Canine Pheochromocytoma: Diagnosis and Management

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ABSTRACT: Pheochromocytoma is a rare adrenal tumor that occurs in various species. Clinical signs are often intermittent and vague and can be the result of catecholamine release or invasion of the tumor into surrounding structures. Abnormalities in routine laboratory tests are usually nonspecific but can be used to rule out concurrent disease. The optimal therapy for pheochromocytoma is surgery; medical therapy is used for nonresectable or metastatic disease. Prognosis is guarded; however, long-term survival is possible for dogs with uncomplicated disease.

Pheochromocytoma is an uncommon endocrine tumor of the sympathetic nervous system that occurs in dogs and more rarely in cats and other domestic animals. Pheochromocytomas originate from the chromaffin cells of the adrenal gland, which are capable of producing, storing, and secreting catecholamines (e.g., epinephrine, norepinephrine). Clinical signs may be the result of excess catecholamine production or local invasion of surrounding structures. Pheochromocytomas can be solitary or bilateral, benign or malignant, and functional or nonfunctional. Because of the high incidence of tumor invasion into the caudal vena cava and confirmed metastasis at time of necropsy, pheochromocytomas should be considered malignant in dogs.

Antemortem diagnosis of pheochromocytomas is challenging and requires a high index of suspicion. Clinical signs can be vague, intermittent, and typical of more common disorders. This article reviews the pathophysiology, diagnosis, and treatment of pheochromocytomas as well as the variable historical findings and clinical signs characteristic of this tumor.

PATHOPHYSIOLOGY

Epinephrine and norepinephrine are secreted by the normal adrenal medulla.

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Although dopamine secretion has also been reported, most human pheochromocytomas secrete predominantly norepinephrine or a mixture of norepinephrine and epinephrine. The excretion patterns of canine pheochromocytomas have not been documented.

Catecholamine synthesis in normal and neoplastic adrenal medulla cells is initiated when tyrosine is hydroxylated to dopa. In turn, dopa is decarboxylated to dopamine and transported to the intracellular granules of chromaffin cells. Dopamine is then hydroxylated to norepinephrine; and in some cases, it is further converted to epinephrine. The rate-limiting step in catecholamine synthesis is the hydroxylation of tyrosine by the enzyme tyrosine hydroxylase. Norepinephrine normally suppresses catecholamine production through inhibition of tyrosine hydroxylase, but this feedback loop is nonfunctional in pheochromocytomas. This could be caused by increased tyrosine hydroxylase activity or such rapid degradation of norepinephrine that accumulation and subsequent feedback do not occur.

Neural impulses mediate secretion of catecholamines by the normal adrenal gland, and excretion occurs by exocytosis of storage granules. Pheochromocytomas are not innervated, and catecholamine release may be initiated by tumor blood flow, direct pressure, or various chemicals and drugs. Excretion occurs mainly by diffusion. Released catecholamines then exert their physiologic effects by interacting with receptors at target tissues. The two classes of catecholamine receptors capable of responding to norepinephrine and epinephrine are α and β receptors. Clinical manifestations of pheochromocytomas (e.g., tachycardia, hypertension, flushing) are the result of the physiologic effects by interacting with receptors at target tissues.

The effects of catecholamines are terminated by an enzyme system present in both neuronal and extraneuronal tissues. Neuronal inactivation of locally released catecholamines occurs primarily at postganglionic nerve endings, whereas extraneuronal inactivation occurs primarily in the liver and kidney. Catecholamines are converted by monoamine oxidase and catechol O-methyltransferase into inactive metabolites (i.e., metanephrine, normetanephrine, vanillylmandelic acid) and are excreted by the kidney. These urinary metabolites can be measured to estimate the amount of catecholamine being produced and released by adrenergic or pheochromocytoma tissue.

