

12

Examining the Endocrine and Lymphatic Systems of the Dog

12.1 Thyroid Gland Neoplasia in the Dog

Endocrine organs are largely inaccessible to the clinician despite the best efforts to perform a comprehensive physical examination. Only in the intact male are normal endocrine organs readily palpable. All other endocrine organs are either too internal to appreciate, such as the endocrine pancreas, or, in the case of the thyroid gland, are palpable only in certain diseased states.

Recall from Section 4.1 that the thyroid gland consists of two lobes. The right lobe is seated more cranial in the cervical region than the left [1, 2].

In health, the thyroid gland is covered by muscle. It is also intimately associated with key vascular, gastrointestinal, and nervous system landmarks. The right lobe lies in close apposition to the common carotid artery, internal jugular vein, and the vagosympathetic trunk. The left lobe abuts the esophagus and the caudal laryngeal nerve. The vascular supply to this region is quite rich, and is capable of supporting aggressive invasion of thyroid-associated tumors into local tissue [1, 3].

The normal thyroid gland is not typically palpable on the physical examination [3]. The abnormal thyroid gland may or may not be appreciated, depending upon the type of pathology. In senior dogs, the two most common diseased states of the thyroid are acquired hypothyroidism and thyroid neoplasia [4]. Of these, only the latter is palpable.

Thyroid tumors represent 1.1–3.8% of all canine neoplasias [5–8]. Neither sex is predisposed to thyroid neoplasia [9–15]. However, the Beagle, Boxer, Golden Retriever, and Husky breeds appear to be at increased risk within the United States [4, 9, 10, 14, 15]. By contrast, the breeds that are over-represented in Scotland are the Shetland Collie, Old English Sheepdog, and Cairn Terrier [16].

When thyroid tumors develop in the dog, they are more likely to be malignant [6, 9, 10]. Only 9% are adenomas [5]. Thyroid tumors also tend to be large and invasive [4]. The regional anatomy supports expansion of the growing tumor by way of the local blood supply. Because the

trachea, larynx, esophagus, and neurovascular structures are neighbors of the thyroid, these vital structures are likely to be compromised [1, 3, 6, 7].

In stark contrast to cats, canine thyroid tumors tend not to be functional [1]. Fewer than one-quarter of canine patients with thyroid tumors present with clinical or biochemical data that support a hyperthyroid state [6, 10, 11, 17, 18]. It is even less likely to see clinical hypothyroidism secondary to thyroid neoplasia [1, 6, 8]. The risk of developing one or more thyroid tumors increases with age: the incidence is 1.1% in 8–12-year-old dogs compared with 4.0% in 12–15-year-old dogs [3].

The etiology of thyroid tumors is better understood in people than in our canine patients [3]. In people, there is a definitive link between excessive exposure to radiation and the development of thyroid cancer [3, 19–21]. Although the possibility of this link in veterinary medicine has been explored experimentally in the laboratory, it has been difficult to extrapolate conclusions to the general canine population [22].

The role of dietary iodine in inducing thyroid cancer has also been studied in people: both deficiencies and excesses of iodine may contribute to thyroidal illness and subsequent neoplasia [3, 23]. However, whether or not this concern is valid in veterinary medicine remains to be determined [3].

Dietary iodine has been researched less extensively in the dog with regard to thyroid cancer and more extensively with regard to feline hyperthyroidism. When it was discovered during the late 1970s that the majority of commercial cat foods contained up to 10 times the recommended level of iodine [24], it was thought that this excess could explain hyperthyroidism. Recommendations for dietary iodine have since been reduced [25], yet hyperthyroidism persists.

Just as more research is necessary to understand the missing links in the etiology of feline hyperthyroidism, so is necessary to explore the causes of thyroid cancer in the dog. Much remains unknown in terms of canine risk factors other than breed. What is known about canine thyroid cancer is that follicular carcinomas predominate [6].

