CAUSES OF HYPOTHYROIDISM
Hypothyroidism results in decreased production of the thyroid hormones thyroxine (T4) and triiodothyronine (T3) from the thyroid gland. At least 95% of cases of canine hypothyroidism are believed to be due to acquired primary hypothyroidism. Destruction of the thyroid gland can result from lymphocytic thyroiditis, idiopathic thyroid atrophy, or rarely neoplastic invasion. Secondary hypothyroidism (deficiency of TSH) is well described in humans but uncommonly recognized in the dog. Causes of acquired secondary hypothyroidism in the dog include pituitary neoplasia and pituitary malformations such as cystic Rathke’s pouch. Tertiary hypothyroidism (deficiency of TRH) has not been documented in dogs.

CANINE THYROIDITIS
Approximately 50% of cases of primary hypothyroidism are due to lymphocytic thyroiditis. Grossly the thyroid gland may be normal or atrophic. Histologically there is multifocal or diffuse infiltration of the thyroid gland by lymphocytes, plasma cells, and macrophages. Remaining follicles are small, and lymphocytes, macrophages and degenerate follicular cells may be found within vacuolated colloid. As thyroiditis progresses, parenchyma is destroyed and replaced by fibrous connective tissue. Canine thyroiditis is believed to be immune-mediated, and anti-thyroglobulin antibodies are present in approximately 50% of hypothyroid dogs. Current evidence suggests that follicular cell destruction is due to binding of thyroid autoantibodies to the plasma membrane of follicular cells and subsequent antibody-dependent cell mediated cytotoxicity. Thyroiditis is heritable in the beagle and the Borzoi. Golden Retrievers, Great Danes, Irish Setters, Doberman Pinschers, and Old English Sheepdogs have an increased prevalence of anti-thyroglobulin antibodies.

In idiopathic follicular atrophy there is loss of thyroid parenchyma and replacement by adipose connective tissue. Degeneration of individual follicular cells occurs, with exfoliation of cells into the colloid. Follicular atrophy may be the final result of thyroiditis, however the absence of fibrosis or inflammation suggests that idiopathic thyroid atrophy is a distinct syndrome.

SIGNALMENT
Any breed may develop hypothyroidism, however some breeds such as the golden retriever and the Doberman pinscher have been reported to be at higher risk in several studies. Many other breeds are suspected to have a predisposition for hypothyroidism. Middle aged dogs are at increased risk of hypothyroidism. In one study, mean age at diagnosis was 7.2 years with a range of 0.5 - 15 years. Spayed females and neutered male dogs are at increased risk for developing hypothyroidism compared with sexually intact animals.

CLINICAL SIGNS
Because thyroid hormones influence the function of many organs, hypothyroidism is considered in the differential diagnosis of a wide range of problems. Clinical signs of hypothyroidism may be nonspecific and insidious in onset, and hypothyroidism is commonly misdiagnosed. Common clinical signs attributable to decreased metabolic rate include lethargy, mental dullness, weight
gain, unwillingness to exercise, and cold intolerance. Obesity occurs in approximately 40 percent of hypothyroid dogs, but most obese dogs suffer from over-nutrition rather than hypothyroidism.

**Dermatologic changes:** Dermatologic changes occur in 60-80 percent of hypothyroid dogs. Common findings include dry scaly skin, changes in haircoat quality or color, alopecia, seborrhea (sicca or oleosa), and superficial pyoderma. Hyperkeratosis, hyperpigmentation, comedone formation, hypertrichosis, ceruminous otitis, poor wound healing, increased bruising, and myxedema may also occur. Alopecia is usually bilaterally symmetric and is first evident in areas of wear, such as the lateral trunk, ventral thorax, and tail. The head and extremities tend to be spared. The hair is often brittle and easily epilated, and loss of undercoat or primary guard hairs may result in a coarse appearance or a puppy-like haircoat. Fading of coat color may also occur, and failure of hair regrowth after clipping is common. Signs of decreased metabolic rate in conjunction with dermatologic abnormalities should increase suspicion of hypothyroidism.

Hypothyroid dogs are predisposed to recurrent bacterial infections of the skin such as folliculitis, pyoderma, and furunculosis. *Malassezia* infections and demodicosis are associated with hypothyroidism. Pruritus may occur with concurrent infection. Myxedema (cutaneous mucinosis) is a rare dermatologic manifestation of hypothyroidism characterized by nonpitting thickening of the skin, especially of the eyelids, cheeks, and forehead. It is caused by deposition of hyaluronic acid in the dermis. A rare complication of myxedema is cutaneous mucinous vesiculation.