**HISTORICAL AND CLINICAL FINDINGS**

Pheochromocytomas are frequently present with serious and more common disorders, including diabetes mellitus, hyperadrenocorticism, hepatic disease, renal disease, and other neoplasms. Therefore, it is difficult to identify the clinical signs caused specifically by the pheochromocytoma. The possibility of pheochromocytoma may also be overlooked if all clinical signs are related to the more recognizable disorder. As a result, the diagnosis is frequently made postmortem. In past studies, pheochromocytoma was suspected antemortem in 15% to 61% of canine cases based on complaints of collapsing episodes and physical examination findings of severe tachycardia and tachypnea. Clinical suspicion was further enhanced by detecting a mass of possible adrenal origin on palpation, radiography, or ultrasonography.

Clinical signs produced by pheochromocytomas are the result of direct pressure and local invasion of the tumor or excessive catecholamine excretion. The clinical signs related to catecholamine excess are believed to occur after the development of systemic hypertension. Hypertension and its related signs can be constant or paroxysmal, depending on the pattern of catecholamine release. Episodic signs resulting from intermittent tumor secretion are frequently present and are considered characteristic of pheochromocytoma.

The clinical signs and historical findings associated with pheochromocytomas are often subtle, vague, and intermittent, making the diagnosis complex. Duration of clinical signs may range from hours to years. Episodes caused by excessive catecholamine release are often separated by intervals in which the animal experiences no clinical signs. The most common historical findings reported by owners include the following:

- Generalized weakness
- Episodic collapse
- Weight loss
- Anorexia
- Panting
- Anxiety and restlessness
- Depression
- Ataxia

**PHYSICAL EXAMINATION**

Most affected dogs are older, with a mean age at diagnosis of 11 years (range, 1 to 18 years). These tumors have no breed or sex predilection. Physical examination findings are variable because of the intermittent nature of catecholamine secretion and depend on the secretory activity of the tumor at the time of examination, tumor size, and the presence of concurrent disease. Many dogs appear normal on presentation, whereas others may be in shock and die during or within hours of initial physical examination. The most common abnormalities on physical examination are secondary to catecholamine excess and include the following:

- Tachycardia
- Cardiac arrhythmias (e.g., premature ventricular contractions, atrioventricular block, atrial tachycardia)
• Panting
• Weakness
• Anxiety

Systolic murmurs may be auscultated; flushing of mucous membranes or pyrexia is also present in some patients.

Other clinical signs associated with pheochromocytomas are attributable to hypertension. Dogs may be tachypneic and have increased bronchovesicular or alveolar sounds secondary to congestion and edema caused by pulmonary hypertension. Mydriasis, retinal hemorrhage, and retinal detachment with associated blindness may develop in patients with severe hypertension. Persistent epistaxis and hemorrhage from surgical sites have been reported in three dogs, presumably secondary to systemic hypertension. Neurologic abnormalities caused by hypertension are generally nonspecific and may include seizures, head tilt, nystagmus, and strabismus.

The space-occupying nature of the tumor causes abnormalities that are detectable on physical examination in some dogs. If the tumor is large, it may be palpable. A palpable abdominal mass was identified in 10% to 25% of reported cases of canine pheochromocytoma. Local tumor invasion may also occur. Progressive paraparesis secondary to spinal cord compression by pheochromocytoma was reported in two dogs.

Partial or complete obstruction of the posterior vena cava has been reported as well. The incidence of dogs that had tumor thrombus invasion of the posterior vena cava ranges from 15% to 38%. Venous distention caudal to the obstruction can cause ascites, peripheral edema of the hindlimbs, and distention of the caudal superficial epigastric veins. One study reported that two dogs had near total obstruction of the caudal vena cava but had no related clinical signs, and two dogs with partial vena caval obstruction had ascites.

**DIAGNOSIS**

The antemortem diagnosis of pheochromocytoma is difficult for numerous reasons. Clinical signs can be vague and intermittent, and physical examination findings can be variable. Therefore, clinicians must maintain a high index of suspicion. Abnormalities in routine laboratory tests are nonspecific and rarely helpful. Patients frequently have concurrent disease that complicates the clinical picture. Finally, the hormonal testing and imaging techniques used in humans are of limited use in dogs because of inaccessibility and high expense.

