos tortoise had T3 and T4 values of 6.9 nmol/l and 3.73 nmol/l, respectively which were significantly lower than three normal Galapagos tortoises (Norton, et al, 1989).

Treatment in these cases involves removal of potentially goitrogenic food items from the diet, and supplementation of levothyroxine. A dose of levothyroxine of 0.02mg/kg every 48 hours was used to successfully maintain a euthyroid state in a Galapagos tortoise (Norton, et al, 1989). An African spurred tortoise was treated with levothyroxine at an initial dose of 0.02mg/kg every 48 hours for three and one half months which decreased clinical signs associated with disease, but was ultimately increased to a dose of 0.025 mg/kg every 24 hours to resolve the associated myxedema (Franco, et al, 2009).

Any tortoise presenting with the above clinical signs should have a total T4 evaluated. If possible also look at fT4. If the patient is determined to be hypothyroid the diet should be adjusted and supplementation with levothyroxine should be instituted. Appropriate dose of medication is based on follow-up total T4 measurements, and resolution of clinical signs. The stimulatory effect of TSH on the reptile thyroid has been well established in squamates and chelonians (Sawin, et al, 1981). In *Chrysemys picta,* housed 17 to 29°C, ovine TSH causes a clear rise in plasma T4 (Sawin, et al, 1981). Adult males turtles (n=8) given 1 mg ovine TSH (1.4 U TSH/mg or 3.8 U TSH/kg average dose) SC in the leg (not stated front or rear) significantly rose from less than 13 nmol/l (1 μg/dL) to roughly 26 nmol/l (2 μg/dL) at 12 hours and 39 nmol/l (3 μg/dL) at 24 hours (i.e. more than doubled and tripled) (Sawin, et al., 1981). More work needs to be done, however, it appears a TSH stimulation test could be validated for reptiles.

Hypothyroidism has not been diagnosed clinically in squamates or crocodilians. From the experimental literature we can predict hypothyroidism to result in lizards shedding less, or producing hyperkeratotic sheds, and snakes shedding more frequently (Lynn, 1970, Chui, et al., 1969, Chui, et al., 1970, Chiu, et al, 1983, Chiu, et al, 1986). Snake thyroid metabolism seems different than other animals as previously discussed. In snakes thyroidectomy, hypophysectomy, administration of propylthiouracil and methimazole administration all resulted in snakes shedding more frequently (Lynn, 1970). Frye, 1991, found that most snakes presented for pathologically frequent shedding shed less frequently after treatment with propylthiouracil (10 mg/kg PO SID x 21-30 days) or methimazole (1 -1.25 mg/kg PO SID x 30 days). Frye recommended checking thyroid values before treatment and again at 21 days and adjusting dosage for ongoing treatment.

Hyperthyroidism

Hyperthyroidism is a multisystemic disorder characterized by a state of abnormally high metabolism the result of elevated concentrations of T3 and T4 produced by the thyroid gland. Hyperthyroidism is most commonly caused by hyperfunctional thyroid nodules, thyroid neoplasia, over supplementation of exogenous thyroid hormone, and/or increased TSH secretion the result of pituitary dysfunction (Rivera and Lock. 2008). The experimental evidence suggests that hyperthyroidism should cause lizards to shed more and snakes to shed less (Lynn, 1970, Chui, et al., 1969,Chui, et al., 1970, Chiu, et al, 1983, Chiu, et al, 1986).

There are few cases of hyperthyroidism confirmed prior to necropsy with elevated total T4 levels. A green iguana, *Iguana iguana,* was diagnosed with a functional thyroid follicular adenoma (Hernandez-Divers, et al, 2001), and a leopard gecko, *Eublepharis macularius* was diagnosed with hyperthyroidism (Boyer, et al, 2010). The iguana presented with signs of polyphagia, weight loss, loss of dorsal spines, hyperactivity, increased aggression, and a palpable mass in the ventral cervical region. Diagnosis of hyperthyroidism was based on a T4 of 30.0 nmol/l compared to normals of 3.81 ± 0.84 nmol/l. Surgical thyroidectomy resulted in return to normal appetite, activity levels, weight, heart rate, and regrowth of dorsal spines. The leopard gecko presented with signs of anorexia, diarrhea, and increased shedding frequency (from monthly to every two weeks). Hyperthyroidism was determined by elevated total T4 levels (20.59 nmol/L, repeat T4 5 weeks later was 64.4 nmol/L, compared to mean normal 12.48 nmol/L). Diagnosis was confirmed with technetium scan which revealed a unilateral, midline, caudal cervical, single structure with technetium uptake. The structure was approximately twice the size of the normal thyroid tissue and consistent with an enlarged thyroid gland, and unilateral hyperthyroidism resulting in negative feedback suppression of the contralateral thyroid gland. The leopard gecko was treated with radioactive Iodine-131 at a dose of 0.1mCi injected subcutaneously in the ventral neck region. The radioactive I-131 treatment resulted in a euthyroid state for 5 months post treatment, and resolution of diarrhea, return to normal appetite, and weight gain, but then T4 rose again. This gecko later died of complications of systemic disease, and Boyer, et al, now recommend a dose of radioactive Iodine-131 of 0.2mCi.

