A

ABORTION, SPONTANEOUS (EARLY PREGNANCY LOSS)—CATS

BASICS

DEFINITION
• Spontaneous abortion—natural expulsion of fetus(es) prior to the point at which they can sustain life outside the uterus. • Early pregnancy loss—generalized term for any loss of conceptus including early embryonic death and resorption.

PATHOPHYSIOLOGY
• Infectious causes result in pregnancy loss directly by affecting the embryo, fetus, or fetal membranes, or indirectly by creating debilitating systemic disease in the queen. • Non-infectious causes of pregnancy loss result from any factor other than infection that leads to the death or premature expulsion of the conceptus (e.g., uterine disease, inadequate maternal nutrition, endocrine dysfunction, toxicity, genetic defects).

SYSTEMS AFFECTED
• Endocrine • Reproductive • Other systems—any debilitating illness can result in pregnancy loss.

GENETICS
Genetic defects are more prevalent in highly inbred individuals; heritability of susceptibility to FIPV thought to be very high.

INCIDENCE/PREVALENCE
Unknown—pregnancy frequently not confirmed, owners may not recognize late pregnancy loss if the queen is fastidious; early embryonic death is difficult to document.

SIGNALMENT
Species
Cat

Breed Predilections
Purebred cats—higher incidence of non-infectious abortion; inbreeding increases risk of genetic disease. Predisposition to developing FIP increased in some breeds including Bengal, Birman, and Himalayan.

Mean Age and Range
Infectious abortion seen in all ages; non-infectious abortion seen more commonly in young and aged queens.

SIGNS
General Comments
Early embryonic death and resorption frequently have no clinical symptoms; any combination of historical and physical examination findings may occur, with some queens displaying no symptoms.

Historical Findings
Failure to deliver litter at expected time, return to estrus sooner than expected, decrease in abdominal diameter and weight loss, discovery of fetal material, behavior change, anorexia, vomiting, diarrhea.

Physical Examination Findings
Purulent, mucoid, watery, or sanguineous vaginal discharge; dehydration, fever, abdominal straining, abdominal discomfort.

CAUSES
Infectious
• Bacterial—organisms implicated in causing abortion via ascending infection include *Escherichia coli, Staphylococcus* spp., *Streptococcus* spp., *Chlamydia* spp., *Pasteurella* spp., *Klebsiella* spp., *Pseudomonas* spp., *Salmonella* spp., *Mycoplasma* spp., and *Ureaplasma* spp. • Protozoal—*Toxoplasma gondii* • Viral—FHV-1, FIV, FIP, FeLV, FPLV.

Non-infectious
• Uterine—cystic endometrial hyperplasia, pyometra, chronic endometritis, anatomical abnormalities of the uterus, mechanical trauma to uterus or fetus. • Ovarian—early termination of corpora lutea function causes a decline in serum progesterone concentrations resulting in early parturition/abortion. Primary hypoluteoidism is rare but secondary hypoluteoidism may result from certain drugs, prolonged stress and uterine inflammation. • Fetal—chromosomal abnormalities resulting in abnormal or arrested development and embryonic or fetal death. • Systemic—malnutrition or nutritional disorders such as taurine deficiency; vitamin A deficiency or toxicity; severe non-reproductive illness; exogenous drug administration: estrogens, glucocorticoids, $PGF_{2\alpha}$, and dopamine agonists (cabergoline, bromocriptine) will disrupt normal corpora lutea function; fetotoxic or teratogenic drugs: chemotherapeutic agents, antifungal agents, some antibiotics (trimethoprim-sulfonamides, tetracyclines, gentamicin); modified live vaccines.

RISK FACTORS
• Previous history of pregnancy loss • Concurrent systemic disease • Recent trauma • Purebred cat with high degree of inbreeding • Very young or old queen • Previous use of progestins to suppress estrus • Malnourishment • Homemade and raw diets • Overcrowded or unsanitary environment

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Early pregnancy loss—failure to conceive, disorder of sexual development, anovulatory cycle • Vulvar discharge—pyometra, mucometra, uterine stump pyometra; vaginitis, metritis, cystitis; impending parturition or dystocia; neoplasia or trauma of urinary bladder, urethra, vagina, or uterus; estrus—very little discharge typically seen • Abdominal straining or discomfort: urethral obstruction; intestinal foreign body; peritonitis; trauma; impending parturition or dystocia

CBC/BIOCHEMISTRY/URINALYSIS
• May be normal. • Inflammatory leukogram or stress leukogram depending on systemic disease response. • Hemoconcentration and azotemia with dehydration.

OTHER LABORATORY TESTS
Infectious Causes
• Cytology and bacterial culture of vaginal discharge, fetus, fetal membranes, or uterine contents (aerobic, anaerobic, and mycoplasma). • FeLV—test for antigens in queens using ELISA or IFA. • FHV-1—IFA or PCR from corneal or conjunctival swabs, viral isolation from conjunctival, nasal, or pharyngeal swabs. • FIP—submit fetal tissue for histopathology and immunohistochemistry. • FIV—ELISA: confirm positive results with Western blot. • FPLV—viral isolation from fetuses submitted for necropsy; document seroconversion in the queen.

Non-infectious Causes
• To rule out anovulatory cycle, confirm progesterone rise > 1.5 ng/mL one week following mating. • Hypoluteoidism—serum progesterone level < 1.0 ng/mL prior to abortion indicates luteal failure but does not determine whether the luteal failure was primary or secondary • Disorder of sexual development can be evaluated with description of external genitalia, karyotype, and histopathology of reproductive tract.

IMAGING
• Abdominal ultrasound in early gestation (21–25 days post-breeding) to confirm pregnancy and screen for evidence of resorption. Later pregnancy, evaluate health and viability of fetus(es) and associated fluid and membranes; abnormal uterine fluid accumulation and non-reproductive disease. • Radiograph— evaluates relative size, number, and position of fetal skeletons; can also be used to screen for fetal monsters, fetal malpresentation, and non-reproductive disease.

DIAGNOSTIC PROCEDURES
• Genetic defects—necropsy aborted fetus(es); submit samples from aborted and stillborn fetus for karyotyping. • Nutrition—submit sample of diet for nutritional analysis: of particular importance when queen is fed a homemade and/or raw diet. • Pedigree analysis to evaluate inbreeding coefficient • Evaluate cattery for vaccination protocols, feeding regime, general sanitation procedures, and quarantine procedures for pregnant queens and new arrivals. • Submit reproductive tract (uterus, ovaries, uterine tubes) and aborted, stillborn, mummified fetus(es) and fetal membranes (fresh, refrigerated, on wet ice) for evaluation of anatomic and pathologic changes, gross

(CONTINUED) ABORTION, SPONTANEOUS (EARLY PREGNANCY LOSS)—CATS

necropsy, histopathology, cultures, and viral isolation.

TREATMENT

APPROPRIATE HEALTH CARE

• Outpatient management: typically no medical management required for non-infectious stable queens; primary hypoluteoidism—can be managed on an outpatient basis with tocolytic drugs in combination with tocodynamometry. • Surgical management: OHE for queens with severe illness due to pyometra or metritis.

ACTIVITY

• Isolation for queens with infectious disease. • No activity restrictions for most non-infectious pregnancy losses. • Restrict activity as indicated for pregnancy loss due to trauma.

DIET

Feed commercially available diet labeled for use in pregnancy. Correct diets with inappropriate taurine or vitamin A concentrations. Avoid feeding raw meats or allowing queens to hunt during pregnancy to reduce risk for ingestion of pathogenic bacteria and *T. gondii*.

CLIENT EDUCATION

• Infectious diseases—verify client is following good vaccination protocols and disease surveillance measures and is utilizing quarantine facilities for pregnant queens and new arrivals. • Breeding management—discuss normal reproductive behavior and good breeding management; advise clients to keep detailed records related to reproductive performance, pedigree analysis, and social behavior of queens within the cattery. • Nutrition—discuss routine diet recommendations for breeding queens; advise homemade diets undergo nutritional analysis. • Genetic disease—increase in inbred individuals; many reproductive traits are heritable. • Discuss risk of zoonotic disease from *Toxoplasma gondii.*

MEDICATIONS

DRUG(S) OF CHOICE

• Will depend on etiology. • Amoxicillin-clavulanic acid 13.75 mg/kg PO q12h or enrofloxacin 5 mg/kg/day PO based on bacterial culture results. • Tocolytic therapy to prevent uterine contractions and help maintain pregnancy: Terbutaline 0.03–1.0 mg PO as needed based on tocodynamometry; 0.03 mg/kg PO q8h if tocodynometry not available. • Hypoluteoidism: progesterone in oil—2.0–3.0 mg/kg IM as needed based on serum progesterone concentration and tocodynamometry.

CONTRAINDICATIONS

• Terbutaline—cardiac or respiratory disease, pyometra, infectious disease, hypertension. • Progesterone in oil—diabetes, pyometra, infectious disease, CEH.

PRECAUTIONS

• Use of tocolytics to maintain pregnancy requires accurate documentation of breeding dates to know when treatment should be discontinued; tocolytics used most successfully in combination with tocodynamometry to establish desired dosing interval based on increasing preterm uterine activity. • Terbutaline can cause hypertension leading to increased hemorrhage from the placental sites during parturition or at the time of c-section.

POSSIBLE INTERACTIONS

• Progesterone administration during pregnancy is associated with masculinization of female fetuses; do not administer in the first half of pregnancy and use with informed consent thereafter. • Use of tocolytics to maintain pregnancy is associated with increased risk of dystocia, failure of normal placental separation at parturition, lack of mammary gland development and milk production, and poor maternal behavior for the first few days postpartum.

FOLLOW-UP

PATIENT MONITORING

• Serial ultrasound evaluation q 5–7 days to evaluate fetal viability for queens receiving tocolytics.

PREVENTION/AVOIDANCE

• Institute infectious disease prevention, control, and surveillance plan. • Replace infertile queens with more reproductively fit individuals. • Avoid exposure to abortifacient, teratogenic, or fetotoxic drugs.

POSSIBLE COMPLICATIONS

• Depends on etiology. • Metritis, endometritis, uterine rupture, sepsis, shock. • Diabetes, CEH, masculinization of female fetuses with progesterone treatment.

EXPECTED COURSE AND PROGNOSIS

• Infectious disease—normal pregnancy, repeated abortion, or infertility possible with viral disease. • Poor prognosis for normal pregnancy in queens with severe CEH. • Fair prognosis for successful pregnancy with treatment for primary hypoluteoidism; significant monitoring required for good outcome. • Pregnancy loss due to genetic abnormalities likely to recur if queen is bred to tom with similar pedigree.

MISCELLANEOUS

AGE-RELATED FACTORS

• Queens > 6 years old have higher incidence of infertility. • Pregnancy loss seen most frequently in very young and old queens.

ZOONOTIC POTENTIAL

Toxoplasma gondii

SEE ALSO

• Breeding, Timing • Sexual Development Disorders

ABBREVIATIONS

• CEH = cystic endometrial hyperplasia • ELISA = enzyme-linked immunosorbent assay • FeLV = feline leukemia virus • FHV-1 = feline herpesvirus 1 • FIPV = feline infectious peritonitis virus • FIV = feline immunodeficiency virus • FPLV = feline panleukopenia virus • IFA = indirect fluorescent antibody • OHE = ovario-hysterectomy • $PGF_{2\alpha}$ = prostaglandin $F_{2\alpha}$

INTERNET RESOURCES

• www.theriojournal.com
• www.whelpwise.com

Suggested Reading

Lamm CG. Clinical approach to abortion, stillbirth, and neonatal death in dogs and cats. Vet Clin North Am: Small Anim Pract 2012, (42)3:501–513.

Pretzer SD. Bacterial and protozoal causes of pregnancy loss in the bitch and queen. Theriogenology 2008, 70(3):320–326.

Verstegen J, Dhaliwal G, Verstegen-Onclin K. Canine and feline pregnancy loss due to viral and non-infectious causes: a review. Theriogenology 2008, 70(3):304–319.

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ABORTION, SPONTANEOUS (EARLY PREGNANCY LOSS)—DOGS

BASICS

DEFINITION
Loss of a fetus because of resorption in early stages or expulsion in later stages of pregnancy.

PATHOPHYSIOLOGY
• Direct causes—congenital abnormality, infectious disease, trauma. • Indirect causes—infectious placentitis, abnormal ovarian function, abnormal uterine environment.

SYSTEMS AFFECTED
• Reproductive. • Any dysfunction of a major body system can adversely affect pregnancy.

GENETICS
• No genetic basis for most causes of abortion.
• Lymphocytic hypothyroidism—single-gene recessive trait in borzois.

INCIDENCE/PREVALENCE
• True incidence unknown. • Resorption estimated between 11–13%, some estimates up to 30% of at least one resorption.
• Incidence of stillbirth reported as 2.2–4.4%; increases with dystocia up to 22.3%.

SIGNALMENT
Species
Dog

Breed Predilections
• Familial lymphocytic hypothyroidism reported in borzoi—prolonged interestrus interval, poor conception rates, abortion midgestation, stillbirths. • Many breeds considered at risk for familial hypothyroidism (see Hypothyroidism).