**Clinical Pathology**

No consistent abnormalities on routine clinical pathology are specific to canine pheochromocytoma. However, these diagnostics are important in identifying concurrent disease. Complete blood cell count is often normal. Packed cell volume and total solids may be elevated because of decreased plasma volume secondary to catecholamine-induced peripheral vasoconstriction, catecholamine stimulated release of erythropoietin by the kidney, or production and secretion of an erythropoietin-like peptide. Some dogs have a decreased packed cell volume presumably caused by anemia associated with chronic disease or blood loss. Leukocytosis characterized by a mature neutrophilia may also occur and can be the result of catecholamine-induced demargination of neutrophils, necrosis or inflammation of the tumor, or unrelated disease.

Serum biochemistry panel results are generally unremarkable. One study reported that elevations in serum alkaline phosphatase and alanine aminotransferase concentrations, which occurred in approximately three fourths of the dogs, were the most common abnormalities. However, there was no correlation between enzyme elevations and metastatic disease of the liver; one third of these dogs were subsequently diagnosed with concurrent hyperadrenocorticism. Additional biochemical abnormalities that may be observed include azotemia, hypercholesterolemia, hypoalbuminemia, and hypocalcemia. Hypercholesterolemia may occur secondary to catecholamine-induced lipolysis and subsequent conversion of fatty acids to cholesterol in the liver but may also be the result of concurrent disease (e.g., hyperadrenocorticism). High-normal blood glucose concentrations have been reported in dogs with pheochromocytomas, but overt hyperglycemia should not be present unless there is concurrent diabetes mellitus. Proteinuria and hematuria are the most consistent abnormalities detected with urinalysis and are likely related to glomerulopathies secondary to hypertension.

**Blood Pressure Measurement**

Hypertension is the most common single finding in humans with pheochromocytomas. The diagnosis is considered in patients with malignant hypertension, patients who are unresponsive to antihypertensive therapy or who have paradoxical hypertensive responses, and individuals who develop hypertension during induction of anesthesia or surgery. Hypertension should be suspected in canine patients with systolic pressure greater than 160 mm Hg or diastolic pressure greater than 95 mm Hg. However, many dogs with pheochromocytomas are normotensive at the time of evaluation because of episodic secretion of catecholamines. Because normal blood pressure measurements do not rule
out pheochromocytoma, multiple measurements should be taken. Hypertension may also be the result of concurrent disease. One retrospective study measured blood pressure in 23 dogs with pheochromocytoma and found 10 to be hypertensive. Of these 10 hypertensive dogs, seven had concurrent hyperadrenocorticism, two had concurrent chronic renal failure, and one had concurrent diabetes mellitus. Of the remaining 13 normotensive dogs, two had hyperadrenocorticism, one had diabetes mellitus, and 10 had only pheochromocytoma.8

Imaging

Abdominal radiography reveals a perirenal mass in 26% to 56% of cases of canine pheochromocytoma.1,7–8,12,14 The tumor mass is calcified approximately 10% of the time (Figure 1).1,12,14 Left adrenal tumors are easier to identify because the left adrenal is not as closely associated with the liver as the right adrenal.6,12,14 A pneumoperitoneogram may aid in visualizing the tumor.12,14 The use of this technique was reported in three dogs with pheochromocytomas and was diagnostic in all three cases.14 Additional abnormalities on abdominal radiographs may include hepatomegaly, renal displacement, abnormal renal contour, ascites, and enlargement or displacement of the caudal vena cava.1,6,13 Cardiomegaly, right or left ventricular enlargement, and pulmonary congestion or edema caused by systemic hypertension may be present on thoracic radiographs.1,6,12,14 Pulmonary nodules consistent with metastatic disease are seen in approximately 8% to 11% of canine cases.7,8