Two-thirds to three-fourths of these malignancies are unilateral [1, 10, 26]. When tumors are bilateral, it is challenging to discern whether each tumor arose independently of the other or whether one tumor was the by-product of the other's metastasis [1].

The rate of metastasis is high in dogs with thyroid carcinomas [1]. At the time of diagnosis, one-third of dogs have detectable metastatic disease [1]. At necropsy, metastasis is recognized in 6–9 out of every 10 dogs [9–11, 14]. The major metastatic sites for thyroid cancer in the dog are the regional lymph nodes and the lungs [6, 7]. Because the nodes cranial to the thyroid are responsible for draining lymph, the submandibular, parotid, and medial retropharyngeal nodes are most commonly implicated [2]. Pulmonary metastasis occurs when neoplastic cells invade the neighboring cranial and caudal thyroid veins [1, 14].

12.2 The Typical Presentation of Thyroid Gland Neoplasia in the Dog

Rarely is thyroid gland neoplasia an incidental finding on physical examination [3, 9, 27]. More often than not, veterinary clients are the ones responsible for identifying a cervical swelling [9, 11, 16, 26–28] and presenting the dog to a veterinarian for evaluation within 1–2 months [3]. Clients typically report rapid growth of a firm, yet apparently non-painful mass that may or may not be freely moveable within the cervical region, depending on how aggressively invasive the tumor is at the time of initial diagnosis [3].

To confirm the presence of a ventral cervical mass, all the clinician needs to do is to firmly cup a hand and guide it down the ventral midline of the neck. To facilitate this motion, the thumb should be on one side of the neck and the fingers should be against the other. The palm is what cups the ventral midline. The author then concentrates on applying firm pressure to the thumb and fingertips to appreciate the ventrolateral structures of the neck. If one or both of the thyroid gland lobes are involved, one or more firm masses should be evident in the region of the throat. An exception would be if the thyroid tumor(s) arose from ectopic thyroid tissue, which may extend well into the thoracic inlet and out of reach of the clinician's fingertips [1, 2, 6, 7].

Because of their tendency to metastasize to regional lymph nodes, thyroid carcinomas may also present for one or more swellings under the angle of the mandible due to submandibular lymphadenopathy [2, 4]. See Section 11.6 to review the proper technique for palpating the submandibular lymph nodes of a dog.

The patient may be otherwise asymptomatic. However, as the enlarging mass begins to compress surrounding soft

tissue structures, additional clinical signs may develop that raise the client's level of concern. When the upper airway or the pharynx is compressed, the patient may present with cough or dysphonia [9, 11, 13, 14]. As the lower airway becomes involved, dyspnea may develop. Compression of the esophagus may lead to dysphagia and retching [1, 11, 14, 26]. Over time, this may cause anorexia and result in weight loss [4]. Rarely, venous and lymphatic drainage are compromised [9]. When this occurs, cervical swelling is exacerbated and the patient may appear to be edematous in the face and throat [3, 4, 9].

Functional thyroid tumors may induce hyperthyroid-associated clinical signs; however, these are not typically as pronounced in the dog as they are when present in the hyperthyroid cat [7, 8, 18]. See Section 4.1.1 to review the typical clinical presentation of a hyperthyroid state.

When the clinician confirms the client's concern that a mass is present along the throat, he should prioritize thyroid tumors as a differential diagnosis given the location. However, until a diagnostic work-up is performed to confirm these suspicions, additional differentials must be considered. Abscesses and granulomas secondary to foreign bodies such as a stick ingestion gone awry cannot be ruled out by palpation alone. Less common, but possible differentials include salivary mucoceles, carotid body tumors, and soft tissue sarcomas [1, 3].

The utility of imaging, particularly ultrasound, as a diagnostic modality is that it helps to differentiate thyroid tumors from aforementioned differentials [1]. Ultrasound is also advantageous because it allows the clinician to make an assessment about the vascularity of the tumor as well as its invasiveness. In addition, ultrasound may facilitate fine needle aspiration (FNA) of samples although biopsies are indicated for definitive diagnosis owing to the low yield and blood contamination that are frequently associated with FNAs [1, 14, 29].