Mean Age and Range
• Infectious causes, pharmacologic agents causing abortion, fetal defects—seen in all ages. • Cystic endometrial hyperplasia—usually > 6 years old.

Predominant Sex
Intact bitches

SIGNS
Historical Findings
• Failure to whelp on time. • Expulsion of recognizable fetuses or placental tissues.
• Decrease in abdominal size; weight loss.
• Anorexia. • Vomiting, diarrhea.
• Behavioral changes.

Physical Examination Findings
• Sanguineous or purulent vulvar discharge.
• Disappearance of vesicles or fetuses previously documented by palpation, ultrasonography, or radiography.
• Abdominal straining, discomfort.
• Depression. • Dehydration. • Fever in some patients.

CAUSES
Infectious
• *Brucella canis.* • Canine herpesvirus.
• *Toxoplasma gondii, Neospora caninum.*
• *Mycoplasma* and *Ureaplasma.*
• Miscellaneous bacteria—*E. coli*, *Streptococcus, Campylobacter, Salmonella.*
• Miscellaneous viruses—distemper virus, parvovirus, adenovirus.

Uterine
• Cystic endometrial hyperplasia and pyometra. • Trauma—acute and chronic.
• Neoplasia. • Embryotoxic drugs.
• Chemotherapeutic agents. • Estrogens.
• Glucocorticoids—high dosages.

Ovarian
• Prostaglandins—lysis of corpora lutea.
• Dopamine agonists—lysis of corpora lutea via suppression of prolactin; bromocryptine, cabergoline. • Hypoluteoidism—abnormal luteal function in the absence of fetal, uterine, or placental disease: progesterone concentrations < 1–2 ng/mL, most often seen at 40–45 days gestation.

Hormonal Dysfunction
• Hypothyroidism; new data shows this is less common than previously thought.
• Hyperadrenocorticism. • Environmental factors—endocrine disrupting contaminants have been documented in human and wildlife instances of fetal loss.

Fetal Defects
• Lethal chromosomal abnormality. • Lethal organ defects.

RISK FACTORS
• Exposure of the brood bitch to carrier animals • Old age • Hereditary factors

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Differentiate infectious from non-infectious causes—*B. canis* of immediate and zoonotic concern. • Differentiate resorption from infertility—helped by early diagnosis of pregnancy. • History of drug use during pregnancy—particularly during the first trimester, or use of drugs (e.g., dexamethasone, prostaglandins, ketoconazole, griseofulvin, doxycycline, tetracycline, dantrolene, among others) known to cause fetal death. • Vulvar discharges during diestrus—may mimic abortion; evaluate discharge and origin to differentiate uterine from distal reproductive tract disease.
• Necropsy of aborted fetus, stillborn puppies, and placenta(s)—enhances chances of a definitive diagnosis, refrigerate but do not freeze prior to submission. • History of systemic or endocrine disease—may indicate problems with the maternal environment.

CBC/BIOCHEMISTRY/URINALYSIS
• Usually normal. • Systemic disease, uterine infection, viral infection, or endocrine abnormalities—may produce changes in CBC, biochemistries, or urinalysis.

OTHER LABORATORY TESTS
• Serologic testing—*B. canis,* canine herpesvirus, and *Toxoplasma, Neospora;* collect serum as soon as possible after abortion; repeat testing for raising titers for canine herpesvirus, *Toxoplasma, Neospora.* • Slide test for *B. canis*—very sensitive; negative results reliable; prevalence of false positives as high as 60% (D-Tec CB®, Synbiotics Corp., (800)733-5500); • PCR for *B. canis* now available; • Definitive diagnosis made via culture. • Tube agglutination test for *B. canis*—gives titers; titers > 1:200 considered positive; titers from 1:50–1:200 considered suspicious. • Agar gel immunodiffusion test for *B. canis*—effectively differentiates between false positives and true positives in agglutination tests; detects cytoplasmic and cell surface antigens (Cornell University Animal Health Diagnostic Laboratory, (607)253-3900). • Baseline T_4 serum concentration (when no infectious agents are identified)—hypothyroidism is a common endocrine disease and has been suggested as a cause for fetal wastage; role in pregnancy loss unclear; subnormal T_4 concentrations indicate need for further testing (see Hypothyroidism). • Serum progesterone concentration (when no infectious agents are identified)—hypoluteoidism may cause fetal wastage; dogs depend on ovarian progesterone production throughout gestation (minimum of 2 ng/mL required to maintain pregnancy); collect sample and determine as soon as possible after abortion; in subsequent pregnancies, start weekly monitoring at week 3, which may be before pregnancy can be documented with ultrasound; start biweekly sampling around the gestational age of previous loss. Pregnancy loss typically occurs during the seventh week of gestation (see Premature Labor). • Vaginal culture—*B. canis* with positive serologic test; *Mycoplasma, Ureaplasma,* other bacterial agents; all except *B. canis* can be normal flora, therefore diagnosis difficult from vaginal cultures alone; *Salmonella* associated with systemic illness in the bitch.

IMAGING
• Radiography—identifies fetal structures after 45 days of gestation; earlier, can determine uterine enlargement but cannot assess uterine contents.
• Ultrasonography—identifies uterine size and contents; assesses fluid and its consistency; assesses fetal remains or fetal viability by noting heartbeats (normal, > 200 bpm; stress, < 150 or > 280 bpm).

DIAGNOSTIC PROCEDURES
• Vaginoscopy—identify source of vulvar discharges and vaginal lesions; use a scope of sufficient length (16–20 cm) to examine the entire length of the vagina. • Cytologic examination and bacterial culture—vagina may reveal an inflammatory process (e.g., uterine infection); technique for culture: use a

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guarded swab culture instrument to ensure an anterior sample (distal reproductive tract is normally heavily contaminated with bacteria), or collection of secretions via transcervical catheterization.

PATHOLOGIC FINDINGS

Histopathologic examination and culture of fetal and placental tissue—may reveal infectious organisms; tissue culture, particularly of stomach contents, to identify infectious bacterial organisms.

TREATMENT

APPROPRIATE HEALTH CARE

• Most bitches should be confined and isolated pending diagnosis. • Hospitalization of infectious patients preferred. • *B. canis*—highly infective to dogs; shed in high numbers during abortion; suspected cases should be isolated. • Outpatient medical management—medically stable patients with non-infectious causes of pregnancy loss, endocrinopathies, or endometrial disease. • Partial abortion—may attempt to salvage the live fetuses; administer antibiotics if a bacterial component is identified.

NURSING CARE

Dehydration—use replacement fluids, supplemented with electrolytes if imbalances are identified by serum biochemistries.

ACTIVITY

Partial abortion—cage rest generally recommended, although the positive effect on reducing further abortion is unknown.

DIET

No special dietary considerations for uncomplicated cases

CLIENT EDUCATION

• Critical for *B. canis*—if confirmed, euthanasia recommended due to lack of successful treatment and to prevent spread of infection; may try OHE and long-term antibiotics; discuss surveillance program for kennel situations: monthly serology for all individuals, culling any positive animals, until three consecutive negative tests are obtained; discuss zoonotic potential. • Primary uterine disease—OHE is indicated in patients with no breeding value; cystic endometrial hyperplasia is an irreversible change. • Infertility or pregnancy loss—may recur in subsequent estrous cycles despite successful immediate treatment. • Prostaglandin treatment—discuss side effects (see Abortion, Termination of Pregnancy). • Infectious diseases—establish surveillance and control measures.

SURGICAL CONSIDERATIONS

OHE—preferred for stable patients with no breeding value.

MEDICATIONS

DRUG(S) OF CHOICE

• $PGF_{2\alpha}$ (Lutalyse, dinoprost tromethamine)—uterine evacuation after abortion; 0.05–0.1 mg/kg SC q8–24h; cloporostenol (Estrumate, cloprostenol)—1–5 μg/kg SC q24h; not approved for use in dogs, but adequate documentation legitimizes its use; use only if all living fetuses have been expelled. • Antibiotics—for bacterial disease; initially institute broad-spectrum agent; specific agent depends on culture and sensitivity testing of vaginal tissue or necropsy of fetus. • Progesterone (Regu-Mate) at 0.088 mg/kg (1 mL/25 kg PO q24h); progesterone in oil at 2 mg/kg IM q48–72h; progesterone (Prometrium®; 10 mg/kg PO q24h, adjust daily dosage based on serum progesterone)—for documented hypoluteodism only to maintain pregnancy, must have accurate due date to know when to discontinue therapy—inadvertently prolonging gestation will result in fetal death.

CONTRAINDICATIONS

Progestogen supplementation—contraindicated in dogs with endometrial or mammary gland disease.

PRECAUTIONS

$PGF_{2\alpha}$—metabolized in the lung; side effects are related to smooth muscle contraction, are dose-related, and diminish with each injection; panting, salivation, vomiting, and defecation common; dosing critical (LD_{50} for dinoprost—5 mg/kg).

ALTERNATIVE DRUG(S)

Oxytocin—1 U/5 kg SC q6–24h for uterine evacuation; should only be considered in cases where uterine evacuation is desired solely through uterine contraction.

FOLLOW-UP

PATIENT MONITORING

• Partial abortion—monitor viability of remaining fetuses with ultrasonography; monitor systemic health of the dam for remainder of pregnancy. • Vulvar discharges—daily; for decreasing amount, odor, and inflammatory component; for consistency (increasing mucoid content is prognostically good). • $PGF_{2\alpha}$—continued for 5 days or until most of the discharge ceases (range 3–15 days). • *B. canis*—monitor after neutering and antibiotic therapy; yearly serologic testing to identify recrudescence. • Hypothyroidism—treat appropriately; neutering recommended (hereditary nature); see Hypothyroidism.

PREVENTION/AVOIDANCE

• Brucellosis and other infectious agents—surveillance programs to prevent introduction to kennel. • OHE—for bitches with no breeding value. • Use of modified-live vaccines (e.g., some distemper, parvovirus, etc., vaccines).

POSSIBLE COMPLICATIONS

• Untreated pyometra—septicemia, toxemia, death. • Brucellosis—discospondylitis, endophthalmitis, recurrent uveitis.

EXPECTED COURSE AND PROGNOSIS

• Pyometra—recurrence rate during subsequent cycle is high (up to 70%) unless pregnancy is established. • CEH—recovery of fertility unlikely; pyometra common complication. • Hormonal dysfunction—often manageable; familial aspects should be considered. • Brucellosis—guarded; extremely difficult to successfully eliminate infection even if combined with neutering.

MISCELLANEOUS

AGE-RELATED FACTORS

Older bitches more likely to have CEH

ZOONOTIC POTENTIAL

B. canis—can be transmitted to humans, especially when handling the aborting bitch and expelled tissues; massive numbers of organisms expelled during abortion. Pathologists should be warned when *B. canis* is suspected. People that are immunocompromised are at greatest risk for infection.

SEE ALSO

• Brucellosis • Hypothyroidism • Infertility, Female—Dogs • Premature Labor • Pyometra

ABBREVIATIONS

• CEH = cystic endometrial hyperplasia • OHE = ovariohysterectomy • $PGF_{2\alpha}$ = prostaglandin $F_{2\alpha}$

Suggested Reading

Givens MD, Marley MSD. Infectious causes of embryonic and fetal mortality. Theriogenology 2008, 70(3):270–285.

Verstegen J, Dhaliwal G, Verstegen-Onclin K. Canine and feline pregnancy loss due to viral and non-infectious causes: A review. Theriogenology 2008, 70(3):304–319.

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Client Education Handout available online

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ABORTION, TERMINATION OF PREGNANCY

BASICS

DEFINITION
Termination of an unwanted pregnancy. May be accomplished by drugs that alter embryo transport in the oviduct impeding establishment of a pregnancy, and/or cause luteal regression, terminating an established pregnancy. Due to their possible side effects (CEH, aplastic anemia and bone marrow suppression), drugs that impair embryonic transit through the oviduct (estrogens) are not commonly used or recommended.

PATHOPHYSIOLOGY
After fertilization the embryo travels the oviduct in a timely manner before entering the uterus. Impaired embryo transport through the oviduct leads to embryonic degeneration and implantation abnormalities. In the dog and cat, pregnancy maintenance is dependent on progesterone production from the corpora lutea. In dogs and cats, maintenance of the corpora lutea during the second half of gestation is also supported by prolactin. Drugs that cause luteal regression, antagonize PRL, and/or compete with progesterone receptors will terminate pregnancy.