Contrast radiography can help detect local invasion by a pheochromocytoma. Intravenous urography identifies renal displacement or invasion of the cranial pole of the kidney in approximately 10% of cases.1,12–14 Vena caval venography is also useful to detect compression, deviation, or obstruction of the caudal vena cava.1,6,12,14 If a tumor thrombus is occluding the vena cava, a filling defect may be observed within the lumen of the vessel. If the obstruction is complete, there may be reflux of contrast media into segmental spinal, renal, and caudal superficial epigastric veins. Abnormalities were detected in 56% to 100% of cases of confirmed canine pheochromocytoma in which venography was performed.7,8,12,14

Abdominal ultrasonography is an effective diagnostic tool that may be superior to radiography in evaluating the adrenal area and detecting adrenal masses.1,6 An adrenal mass can be detected by ultrasonography in 50% to 83% of cases of canine pheochromocytoma.1,7,8 However, failure to visualize a mass does not rule out the diagnosis.1 A case study20 of four dogs reported common ultrasonographic characteristics of pheochromocytoma to include multicystic and/or multilobular architecture, a large mass causing displacement of the kidney(s), and involvement of other structures. Ultra-
sonography may be helpful in detecting abdominal metastasis and local invasion into the kidney or caudal vena cava (Figure 2).1,13

Other techniques that may be used to image pheochromocytomas include computed tomography (CT), magnetic resonance imaging (MRI), and nuclear scintigraphy with 131Iodine (I) or 123I metaiodobenzylguanidine (MIBG). Expense, limited availability, and the need for general anesthesia currently limit the use of CT, MRI, and MIBG scanning in dogs with pheochromocytomas. CT, the modality used most commonly in humans, has an accuracy of 85% to 95% in detecting adrenal masses approaching 1 cm in diameter.6 The disadvantages of CT are that it is less accurate at detecting extraadrenal tumors or tumors smaller than 1 cm in diameter and it cannot differentiate among different histologic types of adrenal tumors. CT abnormalities reported in four dogs with pheochromocytomas included a large, irregular-shaped, soft tissue mass in the middorsal abdomen that caused displacement of surrounding organs, invasion of the caudal vena cava, and compression of the aorta.20 MRI is inferior to CT with respect to resolution but provides superior contrast and is capable of imaging in multiple planes without intravenous contrast dye or radiation exposure. MRI may also be used to differentiate between pheochromocytoma and adrenocortical adenoma or carcinoma.21 Human pheochromocytomas may appear unusually bright on some MRI scans (possibly because of their high water content and increased metabolic activity) and can almost always be separated from adrenocortical carcinomas. However, malignancy cannot be predicted based on signal intensity, thereby requiring demonstration of extraadrenal extension or metastases.22

Metaiodobenzylguanidine scanning is a relatively new technique used to localize adrenal, ectopic, and disseminated pheochromocytomas in humans. The molecular structure of MIBG is similar to norepinephrine, and it is taken up and stored in catecholamine storage vesicles. MIBG is recommended in cases in which the likelihood of pheochromocytoma is high but CT is negative or for follow-up of recurrent or metastatic pheochromocytoma.21 123I MIBG was used in one dog to diagnose pheochromocytoma.23

Hormonal Testing

The diagnosis of pheochromocytoma in humans is confirmed by either demonstration of elevated circulating catecholamine concentrations or increased urinary excretion of catecholamines or their metabolites. If the results of these tests are equivocal, then pharmacologic testing is used to stimulate or inhibit tumor release of catecholamines. These diagnostic tests have limited application to dogs because of restricted availability, high cost, lack of reference ranges, and technical complexity.1,6,12–14

