Ultrasonographic examination of selected small structures in dogs and cats: thyroid glands, lymph nodes and adrenal glands

Echografisch onderzoek van specifieke kleine structuren bij hond en kat: de schildklier, de lymfeknopen en de bijnieren

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ABSTRACT

Ultrasonography has become an important imaging modality for the evaluation of small structures, such as thyroid glands, lymph nodes and adrenal glands, because it is relatively inexpensive, it is non-invasive and it does not require general anesthesia. Both normal and abnormal small structures can be seen, though this depends to a great extent on the quality of the equipment and the operator skills. For thyroid glands, it can be used to assess thyroid carcinomas, canine hypothyroidism and feline hyperthyroidism. Ultrasonography is also a very valuable modality for evaluating superficial and abdominal lymph nodes. By combining different ultrasonographic criteria, it is possible to accurately differentiate normal from reactive or malignant lymph nodes. Finally, the adrenal glands can be evaluated ultrasonographically in cases of hyperadrenocorticism (pituitary- or adrenal-dependent), hyperaldosteronism, hypoadrenocorticism and adrenal neuroendocrine tumors.

SAMENVATTNG

Echografie is een zeer belangrijke beeldvormingsmodaliteit geworden voor de evaluatie van kleine structuren, zoals schildklier, lymfeknopen of bijnieren, en dit omwille van het feit dat de techniek vrij goedkoop en non-invasief is en geen algemene anesthesie vereist. Zowel abnormale als normale structuren kunnen gezien worden, hoewel dit in grote mate afhangt van de kwaliteit van het toestel en de capaciteiten van de operator. Voor de schildklier kan echografie gebruikt worden in het geval van een schildkliercarcinoma of caniene en feliene hypothyroïdie. Echografie is eveneens een waardevolle modaliteit voor het evalueren van opppervlakkige en abdominale lymfeknopen. Door het combineren van verschillende echografische criteria wordt het mogelijk om zeer nauwkeurig normale van reactieve of kwaadaardige lymfeknopen te onderscheiden. Tenslotte kunnen bijnieren echografisch geëvalueerd worden in het geval van hyperadrenocorticisme (hypofyse- of bijnierafhankelijk), hyperaldosteronisme, hyperadrenocorticisme en adrenale neuro-endocriene tumoren.

INTRODUCTION

In small animals, ultrasonography is the method of choice for imaging small organs, whether they are located in the abdomen or superficially. Small organs cannot be detected with radiography, unless severely enlarged or mineralized. Computed Tomography or Magnetic Resonance Imaging could be used for this purpose, but are not routinely performed, as these imaging modalities are more expensive and less available in veterinary clinics. Furthermore, they require deep sedation or general anesthesia.

Hence, ultrasonography is the most common method performed for detecting small organs. It is a non-invasive, inexpensive and rapid technique which avoids the need for general anesthesia. Ultrasonography generally enables the assessment of most of the abdominal organs, including both the largest and the smallest ones, such as the adrenal glands and the lymph nodes. The evaluation of small superficial structures, such as the thyroid gland or the lymph nodes, is also possible. Different parameters of small organs can be evaluated with ultrasonography, including the following: size, shape, margins, echogenicity, structure and vascular flow pattern. Imaging findings coupled with ultrasound-guided fine-needle aspiration or biopsies provide important diagnostic information. However, ultrasonography is equipment and user-dependent and multiple influencing factors may disturb the examination, particularly of small organs.

The aim of this article is to review the usefulness of ultrasonography for the evaluation of the thyroid gland, lymph nodes and adrenal glands in dogs and cats.

ULTRASONOGRAPHY OF THE THYROID GLAND

Imaging anatomy and general principles

Examination of the thyroid gland requires ultrasonographic equipment with a high-frequency transducer (10-12MHz) to increase the spatial resolution of the images. Linear array transducers are recommended, as they provide better visualization of the superficial structures. The entire ventral cervical region should be clipped from caudal to the angle of the mandible to the thoracic inlet, as ectopic thyroid tissue may sometimes be detected. Patients should be positioned in dorsal recumbency, as straight as possible and with the neck extended.

The normal thyroid gland is composed of paired lobes, located adjacent to the lateral walls of the trachea. The thyroid lobes are situated immediately caudal to the cricoid cartilage, which serves as an external landmark for initial transducer placement. The landmarks that are used for the identification of the two thyroid lobes are the medially located trachea, the laterally located common carotid arteries, the ventrally located sternothyroid muscles, and the dorsally located esophagus for the left lobe. Each lobe should first be observed in a longitudinal plane. The landmarks used for the localization of each lobe are the laterally located common carotid arteries and the medially located trachea. The transducer is placed in the jugular groove, just caudal to the larynx to allow visualization of the common carotid artery. The transducer is then angled slightly medially to find the thyroid lobe. Fol-

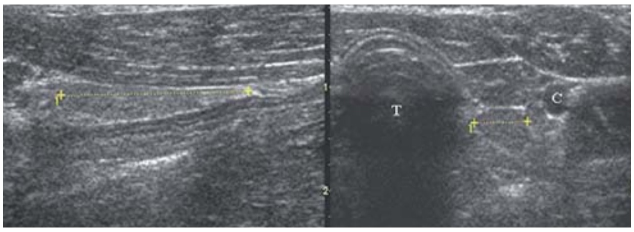

Figure 1. Longitudinal and transverse ultrasound images of a normal canine left thyroid lobe (in between calipers). T = trachea, C = common carotid artery.

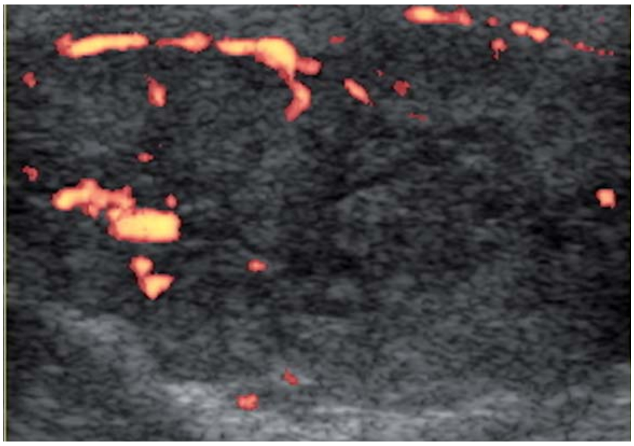

Figure 2. Longitudinal ultrasound image of a canine thyroid carcinoma (with Power Doppler). Note the heterogeneity, increased size and rounding of the lobe. The vascularization of the lobe is increased.