SYSTEMS AFFECTED
• Cardiovascular • Digestive • Neurologic (caused by drugs used for treatment) • Reproductive • Respiratory

GENETICS
N/A

INCIDENCE/PREVALENCE
N/A

GEOGRAPHIC DISTRIBUTION
N/A

SIGNALMENT
Species
Dog and cat

Breed Predilections
N/A

Mean Age and Range
Postpubertal bitch and queen

Predominant Sex
Pregnant bitch or queen

SIGNS
• Depends on stage of gestation: ◦ None ◦ Vaginal discharge ◦ Fetal expulsion

CAUSES
• Impaired oviductal transport • Luteal regression • Progesterone receptor antagonism

RISK FACTORS
N/A

DIAGNOSIS
• Confirm pregnancy first, less than 40% of mismated bitches become pregnant: ◦ Abdominal palpation (bitch: 31–33 days after LH surge; queen: 21–25 days after breeding). ◦ Transabdominal ultrasound (bitch: > 25 days after LH surge; queen: > 16 days after breeding). ◦ Abdominal radiographs (bitch: > 45 days after LH surge; queen: > 38 days after breeding). ◦ Serum relaxin concentration in the bitch (> 28 days after LH surge) (Witness® Relaxin, Synbiotics/Zoetis Corp., http://synbiotics.com/index.html; (800)733-5500). • Ascertain that a breeding took place; a tie in the bitch and coital "after-reaction" in the queen.

DIFFERENTIAL DIAGNOSIS
• Hydrometra • Mucometra • Hematometra • Pyometra • Pseudopregnancy

CBC/BIOCHEMISTRY/URINALYSIS
• Within normal limits during first half of pregnancy in healthy patients. • Decrease in PCV during second half of pregnancy in bitches and queens is normal.
• Recommended as screening test prior to treatment in patients with suspected underlying disease.

OTHER LABORATORY TESTS
• Vaginal cytology—determines stage of estrous cycle and presence of sperm (absence does not rule out a previous breeding). Methods to increase detection of sperm: infuse and recover 5–10 mL of saline from anterior vagina using standard AI pipette, centrifuge, examine pellet; collect routine cytology and allow swab to sit in 1–2 mL of saline, express fluid, centrifuge, examine pellet. • Serum progesterone concentration determines if the female is in diestrus and monitors luteal regression during treatment.

IMAGING
• Transabdominal ultrasound (method of choice): diagnose pregnancy and monitor uterine evacuation during treatment.
• Abdominal radiographs.

PATHOLOGIC FINDINGS
N/A

TREATMENT

APPROPRIATE HEALTH CARE
• Physical examination before initiation of treatment. • Monitor 30–60 minutes after treatment for side effects (vomiting, defecation, hypersalivation, hyperpnea, micturition, tachycardia). • Pregnancy status in early diestrus is unknown; ultrasound confirmation of pregnancy is not possible until ~4 weeks after breeding. • Treatment on day 6–10 of diestrus—may have reduced efficacy compared to midgestation but can be less distasteful to client (less discharge and recognizable fetuses are not passed). • $PGF_{2\alpha}$ and bromocriptine given in combination—improves efficacy of either drug given alone.

NURSING CARE
N/A

ACTIVITY
Normal

DIET
Avoid feeding prior to each treatment and for 1–2 hours after treatments (reduces nausea and vomiting).

CLIENT EDUCATION
• Discuss patient's reproductive future with owner. If no litters are desired, then OHE is the best option. • Discuss with the client the potential side effects of the treatment options; reach a mutual agreement on the treatment plan.

SURGICAL CONSIDERATIONS
OHE is recommended for patients with no reproductive value or when owners do not desire future litters.

MEDICATIONS

DRUG(S) OF CHOICE
• Confirmation of pregnancy before initiating any of the treatment protocols suggested below is recommended. Lengths of treatment suggested may vary; treatments should be continued until abortion is complete.
◦ $PGF_{2\alpha}$: causes luteal regression with subsequent decline in progesterone concentration, cervical relaxation, and uterine contractions; bitches and cats low dose protocol: 10 μg/kg SC q6h for 7–10 days or until pregnancy terminated (in the bitch), then 25 μg/kg q6h for 1–2 days; then 50 μg/kg q6h for 3–4 days (the queen is more resistant to the luteolytic effects of $PGF_{2\alpha}$ than bitches—often higher doses for longer periods are required); bitch standard dose protocol: 100 μg/kg SC q8h for 2 days, then 200 μg/kg SC q8h until pregnancy termination; queens: 0.5–1 mg/kg SC q12h every other day > day 40, or 2 mg/cat IM q24h for 5 days > day 33.
◦ Cloprostenol (prostaglandin analogue): bitches: 2.5 μg/kg SC q8 or q12h every 48 hours until pregnancy termination (~6 days after start of treatment).
◦ Dexamethasone: mode of action is unknown; bitches: 0.2 mg/kg PO q8–12h for 5 days, then decreasing from 0.16 to 0.02 mg/kg over the last five days; treatment failures not uncommon.
◦ Cabergoline (PRL antagonist): causes luteal regression; bitches: 1.65 μg/kg SC q24h for 5 days or 5 μg/kg PO q24h for 5 days > day 40; queens: 1.65 μg/kg SC for

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ABORTION, TERMINATION OF PREGNANCY

5 days > day 30 or 5 μg/kg PO q24h for 5 days > day 35.
◦ Bromocriptine (PRL antagonist): causes luteal regression; bitches: 50–100 μg/kg q12h IM or PO for 4–7 days > day 35 (50% effective); vomiting common side effect, reduce dose and give with meal.
◦ Cloprostenol and cabergoline combination: bitches: cabergoline 5 μg/kg PO q24h for 10 days plus cloprostenol 2.5 μg/kg SC at start of treatment or 1 μg/kg SC at start of treatment and at day 5 of treatment; treatment should be initiated > 28 days post-LH surge; queen: cabergoline 5 μg/kg PO q24h plus cloprostenol 5 μg/kg SC q48h (> 30 days after breeding) until abortion is complete (~ 9 days).
◦ Cloprostenol and bromocriptine combination: bitches; bromocriptine 30 μg/kg q8h PO for 10 days plus cloprostenol 2.5 μg/kg SC or 1 μg/kg SC at start of treatment and at day 5 of treatment; treatment should be initiated > 28 days post-LH surge.

CONTRAINDICATIONS

• $PGF_{2\alpha}$ and analogues: animals with respiratory disease (bronchoconstriction); do not administer intravenously. • Cabergoline and bromocriptine: avoid administration in animals hypersensitive to ergot alkaloids; use with caution in patients with significantly impaired liver function. • Estrogens may cause cystic endometrial hyperplasia, pyometra, and bone marrow suppression leading to pancytopenia.

PRECAUTIONS

• $PGF_{2\alpha}$ and analogues: side effects are dose-dependent and include vomiting, defecation, dyspnea, tachycardia, salivation, restlessness, and anxiety; side effects subside within 60 minutes; the severity of effects can be attenuated with premedication (> 15 minutes) with a combination of atropine (0.025 mg/kg); use extreme caution in dogs and cats with preexisting cardiopulmonary, liver, and renal diseases. • Dexamethasone: polydipsia, polyuria, and polyphagia are reported side effects. Long- term administration has been associated with hyperadrenocorticism. • Cabergoline and bromocriptine: should be administered with caution in patients with impaired liver function. Side effects may include vomiting and anorexia; prolonged use (> 2 weeks) may cause coat color changes.

POSSIBLE INTERACTIONS

• $PGF_{2\alpha}$ and analogues: effect may be reduced by concomitant administration of progestins; use may enhance effects of oxytocin. • Cabergoline and bromocriptine: cabergoline effects may be reduced with concomitant treatment with dopamine (D_2) antagonists; avoid concomitant treatment with hypotensive drugs.

ALTERNATIVE DRUG(S)

• The following drugs are recommended for use in bitches but not available in the United States: ◦ Mifepristone (RU486; progestin and glucocorticoid receptor antagonist): 2.5 mg/kg PO q12h for 4–5 days > day 32 of pregnancy (dog); no side effects have been reported. ◦ Aglepristone (progestin and glucocorticoid receptors antagonists): 10 mg/kg SC q24h for 2 days > 32 days post-LH surge (dog); pregnancy is terminated in 4–7 days; mild reaction at injection site have been reported; mild vaginal discharge may be observed. ◦ Aglepristone and cloprostenol combination: aglepristone (10 mg/kg SC) combined with cloprostenol (1 μg/kg SC) q24h for 2 days > 25 days pregnancy; pregnancy is terminated within 6 days. Side effects after treatment include vomiting and diarrhea. Vaginal discharge may be observed. ◦ Aglepristone (10 mg/kg SC, q24h for 2 days) with intravaginal misoprostol (200–400 μg, depending on body size) daily until abortion complete; abortion complete within 7 days. Vomiting, diarrhea, polydipsia, anorexia not observed with this regimen
◦ GnRH antagonists (Acyline; blocks GnRH receptors at the pituitary gland, causing a decline in gonadotropins concentration): a single treatment with 110–330 μg/kg SC is recommended (dog); pregnancy is terminated within 6–10 days after treatment; prepartum-like behavior has been observed; abortion may be followed by serosanguineous vaginal discharge for 2–3 days; not yet available in the US (currently in Phase I clinical trials for prostate cancer in men).

FOLLOW-UP

PATIENT MONITORING

In animals treated with luteolytic drugs (prostaglandins and PRL antagonists), progesterone assays and transabdominal ultrasound examinations should be performed to monitor decrease of serum progesterone concentration and complete evacuation of uterine contents. In patients treated with progesterone receptor antagonist drugs, transabdominal ultrasound examinations are recommended to monitor complete evacuation of the uterus.

PREVENTION/AVOIDANCE

• OHE for bitches and queens not intended for breeding. • Estrus suppression or confinement of bitches and queens intended for breeding during a later cycle to avoid mismating.

POSSIBLE COMPLICATIONS

Pregnancy termination may not be achieved after one treatment protocol and continuation or change in treatment protocol may be necessary.

EXPECTED COURSE AND PROGNOSIS

• The interestrous interval in bitches treated with prostaglandins and PRL inhibitors may be shortened (~1 month). Queens may resume estrous behavior 7–10 days after pregnancy termination. • Subsequent estrus fertility is not affected.

MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

Induced abortion

SEE ALSO

Breeding, Timing

ABBREVIATIONS

• CEH = cystic endometrial hyperplasia • GnRH = gonadotropin-releasing hormone • LH = luteinizing hormone • OHE = ovariohysterectomy • PCV = packed cell volume • $PGF_{2\alpha}$ = prostaglandin $F_{2\alpha}$ • PRL = prolactin

Suggested Reading

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Client Education Handout available online

A

ABSCESSATION

BASICS

DEFINITION
An abscess is a localized collection of purulent exudate contained within a cavity.

PATHOPHYSIOLOGY
• Bacteria are often inoculated under the skin via a puncture wound; the wound surface then seals.
• When bacteria and/or foreign objects persist in the tissue, purulent exudate forms and collects.
• Accumulation of purulent exudates—if not quickly resorbed or discharged to an external surface, stimulates formation of a fibrous capsule; may eventually lead to abscess rupture.
• Prolonged delay of evacuation—formation of a fibrous abscess wall; to heal, the cavity must be filled with granulation tissue from which the causative agent may not be totally eliminated; may lead to chronic or intermittent discharge of exudate from a draining sinus tract.

SYSTEMS AFFECTED
• Skin/Exocrine—percutaneous (cats > dogs); anal sac (dogs > cats)
• Reproductive—prostate gland (dogs > cats); mammary gland
• Ophthalmic—periorbital tissues
• Hepatobiliary—liver parenchyma
• Gastrointestinal—pancreas (dogs > cats)

GENETICS
N/A

INCIDENCE/PREVALENCE
N/A

GEOGRAPHIC DISTRIBUTION
N/A

SIGNALMENT
Species
Cat and dog

Breed Predilections
N/A

Mean Age and Range
N/A

Predominant Sex
Mammary glands (female); prostate gland (male)

SIGNS
General Comments
• Determined by organ system and/or tissue affected.
• Associated with a combination of inflammation (pain, swelling, redness, heat, and loss of function), tissue destruction, and/or organ system dysfunction caused by accumulation of exudates.

Historical Findings
• Often presented for nonspecific signs such as lethargy and anorexia.
• History of traumatic insult or previous infection.
• A rapidly appearing painful swelling with or without discharge, if affected area is visible.

Physical Examination Findings
• Determined by the organ system or tissue affected.
• Classic signs of inflammation (heat, pain, swelling, and loss of function) are associated with specific anatomic location of the abscess.
• Inflammation and discharge from a fistulous tract may be visible if the abscess is superficial and has ruptured to an external surface.
• A variably sized, painful mass of fluctuant to firm consistency attached to surrounding tissues may be palpable.
• Fever if abscess is not ruptured and draining.
• Sepsis occasionally, especially if abscess ruptures internally.

CAUSES
• Foreign objects.
• Pyogenic bacteria—*Staphylococcus* spp.; *Escherichia coli*; β-hemolytic *Streptococcus* spp.; *Pseudomonas; Mycoplasma* and *Mycoplasma*-like organisms (l-forms); *Pasteurella multocida*; *Corynebacterium; Actinomyces* spp.; *Nocardia; Bartonella*.
• Obligate anaerobes—*Bacteroides* spp.; *Clostridium* spp.; *Peptostreptococcus; Fusobacterium.*

RISK FACTORS
• Anal sac—impaction; anal sacculitis.
• Brain—otitis interna sinusitis oral infection.
• Liver—omphalophlebitis sepsis.
• Lung—foreign object aspiration bacterial pneumonia.
• Mammary gland—mastitis.
• Periorbital—dental disease; chewing of wood or other plant material.
• Percutaneous—fighting, trauma, or surgery.
• Prostate gland—bacterial prostatitis.
• Immunosuppression—FeLV/FIV infection, immunosuppressive chemotherapy, acquired or inherited immune system dysfunctions, underlying predisposing disease (e.g., diabetes mellitus, chronic renal failure, hyperadrenocorticism).