Plasma Catecholamine Concentrations

Patients with functionally secreting pheochromocytomas should have high circulating catecholamine concentrations. However, levels may be normal at the time of evaluation because of variable secretion of catecholamines. Plasma catecholamines can also be falsely elevated because of stress, excitement, or concurrent disease.13 Assay of plasma catecholamines is performed infrequently in dogs because of technical difficulty and lack of reference ranges. Elevated total catecholamine concentrations were demonstrated in one dog with confirmed pheochromocytoma.14
Urinary Catecholamine and Catecholamine Metabolites

Total excretion of urinary catecholamines and their metabolites (i.e., metanephrine, normetanephrine, vanillylmandelic acid), which is the most widely used tool for diagnosing pheochromocytomas in humans, is measured over 24 hours. A diagnosis of pheochromocytoma is based on increased excretion of these compounds. False positives can result from exercise, excitement, radiographic contrast agents, certain medications, and ingestion of foods containing vanilla. Conversely, reduced renal function and intermittent secretion by the tumor may result in lower values. The utility of urinary catecholamine and catecholamine metabolite measurements in dogs with pheochromocytomas has not been evaluated.

Clonidine Suppression Test

Clonidine is a centrally acting \(\alpha\)-adrenergic agonist that decreases neurogenically mediated release of catecholamines. Pheochromocytomas secrete catecholamines independent of neurogenic input; therefore, administration of clonidine should not suppress release of catecholamines in patients with pheochromocytomas. This test is most useful in patients with high levels of circulating catecholamines because results are influenced by the magnitude of serum catecholamine levels. Clonidine suppression testing has not been performed in dogs with pheochromocytomas.

Phentolamine Suppression Test

Phentolamine is an \(\alpha\)-adrenergic antagonist that decreases blood pressure by blocking \(\alpha\)-mediated vasoconstriction. In order for this test to provide useful information, patients suspected of having a pheochromocytoma must be hypertensive. The test is considered positive if blood pressure declines by more than 35 mm Hg (systolic) or 25 mm Hg (diastolic) after administration of phentolamine and the decline lasts for at least 5 minutes. Phentolamine suppression testing has not been evaluated in dogs with pheochromocytomas.

Provocative Tests

Provocative tests increase tumor secretion of catecholamines and precipitate a hypertensive crisis. Histamine, tyramine, metoclopramide, and glucagon all have the potential to stimulate the release of catecholamines from pheochromocytomas. These tests are not recommended because of the potential for life-threatening complications.

TREATMENT

Surgery is the treatment of choice for dogs with pheochromocytomas. Medical therapy permits metabolic and cardiovascular stabilization of patients before surgery and is used to treat intraoperative arrhythmia and episodes of hypertension. It may also play a role in the long-term management of patients with nonresectable or metastatic disease.

Preoperative Management

Administration of \(\alpha\)- and \(\beta\)-adrenergic blocking agents is recommended preoperatively to decrease surgical morbidity and mortality in pheochromocytoma patients. The goals of preoperative medical management are to control blood pressure and expand plasma volume. An \(\alpha\)-adrenergic blocking agent is administered for 2 to 4 weeks in dogs to correct chronic vasoconstriction and allow expansion of plasma volume. Effective \(\alpha\) blockade will also decrease the number and severity of hypertensive responses during induction, intubation, and surgical manipulation of the tumor. Disadvantages of \(\alpha\) blockade include prolongation of the preoperative period, the potential that blockade will mask a hypertensive response that could assist in intraoperative tumor localization, and the possibility of suppressing the drop in blood pressure indicative of complete tumor resection. Effective \(\alpha\) blockade in dogs is phenoxybenzamine. This drug causes a long-acting, noncompetitive \(\alpha\)-adrenergic blockade; therefore, a surge of catecholamine release cannot override the inhibition as it can with competitive agents. The initial dose for dogs is 0.25 mg/kg PO bid, with a range of 0.2 to 1.5 mg/kg. A low dose should be used initially and gradually increased until the patient is normotensive. Therapy should be initiated 2 weeks before surgery; however, the optimal duration of treatment is unknown. \(\beta\)-blocking agents are indicated in patients with cardiac arrhythmias or severe tachycardia. However, these drugs should never be used in the absence of established \(\alpha\) blockade because severe hypertension may develop if \(\alpha\) vasoconstriction is unopposed by \(\beta\) receptor–mediated vasodilatation. Propanolol can be administered at a dose of 0.15 to 0.5 mg/kg PO tid in dogs.