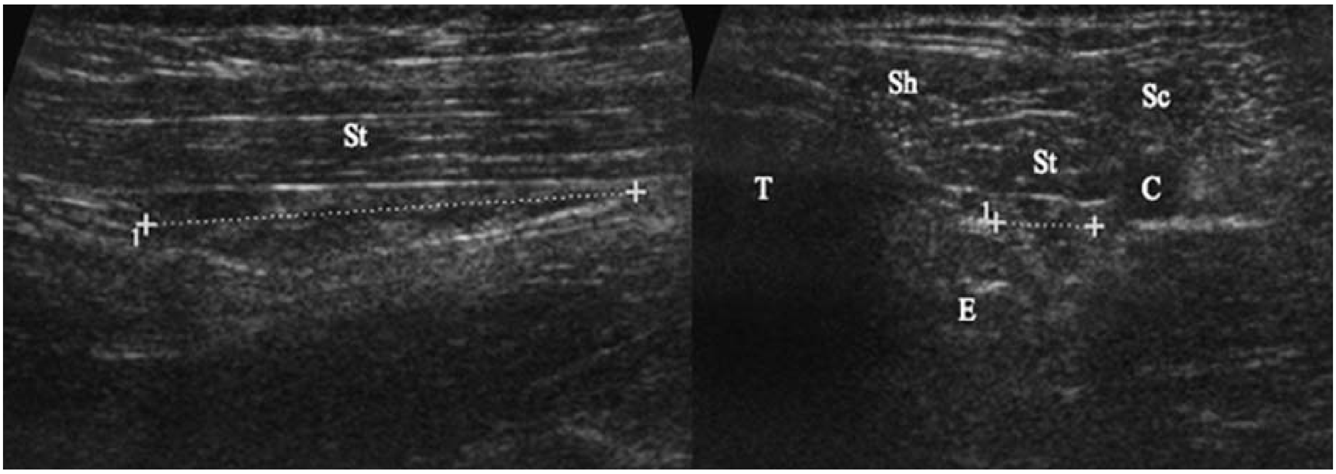

Figure 3. Longitudinal and transverse ultrasound images of the left thyroid lobe of a hypothyroid dog (in between calipers). Note the decrease in size, heterogeneity of the parenchyma and change in shape. T = trachea, C = common carotid artery, E = esophagus, Sh = sternohyoid muscle, St = sternothyroid muscle, Sc = sternocephalic muscle.

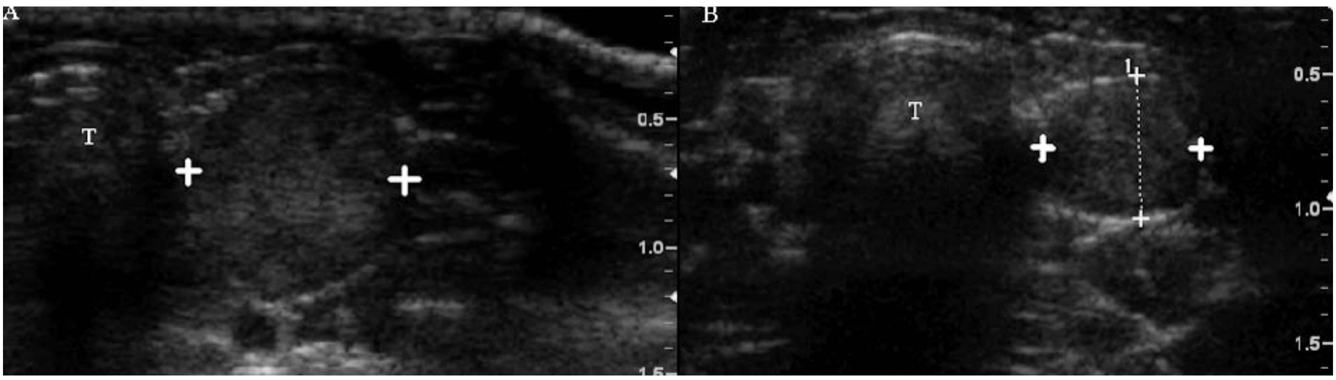

Figure 4. Transverse ultrasound images of the left thyroid lobe of a hyperthyroid cat pre- (A) and post-treatment (B) with radioactive iodine 131I. Pre-treatment, the lobe was very round and heterogeneous with small ill-defined hypoechoic areas. Six months post-treatment, the lobe was graded as moderately round. T: trachea.

lowing this, a transverse image of each lobe may be obtained either by slowly rotating the probe 90° or by using a transverse image of the common carotid artery and the trachea as landmarks. In this case, scanning is started in the midline, just caudal to the larynx, followed by a slow gliding motion of the probe caudally (Wisner *et al.*, 1991; Wisner and Nyland, 1998; Taeymans *et al.*, 2007).

The normal thyroid gland is homogeneous and well delineated, with a hyperechoic capsule. Its parenchyma is most often hyperechoic compared with the surrounding musculature, and its size is correlated with the size of the dog (Wisner *et al.*, 1991; Wisner and Nyland, 1998; Brömel *et al.*, 2006). Each lobe has a more or less triangular shape on a transverse plane and a fusiform shape, with a rounded cranial end and a pointed caudal end, on a longitudinal plane (Figure 1) (Wisner *et al.*, 1991; Wisner and Nyland, 1998).

Ultrasonography of the thyroid gland has three main indications: evaluation of canine thyroid gland carcinoma, canine hypothyroidism and feline hyperthyroidism.

Thyroid gland carcinoma in the dog

The possible origins of undifferentiated neck masses include lymphadenopathy, abscess, granuloma, salivary gland inflammation and neoplasia. To determine the origin of the mass, both thyroid lobes should be identified in order to rule a mass of thyroid origin in or out. It is sometimes difficult to document the thyroidal origin of the mass when its size is such that the normal anatomy of the cervical area is disrupted (Wisner *et al.*, 1994; Wisner and Nyland, 1998).