**Reproductive dysfunction:** Female reproductive abnormalities attributed to hypothyroidism include prolonged interestrus interval, silent estrus, failure to cycle, spontaneous abortion, small or low-birth-weight litters, uterine inertia, and weak or stillborn puppies; however the evidence for this association is weak. Inappropriate galactorrhea apparently due to hyperprolactinemia has been reported in sexually intact hypothyroid bitches. Male reproductive problems attributed to hypothyroidism include low libido, testicular atrophy, hypospermia, and azoospermia. However, a prospective study of six male beagles with $^{131}$iodine-induced hypothyroidism showed no decrease in libido or sperm quality over a two-year period. Decreased testicular size, subfertility, or sterility were reported in association with thyroiditis and orchitis in a colony of beagles.

**Neurologic dysfunction:** Both the peripheral and central nervous systems may be affected by hypothyroidism. Peripheral neuropathy is the best documented neurologic manifestation. Affected dogs have exercise intolerance, weakness, ataxia, quadripareisis or paralysis, deficits of conscious proprioception, and decreased spinal reflexes. Clinical signs resolve with $\text{-thyroxine (T}_4\text{)}$ supplementation. A subclinical myopathy also occurs in hypothyroid dogs. Unilateral lameness reported in hypothyroid dogs may be a manifestation of generalized neuromyopathy.

Dysfunction of multiple cranial nerves (facial, trigeminal, vestibulocochlear) and abnormal gait and postural reactions are also reported in hypothyroidism. Hypothyroid dogs with vestibular deficits have abnormal brain stem auditory-evoked responses and some dogs also have electromyographic abnormalities of appendicular muscles. Clinical signs resolve with $\text{-thyroxine (T}_4\text{)}$ supplementation. Because dogs with vestibular disease may have resolution of clinical signs owing to compensation, a causal relationship is less clear. Although laryngeal paralysis and megaesophagus have been reported in association with hypothyroidism, treatment of hypothyroidism does not consistently result in resolution of clinical signs, and a causal relationship has not been confirmed. Myasthenia gravis has been reported in association with hypothyroidism. Concurrent hypothyroidism may exacerbate clinical signs of myasthenia gravis such as muscle weakness and megaesophagus.
Rarely, cerebral dysfunction occurs in hypothyroidism due to myxedema coma, atherosclerosis, or the presence of a pituitary tumor causing secondary hypothyroidism. Seizures, disorientation, and circling may occur due to severe hyperlipidemia or cerebral atherosclerosis. There is no evidence to suggest that hypothyroidism is a common cause of seizure disorders in dogs, however once dogs are treated with anti-seizure drugs such as phenobarbital, it may become difficult to assess thyroid function because of the effects of these drugs on the pituitary thyroid axis. In myxedema coma, profound mental dullness or stupor is accompanied by nonpitting edema, hypothermia with a lack of shivering, bradycardia, weakness, and inappetence.

**Behavioral changes:** Behavioral abnormalities that have been associated with canine hypothyroidism by some authors include aggression and cognitive dysfunction. Myxedema coma and atherosclerosis can clearly cause cognitive dysfunction in individual dogs, however these manifestations of hypothyroidism are rare. Evidence for causal association between common behavioral problems and hypothyroidism is lacking.

**Cardiovascular system:** Abnormalities of the cardiovascular system such as sinus bradycardia, weak apex beat, low QRS voltages, and inverted T waves occur in hypothyroid dogs. Reduced left ventricular pump function has also been documented, and hypothyroidism may exacerbate clinical signs in dogs with underlying cardiac disease. Although hypothyroidism rarely causes clinically significant myocardial failure in dogs, dilated cardiomyopathy and hypothyroidism may occur concurrently. A recent case report documented dramatic long-term improvement in cardiac function after treatment with l-thyroxine in two Great Danes with concurrent dilated cardiomyopathy and hypothyroidism.

**Ocular changes:** Ocular abnormalities reported in canine hypothyroidism include corneal lipidosis, corneal ulceration, uveitis, lipid effusion into the aqueous humor, secondary glaucoma, lipemia retinalis, retinal detachment, and keratoconjunctivitis sicca, however a definite causal relationship has not been proven. Dogs with experimentally induced hypothyroidism did not develop ocular changes over a 6 month time period.