Hyperthyroidism is a disease that is likely under diagnosed in reptile medicine. Patients presenting with the above clinical signs should be evaluated for elevated total T4 levels. Surgery was effective in one case, and radioactive Iodine-131 shows promise for future cases.

ENDOCRINE DISRUPTING CONTAMINANTS

Endocrine disrupting contaminants are environmental contaminants which have been shown to alter normal thyroid function. Many reptiles have the potential to be exposed to these contaminants in the wild. There are also a few reports of other drugs which alter normal thyroid function as well in the literature.

Much of the information on endocrine disrupting contaminants has been documented in animals other than reptiles. The pesticide endosulfan was shown to block extrathyroidal conversion of T4 to T3, and carbaryl was shown to cause a decrease in T4 levels and an increase in T3 levels in the freshwater catfish (Sinha, et al, 1991). Administration of a PCB mixture resulted in extreme hypothyroidism in weanling rats (Gray, et al, 1993). There is evidence of alteration in normal thyroid function in the American alligator, *Alligator mississippiensis* after exposure to environmental contaminants in Florida (Hewitt, et al, 2002). Propofol was shown to inhibit thyroid activity, promote steroid synthesis, and caused the appearance of both adrenaline and noradrenaline granules in the cytoplasm of the chromaffin cells in the Italian wall lizard, *Podarcis s. sicula* (Laforgia, et al, 1992). Melatonin inhibited thyroid activity as evidenced by reduction in gland weight, follicular epithelial cell height, thyroid peroxidase, and plasma thyroxine levels in the soft-shelled turtle, *Lissemys punctata punctata* (Sarkar, et al, 1997). Metopirone was shown to cause moderate hypertrophy and degranulation of the thyrotrophic cells of the anterior hypophysis as the result of hyperactivity of the thyroid in the rainbow whiptail, *Cnemidophorus l. lemniscatus* (Del Conte, 1972).

When assessing reptiles with thyroid disorders it is important to consider the possible exposure to endocrine disrupting contaminants, and other concurrent therapies which have the potential to alter normal thyroid function.

SUMMARY

Reptiles are one of the most neglected groups in the study of thyroid physiology (Lynn and Wachowski, 1951). Reptile thyroid physiology is much like that of other vertebrates except for several snake species which seem to have less T4 and higher levels of DIT and MIT, which requires further inquiry. Chelonians and snakes have single thyroid glands, lizards and crocodilians have single, paired or lobed thyroid glands. Reptile thyroid levels are well below that of mammals, with snakes being the lowest and chelonians the highest, crocodilians are similar to birds. Thyroid physiology influences many processes such as shedding, growth, development, reproduction, metabolic rate, nutrient assimilation and activity. Many factors also influence thyroid values including age, sex, diurnal changes, seasonal changes, day length, shedding, illness, stress and breeding. Goiter has been reported in chelonians and a snake, hypothyroidism has be reported in chelonians. Thyroid neoplasia, adenomas and carcinomas, have been diagnosed primarily post-mortem (Table 2), but there have been attempts at treatment, one successfully. Veterinarians are encouraged to generate and validate thyroid normals, validate TSH stimulation tests do more thyroid screening and report on thyroid disease in reptiles.

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Table 1. Normal thyroid values in reptiles, values listed as mean ± standard deviation, range, or 10 to 90 percentiles.