Because of the rapid rate with which thyroid carcinomas expand and the high likelihood of invasion into surrounding soft tissue structures, a rapid diagnosis is critical. The prognosis for untreated patients is poor: median survival time is 3 months following the diagnosis [28] compared with more than 3 years when treated with surgical excision [1, 26], and up to nearly 4 years with radiation therapy [30, 31].

12.3 The Pathophysiology of Hypothyroidism

Acquired hypothyroidism is a frequent occurrence in senior dogs [4]. It results from underproduction of thyroxine (T4) and triiodothyronine (T3). In theory, this could arise as a primary disorder (originating from

the thyroid gland itself), secondary disorder [originating from impaired stimulation of the thyroid gland by the pituitary gland via thyroid-stimulating hormone (TSH)], or tertiary disorder [originating from impaired stimulation of the thyroid gland indirectly by the hypothalamus via thyrotropin-releasing hormone (TRH)] [32].

In reality, 95% of the cases of canine hypothyroidism are due to dysfunction at the level of the thyroid itself [32]. Of these cases, 50% are caused by lymphocytic thyroiditis [33], an immune-mediated condition marked by progression destruction of thyroid gland architecture [32]. The remaining 50% of cases of primary hypothyroidism in dogs are caused by idiopathic atrophy: thyroid parenchyma is subsequently replaced by adipose tissue [32].

In health, thyroid hormones contribute to metabolic rate, oxygen consumption, and heart rate. Thyroid hormones act as inotropes and chronotropes, thereby enhancing the response of the heart to catecholamines [32].

Across all age groups of dogs, puppies have the highest T4 concentrations, and as they mature, the levels steadily decline. Dogs older than 6 years of age have total thyroxine (TT4) concentrations that are 21% lower than in young adult dogs [34], and old dogs have TT4 concentrations that are 40% lower than in young adults [4, 32, 35]. This age-related decline in thyroid hormone concentrations is poorly understood. It may be that the thyroid gland becomes less sensitive to TSH or that the thyroid gland degenerates with age [4].

In addition to age, other variables such as pharmaceuticals can adversely impact the hypothalamic–pituitary–thyroid axis. Glucocorticoids, for example, affect the way in which the body metabolizes thyroid hormones. In addition, glucocorticoids inhibit the secretion of TSH. Sulfonamides block the synthesis of thyroid hormones by inhibiting iodination, and phenobarbital decreases TT4 and free T4 (FT4) [4].

Concurrent non-thyroidal illnesses such as hypoadrenocorticism, diabetic ketoacidosis, and organ failure can also suppress the hypothalamic–pituitary–thyroid axis [4, 36–39]. The decline in total thyroid hormone is proportional to the severity of the illness; severe decreases are associated with higher mortality rates [4, 40, 41].

Breed is yet another factor that impacts the hypothalamic–pituitary–thyroid axis. In a study by Shiel *et al.*, 91% of young, healthy Greyhounds were found to have TT4 concentrations either below or at the low end of the normal reference range [42].

However, despite the influence of these factors – age, pharmacologic agents, and breed – some middle-aged to older dogs do in fact develop clinically relevant hypothyroidism.

12.4 The Typical Presentation of a Hypothyroid Dog

The challenge of canine hypothyroidism is that the pathology within the thyroid gland cannot be detected on physical examination. Unlike thyroid neoplasia, in which there is a palpable, sometimes even grossly visible cervical mass, dogs with hypothyroidism palpate as being normal, that is, the clinician is unable to feel the thyroid gland to detect that something is amiss.

At first glance, it may strike the reader as unusual for hypothyroidism to be included in a physical examination textbook, given that the thyroid of a hypothyroid dog is not palpable. However, it is important to mention the hypothyroid dog with regard to the physical examination because very often these patients present with classic historical or examination-related findings.