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Mass Lesions
• Cyst—less or only transiently painful; slower growing.
• Fibrous scar tissue—firm; non-painful.
• Granuloma—less painful; slower growing; generally firmer without fluctuant center.
• Hematoma/seroma—variable pain (depends on cause); non-encapsulated; rapid initial growth but slow increase once full size is attained; unattached to surrounding tissues; fluctuant and fluid filled initially but more firm with organization.
• Neoplasia—variable growth; consistent; painful.

Draining Tracts
• Mycobacterial disease
• Mycetoma—botryomycosis, actinomycotic mycetoma, eumycotic mycetoma
• Neoplasia
• Phaeohyphomycosis
• Sporotrichosis
• Systemic fungal infection—blastomycosis, coccidioidomycosis, cryptococcosis, histoplasmosis, trichosporosis

CBC/BIOCHEMISTRY/URINALYSIS
• CBC—normal or neutrophilia with or without regenerative left shift. Neutropenia and degenerative left shift if sepsis present.
• Urinalysis and serum chemistry profile—depends on system affected.
• Prostatic—pyuria.
• Liver and/or pancreatic—high liver enzymes and/or total bilirubin.
• Pancreatic (dogs)—high amylase/lipase.
• Diabetes mellitus—persistent hyperglycemia and glucosuria.

OTHER LABORATORY TESTS
• FeLV and FIV—for cats with recurrent or slow-healing abscesses.
• CSF evaluation—increase in cellularity and protein expected with brain abscess.
• Adrenal function— evaluate for hyperadrenocorticism.

IMAGING
• Radiography—soft-tissue density mass in affected area; may reveal foreign body.
• Ultrasonography—determine if mass is fluid filled or solid; determine organ system affected; reveal flocculent-appearing fluid characteristic of pus; may reveal foreign object.
• Echocardiography—helpful for diagnosis of pericardial abscess.
• CT or MRI—helpful for diagnosis of brain abscess.

DIAGNOSTIC PROCEDURES
Aspiration
• Reveals a red, white, yellow, or green liquid.
• Protein content > 2.5–3.0 g/dL.
• Nucleated cell count—3,000–100,000 (or more) cells/μL; primarily degenerative neutrophils with lesser numbers of macrophages and lymphocytes.
• Pyogenic bacteria—may be seen in cells and free within the fluid.
• If the causative agent is not readily identified with a Romanowsky-type stain, specimens should be stained with an acid-fast stain to detect mycobacteria or *Nocardia* and PAS stain to detect fungus.

Biopsy
• Sample should contain both normal and abnormal tissue in the same specimen.
• Impression smears—stained and examined.
• Tissue—submit for histopathologic examination and culture.

• Contact the diagnostic laboratory for specific instructions.

Culture

• Affected tissue and/or exudate—aerobic and anaerobic bacteria and fungus.
• Blood and/or urine—isolate bacterium responsible for possible sepsis.
• Bacterial sensitivity.

PATHOLOGIC FINDINGS

• Pus-containing mass lesion accompanied by inflammation.
• Palpable—variably firm or fluctuant mass.
• Ruptured—may see pus draining directly from the mass or an adjoining tract.
• Exudate—large numbers of neutrophils in various stages of degeneration; other inflammatory cells; necrotic tissue.
• Surrounding tissue—congested; fibrin; large number of neutrophils; variable number of lymphocytes; plasma cells; macrophages.
• Causative agent variably detectable.

TREATMENT

APPROPRIATE HEALTH CARE

• Depends on location of abscess and treatment required.
• Outpatient—bite-induced abscesses.
• Inpatient—sepsis; extensive surgical procedures; treatment requiring extended hospitalization.
• Establish and maintain adequate drainage.
• Surgical removal of nidus of infection or foreign object(s) if necessary.
• Institution of appropriate antimicrobial therapy.

NURSING CARE

• Depends on location of abscess.
• Apply hot packs to inflamed area as needed.
• Use protective bandaging and/or Elizabethan collars as needed.
• Accumulated exudate—drain abscess; maintain drainage by medical and/or surgical means.
• Sepsis or peritonitis—aggressive fluid therapy and support.

ACTIVITY

Restrict until the abscess has resolved and adequate healing of tissues has taken place.

DIET

• Sufficient nutritional intake to promote a positive nitrogen balance.
• Depends on location of abscess and treatment required.

CLIENT EDUCATION

• Discuss need to correct or prevent risk factors.
• Discuss need for adequate drainage and continuation of antimicrobial therapy for an adequate period of time.

SURGICAL CONSIDERATIONS

• Appropriate debridement and drainage—may need to leave the wound open to an external surface; may need to place surgical drains.
• Early drainage—to prevent further tissue damage and formation of abscess wall.
• Remove any foreign objects(s), necrotic tissue, or nidus of infection.

MEDICATIONS

DRUG(S) OF CHOICE

• Antimicrobial drugs—effective against the infectious agent; gain access to site of infection.
• Broad-spectrum agent—bactericidal and with both aerobic and anaerobic activity; until results of culture and sensitivity are known. Dogs and cats: amoxicillin (11–22 mg/kg PO q8–12h); amoxicillin/clavulanic acid (12.5–25 mg/kg PO q12h); clindamycin (5 mg/kg PO q12h); and trimethoprim/sulfadiazine (15 mg/kg PO IM q12h). Cats with *Mycoplasma* and l-forms: doxycycline (5 mg/kg PO q12h).
• Aggressive antimicrobial therapy—sepsis or peritonitis.

CONTRAINDICATIONS

N/A

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

FOLLOW-UP

PATIENT MONITORING

Monitor for progressive decrease in drainage, resolution of inflammation, and improvement of clinical signs.

PREVENTION/AVOIDANCE

• Percutaneous abscesses—prevent fighting.
• Anal sac abscesses—prevent impaction; consider anal saculectomy for recurrent cases.
• Prostatic abscesses—castration possibly helpful.
• Mastitis—prevent lactation (spaying).
• Periorbital abscesses—do not allow chewing on foreign object(s).

POSSIBLE COMPLICATIONS

• Sepsis.
• Peritonitis/pleuritis if intra-abdominal or intrathoracic abscess ruptures.
• Compromise of organ function.
• Delayed evacuation may lead to chronically draining fistulous tracts.

EXPECTED COURSE AND PROGNOSIS

Depends on organ system involved and amount of tissue destruction.

MISCELLANEOUS

ASSOCIATED CONDITIONS

• FeLV or FIV infection
• Immunosuppression

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

• Minimal for pyogenic bacteria.
• Mycobacteria and systemic fungal infections carry some potential.

PREGNANCY/FERTILITY/BREEDING

Teratogenic agents—avoid use in pregnant animals.

SEE ALSO

• Actinomycosis
• Anaerobic Infections
• Colibacillosis
• Mycoplasmosis
• Nocardiosis
• Sepsis and Bacteremia

ABBREVIATIONS

• CSF = cerebrospinal fluid
• CT = computed tomography
• FeLV = feline leukemia virus
• FIV = feline immunodeficiency virus
• MRI = magnetic resonance imaging
• PAS = periodic acid-Schiff

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Client Education Handout available online

A

ACETAMINOPHEN (APAP) TOXICOSIS

BASICS

DEFINITION
Results from accidental animal ingestion or owner administration of over-the-counter acetaminophen-containing analgesic and antipyretic medications.

PATHOPHYSIOLOGY
When the normal biotransformation mechanisms for detoxification (glucuronidation and sulfation) are saturated, cytochrome P450-mediated oxidation produces a toxic metabolite (*N*-acetyl-p-benzoquinone imine) that is electrophilic, conjugates with glutathione, and binds to sulfhydryl groups leading to hepatic necrosis.

Dogs
• Liver is most susceptible to toxicity.
• Signs commonly observed at exposures > 100 mg/kg.
• Methemoglobinemia may develop at doses > 200 mg/kg.

Cats
• Cannot effectively glucuronidate; more limited capacity for acetaminophen elimination than dogs.
• Saturate glucuronidation and sulfation biotransformation routes.
• RBCs are most susceptible to oxidative injury following glutathione depletion.
• Develop toxic cytochrome P450 metabolite at much lower doses than dogs.
• Poisoned by as little as 50–60 mg/kg (often as little as one-half tablet); deacetylation of acetaminophen to p-aminophenol (PAP) causes oxidative damage to RBCs, rapidly producing methemoglobinemia by binding to sulfhydryl groups on hemoglobin.
• Slower-developing hepatotoxicosis may not be fully expressed before development of fatal methemoglobinemia.

SYSTEMS AFFECTED
• Hemic/Lymph/Immune—RBCs are damaged by glutathione depletion, allowing oxidation of hemoglobin to methemoglobin.
• Hepatobiliary—liver necrosis (more common in dogs).
• Cardiovascular (primarily cats)—edema of the face, paws, and (to a lesser degree) forelimbs through an undefined mechanism.

GENETICS
Cats—genetic deficiency in the glucuronide conjugation pathway makes them vulnerable.

INCIDENCE/PREVALENCE
Common drug toxicity in cats; less frequent in dogs.

GEOGRAPHIC DISTRIBUTION
N/A

SIGNALMENT
Species
Cats more often than dogs

SIGNS
General Comments
Relatively common—owing to widespread human use.

Historical Findings
• Depression
• Hyperventilation
• Darkened mucous membranes
• Signs may develop 1–4 hours after dosing

Physical Examination Findings
• Progressive depression
• Salivation
• Vomiting
• Abdominal pain
• Tachypnea and cyanosis or muddy mucous membranes—reflect methemoglobinemia
• Edema—face, paws, and possibly forelimbs; after several hours
• Chocolate-colored urine—hematuria and methemoglobinuria; especially in cats
• Icterus
• Hypothermia
• Shock
• Death

CAUSES
Acetaminophen toxicosis

RISK FACTORS
• Nutritional deficiencies of glucose and/or sulfate
• Simultaneous administration of other glutathione-depressing drugs

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Other causes of liver injury
• Hepatotoxic mushrooms
• Blue-green algae
• Aflatoxins
• Iron, copper, zinc
• Xylitol
• Cycad palms
• NSAIDs

Other causes of methemoglobinemia
• Onions/garlic
• Naphthalene
• Chlorates
• Nitrites
• Sulfites
• Phenol
• Benzocaine
• Propylene glycol (cats)

CBC/BIOCHEMISTRY/URINALYSIS
• Methemoglobinemia and progressively rising serum concentrations of liver enzymes (ALT, AST)—characteristic.
• As hepatic function becomes impaired—decreased BUN, cholesterol, and albumin, and increased serum bilirubin.
• Heinz bodies (cats)—prominent in RBCs within 72 hours.
• Anemia, hemoglobinemia, and hemoglobinuria or hematuria.

OTHER LABORATORY TESTS
Acetaminophen plasma, serum, or urine concentrations

IMAGING
N/A

DIAGNOSTIC PROCEDURES
N/A

PATHOLOGIC FINDINGS
• Methemoglobinemia.
• Pulmonary edema.
• Centrilobular necrosis and congestion of the liver.
• Renal tubular edema and degeneration with proteinaceous tubular casts.

TREATMENT

APPROPRIATE HEALTH CARE
• With methemoglobinemia—must evaluate promptly.
• With dark or bloody colored urine or icterus—inpatient.

NURSING CARE
• Gentle handling—imperative for clinically affected patients.
• Induced emesis and gastric lavage—useful within 4–6 hours of ingestion.
• Anemia, hematuria, or hemoglobinuria—may require whole blood transfusion.
• Fluid therapy—maintain hydration and electrolyte balance.
• Oxygen therapy may be needed.
• Drinking water—available at all times.
• Food—offered 24 hours after initiation of treatment.

(CONTINUED)

ACETAMINOPHEN (APAP) TOXICOSIS

A

ACTIVITY
Restricted

DIET
N/A

CLIENT EDUCATION
• Warn client that treatment in clinically affected patients may be prolonged and expensive.
• Inform client that patients with liver injury may require prolonged and costly management.

SURGICAL CONSIDERATIONS
N/A

MEDICATIONS

DRUG(S) OF CHOICE
• Activated charcoal 2 g/kg PO; immediately after completion of emesis or gastric lavage.
• *N*-acetylcysteine (Mucomyst) 140 mg/kg diluted in D5W as loading dose PO, IV; then 70 mg/kg diluted in D5W PO, IV, q6h for 5–7 additional treatments.
• S-adenosylmethionine (SAMe) as a glutathione donor; 40 mg/kg PO × 1 dose, then 20 mg/kg q24h PO × 7 days.
• Added benefit of using methylene blue, cimetidine, and/or ascorbic acid is controversial.