**Secondary hypothyroidism:** Clinical signs of secondary hypothyroidism are similar to those of primary hypothyroidism, but clinical signs related to a deficiency of other pituitary functions may predominate, particularly if a pituitary neoplasm is present.

**Congenital hypothyroidism:** Congenital hypothyroidism results in mental retardation and stunted disproportionate growth due to epiphyseal dysgenesis and delayed skeletal maturation. Affected dogs are mentally dull and have large, broad heads, short thick necks, short limbs, macroGLOSSIA, hypothermia, delayed dental eruption, ataxia, and abdominal distention. Dermatologic findings are similar to those seen in the adult hypothyroid dog. Other clinical signs may include gait abnormalities, stenotic ear canals, sealed eyelids, and constipation. Affected puppies are often the largest in the litter at birth but start to lag behind their littermates within three to eight weeks of age. It is likely that many severely affected puppies die without a diagnosis in the first few weeks of life. Vertebral physeal fracture causing tetraparesis was reported in a dog with congenital hypothyroidism.

Congenital hypothyroidism with goiter due to an autosomal recessive trait is recognized in Toy Fox Terriers. The defect is due to thyroid peroxidase deficiency and a nonsense mutation in the thyroid peroxidase gene of affected dogs has been identified. A DNA based carrier test is available for screening of breeding animals.

**Hemostasis:** Decreased plasma von Willebrand factor antigen (vWF:Ag) concentration has been reported in hypothyroid dogs; however, studies have failed to demonstrate a relationship between vWF:Ag or Factor VIII activity and thyroid hormone status. Canine hypothyroidism is rarely
associated with clinical bleeding, and platelet function and bleeding times are normal. Concentrations of vWF:Ag do not consistently increase during l-thyroxine treatment of hypothyroid dogs or euthyroid dogs with von Willebrands disease.

**Polyendocrinopathies:** Canine hypothyroidism may occur in association with other immune-mediated endocrine disorders such as hypoadrenocorticism and diabetes mellitus. Hypothyroidism causes insulin resistance and may mask the classic electrolyte changes of hypoadrenocorticism.

**DIAGNOSIS OF HYPOTHYROIDISM**

A clinical suspicion of hypothyroidism should be obtained by evaluation of the signalment, history and physical examination, results of a hemogram, biochemical panel and urinalysis, and measurement of total T<sub>4</sub> concentration. Tests that may be utilized to confirm the diagnosis include measurement of free T<sub>4</sub> and TSH concentration, provocative thyroid function tests, and response to thyroid hormone supplementation. Choice and interpretation of diagnostic tests is based heavily on the index of suspicion for hypothyroidism.

**Clinical Pathology:** Clinico-pathologic changes that are commonly observed in dogs with hypothyroidism are a normocytic normochromic non-regenerative anemia, fasting hypertriglyceridemia, and hypercholesterolemia.

**Basal thyroid hormone concentrations:** The two most important thyroid hormones secreted by the thyroid gland are thyroxine (T<sub>4</sub>) and 3,5,3’-triiodothyronine (T<sub>3</sub>). Thyroxine is the major secretory product of the thyroid gland, while the majority of serum T<sub>3</sub> is derived from the extrathyroidal deiodination of T<sub>4</sub>. Both T<sub>3</sub> and T<sub>4</sub> are highly protein bound to serum carrier proteins such as thyroid binding globulin, transthyretin, and albumin. Only unbound (free) hormone penetrates cell membranes, binds to receptors and has biological activity. Protein-bound hormone acts as a reservoir and buffer to maintain a steady concentration of free hormone in the plasma despite rapid alterations in release and metabolism of T<sub>3</sub> and T<sub>4</sub> and changes in plasma protein concentrations. Free T<sub>4</sub> is mono-deiodinated within cells to T<sub>3</sub>, which binds to receptors and induces the cellular effects of thyroid hormone.