The typical canine patient with hypothyroidism is a purebred dog [43, 44]. Specifically, the breeds considered at an increased risk for developing this endocrinopathy are Golden Retrievers, Doberman Pinschers, Labrador Retrievers, and Cocker Spaniels [4, 32]. Boxers, Dachshunds, Miniature Schnauzers, Great Danes, and Old English Sheepdogs are also overrepresented in the literature [45, 46].

With the exception of congenital hypothyroidism, which has been reported in the juvenile Giant Schnauzer [47], Boxer [48], and Scottish Deerhound [49], the majority of hypothyroid patients are middle- to older-aged [33].

Because thyroid hormones regulate metabolism and hypothyroidism implies a sluggish metabolic rate, clients may report unusually sloth-like behavior. The patient may be inactive or sedentary. Initially clients may liken this to a normal by-product of aging; however, its persistence may become concerning. Clients may also report decreased mental stimulation: the patient may be less engaged with the client and/or its surroundings. Both the client and veterinarian may remark upon the patient's weight gain despite the client's insistence that there has been no change in diet [4, 45, 50].

On physical examination, 60–80% of hypothyroid dogs display a classic dermatopathy [51, 52]: bilaterally symmetrical, non-pruritic truncal alopecia with an alopecic “rat tail.” The head and distal limbs tend to remain unaffected compared with the areas of wear along the body. What coat remains tends to be dull, coarse, and/or brittle. In some cases, the undercoat may be lost altogether, with or without the loss of primary guard hairs, giving the patient the appearance of having retained its puppy coat [4, 32, 45, 50].

Because the anagen phase of hair growth requires thyroid hormones, the lack thereof may cause a patient

not to regrow its fur post-clipping. As a result, many patients present for coat-related concerns following grooming [4, 50].

The skin itself may be normal or it may become excessively flaky and/or greasy. In areas of wear where the coat has thinned, the underlying skin may exhibit hyperpigmentation or even hyperkeratosis [50].

Other hypothyroid patients may present for recurrent bacterial skin infections [50]: 20–30% of dogs with hypothyroidism are diagnosed with pyoderma [51, 52]. Systemic *Malassezia* overgrowth is also not uncommon [50]. When these secondary infections develop, hypothyroid patients become pruritic [50].

Rarely does myxedema, the deposition of hyaluronic acid in the dermis, causing edema, occur [50]. Hyaluronic acid is in excess in these patients because the lack of thyroid hormone reduces the metabolic breakdown of glycosaminoglycans [53]. The result is thickened, puffy skin over the forehead, eyelids, and cheeks [50]. Vesicles develop on the surface of the affected skin [50, 54]. Mucin may be expressed digitally from these vessels as a clear, stringy substance [50].

When a canine patient of the “right” age and breed presents with a history and/or physical examination findings that mirror the above, then a diagnosis of hypothyroidism should be considered until proven otherwise.

12.5 The Atypical Presentation of a Hypothyroid Dog

Hypothyroid dogs may also present, albeit rarely, with neurologic signs in the absence of dermatopathy [4, 55–58]. Although the etiology remains unknown in dogs, it has been demonstrated in rats that hypothyroid-induced reduction in axonal transport leads to peripheral neuropathy [59]. The mechanism underlying cranial nerve dysfunction secondary to hypothyroidism is even more unclear; however, it has been hypothesized that the deposits of mucin compress the cranial nerves where they exit the skull [60, 61]. Of all cranial nerves, the trigeminal, facial, and vestibulocochlear nerves are most likely to be impacted [55, 60].

Although the canine neurologic examination will be reviewed in detail in Chapter 16, it should be recognized that endocrinopathy can result in peripheral neuropathy or peripheral vestibular syndrome, and that a patient that presents with either may not have a primary neurologic disease [55].