CONTRAINDICATIONS
Drugs that contribute to methemoglobinemia or hepatotoxicity.

PRECAUTIONS
Drugs requiring extensive liver metabolism or biotransformation—use with caution; expect their half-lives to be extended.

POSSIBLE INTERACTIONS
Drugs requiring activation or metabolism by the liver have reduced effectiveness.

FOLLOW-UP

PATIENT MONITORING
• Continual clinical monitoring of methemoglobinemia—vital for effective management; laboratory determination of methemoglobin percentage every 2–3 hours.
• Serum liver enzyme activities (ALT, ALP) every 12 hours; monitor liver damage.

PREVENTION/AVOIDANCE
• Never give acetaminophen to cats.
• Give careful attention to the acetaminophen dose in dogs.

POSSIBLE COMPLICATIONS
Liver necrosis and resulting fibrosis—may compromise long-term liver function in recovered patients.

EXPECTED COURSE AND PROGNOSIS
• Rapidly progressive methemoglobinemia—serious sign.
• Methemoglobin concentrations ≥ 50%—grave prognosis.
• Progressively rising serum liver enzymes 12–24 hours after ingestion—serious concern.
• Expect clinical signs to persist 12–48 hours; death owing to methemoglobinemia possible at any time.
• Dogs and cats receiving prompt treatment that reverses methemoglobinemia and prevents excessive liver necrosis—may recover fully.
• Dogs—death as a result of liver necrosis may occur within 72 hours.
• Cats—death as a result of methemoglobinemia occurs 18–36 hours after ingestion.

MISCELLANEOUS

ASSOCIATED CONDITIONS
Keratoconjunctivitis sicca (KCS) may develop in small-breed dogs as a sequela.

AGE-RELATED FACTORS
Young and small dogs and cats—greater risk from owner-given single-dose acetaminophen medications.

ZOONOTIC POTENTIAL
None

PREGNANCY/FERTILITY/BREEDING
Imposes additional stress and higher risk on exposed animals.

SYNONYMS
• Paracetamol
• Tylenol

SEE ALSO
Poisoning (Intoxication) Therapy

ABBREVIATIONS
• PAP = p-aminophenol
• ALT = alanine aminotransferase
• AST = aspartate transaminase
• RBC = red blood cell
• D5W = 5% dextrose injection

INTERNET RESOURCES
http://www.aspca.org/pet-care/poison-control/

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Client Education Handout available online

A

ACIDOSIS, METABOLIC (TRADITIONAL APPROACH)

BASICS

DEFINITION

A process in the body that leads to a decrease in pH below the reference interval for that species. A decline in blood pH is specifically termed acidemia. Associated with a decrease in plasma bicarbonate concentration (HCO_3^-) (dogs, > 18 mEq/L; cats, > 16 mEq/L) and base excess (BE) (< – 4 mmol/L) with a compensatory decrease in carbon dioxide tension (PCO_2).

PATHOPHYSIOLOGY

• Metabolic acidosis may develops either from a *loss of* HCO_3^- (hyperchloremic acidosis) or a *gain in acid* (high anion gap acidosis). It is usually secondary to an accumulation of metabolically produced strong anions (strong ion gap or high anion gap acidosis), accumulation of weak acids (hyperphosphatemia), corrected hyperchloremia (hyperchloremic acidosis), or as a compensatory mechanism for respiratory alkalosis. • *High anion gap* acidosis: Increase in the concentration of other strong anions through addition (e.g., ethylene glycol toxicity), excessive production (e.g., lactate produced by prolonged anaerobic metabolism), or renal retention (e.g., renal failure) of strong anions other than chloride causes metabolic acidosis without increasing chloride concentration (so-called normochloremic or high AG metabolic acidosis). • *Hyperphosphatemic* acidosis: Increase in plasma weak acids (e.g., inorganic phosphate) is associated with metabolic acidosis and increased anion gap. At pH of 7.4, a 1 mg/dL increase in phosphate concentration is associated with a 0.58 mEq/L decrease in HCO_3^- and a 0.58 mEq/L increase in AG. Hyperphosphatemia commonly develops with decrease renal phosphorous excretion (e.g., renal failure, hypoparathyroidism, etc), cellular lysis (e.g., tumor lysis syndrome, trauma, rhabdomyolysis), bone neoplasms (increased bone resorption), and hypervitaminosis D. • *Hyperchloremic* acidosis: Hyperchloremic acidosis may be caused by chloride retention (e.g., renal failure, renal tubular acidosis) that typically occurs in response to HCO_3^- loss. Chloride and HCO_3^- are reciprocally related; a loss of HCO_3^- generally results in retention of chloride. Other mechanisms for hyperchloremic acidosis include: excessive loss of sodium relative to chloride (e.g., diarrhea, Addison's) and administration of substances containing more chloride than sodium as compared with normal extracellular fluid composition (e.g., administration of KCl, 0.9% NaCl). Acidemia is usually not severe in patients with hyperchloremic acidosis.

SYSTEMS AFFECTED

• Cardiovascular—a fall in pH results in an increase in sympathetic discharge but simultaneously causes a decrease in the responsiveness of the cardiac myocytes and vascular smooth muscle to the effects of catecholamines. In mildly acidemic conditions (pH > 7.2), the effects of increased sympathetic stimulation predominate and result in a mild increase in heart rate and cardiac output. More severe acidemia (pH < 7.1), especially if acute, may decrease cardiac contractility and predispose the heart to ventricular arrhythmias and ventricular fibrillation. • Respiratory—increased $[H^+]$ stimulates peripheral and central chemoreceptors to increase alveolar ventilation; hyperventilation decreases PCO_2, which counters the effects of low plasma HCO_3^- on pH. In dogs, a decrease of approximately 0.7 mmHg in PCO_2 is expected for each 1 mEq/L decrease in plasma HCO_3^-. Little is known about compensation in cats, but it appears to be almost nonexistent. • Renal/Urologic—the kidneys increase net acid excretion, primarily by increasing excretion of NH_4^+ and chloride. This compensatory mechanism is not very effective in cats.

SIGNALMENT

Any breed, age, or sex of dog and cat

SIGNALMENT

Historical Findings

• Chronic disease processes that lead to metabolic acidosis (e.g., renal failure, diabetes mellitus, and hypoadrenocorticism), acute circulatory shock (hemorrhagic), exposure to toxins (e.g., ethylene glycol, salicylate, and paraldehyde), diarrhea, administration of carbonic anhydrase inhibitors (e.g., acetazolamide and dichlorphenamide).

Physical Examination Findings

• Generally relate to the underlying disease. • Depression, stupor, seizures, and or generalized muscle weakness in severely acidotic patients. • Tachypnea in some patients results from compensatory increase in ventilation. • Kussmaul's respiration, typically seen in human beings with metabolic acidosis, is not commonly observed in dogs and cats. • Vomiting and/or diarrhea.

CAUSES

Associated with Hyperchloremia (Hyperchloremic Metabolic Acidosis)

• Renal: Renal tubular acidosis; carbonic anhydrase inhibitors. • GI: Diarrhea. • Other: Chloride-rich fluids (e.g., 0.9% NaCl, KCl supplementation); total parenteral nutrition with cationic amino acids: lysine, arginine, and histidine; rapid correction of hypocapnia (chronic respiratory alkalosis); NH_4Cl or HCl.

Associated with Normochloremia (High Anion Gap Metabolic Acidosis)

• Renal: uremic acidosis, acute renal failure. • Ketoacidosis: diabetic ketoacidosis, starvation liver disease. • Lactic acidosis: impaired perfusion, impaired carbohydrate metabolism. • Toxins: ethylene glycol, salicylate, paraldehyde, and methanol intoxication. • Hyperphosphatemia (see Hyperphosphatemia): raises the anion gap. At a pH of 7.4, each 1 mg/dL increase in phosphate concentration is associated with a 0.58 mEq/L increase in anion gap.

RISK FACTORS

• Chronic renal failure, diabetes mellitus, and hypoadrenocorticism • Poor tissue perfusion or hypoxia—lactic acidosis • Tumor lysis syndrome or osteosarcoma—hyperphosphatemia • Trauma, snake envenomation, or malignant hyperthermia—rhabdomyolysis

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Low plasma HCO_3^- and hyperchloremia may also be compensatory in animals with chronic respiratory alkalosis, in which PCO_2 is low and pH is high or near normal, despite decreased HCO_3^- and increase in chloride concentration. Blood gas determination is required to differentiate.

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

Potassium bromide is measured as chloride in most analyzers, so potassium bromide administration artificially decreases the anion gap.

Disorders That May Alter Laboratory Results

• Too much heparin (> 10% of the sample) decreases HCO_3^-. • Blood samples stored at room temperature for > 15 minutes have low pH because of increased PCO_2. • Hypoalbuminemia lowers AG; negative charges of albumin are the main component of the anion gap.

Valid if Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

• Low total CO_2—total CO_2 in serum samples handled aerobically closely approximates the serum HCO_3^- concentration; unfortunately, patients with chronic respiratory alkalosis also have low total CO_2, and the distinction cannot be made without blood gas analysis. • Metabolic acidoses are traditionally divided into hyperchloremic and high anion gap by means of the anion gap. Anion gap, the difference between the measured cations and the

(CONTINUED)

ACIDOSIS, METABOLIC (TRADITIONAL APPROACH)

measured anions, is calculated as AG = $[Na^+] - (HCO_3^- + [Cl^-])$ or AG = $([Na^+] + [K^+]) - (HCO_3^- + [Cl^-])$, depending on the preference of the clinician or laboratory. Normal values with potassium included in the calculation are usually 12–24 mEq/L in dogs and 13–27 mEq/L in cats. The negative charges of albumin are the major contributors to the normal anion gap; this should be taken into account when evaluating anion gap in patients with hypoalbuminemia. At pH 7.4 in dogs, a decrease of 1 g/dL in albumin is associated with a decrease of 4.1 mEq/L in the anion gap. • Normal anion gap (i.e., hyperchloremic metabolic acidosis). • High anion gap (i.e., normochloremic metabolic acidosis). • Hyperglycemia—see Hyperglycemia. • Azotemia—see Azotemia. • Hyperphosphatemia—see Hyperphosphatemia. • High lactate concentration—see Lactic Acidosis. • Hyperkalemia—see Hyperkalemia (*formulas to adjust potassium concentration based on pH changes should not be used*).

OTHER LABORATORY TESTS

Blood gas analysis reveals low HCO_3^-, low PCO_2, and low pH.

DIAGNOSTIC PROCEDURES

None

TREATMENT

• Acid-base disturbances are secondary phenomena; successful resolution depends on diagnosis and treatment of the underlying disease process. • Restore blood volume and perfusion deficits before considering $NaHCO_3$. • Treat patients with blood pH ≤ 7.1 aggressively while pursuing the definitive diagnosis. • Discontinue drugs that may cause metabolic acidosis. • Nursing care—Isotonic, *buffered* electrolyte solution is the fluid of choice for patients with mild metabolic acidosis and normal liver function.

MEDICATIONS

DRUG(S) OF CHOICE

• $NaHCO_3$ may help patients with hyperchloremic, hyperhosphatemic, or uremic acidosis, but not patients with lactic acidosis or diabetic ketoacidosis.
• $NaHCO_3$ may be considered for alkaline diuresis in salicylate toxicity.
  ◦ Estimation of HCO_3^- dose: dogs, 0.3 × body weight (kg) × (21 – patient HCO_3^-); cats, 0.3 × body weight (kg) × (19 – patient HCO_3^-). Give half of this dose slowly IV and reevaluate blood gases before deciding on the need for additional administration. An empirical dose of 1–2 mEq/kg followed by reevaluation of blood gas status is safe in most patients.
  ◦ Potential complications of $NaHCO_3$ administration: volume overload resulting from administered sodium, tetany from low ionized calcium concentration, increased affinity of hemoglobin for oxygen, paradoxical CNS acidosis, overshoot metabolic alkalosis, and hypokalemia.
• Hyperchloremic acidosis: $NaHCO_3$ may be effective and considered whenever pH < 7.1.
• Uremic acidosis: efficacy of $NaHCO_3$ in acute therapy of uremic acidosis is related to the shift of phosphate inside the cells and consequent amelioration of hyperphosphatemic acidosis.
• Lactic acidosis: $NaHCO_3$ increases lactate production and is of little to no value in lactic acidosis. Therapy should be directed at augmenting oxygen delivery to the tissues and reestablishing cardiac output. Small titrated doses of $NaHCO_3$ can be used as a temporizing measure to maintain HCO_3^- above 5 mEq/L, if needed.
• Diabetic ketoacidosis: $NaHCO_3$ adversely affects outcome in humans with diabetic ketoacidosis even when pH is < 7.0.
• Administration of $NaHCO_3$ to ketoacidotic patients cannot be recommended at any pH. Therapy should be direct at insulin and fluid administration. Reestablishing plasma volume and renal perfusion will allow the kidneys to excrete ketoanions, replacing them with chloride.