Species	T4 nmol/l	T3 nmol/l	fT4 pmol/l	fT3 pmol/l	Sex #	Temp ^{0}C	Month	S	Reference
Alligators, *Alligator mississippiensis*	4.18 ± 0.31	ND[a]	ND	ND	ND	ND	May	ND	Hewitt, et al, 2002
Freshwater crocodiles, *Crocodylus johnstoni*	3.24 ± 0.6	0.51 ± 0.02	ND	ND	U, 5	30-32	ND	C	Hulbert and Williams, 1988
Garter snakes, *Thamnophis sirtalis*	0.9 ± 0.4	0.28 ± 0.06	ND	ND	U, 6	24-36	Spring	OS	Etheridge, 1993
Garter snakes, *Thamnophis sirtalis*	1.4 ± 0.9	0.46 ± 0.11	ND	ND	U, 6	24-36	Spring	OS	Etheridge, 1993
Corn snakes, *Elaphe guttata*	0.45 -6.06 m = 2.75	ND	ND	ND	U, 10	ND	ND	TV	Greenacre, et al, 2001
Milk snakes, *Lampropeltis triangulum*	0.27 -2.94 m = 1.88	ND	ND	ND	U, 10	ND	ND	TV	Greenacre, et al, 2001
Ball pythons, *Python regius*	0.93 -4.79 m = 2.58	ND	ND	ND	U, 11	ND	ND	TV, C	Greenacre, et al, 2001
Boas, *Boa constrictor*	≤0.24 to 3.98 m = 2.50	ND	ND	ND	U, 11	ND	ND	TV, C	Greenacre, et al, 2001
Eastern fence lizards, *Sceloporus undulates*	13.1 ± 1.71	3.8 ± 0.80	ND	ND	M, 17	23-41	July	IO	John-Alder, et al, 1991
Western fence lizards, *Sceloporus occidentalis*	6.2 ± 0.60	ND	ND	ND	U, 59	21-26	Jan	IO	John-Alder, 1990
Six lined racerunners, *Cnemidophor-us sexlineatus*	1.3 to 5.4	ND	ND	ND	M, 102 F, 140	5 to 31	YR	TV	Sellers, et al, 1982
Desert iguanas, *Dipsosaurus dorsalis*	12.2 ± 2.8	ND	ND	ND	M, 8	24-30	May	IO	John-Alder, 1984
Desert iguanas, *Dipsosaurus dorsalis*	16.7 ± 6.6	ND	ND	ND	M, 16	24-30	May	IO	John-Alder, 1984
Indian garden lizards, *Calotes versicolor*	0.21 - 5.96	0- 2.70	ND	ND	M, 128-160	ND	YR	C	Kar, et al, 1985
Green iguanas, *Iguana iguana*	3.81 ± 0.84	ND	ND	ND	M, 3 F, 4	ND	ND	TV	Hernandez, et al, 2001
Leopard geckos, *Eublepharis macularius*	6.05 -19.3 m =12.48	ND	ND	ND	M, 2 F, 4	ND	ND	TV	Boyer, et al, 2010

Green sea turtles, *Chelonia mydas*	11.4 - 13.5	ND	ND	ND	M, 73	ND	Jan Mar Sept	DCS	Licht, et al, 1985
Shingleback skinks, *Trachydosaurus rugosus*	1.48 ± 0.42	0.14 ± 0.03	ND	ND	U, 9	20-22	ND	C	Hulbert & Williams, 1988
Shingleback skinks, *Trachydosaurus rugosus*	2.62 ± 0.30	0.28 ± 0.05	ND	ND	U, 9	30-32	ND	C	Hulbert and Williams, 1988
Snake necked tortoises, *Chelodina longicollis*	0.69 ± 0.11	0.31 ± 0.03	ND	ND	U, 10	20-22	ND	JV	Hulbert and Williams, 1988
Snake necked tortoises, *Chelodina longicollis*	0.55 ± 0.11	0.28 ± 0.05	ND	ND	U, 10	30-32	ND	JV	Hulbert and Williams, 1988
Painted turtles, *Chrysemys picta*	13.0 ± 2.3	< 0.192	ND	ND	M, 24	17-29	June	TC	Sawin, et al, 1981
Painted turtles, *Chrysemys picta*	24 ± 6	ND	ND	ND	F, 20	17-29	June	TC	Sawin, et al, 1981
Painted turtles, *Chrysemys picta*	6 to 97	ND	ND	ND	M, 128	ND	May - Oct	TC	Licht, et al, 1985
Desert tortoises, *Gopherus agassizii*	0.46 ± 0.12 to 3.15 ± 0.36	< 0.15	ND	ND	M, U	ND	YR	JV	Kohel, et al, 2001
Desert tortoises, *Gopherus agassizii*	0.55 ± 0.10 to 3.69 ± 0.31	< 0.15	ND	ND	F, U	ND	YR	JV	Kohel, et al, 2001
Spurred tortoises, *Geochelone sulcata*	2.0 - 9.0 (10 -90%)	0 - 0.8 (10-90%)	3.0 - 6.0 (10 -90%)	1.5 -4.8 (10 - 90%)	M, 4 F, 8	ND	ND	JVSCP	Franco, et al, 2009
Galapagos tortoises, *Geochelone elephantopus*	10.39 ± 18.72	ND	ND	ND	M, 2 F, 3	ND	ND	BV	DiGesualdo, et al, 2004
Greek tortoises, *Testudo hermanni*	12.8 ± 7.0	0.2 ± 0.1	< 0.45	8.1 ± 2.9	69	ND	YR	TV	Buhler, 2006
Moorish tortoises, *Testudo graeca*	12.3 ± 3.9	0.2 ± 0.04	< 0.45	7.2 ± 1.7	11	ND	YR	TV	Buhler, 2006
Russian tortoises, *Agrionemys horsfeildi*	9.9 ± 4.1	0.1 ± 0.03	< 0.45	5.6 ± 1.4	11	ND	YR	TV	Buhler, 2006