Thyroid carcinomas appear as large non-homogeneous or complex masses, sometimes containing multiple cysts. The echogenicity of the carcinomatous gland is often decreased, without distal enhancement. Hyperechoic foci representing calcification or dense connective tissue can be found. Thyroid carcinomas can be either well marginated with a definable capsule or poorly marginated. Particularly in poorly delineated neoplasms, the invasion of surrounding structures such as the esophagus, the fascial sheaths and the cervical vasculature can be detected. This information is very useful in determining whether surgical treatment is a possible option. The masses are highly vascular on Power or Color Doppler, and a large arterial vascular plexus may be distributed in and around the thyroid mass (Figure 2). The development of arteriovenous malformations either on initial presentation or after surgical intervention has been reported (Wisner *et al.*, 1994; Wisner and Nyland, 1998).

Diagnosis can be confirmed preferentially by fine needle aspiration, or else by tissue core biopsy, both performed using ultrasound-guidance to avoid large arterial vessels. Ultrasonography is also used to evaluate the regional lymph nodes (generally the retropharyngeal lymph nodes) for detecting metastatic lesions. Other common sites of metastasis of thyroid carcinomas are the regional lymph nodes (generally the retropharyngeal lymph nodes) and the lung, hence thoracic radiographs are necessary (Wisner and Nyland, 1998). Other potential but less frequent sites of metastases are liver, kidneys, adrenals, spleen, prostate, brain, spinal cord, bone, and bone marrow (Feldman and Nelson, 2004a).

Canine hypothyroidism

Ultrasonography of the thyroid gland may be used as an aid in the diagnosis of primary hypothyroidism and in the differentiation between euthyroid sick syndrome and primary hypothyroidism. The appearance of the gland is normal in dogs with euthyroid sick syndrome (Brömel *et al.*, 2005; Reese *et al.*, 2005). Ultrasonographic features of the thyroid gland in dogs with primary hypothyroidism include a hypoechoic parenchyma compared with the overlying sternothyroid muscle, a heterogeneous parenchyma, an irregular outline, a decrease in size, and a more rounded shape of the lobe on transverse images (Figure 3). One or several of these changes may be present at the same time in the same lobe, and the ultrasonographic features may differ between the two lobes (Brömel *et al.*, 2002; Brömel *et al.*, 2005; Reese *et al.*, 2005; Taeymans *et al.*, 2007). An increasing number of abnormalities detected in the same gland results in a sensitivity of 98% for diagnosing hypothyroidism in dogs (Reese *et al.*, 2005; Taeymans *et al.*, 2007). Care should be taken, however, when measuring the gland because of relatively high interobserver variability. When comparing different dogs or when performing a follow-up of the gland size over time, it is advisable that the same sonographer performs the measurements. Using the height and volume of the gland results in the lowest intra- and interobserver variability in evaluating the gland size (Taeymans *et al.*, 2005).

Feline Hyperthyroidism

Feline hyperthyroidism is the most frequent endocrine disease in cats and is most commonly due to multinodular adenomatous hyperplasia or adenoma(s). It is bilateral in 70% of the cases. It is generally diagnosed by a combination of signalment, clinical signs, physical examination, serum thyroid hormone levels and scintigraphy. Thyroid scintigraphy can determine whether the lesion is unilateral or bilateral and is valuable in detecting ectopic hyperfunctioning thyroid tissue, particularly in the mediastinum. It may also detect metastases in rare cases of thyroid carcinomas. However, scintigraphy involves radiation exposure to the patient and personnel and it is not widely available (Feldman and Nelson, 2004b).

When scintigraphy is not available, thyroid ultrasonography may be useful in detecting abnormal thyroid lobes, calculating thyroid lobe volume and differentiating bilateral from unilateral disease (in order to select the most appropriate treatment). The normal feline thyroid gland appears as two moderately echogenic and homogeneous fusiform lobes, bounded by a thin hyperechoic fascia. The normal total thyroid volume is inferior to 200 mm^3 (Wisner *et al.*, 1994;

Wisner and Nyland, 1998). In hyperthyroid cats, thyroid lobes may become severely enlarged (mean total thyroid volume > 800 mm^3) and severely rounded because of a dramatic increase in thickness. The lobes may also appear diffusely hypoechoic and/or heterogeneous, with some hypoechoic to anechoic cyst-like areas (Wisner *et al.*, 1994; Wisner and Nyland, 1998; Barberet *et al.*, 2010). With Color or Power Doppler ultrasonography, the vascularity of the thyroid gland can be assessed in hyperthyroid cats; this vascularity is usually moderately to severely increased (Barberet *et al.*, 2010). Thyroid ultrasonography shows good correlation with scintigraphy in differentiating unilateral from bilateral disease, with 85.7% agreement between the two techniques (Wisner *et al.*, 1994; Barberet *et al.*, 2010). However, ultrasonography does not provide information about the functional activity of the thyroid lobes and cannot detect ectopic thyroid tissue (if mediastinal) or potential metastases in the case of thyroid carcinoma (Wisner and Nyland, 1998).

Thyroid ultrasonography may also be used to monitor the response of radioactive iodine treatment. Six months post ^{131}I radioactive iodine treatment, thyroid lobes of hyperthyroid cats show a significant decrease in volume, reduced rounding and reduced heterogeneity (Figure 4). With Power Doppler, the vascularity of the thyroid lobes is significantly decreased after treatment (Barberet *et al.*, 2010).

Ultrasound-guided techniques have been developed for treating hyperthyroid cats. Percutaneous radiofrequency heat ablation is effective transiently but not permanently (Mallery *et al.*, 2003). Percutaneous ethanol injection in thyroid nodules of hyperthyroid cats is not recommended as it is only effective transiently and risks of laryngeal paralysis have been observed (Wells *et al.*, 2001).

ULTRASONOGRAPHY OF LYMPH NODES

Imaging anatomy and general principles

The identification of normal and abnormal lymph nodes ultrasonographically requires careful regional scanning using organ and vascular landmarks. Vascular landmarks are usually preferred, as most lymph nodes are closely associated with well-defined large vessels (Saunders *et al.,* 1992; Spaulding, 1997). For example, the medial iliac lymph nodes are consistently located laterally to the caudal vena cava and aorta, at the level of the aortic trifurcation. The cranial mesenteric arteries are used to detect jejunal lymph nodes. When an abnormal lymph node is seen, it is important to know the anatomic structures drained by this lymph node and to closely check those areas. Conversely, one should also know which lymph nodes to evaluate when a particular organ is abnormal (Nyman and O'Brien, 2007).