CONTRAINDICATIONS

• Avoid $NaHCO_3$ in patients with respiratory acidosis because it generates CO_2. • Patients with respiratory acidosis cannot adequately excrete CO_2, and increased PCO_2 will further decrease the pH. • Avoid diuretics that act in the distal nephron (e.g., spironolactone). • Avoid carbonic anhydrase inhibitors (e.g., acetazolamide, dichlorphenamide). • Avoid $NaHCO_3$ in acute (< 10 minutes) cardiac arrest as it may impair tissue oxygen unloading.

PRECAUTIONS

Use $NaHCO_3$ cautiously in patients with congestive heart failure because the sodium load may cause decompensation of the heart failure.

POSSIBLE INTERACTIONS

None

ALTERNATIVE DRUG(S)

None

FOLLOW-UP

PATIENT MONITORING

Recheck acid-base status; frequency dictated by the underlying disease and patient response to treatment.

POSSIBLE COMPLICATIONS

• Hyperkalemia in acute hyperchloremic acidosis • Myocardial depression and ventricular arrhythmias

MISCELLANEOUS

ASSOCIATED CONDITIONS

• Hyperkalemia • Hyperchloremia

AGE-RELATED FACTORS

None

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

• Dilutional acidosis—metabolic acidosis resulting from increased free water in plasma. • Hyperchloremic acidosis—normal anion gap acidosis. • Hyperphosphatemic acidosis—metabolic acidosis resulting from high phosphate concentration.
• Non-respiratory acidosis.
• Normochloremic acidosis—high anion gap acidosis. • Organic acidosis—metabolic acidosis resulting from accumulation of organic anions (e.g., ketoacidosis, uremic acidosis, and lactic acidosis).

SEE ALSO

• Azotemia • Diabetes Mellitus with Ketoacidosis • Hyperchloremia
• Hyperkalemia • Hyperphosphatemia
• Lactic Acidosis

ABBREVIATIONS

• AG = anion gap • BE = base excess
• CNS = central nervous system
• H^+ = hydrogen ion • HCO_3^- = bicarbonate
• $NaHCO_3$ = sodium bicarbonate
• O_2 = oxygen • PCO_2 = carbon dioxide tension

Suggested Reading

de Morais HA, Constable PD. Strong ion approach to acid-base disorders. In: DiBartola SP, ed., Fluid, Electrolyte and Acid-Base Disorders, 4th ed. St. Louis, MO: Saunders, 2012, pp. 316–330.
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Authors Helio S. Autran de Morais and Lee E. Palmer
Consulting Editor Carl A. Osborne

A

ACNE—CATS

BASICS

OVERVIEW
• Inflammatory dermatitis affecting the chin and lips
• Symptoms may be recurrent or persistent
• Precise etiology unknown

SIGNALMENT
• Cats
• Prevalence for sex, age, or breed not reported

SIGNS
• Cats may have a single episode, a life-long recurrent problem, or a continual disease.
• Frequency and severity of each occurrence varies with the individual.
• Comedones, mild erythematous papules, serous crusts, and dark keratin debris develop on the chin and less commonly on the lips.
• Swelling of the chin.
• Severe cases—nodules, hemorrhagic crusts, pustules, cysts, fistulae, severe erythema, alopecia, and pain.
• Pain often associated with bacterial furunculosis.

CAUSES & RISK FACTORS
Precise etiology unknown; may be a disorder of keratinization, poor grooming, abnormal sebum production, immunosuppression, viral infection, or stress.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Bacterial folliculitis
• Demodicosis
• *Malassezia* infection
• Dermatophytosis
• Neoplasia of sebaceous or apocrine glands
• Eosinophilic granuloma
• Contact hypersensitivity

CBC/BIOCHEMISTRY/URINALYSIS
N/A

OTHER LABORATORY TESTS
N/A

IMAGING
N/A

DIAGNOSTIC PROCEDURES
• Skin scrapings—demodicosis.
• Fungal culture—dermatophytosis.
• Cytology—bacteria, *Malassezia.*
• Biopsy—rarely needed; necessary in selected cases to characterize changes such as cystic follicles, to differentiate acne from other diseases such as demodicosis, infections (bacterial, yeast, or dermatophytes), or to diagnose neoplasia.

PATHOLOGIC FINDINGS
• Mild disease—follicular distention with keratin (comedo), hyperkeratosis, and follicular plugging.
• Severe disease—mild to severe folliculitis and perifolliculitis with follicular pustule formation leading to furunculosis and pyogranulomatous dermatitis.
• Bacteria and *Malassezia* in these lesions are considered secondary invaders and not causative agents.
• *Demodex* mites can be primary agents of this disease.

TREATMENT
• Initial treatment—gentle clipping and soakings to soften crusts.
• Continue one or a combination of the therapies listed below until all lesions have resolved.
• Discontinue treatment by tapering medication over a 2- to 3-week period.
• Recurrent episodes—once the recurrence rate is determined, an appropriate maintenance protocol can be designed for each individual.
• Continual episodes—life-long maintenance treatment necessary.

MEDICATIONS

DRUG(S)
Topical
• Shampoo—once or twice weekly with antiseborrheic (sulfur-salicylic acid, benzoyl peroxide, or ethyl lactate).
• Cleansing agents—benzoyl peroxide, salicylic acid, chlorhexidine-phytosphingosine.
• Wet wipes—Douxo Chlorhexidine pads®, Malaseb® wipes, MalAcetic® wipes, GlycoZoo® wipes.
• Antibiotic ointment—mupirocin 2%.
• Other topicals—clindamycin or erythromycin solution or ointment.
• Combination topicals—benzoyl peroxide-antibiotic gels (e.g., Benzamycin).
• Topical retinoids—Tretinoin (Retin-A 0.01% gel).
• In severe inflammatory periods 10–14 days of oral prednisolone (1–2 mg/kg q24h) may help to reduce scar tissue formation.

Systemic
• Antibiotics—amoxicillin with clavulanate, cephalosporin, or fluoroquinolone.
• Severe cases may warrant treatment with isotretinoin (Accutane) or cyclosporine, modified (Atopica).
• Demodicosis—oral ivermectin 400 μg/kg daily until mites are cleared.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
• Benzoyl peroxide and salicylic acids—can be irritating.
• Some wipes contain alcohols that can be irritating.
• Systemic isotretinoin—use with caution, if animal will not allow application of topical medications; potential deleterious side effects in human beings (drug interactions and teratogenicity); container should be labeled for animal use only and kept separate from human medications to avoid accidental use; currently difficult to obtain for animal patients.

FOLLOW-UP
• Monitor for relapses.
• Maintenance cleansing programs can be used to reduce relapses. Affected cats are likely to have variable numbers of comedones life-long, often are just cosmetic and treatment is not necessary.

MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING
Systemic isotretinoin should not be used on breeding animals.

Suggested Reading
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White SD. Feline acne and results of treatment with mupirocin in an open clinical trial: 25 cases (1994–96). Vet Dermatol 1997, 8:157.
Author David D. Duclos
Consulting Editor Alexander H. Werner

ACNE—DOGS

BASICS

OVERVIEW
• Also called muzzle folliculitis and furunculosis.
• Chronic inflammatory disorder of the chin and lips of young animals.
• Characterized by folliculitis and furunculosis; rarely comedogenic as seen in "true acneiform" lesions of human beings.
• Recognized almost exclusively in short-coated breeds.
• Genetic predisposition and local trauma may play a more important role than hormonal effects.

SIGNALMENT
• Dogs.
• Predisposed short-coated breeds—boxer, Doberman pinscher, English bulldog, Great Dane, Weimaraner, mastiff, rottweiler, German shorthaired pointer, pit bull terrier.

SIGNS
• Ventral chin and lip margins may be minimally to markedly swollen with numerous erythematous papules and pustules.
• Initial lesions are sterile; bacteria may not be isolated and lesions may not respond to antibiotics.
• Advanced stages—lesions may be exudative, indicating secondary deep bacterial folliculitis-furunculosis.
• Lesions may be painful on palpation; most are non-painful and non-pruritic.
• Chronic resolved lesions may be scarred and lichenified.

CAUSES & RISK FACTORS
Some short-coated breeds appear to be genetically predisposed to follicular hyperkeratosis and secondary bacterial infection.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Dermatophytosis
• Demodicosis
• Foreign body
• Contact dermatitis

CBC/BIOCHEMISTRY/URINALYSIS
N/A

OTHER LABORATORY TESTS
N/A

IMAGING
N/A

DIAGNOSTIC PROCEDURES
• Bacterial culture and sensitivity testing—in patients with suppurative folliculitis and furunculosis that are non-responsive to initial antibiotic selection.
• Biopsy—histologic confirmation for cases in which diagnosis is in question.
• Skin scrape—demodicosis.
• Dermatophyte culture—dermatophytosis.

PATHOLOGIC FINDINGS
• Clinical signs and histopathologic findings are diagnostic.
• Initial lesions—hairless follicular papules; characterized histopathologically by marked follicular keratosis, plugging, dilatation, and perifolliculitis.
• Bacteria—not present and cannot be isolated from lesions in early stages.
• As disease progresses, papules enlarge and rupture, promoting a suppurative folliculitis and furunculosis.

TREATMENT

• Depends on the severity and chronicity of the disease.
• Reduce behavioral trauma to the chin (e.g., rubbing on the carpet, chewing bones that increase salivation).
• Frequent cleaning with benzoyl peroxide shampoo or gel.
• Mupirocin 2% ointment to reduce the bacterial numbers on the surface of the skin.
• Instruct owners to avoid expressing the lesions, which may cause internal rupture of the papule and massive inflammation.

MEDICATIONS

DRUG(S)
Topical
• Benzoyl peroxide shampoo or gel (antibacterial).
• Mupirocin 2% ointment (antibacterial-staphylococcus).
• Tretinoin (Retin-A)—may reduce follicular keratosis.
• Corticosteroids—may be necessary to reduce inflammation; limit frequency of use to avoid local and systemic effects.

Systemic
• Antibiotics appropriate for deep bacterial infection—when indicated (e.g., cephalexin, 22 mg/kg PO q8–12h for 6–8 weeks).
• May need to perform bacterial culture and sensitivity test.
• Isotretinoin (Accutane)—1–2 mg/kg/day.
• Oral corticosteroids: tapering dosages of prednisolone (initial 0.5 mg/kg/day) to reduce significant inflammation; not for continued use.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
• Benzoyl peroxide—may bleach carpets and fabrics; may be irritating.
• Mupirocin ointments—greasy; may be prudent to reserve for use in multidrug-resistant cases.
• Topical retinoids—may be drying and irritating.
• Topical steroids—may cause adrenal suppression and thinning of skin with repeated use.
• Isotretinoin—may cause keratoconjunctivitis sicca, hyperactivity, ear pruritus, erythema of mucocutaneous junctions, lethargy with vomiting, abdominal distension, anorexia with lethargy, collapse, and swollen tongue; CBC and chemistry screen abnormalities include high platelet count, hypertriglyceridemia, hypercholesterolemia, and high alanine transaminase.

FOLLOW-UP

PATIENT MONITORING
• Continue antibiotics until lesions have healed.
• Repeat bacterial culture/sensitivity if lesions worsen.
• Discontinue topical corticosteroids when possible.

EXPECTED COURSE AND PROGNOSIS
• Long-term topical treatment may be required.
• Chronic scarring may be prevented by early and aggressive therapy.

MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING
Synthetic retinoids—teratogens; do not use in pregnant animals, animals intended for reproduction, or intact female animals; should not be handled by women of childbearing age.

Suggested Reading
Miller WH, Griffin CE, Campbell KL. Muzzle folliculitis and furunculosis. In: Muller & Kirk's Small Animal Dermatology, 7th ed. St. Louis, MO: Elsevier, 2013, pp 201 and 640.

Author Karen Helton Rhodes
Consulting Editor Alexander H. Werner

A

ACRAL LICK DERMATITIS

BASICS

OVERVIEW
• Chronic lesions directly caused by self-trauma.
• A cycle of licking, pruritus, and secondary infection develops.

SYSTEMS AFFECTED
Skin/Exocrine

SIGNALMENT
• Dogs.
• Most common in large breeds—especially Doberman pinschers, Labrador retrievers, Great Danes, Irish and English setters, golden retrievers, Akitas, Dalmatians, boxers, Shar-Peis, and Weimaraners.
• Age at onset—varies (especially with cause).
• No sex predilection.

SIGNS
• Excessive licking of the affected area.
• Alopecic, eroded, thickened, and raised firm plaques with scabs and exudation, usually located on the dorsal aspect of the carpus, metacarpus, tarsus, or metatarsus.
• Lesions often occur singly or may be multiple.

CAUSES & RISK FACTORS
• Focal trauma to the area initiating a lick-itch cycle.
• Anything causing a local irritation or lesion may initiate response.
• Associated diseases—staphylococcal furunculosis, hypersensitivity, endocrinopathy, demodicosis, dermatophytosis, foreign body reaction, neoplasia, underlying joint disease or arthritis, trauma, neuropathy, psychogenic, or sensory nerve dysfunction.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Neoplasia
• Bacterial furunculosis
• Focal demodicosis
• Focal dermatophytosis

CBC/BIOCHEMISTRY/URINALYSIS
Normal except in cases of endocrinopathy.