**Total T<sub>4</sub> concentration:** Total T<sub>4</sub> concentration is the most commonly performed static thyroid hormone measurement and is a good initial screening test for canine hypothyroidism. In general a dog with a T<sub>4</sub> concentration well within the normal range may be assumed to have normal thyroid function, however a basal T<sub>4</sub> concentration below the normal range is not diagnostic for hypothyroidism. In this case the animal may be normal, hypothyroid, or suffering from a non-thyroidal illness with a secondary decrease in the basal T<sub>4</sub> concentration (sick euthyroid syndrome). Factors such as time of day, age, breed, and ambient temperature, may affect the total T<sub>4</sub> concentration without altering metabolically active free thyroid hormone concentrations. In one study, 50-60% of normal dogs had a low serum total T<sub>4</sub> at some time during the day. Estrus, pregnancy, obesity, malnutrition, exogenous glucocorticoids, and drugs such as trimethoprim/sulfamethoxazole, anticonvulsants, salicylates, and phenylbutazone may also change the basal T<sub>4</sub> concentration. Systemic illnesses that are particularly likely to decrease basal T<sub>4</sub> concentrations include hyperadrenocorticism, diabetes mellitus, hypoadrenocorticism, renal failure, hepatic failure, and infection. Changes in protein binding, decreased conversion of T<sub>4</sub> to T<sub>3</sub>, inhibition of TSH secretion, and inhibition of thyroid hormone synthesis by the thyroid gland are potential mechanisms for decreased total T<sub>4</sub> concentrations in sick euthyroid dogs.

**Free T<sub>4</sub> concentration:** Since only the unbound fraction of serum T<sub>4</sub> is biologically active, measurement of free T<sub>4</sub> has been hypothesized to be useful in differentiating euthyroid dogs from hypothyroid dogs. Despite the usefulness of free T<sub>4</sub> assays in humans, most single stage solid phase (analogue) commercial assays for free T<sub>4</sub> do not appear to be superior to measurement of total T<sub>4</sub> in the dog, probably due to differences in serum binding proteins. A free T<sub>4</sub> assay which utilizes an equilibrium dialysis step (direct dialysis) has better accuracy than the analogue methods, and is more sensitive and specific for diagnosis of hypothyroidism than total T<sub>4</sub>.
**Total T₃ concentration:** T₃ concentrations are less accurate in distinguishing euthyroid from hypothyroid dogs since T₃ concentrations fluctuate in and out of the normal range even more than T₄ concentrations in euthyroid dogs. Spurious T₃ measurements may also occur due to the presence of anti- T₃ antibodies that may interfere with commercial assays for T₃. Anti- T₃ antibodies result in spuriously high values for T₃ with most assays.

**TSH concentration:** Measurement of canine TSH concentration is useful in dogs with a low total T₄ concentration, because a low T₄ in conjunction with a high TSH is highly specific for diagnosis of hypothyroidism. The main disadvantage of measurement of TSH is the lack of sensitivity for diagnosis of hypothyroidism in the dog. Approximately thirty percent of hypothyroid dogs have a TSH concentration within the reference range. The reasons for this lack of sensitivity are unclear. It has been hypothesized that the current TSH assay may only measure certain isoforms of TSH. Other possibilities include diurnal fluctuation in TSH, effect of concurrent illness or drugs, and pituitary exhaustion.

**TSH stimulation test:** The TSH stimulation test evaluates the response of the thyroid gland to exogenously administered TSH and is a test of thyroid reserve. It is an accurate test of thyroid function in dogs but its use is limited by the expense and limited availability of TSH. The cost of the TSH stimulation test may be decreased by storing reconstituted TSH either refrigerated for up to 1 month or frozen at -20°C for up to 3 months. The protocol requires collection of a serum sample for measurement of a basal T₄ followed by administration of bovine TSH IV at a dose of 0.1 units/kg (maximum dose 5 units). A second sample for measurement of T₄ is collected 6 hours later. Results may reveal a normal response, a blunted response (sick euthyroid syndrome) or no response (hypothyroidism). A diagnosis of hypothyroidism can be confirmed if both the pre and the post T₄ samples are below the reference range for basal total T₄ concentration. A euthyroid state is confirmed if the post T₄ concentration is greater than approximately 3µg/dl. Interpretation of intermediate results is more difficult and should take into consideration the clinical signs and severity of concurrent systemic disease. Human recombinant TSH is also now available, although quite expensive. The recommended dose is 50-100 µg IV with collection of 0 and 4 hour samples. Results are similar to those obtained using the bovine product and this product may be frozen for at least 8 weeks with no loss of potency.