The abdominal lymph nodes that are more often detected and evaluated are the medial iliac and the jejunal lymph nodes, because of their larger size and their consistent vascular landmarks (Figures 5 and 6). In dogs, the medial iliac lymph nodes were detected in 54% of the cases in one study (Barberet *et al.*, 2008). They are more easily detected with a dorsal approach, through the lateral sublumbar skin, rather than with a ventral approach (Llabres-Diaz, 2004). The medial iliac lymph nodes were detected in 100% of the cats in another study (Schreurs *et al.*, 2008). The jejunal lymph nodes are reported to be more difficult to image routinely because of gastrointestinal gas interference (Saunders *et al.*, 1992). The detection rate of canine jejunal lymph nodes was reported as 51% in one study (Barberet *et al.*, 2008) and as 100% in another study (Agthe *et al.*, 2009), this difference possibly being explained by the different recumbencies, scanning planes or fasting periods of the dogs. In cats, a detection rate of 90% was reported for the jejunal lymph nodes (Schreurs *et al.*, 2008). Some peripheral lymph nodes, such as the mandibular and popliteal lymph nodes, can also be easily imaged with ultrasonography. It can, however, be more difficult to detect axillary, inguinal and prescapular lymph nodes, especially if they are normal (Nyman and O'Brien, 2007).

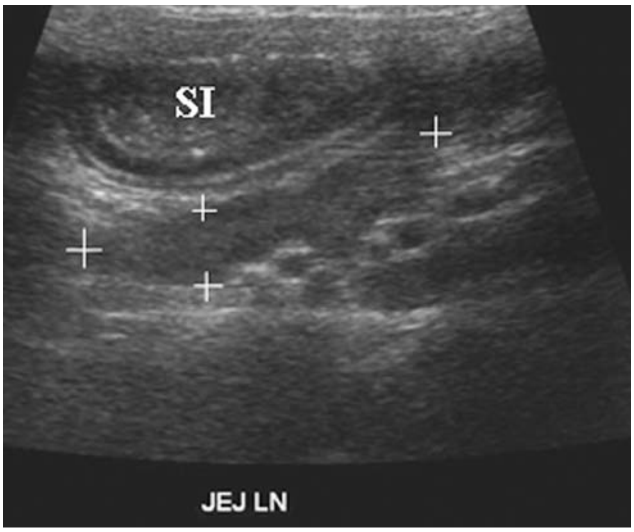

Figure 5. Longitudinal ultrasound image of a normal canine jejunal lymph node. SI = small intestinal loop.

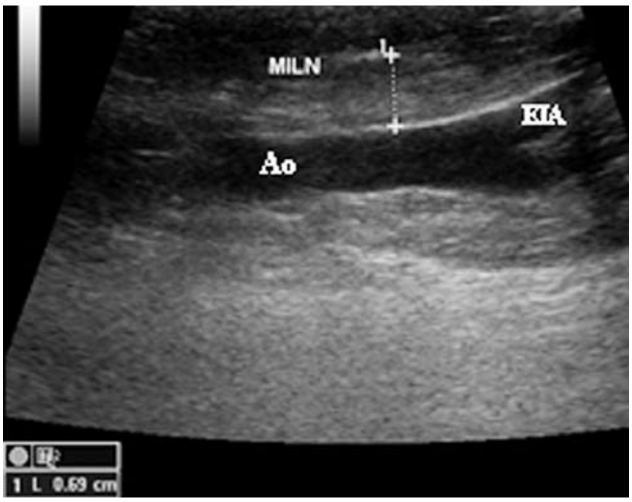

Figure 6. Longitudinal ultrasound image of a normal canine medial iliac lymph node. Ao = aorta, EIA = external iliac artery, MILN = medial iliac lymph node.

Lymph node echogenicity and echotexture

Normal lymph nodes are homogeneous and either isoechoic or slightly hypoechoic to the surrounding tissue or fat (Saunders *et al.*, 1992; Pugh, 1994; Spaulding, 1997; Llabres-Diaz, 2004). They have a thin hyperechoic capsule that is best seen when imaged perpendicular to the ultrasound beam. A hyperechoic line can often be seen at the level of the hilus. It is due to the presence of fat and fibrous tissue (Spaulding, 1997, Nyman *et al.*, 2006). A thin hypoechoic rim may sometimes be present (Lamb, 1999). In a recent study evaluating normal canine jejunal lymph nodes, the lymph nodes were mildly hypoechoic to the mesentery in 71% of the dogs and isoechoic in 29% of them (Agthe *et al.*, 2009). All dogs less than 2 years of age had hypoechoic lymph nodes. All dogs 6 years of age or older had lymph nodes of uniform echogenicity. However, in dogs less than 6 years of age, nonuniform lymph nodes were observed with either a thin hypoechoic rim at the periphery or a wide undulating hypoechoic rim with an uneven thickness and with or without a separate hypoechoic nodule. This was speculated to be related to an immunologically active lymph node cortex, as the gastrointestinal tract of young animals is continuously being exposed to new antigens (Agthe *et al.*, 2009).

Benign reactive lymph nodes usually remain isoechoic or sometimes appear with a varied echogenicity. Malignant lymph nodes tend to be more hypoechoic, with a varied echotexture. The mixed echotexture may then be a consequence of necrosis, metastatic lesions, edema or hemorrhage within the nodes. For example, liquefaction and coagulation necrosis may be responsible for the presence of hypoechoic or hyperechoic areas, respectively (Nyman *et al.*, 2004, 2005 and 2006). Fluid-filled or necrotic lesions often result in acoustic enhancement (through transmission). Occasionally, some mineralizations responsible for acoustic shadowing may be detected in abnormal lymph nodes (Nyman *et al.*, 2006; Nyman and O'Brien, 2007). In another study evaluating the medial iliac lymph nodes (Llabres-Diaz, 2004), heterogeneity, together with an increase in the size or number of the detected nodes, was used to differentiate normal lymph nodes from malignant lymph nodes affected by lymphoma or metastases of adenocarcinoma of the apocrine glands of the anal sacs. A significant association was found between heterogeneity and malignancy in canine abdominal lymph nodes (Kinns and Mai, 2007). In the same study, although 63% of the heterogeneous feline abdominal lymph nodes were malignant, no significant association was found between heterogeneity and malignancy in cats.

The detection of a hyperechoic hilus is subject to controversy. Some human studies state that the ultrasonographic detection of the hilus is a benign sign whereas the lack of detection is a malignant sign due to neoplastic infiltration of the hilus (Rubaltelli *et al.*, 1990). The same principle could be applied in veterinary medicine, although no significant difference was found in ultrasonographic detection of a hilus between benign and malignant lymph nodes (Nyman *et al.*, 2005 and 2006). However, in another study evaluating lymphomatous lymph nodes, loss of the central hyperechoic band was detected in 81.8% of the cases (Salwei *et al.*, 2005).