OTHER LABORATORY TESTS
Endocrinopathy—free T_4/TSH; ACTH stimulation test or LDDST.

IMAGING
Radiology—neoplasia; local trauma; radiopaque foreign bodies; bony proliferation may be seen secondary to the chronic irritation; evidence of underlying arthritis if over a joint.

DIAGNOSTIC PROCEDURES
• Skin scrapings—demodicosis.
• Dermatophyte culture—fungal infection.
• Epidermal cytology—bacterial infection.
• Bacterial culture and sensitivity—tissue cultures may differ from surface culture.
• Food-elimination diet—determine food allergy.
• Intradermal allergy testing—atopy.
• Biopsy—to rule out neoplasia, other infections.
• Behavioral history.
• Neurologic and orthopedic evaluation.

PATHOLOGIC FINDINGS
Histopathology—epidermal hyperplasia, plasmacytic dermal inflammation, folliculitis, furunculosis, perihidradenitis, hidradenitis, and vertical streaking fibrosis.

TREATMENT

• Behavioral therapy: attempt to identify psychological causes and remediate.
• Physical restraints—Elizabethan collars and bandaging permit healing.
• Therapeutic laser—one controlled study did not demonstrate efficacy.
• Diet—no modification unless food hypersensitivity is suspected.
• Difficult to treat, especially if no underlying cause is found; warn owner that patience and time are necessary.
• Surgery (laser or standard)—may cause increased licking and attention to a larger affected area; if underlying causes are not addressed, recurrence is likely.

MEDICATIONS

DRUG(S)

Antibiotics
• Based on bacterial culture and sensitivity.
• Administer until infection is completely resolved; often at least 6 weeks.

Systemic
• Antihistamines—e.g., hydroxyzine (1–2 mg/kg PO q12h); chlorpheniramine (4–8 mg/dog PO q12h; maximum of 0.5 mg/kg q12h).
• SSRIs: e.g., fluoxetine (1 mg/kg PO q24h); paroxetine (0.5–1 mg/kg PO q24h).
• Dopamine antagonists: e.g., naltrexone (2.2 mg/kg PO q12–24h).
• TCAs: e.g., amitriptyline (1.1–2.2 mg/kg PO q12h; doxepin (3–5 mg/kg PO q12h; maximum 150 mg q12h); clomipramine (1–3.5 mg/kg PO q12–24h).
• Combine and/or withdraw administration of these medications carefully.

Topical
• Flunixin meglumine and fluocinolone in dimethyl sulfoxide (combined).
• Topical capsaicin products.
• Intralesional corticosteroids rarely helpful.
• Topical medications should be applied with gloves.
• Animals should be kept from licking the area for 10–15 minutes.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
• Doxepin—caution using with monoamine oxidase inhibitors, clonidine, anticonvulsants, oral anticoagulants, steroid hormones, antihistamines, or aspirin.
• Antihistamines—may cause sedation.
• Psychotropic medications should be combined and/or withdrawn carefully.
• Cardiotoxicity and hepatoxicity—rare cases in animals on TCAs. Routine monitoring recommended.

FOLLOW-UP

• Monitor level of licking and chewing closely.
• Treat underlying disease to prevent recurrence.
• If no underlying disease is detected, suspect psychogenic causes (compulsive or self-mutilation disorder); prognosis is guarded.

MISCELLANEOUS

AGE-RELATED FACTORS
Dogs < 5 years old—strongly consider allergy

ZOONOTIC POTENTIAL
• Transmitted to humans only if dermatophytosis is the underlying cause; exceedingly rare.
• Methicillin resistant *Staphylococcus aureus* may have zoonotic implications.

ABBREVIATIONS
• ACTH = adrenocorticotropin hormone
• LDDST = low-dose dexamethasone suppression test
• SSRI = selective serotonin reuptake inhibitor
• TCA = tricyclic antidepressant
• TSH = thyroid stimulating hormone

Suggested Reading
Shumaker AK, Angus JC, et al. Microbiological and histopathological features of canine acral lick dermatitis. Vet Dermatol 2008, 19(5):288–298.

Author Alexander H. Werner
Consulting Editor Alexander H. Werner
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ACROMEGALY—CATS

BASICS

OVERVIEW

• Syndrome resulting from growth hormone (somatotropin) hypersecretion by tumorous or hyperplastic somatotrophs in the anterior pituitary.
• Clinical signs are due to growth hormone's direct catabolic/diabetogenic effects and its indirect anabolic effects mediated through insulin-like growth factor I, which is secreted by the liver in response to growth hormone stimulation.
• Elevated IGF1 activity induces excessive soft tissue growth, visceral organomegaly, bone remodeling and thickening (especially in bones formed from membranous ossification) resulting in arthropathy, broad facial features, and enlarged "clubbed" paws.
• Myocardial hypertrophy occurs in many cats, but heart failure is uncommon.
• The catabolic actions of GH result from insulin antagonism leading eventually to pancreatic β cell exhaustion and DM. Between 25 and 33% of diabetic cats may have acromegaly.
• Like most diabetic cats the potential for remission remains if the excessive GH production can be normalized; likelihood of remission is inversely related to the duration of DM.

SIGNALMENT

• Cat
• Median age—11 years (range of 6–17 years)
• Approximately 80% are males

SIGNS

• Initial signs relate to unregulated DM with the vast majority of cases presenting with polyuria, polydipsia, and often profound polyphagia accompanied with concurrent weight gain (weight loss has also been reported).
• Many patients gain weight and have increased body size due to increased bone and soft tissue mass, not from increased adipose tissue. Weight gain in an unregulated diabetic cat strongly suggests acromegaly.
• Broadening of facial features, prognathia inferior, and increased paw size reflect long-standing or severe disease.
• Organomegaly—most commonly bilateral renomegaly and hepatomegaly.
• Murmur and/or gallop rhythm occasionally present; signs of heart failure uncommon.
• Lameness may develop.
• Neurologic signs referable to intracranial disease through an expanding pituitary mass lesion possible.
• Recent reports suggest the majority of acromegalic cats are indistinguishable phenotypically from non-acromegalic diabetic cats.

CAUSES & RISK FACTORS

• GH hypersecretion.
• Progestins do not cause GH secretion and acromegaly in cats as they do in dogs.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Uncomplicated DM or DM secondary to hyperadrenocorticism
• Pituitary-dependent hyperadrenocorticism and acromegaly can both produce insulin-resistant DM with an associated pituitary mass lesion. Differentiation may require use of a low-dose dexamethasone suppression test to rule out PDH.
• Acromegaly and PDH can occur concurrently.
• Other disorders causing weight loss with polyphagia, polyuria, and polydipsia such as hyperthyroidism are not usually associated with significant glucose intolerance.
• Insulin-resistant DM (> 2.0 U of insulin/kg/12h) is to be expected in all acromegalic cats and the dose tends to increase over time, with doses of 12–50 U/cat/12h not uncommon.
• Acromegaly should be suspected in any diabetic cat demonstrating signs of otherwise unexplained insulin resistance.

CBC/BIOCHEMISTRY/URINALYSIS

• Most abnormalities attributed to poorly controlled DM—hyperglycemia, glucosuria, and elevated fructosamine levels are consistent findings in most acromegalic cats.
• Hyperproteinemia.
• Traditionally associated with renal failure and hypertension, but more recent studies suggest this is not the case.

OTHER LABORATORY TESTS

• IGF1—diabetic cats receiving insulin can have higher IGF1 levels than normal; hence there is significant potential for overlap between acromegalic and non-acromegalic diabetic cats; however, dramatically elevated IGF1 levels (e.g., > 1,000 ng/ml) are strongly suggestive of the acromegaly.
• IGF1 is well preserved across the species, so valid assays are commonly available.
• GH—elevated basal serum levels are diagnostic. However, as GH is not well preserved across the species, a validated fGH assay has limited availability.

IMAGING

• Intracranial imaging to demonstrate a pituitary mass lesion; MRI is more sensitive than contrast-enhanced CT, although the difference is modest and from a cost-benefit perspective CT is generally preferred.
• Echocardiographic abnormalities may include left atrial enlargement, asymmetric septal and left ventricular free-wall thickening, systolic anterior motion of the mitral valve, and diastolic dysfunction.
• Radiographic changes include increased oropharyngeal soft tissue, degenerative arthropathy with periarticular osteophytosis, spinal spondylosis deformans, and variable abdominal organomegaly.

TREATMENT

RADIOTHERAPY

• The only currently available means of reducing autonomous overproduction of GH from the anterior pituitary. Unfortunately, radiotherapy is more suited to reducing the size of the tumor than achieving clinically significant reductions in GH secretion.
• A total dose of between 3,500 and 5,500 cGY, administered in variably fractionated doses is often suggested. Recent reports suggest that the greatest success may be achieved with a total dose of 3,700 cGy administered as an incremental hypofractionated dosage protocol of 10 doses. Using this method, 13 of 14 acromegalic cats had markedly improved diabetic control.

SURGERY

• Hypophysectomy is considered the treatment of choice in human hypersomatotropism. It has also proven to be the only consistently effective and reliable method to cure HS in cats.
• An experienced neurosurgeon and appropriate pre-, peri- and postoperative care are essential for success. A transsphenoidal approach is currently preferred (incising the soft palate).
• In the long run, cats need to be supplemented with thyroid hormone and a glucocorticoid; synthetic ADH (DDAVP) supplementation can often be ceased 6–8 weeks postoperatively. When performed early in the disease process, diabetic remission is a realistic outcome and often occurs within 2 months after the procedure.

MEDICATIONS

Somatostatins and dopamine agonists have been used to try to inhibit GH secretion by the pituitary, mostly without success. Recently, a novel somatostatin analog, pasireotide (Novartis, Basel, Switzerland) has been shown to be effective at achieving this, although further research is required to evaluate the use of this drug, including dosing regimes, in the long run.

A

ACROMEGALY—CATS (CONTINUED)

PALLIATIVE TREATMENT

• When definitive treatment is not possible, the focus should lie on gaining more control of the diabetes mellitus and treating possible comorbidities.
• Eventually most cats tend to need high dosages of insulin and/or combinations of short-acting and long-acting insulin types to ensure an adequate quality of life for both pet and owner.
• Nevertheless, a minority achieve an adequate quality of life.
• Regular veterinary assessment is recommended.
• Iatrogenic hypoglycemia is a major concern given the pulsatile nature of GH secretion (and therefore associated insulin resistance).

FOLLOW-UP

• Clinical signs that might be attributed to poor diabetic control (e.g., profound polyphagia) will not improve with improved diabetic control; thus levels of glycated proteins or blood glucose levels are better indicators of diabetic control than clinical signs.
• Serum IGF1 levels are not suitable for monitoring therapy as they do not change during or after radiotherapy.
• Reported survival times vary enormously—from a few months to many years, and dying from causes unlikely to be related to acromegaly.

MISCELLANEOUS

Suggested Reading

Berg RI, Nelson RW, Feldman EC, et al. Serum insulin-like growth factor-I concentration in cats with diabetes mellitus and acromegaly. J Vet Intern Med 2007, 21(5):892–898.
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ACTINOMYCOSIS

A

BASICS

OVERVIEW

• An infectious disease caused by Gram-positive, branching, pleomorphic, rod-shaped bacteria of the genus *Actinomyces.* • *A. viscosus* and *A. hodeovulneris*—most commonly identified isolates (though most isolates are not identified to the species level); survives in microaerophilic or anaerobic conditions. • Rarely found as the single bacterial agent in a lesion; more commonly, it is a component of a polymicrobial infection. • There may be synergism between *Actinomyces* and other organisms. • Organ systems affected may include: ◦ Skin ◦ Respiratory ◦ Cardiovascular ◦ Musculoskeletal ◦ Nervous.

SIGNALMENT

• Dogs and cats (uncommon). • Most common in young male dogs of sporting breeds.

SIGNS

• Infections—usually localized; may be disseminated; cervicofacial area commonly involved. • Cutaneous swellings or abscesses with draining tracts—yellow granules ("sulfur granules") may be seen in associated exudates. • Pain, fever, and weight loss. • Exudative pleural or peritoneal effusions; occasionally pericardial effusion noted. • Cough, dyspnea, decreased ventral lung sounds (empyema). • Retroperitonitis—lumbar pain; rear limb paresis or paralysis. • Osteomyelitis of vertebrae or long bones—probably secondary to extension of cutaneous infection; lameness or a swollen extremity may develop. • Motor and sensory deficits—reported with spinal cord compression by granulomas. • Pyothorax and subcutaneous bite wounds are the most common presenting signs in cats.

CAUSES & RISK FACTORS

• *Actinomyces* spp. normal inhabitants of the oral cavity of dogs and cats. • Loss of normal protective barriers (mucosa, skin), immunosuppression, or change in the bacterial microenvironment can predispose; thought to occur as an opportunistic infection. • Specific risk factors—trauma (bite wound), migrating foreign body (grass awn or, in the western United States, a foxtail), and periodontal disease.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Nocardiosis—primary differential diagnosis; *Actinomyces* not reliably distinguished from *Nocardia* spp. by Gram staining, cytology, or clinical signs. • Other causes of chronic draining tracts and pleural or peritoneal effusions must be addressed.