**TRH stimulation test:** In people this test is utilized to evaluate pituitary gland function (change in TSH after TRH adminstration), however in dogs the test has predominantly been used to evaluate thyroid gland function by measurement of change in T₄ concentration after TRH administration. Unfortunately the change is not as large as after TSH administration, and some dogs with normal thyroid function have a decreased response to TRH. For this reason the test is of limited clinical utility. Various protocols have been reported with the most commonly used dose being 0.1 mg/kg of TRH administered IV with samples for measurement of T₄ collected prior to, and 4-6 hours after TRH administration. Side effects such as salivation, vomiting, urination, defecation, miosis, tachycardia, and tachypnea may be observed. Recent studies have suggested that a lower fixed dose of 100 - 600 µg TRH IV, with samples collected at 0 and 4 hours is as reliable as the higher dose and less likely to result in side effects. Change in TSH after TRH administration has also been evaluated as a diagnostic test for hypothyroidism in dogs, however this has no diagnostic advantage over other tests of thyroid function.

**Thyroid ultrasound:** Determination of thyroid gland size and volume by ultrasound may also be a useful adjunctive test for differentiating between hypothyroid and euthyroid dogs. It is important that the study is performed by an experienced operator. Studies suggest that ultrasoundography has low sensitivity but relatively high specificity for diagnosis of hypothyroidism.

**Therapeutic trial:** In some cases the most practical approach to confirming the diagnosis of hypothyroidism is a therapeutic trial. This is an acceptable practice providing the following guidelines are followed: Every attempt should be made to rule out non-thyroidal illness prior to starting a therapeutic trial. There is no evidence that thyroid hormone supplementation is beneficial in dogs with sick euthyroid syndrome, and it may be detrimental. Thyroxine supplementation should be initiated at a dose of 20 µg/kg (0.1 mg/10 lbs) q 12 hours. There are no studies documenting the comparative efficacy of available thyroxine products in the dog. It is
however important to use a product that the clinician is familiar with and that gives a consistent
response in their experience. Small differences between product bioavailability are unimportant
provided therapeutic monitoring is used to guide the choice of final dose, however it is
recommended to use the same product consistently rather than switching brands frequently.
Objective criteria should be used to assess response to treatment. If a positive response to
treatment occurs, the clinician should be prepared to withdraw therapy to confirm that clinical
signs return. This will ensure that dogs with thyroid responsive diseases do not remain on
thyroid supplementation for life. Dogs with thyroid responsive diseases are those dogs in which
the clinical signs improve due to the nonspecific effects of thyroid hormone or unrelated to
therapy. If therapy is unsuccessful, therapeutic monitoring should be performed to identify the
cause of treatment failure. Since an incorrect diagnosis is the most common cause of treatment
failure, the clinician should be prepared to withdraw therapy and pursue other diagnoses.

DIAGNOSIS OF THYROIDITIS

Anti-Thyroglobulin Antibody: Anti-thyroglobulin antibodies (ATA) are found in 42 to 59% of
hypothyroid dogs and are believed to be the result of leakage of thyroglobulin into circulation
due to lymphocytic thyroiditis. A commercially available ELISA assay for ATA is a sensitive
and specific indicator of thyroiditis, with false positive results occurring in less than 5% of dogs
with other endocrine disorders. Because anti-thyroglobulin antibodies are more common in
hypothyroid dogs than euthyroid dogs, their presence may be useful in interpretation of other
tests of thyroid function. It is important however, to recognize that a positive ATA titer may
occur in euthyroid dogs. The proportion of euthyroid dogs with ATA that ultimately develop
hypothyroidism is unknown. In one study, approximately 20% of euthyroid dogs with thyroiditis
developed some evidence of thyroid dysfunction within one year. A small percentage of dogs
(15%) became ATA negative after 12 months. Studies in our laboratory suggest that vaccination
may also cause a short term positive result for ATA. Whether other variables such as viral
infections can also cause transient thyroiditis is unknown. Measurement of ATA has been
advocated for screening breeding stock with the aim of ultimately eliminating heritable forms of
thyroiditis. It has yet to be proven that this is an effective approach.