Lymph node size, shape and margins

Normal or reactive superficial lymph nodes are longer in length than in thickness, and have an oval shape. A quantitative means of assessing lymph node shape and size is the short-to-long axis ratio (S/L), which remains inferior to 0.6 in normal or reactive superficial lymph nodes. The lymphoma nodes have a plump shape with rounded edges and a S/L ratio superior to 0.7. Metastatic lymph nodes have a more varied shape, but the S/L ratio is also superior to 0.7. This is due to the fact that infiltration of the node by malignant tissue results in early distortion of the internal nodal architecture. Malignant cells may in some cases infiltrate only part of a node, where they may block the draining lymphatic channels, leading to focal cortical widening. In reactive lymph nodes, pathogens spread throughout the entire node, leading to a diffuse widening of the entire cortex (Nyman *et al.*, 2004 and 2005).

This S/L ratio is valid for superficial lymph nodes, but is probably not applicable to all the abdominal lymph nodes for the purpose of determining if they are malignant. For example, normal jejunal lymph nodes have an oblong shape and may measure up to 6 cm long, 2 cm wide and 0.8 cm thick (Agthe *et al.*, 2009). A maximal length of 20 cm has also been reported (Pugh, 1994). Some variations in shape may be seen with a focal distal enlargement and lobulation (Agthe *et al.*, 2009). Hence, the S/L ratio may not be appropriate, as it is often not possible to ensure that the entire long axis of the jejunal lymph node is included in a single image.

The medial iliac lymph nodes may be singular or double, and paired or unpaired (Pugh, 1994). They are the largest nodes of the parietal group, measuring 4 cm long, 2 cm wide and 0.5 cm thick, but maximal lengths of up to 6 cm have been described (Pugh, 1994; Llabres-Diaz, 2004). In a study evaluating medial iliac lymph nodes (Llabres-Diaz, 2004), malignant lymph nodes affected by lymphoma or metastases were larger compared with normal nodes. They also showed a rounder shape, the rounded shape corresponding in that study to a S/L ratio superior to 0.5.

Concerning the size of the lymph nodes, it is frequently reported that younger dogs have significantly larger lymph nodes than adult dogs, in the case of jejunal (Barberet *et al.*, 2008; Agthe *et al.*, 2009) or medial iliac lymph nodes (Barberet *et al.*, 2008). This has also been described for the medial retropharyngeal lymph nodes of dogs (Burns *et al.*, 2008). The finding of thicker and wider lymph nodes in young dogs supports the assumption that lymph nodes have a higher immunologic activity in young dogs (Agthe *et al.*, 2009). So, patient age should be taken into consideration when interpreting the size and aspect of jejunal lymph nodes in young dogs. The size of lymph nodes is also correlated to body weight, with larger lymph nodes being detected in large dogs (Barberet *et al.*, 2008; Burns *et al.*, 2008).

Border definition describes the sharpness of a lymph node. Normal or reactive nodes often have a regular and smooth border, but which is sometimes hard to delineate. On the contrary, malignant lymph nodes have more irregular borders suggestive of invasiveness. They are also more sharply delineated; this could be explained by the fact that normal tissue has been replaced by infiltrating neoplastic cells, which can lead to an increased difference in acoustic impedance, and hence a short transition zone between the node and surrounding tissues (Nyman *et al.*, 2005; Nyman and O'Brien, 2007).

Lymph node vascularization

Some studies have evaluated the vascularization of superficial lymph nodes using either Doppler ultrasonography (Color or Power Doppler) or contrast harmonic ultrasonography, in order to differentiate benign from malignant lymph nodes (Nyman *et al.*, 2005; Salwei *et al.*, 2005). The Doppler technique may demonstrate the amount and distribution of blood vessels within the lymph nodes. Normal vascular structures within the lymph node are characterized by branching arteries entering at the level of the hilus. Generally, patterns of vascular distribution within the node are divided into three groups: hilar, peripheral and mixed hilar/peripheral. Normal nodes have hilar vascularity or appear avascular with Doppler ultrasonography. Reactive nodes may show prominent hilar vascularity because of an increase in blood flow secondary to the inflammatory process. Metastatic lymph nodes more often have a peripheral perfusion, most likely due to the deposition of neoplastic cells at the margins of the nodes, which induces aberrant feeding vessels in the periphery by tumor angiogenesis. As tumor infiltration progresses, increased vascularization is sometimes visible both centrally and peripherally within the node (Nyman *et al.*, 2005; Nyman and O'Brien, 2007). In another study evaluating the perfusion of lymphomatous superficial lymph nodes, 2.13 times more vessels were detected with contrast harmonic ultrasonography than with Power Doppler ultrasonography. The angioarchitecture of these lymph nodes was also disturbed and predominantly peripheral, with 45.5% consisting of aberrant vessels, 63.6% of pericapsular vessels and 36.4% of subcapsular vessels. Displacement of the central hilar vessel was also seen in 45.5% of the cases and could be explained by the mass effect created by the neoplastic cells (Salwei *et al.*, 2005).

Some of these abnormal vascular features can be indirectly assessed by using Spectral Doppler, which can be used to determine flow indices within blood vessels of lymph nodes. These flow indices are the resistive index RI and the pulsatility index PI:

RI = (peak systolic velocity - end diastolic velocity)/peak systolic velocity

PI = (peak systolic velocity - end diastolic velocity)/time-averaged maximum velocity.