In particular, a middle-aged to older, middle- to large-sized breed that presents for slowly progressive neurologic deficits may in fact be hypothyroid. These patients tend to show mild gait deficits that then

develop into paraparesis or tetraparesis. They may or may not be ataxic. Spinal reflexes may be reduced in all four limbs, although the hind limbs tend to be the most impaired. Although these patients necessitate a full orthopedic and neurologic work-up to rule out potential pathology that could require surgery, it is important that the clinician not wear blinders and be cognizant that hypothyroidism is a possibility. When hypothyroidism is implicated in neurologic disease, the patient can recover: neurologic signs are reversible after 2–3 months of supplementing the patient with thyroxine [55, 59, 62].

Atypical hypothyroid patients may also exhibit intermittent or constant forelimb lameness that is responsive to treatment with thyroxine [55, 58, 59]. In addition, hypothyroid-induced facial paralysis and vestibular dysfunction, characterized by a head tilt, ataxia, circling, strabismus, and nystagmus, are responsive to thyroxine supplementation [55, 56, 60, 61].

Although these clinical signs represent atypical presentations of hypothyroidism, they serve as good reminders that a systems-based approach to the physical examination, although effective in teaching the novice clinician to be comprehensive, must ultimately integrate physical examination findings, given the overlap between systems. The astute clinician must learn to construct the isolated details into a complete clinical picture. Neurologic disease may not simply be neurologic disease; dermatologic disease may not simply be dermatologic disease; endocrinopathy may not simply be straightforward endocrinopathy. In other words, they may be inextricably linked. It is up to the clinician to recognize that link if diagnosis and treatment are to be facilitated.

12.6 Assessing the Lymphatic System

Just as the clinician is limited by which components of the endocrine system are palpable on the physical examination, the clinician is granted few opportunities to evaluate the lymphatic system.

As discussed in Section 4.2, the lymphatic system neighbors the vasculature. Its series of lymph vessels exist to collect fluid and proteins that are forced out of blood vessels by hydrostatic pressure. The vessels then return this excess fluid to the general circulation via lymphatic ducts. Without this network, peripheral tissues would rapidly drown in edema [63].

With the exception of lymphatic obstruction, which causes grossly visible edema, the clinician is unable to evaluate the lymphatic vasculature individually. The only structures of the lymphatic system that the clinician is able to assess at each visit are the lymph nodes.

Think of the lymph nodes as filters of lymph as well as sites for lymphocytes to proliferate and differentiate [63].

Lymph nodes are positioned in the body where they interfere least with mobility and the circulation [63]. The peripheral lymph nodes tend to be paired. Three sets are typically palpable in the normal patient [64]:

- the submandibular lymph nodes;
- the superficial cervical lymph nodes, otherwise referred to as pre-scapular lymph nodes;
- the popliteal lymph nodes.

These sets of lymph nodes should be palpated at each visit, with the clinician noting their size, shape, consistency, and symmetry, and whether palpation is painful. Lymph nodes should feel rubbery [65], like scallops. They should not be tender to the touch.

12.7 Examining the Submandibular Lymph Nodes

See Section 11.6.

12.8 Examining the Superficial Cervical or Pre-Scapular Lymph Nodes

The superficial cervical or pre-scapular lymph nodes are located at the cranial border of each scapula, covered by the cleidocervical and omotransversarius muscles. These nodes are oval, flat, and typically paired when comparing the left and right sides of the body. There may be as few as one and as many as four on each side, the right and the left. They collectively drain the neck, shoulder, and corresponding forelimb [63, 66].

To palpate the superficial cervical or pre-scapular lymph nodes, the clinician may stand directly behind the patient or immediately in front. The author prefers the former approach, using her left hand to palpate the left nodes and the right hand to palpate the right nodes. Both hands are used simultaneously to appreciate significant differences in symmetry, size, and consistency between sides.

The patient can be seated or standing for this exercise. The clinician simply follows his fingertips up from the humerus to the point of the shoulder. At the point of the shoulder, the clinician's thumb and index finger should grasp deep to the scapular border. As the clinician then moves his thumb and index finger from deep to superficial, the lymph nodes should "slip" through, much like a thyroid nodule can be felt to "slip" through the fingertips upon ventral neck palpation (Figure 12.1).