Anesthetic Considerations

When anesthetizing dogs with pheochromocytomas, consideration must be given to the choice of preanesthetic, induction, and maintenance agents. Atropine should be avoided because of its ability to cause profound tachycardia in patients with pheochromocytomas. Phenothiazines should also be avoided because their \(\alpha\) blocking effects can result in unopposed \(\beta\) effects, leading to vasodilation and shock.
Invasive tumors, especially those involving \( \alpha \)-blocking agents, are good choices as preanesthetic or induction agents; the tendency of barbiturates to be arrhythmogenic makes them less ideal.\(^{1,12,14}\) Isoflurane or methoxyflurane are recommended for maintenance because halothane potentiates catecholamine-induced arrhythmias.\(^{6,12,14}\) One canine study described the use of oxymorphone and atropine or glycopyrrolate for preanesthesia, fentanyl citrate and diazepam for induction, and isoflurane with or without concurrent intravenous infusion of fentanyl citrate for maintenance of anesthesia. This protocol was used in 10 dogs with pheochromocytomas and did not result in complications during induction. However, intraoperative complications were common.\(^1\)

**Surgical Considerations**

Surgical resection of invasive pheochromocytomas can be technically demanding,\(^{6,13}\) but tumors without extensive local invasion can often be completely resected.\(^{12,14}\) Nonresectable tumors should be debulked as much as possible to decrease circulating catecholamine concentrations and improve the efficacy of long-term medical management.\(^6\) Most canine pheochromocytomas are unilateral; however, a complete abdominal exploration should be performed to evaluate the retroperitoneal area, the sympathetic chain surrounding the aorta, local lymph nodes, liver, and the posterior vena cava for potential sites of metastasis.\(^{1,4}\) Evidence of local invasiveness or distant metastasis should always be carefully assessed during surgery because determination of malignancy through histologic appearance alone can be difficult.\(^{1,12,14}\) A decrease in arterial blood pressure should occur following removal of the tumor, even if the patient has received preoperative \( \alpha \)-blocking agents.\(^{12,14}\) If blood pressure fails to decline, unidentified metastases are likely.\(^{1,6,12–14}\) Postoperative glucocorticoid and mineralocorticoid replacement therapy is necessary in patients undergoing bilateral adrenalectomy.\(^{1,12,14}\)

**Intraoperative and Postoperative Considerations**

The most serious complications that occur during induction of anesthesia or intraoperative manipulation of the tumor include the following:

- Severe hypertension (systolic arterial blood pressure greater than 300 mm Hg)
- Severe tachycardia (heart rate over 250 beats/min)
- Arrhythmia
- Hemorrhage\(^{1,12,14}\)

Because close patient monitoring is central to a successful outcome, an intraarterial catheter should be placed for direct blood pressure measurements, a jugular catheter placed to assess central venous pressure, and cardiac rhythm should be followed with an electrocardiogram.\(^{1,12,14}\) These parameters must be monitored closely throughout anesthesia, and for 24 to 48 hours postoperatively. This will allow rapid recognition and initiation of therapy if cardiac arrhythmia, hypovolemia, or blood pressure abnormalities develop.\(^1\)