These indices may be valuable for detecting lymph node malignancy. The flow indices may possibly be increased in malignant nodes, since vascular resistance would be augmented by the compression of the vessels by tumor cells and/or tumor angiogenesis. On the contrary, vascular resistance in the vessels of inflamed lymph nodes may be decreased because of vasodilatation, in which case the indices would be lower (Nyman and O'Brien, 2007). In a study by Nyman *et al.* (2005), there was a significant difference in RI and PI between benign and malignant superficial lymph nodes, with cut-off values suggested at 0.68 for RI and 1.49 for PI, in order to discriminate between normal and metastatic lymph nodes. Lymphomatous lymph nodes showed values situated in between. Another study (Della Santa *et al.*, 2008) performed on superficial lymph nodes evaluated RI and different flow indices to discriminate inflammatory and neoplastic (lymphomatous or metastatic) lymph nodes. The Doppler index with the highest diagnostic accuracy appeared to be the S:D ratio (peak systolic-to-end diastolic velocity ratio), with a cut-off value of 3.22, which yields a sensitivity of 91% and a specificity of 100%. At a sensitivity of 100%, the most accurate index was the N:S ratio (diastolic notch velocity-to-peak systolic velocity ratio), with a cut-off value of 0.45, which yields a specificity of 67%. Finally, the use of RI and PI has been evaluated for differentiating normal, reactive and neoplastic abdominal lymph nodes. Values higher than 0.67 for RI and 1.02 for PI in medial iliac lymph nodes and higher than 0.76 for RI and 1.23 for PI in mesenteric lymph nodes had a high sensitivity and specificity for differentiating benign from neoplastic lymph nodes (Prieto *et al.*, 2009).

Ultrasonographic characteristics of malignant and benign lymph nodes

In conclusion, ultrasonography is a very valuable modality for evaluating superficial and abdominal lymph nodes. By combining different ultrasonographic criteria, it is possible to accurately differentiate normal, reactive and malignant lymph nodes. To summa-

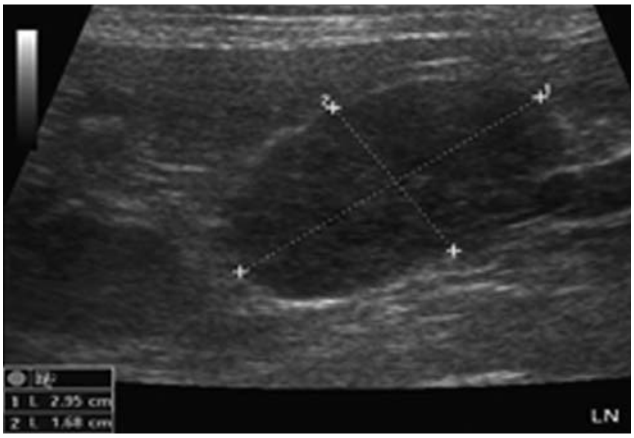

Figure 7. Longitudinal ultrasound image of a lymphomatous abdominal lymph node. Note the enlarged size, the rounded shape and the hypoechoic parenchyma of the lymph node.

Figure 8. Longitudinal ultrasound image of a normal left adrenal gland. Ao = aorta, LRa = left renal artery.

rize, normal or reactive lymph nodes are usually oval in shape and isoechoic to surrounding tissues, and their hilus may be visible. Their blood flow pattern is hilar and their vascular flow indices are low (RI < 0.65, PI < 1.45). By contrast, malignant lymph nodes are increased in size, rounded, and hypoechoic, with possible loss of delineation of the central hilus (Figure 7). They may show a heterogeneous parenchyma. Their blood flow is mixed or peripheral, with increased vascular flow indices (RI > 0.65, PI > 1.45). The size of the lymph node, the distribution of the vascular flow within the node and the PI, in combination, may result in a classification error of 11% for dividing the lymph nodes into two groups: malignant or benign (Nyman *et al.*, 2005).

Ultrasonography is also very helpful for guiding fine-needle aspirations or biopsies, in order to avoid closely located vessels. Cytology or histology is always necessary to obtain a final diagnosis, as they remain the most sensitive and specific tests for assessing lymph node status (Langenbach *et al.*, 2001).

ULTRASONOGRAPHY OF ADRENAL GLANDS

Imaging anatomy and general principles

Earlier reports claimed that normal adrenal glands could not be imaged with ultrasonography, as they were too small and had the same echogenicity as surrounding tissue (Kantrowitz *et al.*, 1986). It is now accepted that ultrasonography is the most practical method of imaging the adrenal glands because both normal and abnormal adrenal glands can be seen quickly and without the need for general anesthesia. However, the visualization of the glands is highly dependent on the quality of the instrumentation (a frequency of 7-8 MHz is recommended) and on the operator's skills (Tidwell *et al.*, 1997; Barthez *et al.*, 1998). In one study, 91% of the left adrenal glands and 86% of the right adrenal glands were visualized during routine ultrasonographic examinations (Barberet *et al.*, 2008). In a less recent study, the left adrenal gland was identified in 96% and the right one in 72% of the cases (Grooters *et al.*, 1994).

It is often reported that the right adrenal gland is more difficult to visualize than the left due to its smaller

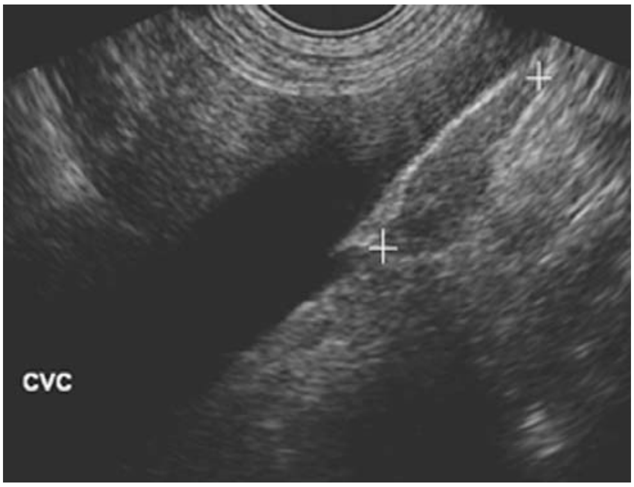

Figure 9. Longitudinal ultrasound image of a normal right adrenal gland. CVC = caudal vena cava.

size, its deeper and more cranial location under the rib cage, the respiratory motion and the presence of gas in the pylorus, duodenum and colon (Grooters *et al.*, 1994; Barthez *et al.*, 1998; Nyland *et al.*, 2002). Obesity and lack of patient compliance were also reported to interfere with the visualization of both adrenal glands (Nyland *et al.*, 2002). In a recent study, however, the only factor influencing visualization of the adrenal glands was the body condition score. In that study, a high body condition score had a positive influence on the visibility of the right adrenal gland, which is contrary to other reports (Barberet *et al.*, 2008).