Figure 12.1 Palpating the superficial cervical lymph nodes by grasping deep to the scapular border at the point of the shoulder. Source: Courtesy of the Media Resources Department at Northwestern University.

12.9 Examining the Popliteal Lymph Nodes

The popliteal lymph nodes are located at the caudal aspect of each stifle, sandwiched between the biceps femoris and semitendinosus muscles. These nodes are more round than the superficial cervical lymph nodes. They are paired structures, with typically one on each side, the right and the left. They collectively drain the distal hind limbs [63, 66].

To palpate the popliteal lymph nodes, the clinician should stand behind the patient with the patient facing in the same direction as the clinician. The clinician should pinch the thumb and index finger of each hand together as if crimping pie crust. Together, the thumb and index finger of the left hand are placed over the left caudal thigh; the thumb and index finger of the right hand are placed over the right caudal thigh. Beginning at the caudal thigh, the thumb and index finger are then progressively slid down the thigh to the caudal stifle, applying firm and constant pressure all the way. At the level of the caudal stifle, the clinician can grasp deep to the skin. As the clinician's fingertips move from deep to superficial, the lymph nodes should "slip" through (Figure 12.2).



Figure 12.2 Palpating the popliteal lymph nodes. This patient had a tendency to want to sit down, so the clinician has supported the dog's weight to keep it standing by placing her knee under the dog's caudal abdomen. Source: Courtesy of the Media Resources Department at Midwestern University.

12.10 Feeling for Lymph Nodes That Should Not Be Present

Compared with the submandibular, superficial cervical, and popliteal lymph nodes, which should be appreciated at every visit, there are two sets of lymph nodes that are not typically palpable in health:

- 1) the axillary lymph nodes;
- 2) the superficial inguinal lymph nodes.

The axillary lymph nodes are located, as their name implies, within the arm pit, caudal to the shoulder joint. The teres major muscle forms its lateral boundary, and the rectus thoracis muscle forms its medial boundary. The axillary lymph nodes are disc-shaped and deeper than expected, which is why they are not normally palpable. They drain the thoracic wall and the thoracic limbs and also the thoracic and cranial abdominal mammary glands [63, 66].

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Even though the axillary lymph nodes are not typically palpable, the clinician should feel for their presence at each visit. The only way that the clinician will know if they are enlarged is if he feels for them. By including this palpation in each examination, the clinician develops consistency in his approach to the physical examination and is less likely to miss them on the rare occasion when they are enlarged and in need of a more extensive work-up.

To feel for the axillary lymph nodes, the clinician should stand behind the patient with the patient facing in the same direction as the clinician. The clinician should take flattened hands with fingers pressed together and slide them into the axilla: the left palm against the left axillary and the right palm against the right axilla. Using his fingertips as a paddle, the clinician should start by reaching rostrally and then moving caudally. The act of strumming one's fingers back and forth should allow the lymph nodes to “blip” past the clinician's fingertips if they are indeed enlarged.

The superficial inguinal lymph nodes are located where the caudoventral abdominal wall meets the medial thighs. There are one to two nodes per side, and their shape is typically oval. These drain the abdominal and inguinal mammary glands. They also receive drainage from the popliteal nodes, ventral pelvis, tail, and the medial thigh, stifle, and crus. In the male, drainage includes the penis, prepuce, and scrotum [63, 66].

To palpate for the superficial inguinal lymph nodes, which are appreciated only in diseased states involving lymph drainage, the clinician should stand behind the patient with the patient facing in the same direction as the clinician. The clinician should take flattened hands with fingers pressed together and slide them into the crease between the medial thigh and the abdominal wall: the left palm against the left crease and the right palm against the right crease. Using his fingertips as a paddle, the clinician should feel dorsolateral to the last mammary gland. The act of strumming one's fingers back and forth should allow the lymph nodes to “blip” past the clinician's fingertips if they are indeed enlarged. Alternatively, the clinician may palpate this region one side at a time with the patient in lateral recumbency and each hind limb gently abducted.

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