[a]ND = No data, m = mean, M = male, F = female, U = Unknown sex, YR = year round, S = Blood collection site, C = Cardiocentesis, OS = Orbital, infra or suborbital sinus, TV = Tail vein, DCS – Dorsal cervical sinus, JV = Jugular vein, BV = Brachial vein, TC = Tail cut, SCP = Subcarapacial plexus

Table 2. Thyroid and pituitary neoplasias reported in reptiles.

Species	Tumor	Signs related to thyroid disease	Treatment / Response to treatment	Reference
LIZARDS				
Cordylus polyzonas, African sungazer lizard	Thyroid gland adenoma	None listed	None listed	Harshbarger, 1974
Iguana iguana, Green Iguana	Thyroid adenoma	Polyphagia, loss of dorsal spines, hyperactivity, increased aggression, cervical mass, tachycardia	Surgical thyroidectomy. No recurrence at least one year post-surgery, patient became euthyroid.	Hernandez-Divers, et al, 2001
Iguana iguana, Green Iguana	Thyroid c-cell adenoma	None listed	None listed	Frye, 1994
Shinisaurus crocodiluris, Crocodile Lizard	Thyroid adenocarcinoma	Anorexia, lethargy	No response to general treatment, no attempt at treating tumor, found on necropsy	Whiteside and Garner, 2001
Varanus komodoensis, Komodo Dragon	Thyroid follicular adenoma	None listed	None listed	Harshbarger, 1976
SNAKES				
Acrantophis dumerili, Dumerils Ground Boa	Pituitary adenoma	Slowed righting reflex, no other signs could be contributed to the tumor	None, died	Zoltan and Garner, 2007
Elaphe obsoleta rossalleni, Everglades Ratsnake	Pituitary cystadenoma	Dysecdysis, hyperkeratosis, anorexia, slowed righting reflex	No response to general treatment; Euthanized not due to tumor	Dadone, et al, 2010

Pituophus melanoleucus, Gopher Snake	Thyroid adenoma	None listed	None listed	Ramsay, et al, 1992
TURTLES TORTOISES				
Caretta caretta, Loggerhead Sea Turtle	Multicentric lymphoblastic lymphoma (white nodules in thyroid gland)	None listed	None listed	Oros, et al, 2001
Chrysemys picta, Painted Turtle	Thyroid carcinoma	None listed	None listed	Harshbarger, 1976
Geochelone chilensis, Chaco Tortoise	Thyroid adenoma	Incidental finding, chronic renal disease	None listed	Raiti, 2008
Gopherus agassizii, Desert tortoise	Thyroid colloid adenoma (papillary pattern)	None listed	None listed	Frye, 1994
Geomyda trijuga, Indian Black Turtle	Thyroid carcinoma	Metastasis to mediastinum	None listed	Cowan, 1968
Pseudemys geoffronamus, Freshwater Turtle	Thyroid adenoma	None listed	None listed	Machota, 1984
Sternotherus odoratus, Stinkpot Turtle	Thyroid adenoma	Apathy, anorexia, full body edema, anemia	Euthanized	Kolle and Hoffman, 2002
Trachemys scripta elegans, Red-eared Slider	Papillary cystic thyroid carcinoma	Enlarged thyroid gland shifted base of heart caudally	None listed	Gal, et al; 2010