Anti- T₃ And T₄ Antibodies: Antibodies directed against T₃ and T₄ also occur in canine
thyroiditis, although they are less prevalent than ATA. Anti- T₃ antibodies can be identified in
approximately 30% of hypothyroid dogs. Anti-T₄ antibodies also occur although they are less
common (15% hypothyroid dogs). Since some euthyroid dogs also may have anti- T₃ or T₄
antibodies however, their presence is not diagnostic for hypothyroidism. In the presence of other
equivocal results however, the presence of anti-thyroid antibodies increases the likelihood for
hypothyroidism. Because T₃ and T₄ alone are small molecules, these anti-thyroid hormone
antibodies probably develop against T₃ and T₄ containing epitopes of thyroglobulin. There is a
higher prevalence of antithyroid antibodies in hypothyroid compared with euthyroid dogs, and
antibodies are most prevalent in younger dogs and in breeds with a high prevalence of
hypothyroidism. Antibodies directed against T₃ and T₄ may interfere with hormone assays
leading to a spurious increase (most common) or decrease in the measured hormone
concentration. In theory these antibodies could also increase a low T₄ concentration into the
normal or high range and result in a false diagnosis of euthyroidism or hyperthyroidism. Anti-
thyroid antibodies do not interfere with response to thyroid supplementation in dogs with
hypothyroidism.

TREATMENT OF HYPOTHYROIDISM

Synthetic thyroid hormone products are preferable to those of animal origin since synthetic
products (salts of T₃ or T₄) are more stable and better standardized for potency. Sodium
levothyroxine (synthetic T₄) is the initial thyroid supplement of choice. Levothyroxine has a
serum half-life of 12 - 16 hours and peak concentrations are achieved at 4 - 12 hours after
administration. Recommendations for initiation of therapy are to administer levothyroxine at a
dose of 20 µg/kg twice a day. Some dogs will ultimately only require supplementation once a
day. Once a clinical response is achieved, a trial with once a day therapy can be instituted.
Some authors recommend dosing based on body surface area (0.5 mg/m\(^2\)). In animals with concurrent heart disease a sudden increase in the basal metabolic rate due to initiation of therapy can lead to cardiac destabilization. These animals should be started on 50% of the recommended starting dose for thyroxine and the dose then adjusted using therapeutic monitoring.

Synthetic triiodothyronine administration is only indicated in those few situations when T\(_4\) supplementation has failed to achieve a response in a dog with confirmed hypothyroidism. This may occur due to impaired T\(_4\) absorption from the gastrointestinal tract. T\(_3\) supplementation is not recommended for initial therapy because only serum T\(_3\) concentrations are normalized while T\(_4\) levels remain low. Dogs receiving T\(_3\) supplementation may be more susceptible to iatrogenic thyrotoxicosis since serum T\(_4\) concentrations are important in the feedback regulation of the hypothalamic-pituitary-thyroid axis. Combination products which contain both T\(_3\) and T\(_4\) should be avoided for similar reasons. The plasma half-life of synthetic T\(_3\) is 5 - 6 hours so it needs to be administered three times a day. The initial starting dose is 4 - 6 µg/kg q 8 hours.

**Response to therapy:** Clinical improvement should be observed in 4 - 6 weeks from initiation of therapy although an improvement in the patient's activity level may occur within 1 week. Dermatologic abnormalities may take several months to completely resolve, and initially the appearance of the hair coat may worsen as old hair is shed. Reproductive and clinicopathologic abnormalities are usually the last to resolve.

**Poor response to therapy:** An absent or inadequate response to therapy may be due to incorrect diagnosis, poor owner compliance, inadequate dose of thyroid supplementation, poor oral absorption of thyroid supplement, or use of thyroid supplements of animal origin. Defective conversion of T\(_4\) to T\(_3\), and resistance of peripheral tissues to the action of thyroid hormone are theoretical causes of treatment failure that have not been well documented in dogs.

**Therapeutic monitoring:** Monitoring of serum T\(_4\) and T\(_3\) concentrations will allow the clinician to identify the reason for failure to respond to thyroid supplementation and allow individualization of the dose and dosing frequency. Measurement of serum T\(_3\) and T\(_4\) concentrations should be performed after at least one month of therapy. A serum sample is taken prior to, and 4-6 hours after treatment and submitted for measurement of T\(_4\) concentrations. Dosage and frequency of thyroid supplementation can then be adjusted appropriately. Both T\(_4\) measurements should be in the normal reference range, and typically the post-pill T\(_4\) concentration is slightly above the reference range (up to 6µg/dl is considered acceptable). If it is only possible to collect one sample a post-pill sample should be collected. The utility of measurement of TSH concentration during therapeutic monitoring is unclear since assay sensitivity does not allow detection of mild hyperthyroidism. Documentation of a TSH in the normal range however would be additional evidence of adequate supplementation.

**REFERENCES:**