The adrenal glands are situated at the craniomedial aspect of the kidneys. Usually, the sonographer relies on consistent anatomic landmarks to locate them. The left adrenal gland is located ventrolateral to the aorta, just cranial to the curvature of the left renal artery and caudal to the origin of the celiac and cranial mesenteric arteries from the aorta (Figure 8). The right adrenal gland is dorsolateral to the caudal vena cava, just cranial to the level of the origin of the celiac and cranial mesenteric arteries (Figure 9). The phrenico-abdominal vein (ventral) and artery (dorsal) course in the groove between the two poles, but may not be readily seen without Color Doppler. The left adrenal gland has a 'bean' or 'peanut' shape with a narrowed mid-portion, while the right adrenal gland is described as comma- or wedge-shaped or as an 'L' or a 'bent arrow' (Saunders *et al.*, 1992; Spaulding, 1997; Tidwell *et al.*, 1997; Barthez *et al.*, 1998). Both adrenal glands are usually isoechoic or hypoechoic to the cortex of the kidney and hypoechoic to surrounding fat (Grooters *et al.*, 1995; Barthez *et al.*, 1998). Sometimes the cortex and medulla of the adrenal gland can be distinguished, with the cortex being hypoechoic and the medulla being hyperechoic (Tidwell *et al.*, 1997; Barthez *et al.*, 1998).

Variable ultrasonographic measurements of normal and abnormal canine adrenal glands have been reported (Grooters *et al.*, 1995 and 1996; Barthez *et al.*, 1995; Douglass *et al.*, 1997). However, little is known about the reliability of these measurements. Moderate correlation was present between ultrasonographic and gross measurements of thickness (dorsoventral measure) for both left and right glands, but no correlation was found for the width (mediolateral measure) or length (Grooters *et al.*, 1995). In two studies by the same author, adrenal glands measured a thickness of 2-5 mm in normal young adult medium-sized dogs and 4-7 mm in middle-aged to older dogs (Grooters *et al.*, 1995 and 1996). Another study reported a range of thickness of 1.8-6.7 mm and a range of width of 3.6-8.1 mm in healthy dogs (Barthez *et al.*, 1995). Finally, the length of the adrenal glands has been reported to vary between 10 and 50 mm (Barthez *et al.*, 1995; Grooters *et al.*, 1995; Douglass *et al.*, 1997). The length of the adrenal glands is significantly correlated with body weight, but not their thickness or width (Barthez *et al.*, 1995; Douglass *et al.*, 1997).

Similar anatomical landmarks may be used to detect feline adrenal glands, which are short, ovoid and hypoechoic. Adrenal gland mineralization is common in older cats and should not be considered a sign of malignancy (Barthez *et al.*, 1998). The normal feline adrenal glands measure 4.3 ± 0.3 mm in width, 3.9 ± 0.2 mm in thickness and 10.7 ± 0.4 mm in length. Ultrasonographic measurements of length and thickness correlated well with gross measurements (Cartee *et al.*, 1993).

Ultrasonography of the adrenal glands has four main indications: hyperadrenocorticism (pituitary- or adrenal-dependent), hyperaldosteronism, hypoadrenocorticism and the evaluation of adrenal neuroendocrine tumors.

Hyperadrenocorticism

There are two major causes of hyperadrenocorticism in dogs: oversecretion of AdrenoCorticoTropic Hormone (ACTH) by the pituitary gland (80%) and cortisol-secreting adrenocortical neoplasia (20%). Once a diagnosis of hyperadrenocorticism has been confirmed with blood tests, the next step in the workup is to distinguish a pituitary-dependent hyperadrenocorticism (PDH) from an adrenal-dependent hyperadrenocorticism (ADH) using laboratory tests and diagnostic imaging, mostly ultrasonography. In contrast to dogs, hyperadrenocorticism is uncommon in cats and can be of adrenal or pituitary origin. The ultrasonographic criteria are similar to those in dogs (Feldman and Nelson, 2004c).

In dogs with PDH, both adrenal glands may sometimes appear normal in size, but in general they are uniformly and symmetrically enlarged. In both cases, their shape is usually either normal or described as "plump" (Figure 10). The parenchyma may appear slightly more hypoechoic than normal (Tidwell *et al.*, 1997; Barthez *et al.*, 1998), which is difficult to determine objectively on an individual examination. Infrequently, hyperplasia may appear as a rounded mass or nodule (Besso *et al.*, 1997). Sometimes, affected adrenal glands may show heterogeneous parenchyma and focal areas of increased echogenicity, which may indicate nodular hyperplasia. Mineralizations are rarely seen (Grooters *et al.*, 1996). Depending on the authors, either the thickness (Grooters *et al.*, 1996) or the width (Barthez *et al.*, 1995 and 1998) of the gland has been found to be a better indicator of the adrenomegaly than the length. A threshold of 7.4 mm for adrenal width offers a reasonable combination of sensitivity (77%) and specificity (80%) in the diagnosis of PDH, but it should not be used as the sole criterion. There is indeed a substantial overlap between adrenal gland size in normal dogs and those with PDH. Interpretation of ultrasonographic images should be made in conjunction with clinical findings and the results of biochemical and endocrine tests (Barthez *et al.*, 1995 and 1998). Trilostane treatment induces an enlargement of the adrenal gland thickness, width and length, which may occur as a result of suppression of the negative feedback mechanism affecting cortisol production. The distinction between the two parts of the gland may become more apparent because of a decrease in echogenicity of the hypoechoic outer zone and an increased echogenicity in the hyperechoic centre (Ruckstuhl *et al.*, 2002; Mantis *et al.*, 2003). This appearance was described in dogs receiving a high dose of trilostane (dogs weighing 5 to 20 kg received 60 mg of trilostane once daily; dogs weighing more than 20 kg received 120 mg once daily). However,

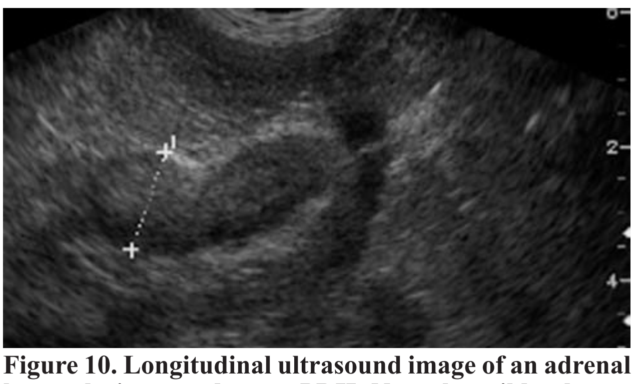

Figure 10. Longitudinal ultrasound image of an adrenal hyperplasia secondary to PDH. Note the mild enlargement and plump shape of the gland.