Intraoperative episodes of hypertension can be treated by administering phentolamine (0.02 to 0.1 mg/kg IV as needed) or sodium nitroprusside (5 to 15 \( \mu \)g/kg/min via constant-rate infusion).\(^{1,13}\) Hypotension caused by decreased plasma volume secondary to chronic catecholamine-induced vasoconstriction may develop after removal of the tumor\(^{1,12,14}\) but commonly responds to vigorous intravenous fluid administration.\(^{1,12,14,21}\) Central venous pressure monitoring is essential to assess blood volume and direct fluid replacement during surgery.\(^{1,12,14}\) Pressor agents should be used only if hypotension does not respond to volume replacement.\(^{21}\) Cardiac arrhythmia and tachycardia may be treated with intravenous administration of propanolol (0.02 to 0.1 mg/kg) or esmolol (slow bolus of 500 mg/kg or infusion of 50 to 200 \( \mu \)g/kg/min).\(^{12–14}\)

**Postoperative Chemotherapy**

Chemotherapy has been used in humans with advanced, malignant pheochromocytomas. In one study, combination chemotherapy consisting of cyclophosphamide, vincristine, and dacarbazine resulted in a combined complete and partial response rate of 57% (median duration, 21 months; range, 7 to more than 34).\(^{24}\) Treatment of malignant pheochromocytoma with chemotherapy has not been reported in dogs.

**PROGNOSIS**

The prognosis for dogs with pheochromocytomas depends on the presence of concurrent disease, metastasis, or local invasion as well as perioperative complications.\(^1\) Invasive tumors, especially those involving the posterior vena cava, have a guarded prognosis.\(^{14}\) One study found that neurologic signs, abdominal distention, and weight loss were frequently associated with more advanced tumors and a poorer prognosis.\(^7\) However, if the adrenal mass can be excised, metastatic disease is not present, and perioperative complications are avoided, long-term survival of months to years is possible.\(^{1,14}\)

**REFERENCES**


The article you have read qualifies for 1.5 contact hours of Continuing Education Credit from the Auburn University College of Veterinary Medicine. *Choose the best answer* to each of the following questions; then mark your answers on the postage-paid envelope inserted in *Compendium*.

1. Pheochromocytomas arise from ____________ cells.
   a. chief
   b. chromaffin
   c. β
   d. acinar

2. The rate-limiting step of catecholamine synthesis is
   a. decarboxylation of adenosine.
   b. hydroxylation of tyrosine.
   c. oxidation of alanine.
   d. hydroxylation of glutamine.

3. Catecholamine release from neoplastic adrenal medulla cells is initiated by all of the following except
   a. blood flow.
   b. direct pressure.
   c. neural impulses.
   d. drugs.

4. All the following abnormalities are associated with canine pheochromocytoma except
   a. tachycardia.
   b. panting.
   c. lymphadenopathy.
   d. weakness.

5. Which of the following statements regarding canine pheochromocytoma is true?
   a. Most dogs have palpable abdominal masses.
   b. The lung is the most common site of metastasis.
   c. Increased liver enzymes indicate hepatic metastases.
   d. As many dogs are normotensive as hypertensive.

6. Which of the following is the least common finding on thoracic radiographs in dogs with pheochromocytomas?
   a. cardiomegaly
   b. pulmonary edema
   c. pulmonary nodules
   d. left ventricular enlargement

7. Which of the following urinary metabolites can be measured to estimate the amount of catecholamine being produced and released?
   a. vanillylmandelic acid
   b. metanephrine
   c. normetanephrine
   d. all of the above
8. ___________ is the drug of choice for α blockade.
   a. Labetalol
   b. Nifedipine
   c. Phenoxybenzamine
   d. Prazosin

9. Which of the following statements regarding the surgical management of canine pheochromocytoma is true?
   a. Preanesthetic management should include administration of atropine.
   b. Surgical debulking of nonresectable disease has no therapeutic benefit.
   c. Intraoperative appearance may be a better indicator of malignancy than histology.
   d. Posttumor resection hypotension should be managed with pressor agents.

10. Which of the following chemotherapeutic drugs is used in humans with pheochromocytomas?
    a. cyclophosphamide
    b. vincristine
    c. dacarbazine
    d. all of the above