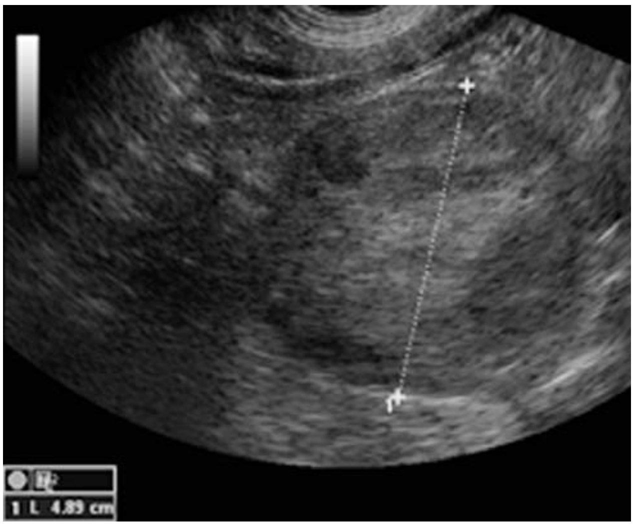

Figure 11. Longitudinal ultrasound image of an adrenal carcinoma. Note the severe enlargement, rounding and heterogeneity of the gland.

these modifications have not been observed with the dose of trilostane currently used at our institution (1-2 mg/kg BID). In contrast, treatment with mitotane results in a substantial decrease in the size of the adrenal cortex because of its adrenocorticolytic effect (Hoerauf and Reusch, 1999a). ADH is caused by functional adrenocortical tumors, which may be adenomas or carcinomas. Usually, ultrasonography is valuable in helping to differentiate dogs with PDH from dogs with functional adrenal tumors. ADH should be suspected if one adrenal gland is enlarged or shows a nodule or a mass with variable echogenicity and possible mineralizations (Figure 11). The contralateral adrenal gland may be either of normal size or decreased in size due to suppression. Carcinomas tend to be larger than adenomas, but neither the echogenicity of the mass nor the presence of mineralization nor bilateral involvement can be used for differentiation (Besso *et al.*, 1997). Adenocarcinoma cannot be distinguished ultrasonographically from other malignant tumors such as metastases or pheochromocytoma. Invasion of adjacent structures such as kidneys and adjacent vessels should be evaluated carefully with ultrasonography. Although vascular invasion and thrombosis usually indicate malignancy, thrombosis secondary to hypercoagulability can be detected with PDH (Tidwell *et al.*, 1997; Barthez *et al.*, 1998). Concurrent adenocarcinoma and pheochromocytoma have been reported in the dog, as have concurrent PDH and ADH (Feldman and Nelson, 2004c). Associated with biochemistry, ultrasonography becomes more sensitive and specific. For instance, the sensitivity and specificity of adrenal ultrasonography and endogenous ACTH determinations to identify the cause of hyperadrenocorticism were demonstrated to be 100% and 95%, respectively, for ADH (Gould *et al.*, 2001).

Hyperaldosteronism

Primary hyperaldosteronism results either from an adrenal tumor or from adrenal hyperplasia affecting the mineralocorticoid-producing zona glomerulosa of the adrenal cortex. It is rare, though it has been described in dogs and in cats. It can be suggested on the basis of inappropriately elevated serum aldosterone concentration, supported by an abnormal adrenal gland on imaging. On ultrasonography, the adrenal gland is often enlarged or shows a mass lesion, which may be hypoechoic, and homogeneous or heterogeneous (Tidwell *et al.,* 1997; Feldman and Nelson, 2004c).

Hypoadrenocorticism

Hypoadrenocorticism results from deficient secretion of both mineralocorticoids and glucocorticoids. Hypoadrenocorticism may be primary (Addison's disease) or secondary to infection, infarction, neoplasia, amyloidosis, trauma or medication. The interest of imaging in Addison's disease is quite limited since the diagnosis mainly relies on laboratory findings such as the ionogram and the ACTH stimulation test (Feldman and Nelson, 2004c). A diagnosis of Addison's disease cannot be based on ultrasonographic findings alone. On ultrasonography, the adrenal glands of affected dogs show a significant reduction in length (9.5-19.7 mm) and thickness (2.2-3.4 mm) compared with normal dogs (Hoerauf and Reusch, 1999b). Therefore, in a patient with consistent clinical and laboratory findings, the detection of small glands or failure to detect them may support a diagnosis of hypoadrenocorticism.

Adrenal neuroendocrine tumors

Pheochromocytoma is an uncommon catecholamine-secreting tumor arising from chromaffin cells of the adrenal medulla. The excessive catecholamines produce hypertension, which may be intermittent. Imaging has a significant role in the diagnosis of this disorder because clinical signs may be non-specific and laboratory findings are sometimes inconclusive. A pheochromocytoma is often considered only after an adrenal mass has been identified on routine abdominal ultrasonography (Tidwell *et al.*, 1997; Rosenstein, 2000). Small pheochromocytomas (less than 1 cm in size) are usually incidental findings at necropsy (Feldman and Nelson, 2004c). An obvious heterogeneous adrenal mass is usually present (Besso *et al.*, 1997; Rosenstein, 2000). Pheochromocytoma may also develop in both adrenal glands, resulting in bilateral adrenal masses, or it may occur simultaneously with an adrenal carcinoma (Barthez *et al.*, 1997). As for other neoplasms, ultrasonography can also provide useful information regarding metastases (in the liver, for example), abdominal effusion secondary to tumor rupture or vascular invasion, or local invasion of the mass into surrounding structures, which is quite common with pheochromocytomas (Rosenstein, 2000). However, vascular invasion is detected more commonly by necropsy or histopathology than by ultrasonography, because the affected vessels (for example, renal or adrenal veins or phrenicoabdominal vessels) may be quite small. Calcification of the adrenal gland is rarely observed in dogs with pheochromocytoma (Besso *et al.*, 1997).

In conclusion, ultrasonography has become an important imaging modality for the evaluation of small structures such as thyroid glands, lymph nodes and adrenal glands. Both normal and abnormal small structures can be seen, however this is highly dependent on the quality of the equipment and the operator skills. Although ultrasonographic findings for each disorder are described, some overlap may exist between normal and abnormal structures. For this reason, ultrasonography should be used to complement clinical and laboratory evaluation and guide aspiration or biopsy procedures.

LITERATURE

The complete reference list is available on request.