CBC/BIOCHEMISTRY/URINALYSIS

• Nonspecific changes. • Leukocytosis with a left shift and monocytosis—reported. • Nonregenerative anemia—may develop. • Hypoglycemia and hyperglobulinemia—reported.

IMAGING

• Radiographs of infected bone—periosteal new bone production, reactive osteosclerosis, and osteolysis. • Thoracic radiographs—alveolar and interstitial lung patterns with possible lung consolidation; pleural effusion; pericardial effusion; subcutaneous masses on lateral thorax. • Abdominal radiographs—peritoneal effusion; mass effect in abdomen. • Vertebral column radiographs—periosteal new bone formation, especially T13–L3.

DIAGNOSTIC PROCEDURES

• Pus or osteolytic bone fragments submitted in anaerobic specimen containers for culture (see Anaerobic Infections) can provide a definitive diagnosis; inform the lab to check for actinomycosis; advisable to submit aerobic culture, as well. • Fresh smears—Gram staining, cytology, and acid-fast staining; staining does not preclude the need for culture; *Actinomyces* does not stain acid-fast; *Nocardia* is variable.

PATHOLOGIC FINDINGS

Histopathologic examination—sulfur granules can be difficult to find so multiple tissue sections should be submitted; special stains may enhance visualization of organisms; granules are a useful diagnostic tool when present; pyogranulomatous or granulomatous cellulitis with colonies of filamentous bacteria is characteristic.

TREATMENT

• Exudative fluid (thorax, abdomen, subcutaneous tissue) should be drained and lavaged. • A chest tube with continuous suction is needed for cats with pyothorax; dogs are best served with surgical exploration of the chest prior to tube placement in order to identify and remove any grass awns. • Diseased lung lobes may need to be removed. • Dogs with solitary masses involving the thoracic or abdominal wall may experience cure with radical surgical excision.

MEDICATIONS

DRUG(S)

• Important to distinguish between *Actinomyces* and *Nocardia* for appropriate antimicrobial selection. • Antibiotics—a retrospective study suggests administration for a minimum of 3–4 months after resolution of all signs; may need to be directed against other associated microbes. • Penicillins—considered the drug of choice; in most cases, oral therapy can be initiated and parenteral is not needed; amoxicillin should be administered at 20–22 mg/kg q8h PO.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

• Metronidazole—avoid use; actinomycosis unlikely to respond. • Aminoglycosides—do not use; ineffective against anaerobic infections. • *A. hordeovulneris*—cell-wall deficient variant (l-phase); does not usually respond well to penicillin; consider clindamycin, erythromycin, and chloramphenicol.

FOLLOW-UP

PATIENT MONITORING

Monitor patients closely for recurrence in the months after therapy discontinued.

PREVENTION/AVOIDANCE

Avoidance of contact with grass awns and prevention of bite wounds.

POSSIBLE COMPLICATIONS

Concurrent immune-suppressive disease or therapy may complicate management.

EXPECTED COURSE AND PROGNOSIS

Redevelopment of infection at the initial site may be expected in about half of all cases.

MISCELLANEOUS

AGE-RELATED FACTORS

Young outdoor dogs.

ZOONOTIC POTENTIAL

There are no reported cases of actinomycosis being transmitted from animals to man; transmission by bite wound may be possible so appropriate attention should be given to bite wounds.

Suggested Reading

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A

ACUTE ABDOMEN

BASICS

DEFINITION
An emergency condition characterized by historical and physical examination findings of a tense, painful abdomen. May represent a life-threatening condition.

PATHOPHYSIOLOGY
• A patient with an acute abdomen has pain associated with either distention of an organ, inflammation, traction on the mesentery or peritoneum, or ischemia.
• The abdominal viscera are sparsely innervated, and diffuse involvement is often necessary to elicit pain; nerve endings also exist in the submucosa-muscularis of the bowel wall.
• Any process that causes fluid or gaseous distension (i.e., intestinal obstruction, gastric dilatation-volvulus, ileus) may produce pain.
• Inflammation produces abdominal pain by releasing vasoactive substances that directly stimulate nerve endings.
• Many nerves in the peritoneum are sensitive to a diffuse inflammatory response.

SYSTEMS AFFECTED
• Behavioral—trembling, inappetence, vocalizing, lethargy, and abnormal postural changes such as the praying position to achieve comfort.
• Cardiovascular—severe inflammation, ischemia, and sepsis may lead to acute circulatory collapse (shock). May be associated with SIRS and septic shock.
• Gastrointestinal—vomiting, diarrhea, inappetence, generalized functional ileus; pancreatic inflammation, necrosis, and abscesses may lead to cranial abdominal pain, vomiting, and ileus.
• Hepatobiliary—jaundice associated with extrahepatic cholestasis from biliary obstruction (including pancreatitis) and bile peritonitis. Hyperbilirubinemia may occur secondary to sepsis.
• Renal/Urologic—azotemia can be due to prerenal causes (dehydration, hypovolemia, and shock), renal causes (acute pyelonephritis and acute renal failure), and post-renal causes (ureteral obstruction, urethral obstruction and uroperitoneum from bladder rupture).
• Respiratory—increased respiratory rate due to pain or metabolic/acid-base disturbances.

SIGNALMENT
• Dogs and cats.
• Dogs more commonly.
• Younger animals tend to have a higher incidence of trauma-related problems, intussusceptions, and acquired diet- and infection-related diseases; older animals have a greater frequency of malignancies.
• Male cats and dogs are at higher risk for urethral obstruction.
• Male Dalmatians in particular have a higher risk of urethral obstruction because of the high incidence of urate urinary calculi.
• German shepherds with pancreatic atrophy have a higher risk of mesenteric volvulus.
• Patients treated with corticosteroids and non-steroidal anti-inflammatory drugs are at higher risk for gastrointestinal ulceration and perforation.

SIGNS
General Comments
Clinical signs vary greatly depending on the type and severity of the disease leading to an acute abdomen.

Historical Findings
• Trembling, reluctance to move, inappetence, vomiting, diarrhea, vocalizing, and abnormal postures (tucked up or praying position)—signs that the owner may notice.
• Question owner carefully to ascertain what system is affected; for example, melena with a history of NSAID treatment may suggest GI mucosal disruption (ulceration).

Physical Examination Findings
• Abnormalities include abdominal pain, splinting of the abdominal musculature, gas- or fluid-filled abdominal organs, abdominal mass, ascites, pyrexia or hypothermia, tachycardia, and tachypnea.
• Once abdominal pain is confirmed, attempt to localize the pain to cranial, middle, or caudal abdomen.
• Perform a rectal examination to evaluate the colon, pelvic bones, urethra, and prostate, as well as for the presence of melena.
• Rule out extra-abdominal causes of pain by careful palpation of the kidneys and thoracolumbar vertebrae.
• Pain associated with intervertebral disc disease often causes referred abdominal guarding and is often mistaken for true abdominal pain. Renal pain can be associated with pyelonephritis.

CAUSES
Gastrointestinal
• Stomach—gastritis, ulcers, perforation, foreign bodies, gastric dilatation-volvulus.
• Intestine—obstruction (foreign bodies, intussusception, hernias), enteritis, ulcers, perforations.
• Rupture after obstruction, ulceration, or blunt or penetrating trauma, or due to tumor growth.
• Vascular compromise from infarction, mesenteric volvulus, or torsion.

Pancreas
• Pain associated with inflammation, abscess, ischemia.
• Pancreatic masses or inflammation obstructing the biliary duct/papilla may cause jaundice.

Hepatic and Biliary System
• Rapid distention of the liver and its capsule can cause pain.
• Biliary obstruction, rupture, or necrosis may lead to bile leakage and peritonitis. Gallbladder mucocele may be identified on ultrasound examination.
• Hepatic abscess.

Spleen
• Splenic torsion, splenic masses, splenic thrombus, splenic abscess.

Urinary Tract
• Distention is the main cause of pain in the urinary tract.
• Lower urinary tract obstruction can be due to tumors of the trigone area of the bladder or urethra, urinary calculi, or granulomatous urethritis.
• Traumatic rupture of the ureters or bladder are associated with blunt trauma and increased intra-abdominal pressure.
• Urethral tears can be associated with pelvic fractures from acute trauma.
• Free urine in the peritoneal cavity leads to a chemical peritonitis.
• Acute pyelonephritis, acute renal failure, nephroliths, and ureteroliths are uncommon causes of acute abdomen.

Genital Tract
• Prostatitis and prostatic abscess, pyometra; a ruptured pyometra or prostatic abscess can cause endotoxemia, sepsis, and cardiovascular collapse.
• Infrequent causes include ruptures of the gravid uterus after blunt abdominal trauma, uterine torsion, ovarian tumor or torsion, and intra-abdominal testicular torsion (cryptorchid).

Abdominal Wall/Diaphragm
• Umbilical, inguinal, scrotal, abdominal, or peritoneal hernias with strangulated viscera.
• Trauma or congenital defects leading to organ displacement or entrapment in the hernia will lead to abdominal pain if the vascular supply of the organs involved becomes impaired or ischemic.

RISK FACTORS
• Exposure to NSAIDs or corticosteroid treatment (increased risk when used concurrently)—gastric, duodenal, or colonic ulcers.
• Garbage or inappropriate food ingestion—pancreatitis.
• Foreign body ingestion—intestinal obstructions.
• Abdominal trauma—hollow viscus rupture.
• Hernias—intestinal obstruction/strangulation.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Renal-associated pain, retroperitoneal pain, spinal or paraspinal pain, and disorders causing diffuse muscle pain may mimic abdominal pain; careful history and physical

(CONTINUED) # ACUTE ABDOMEN A

examination are essential in pursuing the appropriate problem.
• Parvoviral enteritis can present similarly to intestinal obstructive disease; fecal parvoviral antigen assay and CBC (leukopenia) are helpful differentiating diagnostic tests.

CBC/BIOCHEMISTRY/URINALYSIS
• Inflammation or infection may be associated with leukocytosis or leukopenia.
• Anemia may be seen with blood loss associated with GI ulceration.
• Azotemia is associated with prerenal, renal, and post-renal causes.
• Electrolyte abnormalities can help to evaluate GI disease (i.e., hypochloremic metabolic alkalosis with gastric outflow obstruction) and renal disease (i.e., hyperkalemia with acute renal failure or post-renal obstruction).
• Hyperbilirubinemia and elevated hepatic enzymes help localize a problem to the liver or biliary system.
• Urine specific gravity (before fluid therapy) is needed to help differentiate prerenal, renal, and post-renal problems.
• Urine sediment may be helpful in acute renal failure, ethylene glycol intoxication, and pyelonephritis.

OTHER LABORATORY TESTS
• Venous blood gas analysis including lactate concentration may indicate acid-base abnormalities, and increased lactate may be associated with hypoperfusion.
• Canine and feline pancreatic lipase immunoreactivity can be useful in evaluating pancreatitis.

IMAGING
Abdominal Radiography
• May see abdominal masses or changes in shape or shifting of abdominal organs.
• Loss of abdominal detail with abdominal fluid accumulation is an indication for abdominocentesis.
• Free abdominal gas is consistent with a ruptured GI viscus or infection with gas-producing bacteria and is an indication for emergency surgery.
• Use caution when interpreting radiographs following abdominocentesis with an open needle. Free gas may be introduced with this technique.
• Use caution when evaluating postoperative radiographs; free gas is a normal postoperative finding.
• Ileus is a consistent finding with peritonitis.
• Characterize ileus as functional (due to metabolic or inflammatory causes) or mechanical (due to obstruction).
• Foreign bodies may be radiopaque.
• Upper GI barium contrast radiographs are useful in evaluating the GI tract, particularly for determination of GI obstruction.
• Loss of contrast or radiographic detail in the area of the pancreas can be observed with pancreatic inflammation.

Abdominal Ultrasound
• A sensitive diagnostic tool for the detection of abdominal masses, abdominal fluid, abscesses, cysts, lymphadenopathy, and biliary or urinary calculi.
• FAST ultrasound is a published technique meaning Focused Assessment with Sonography in Trauma.

Abdominal CT
• Very sensitive diagnostic tool that may be used especially when surgeon requires additional information.

DIAGNOSTIC PROCEDURES
Abdominocentesis/Abdominal Fluid Analysis
• Perform abdominocentesis on all patients presenting with acute abdomen.
Four-quadrant approach may improve yield.
Fluid can often be obtained for diagnostic evaluation even when only a small amount of free abdominal fluid exists, well before detectable radiographic sensitivity.
Ultrasound is much more sensitive than radiography for the detection of fluid and can be used to direct abdominocentesis. Blind abdominocentesis can be performed safely without ultrasound guidance. Abdominal fluid analysis with elevated WBC count, degenerate neutrophils, and intracellular bacteria is consistent with septic peritonitis and is an indication for immediate surgery.
• Diagnostic peritoneal lavage can be performed by introducing sterile saline (10–20 ml/kg) and performing abdominocentesis with or without ultrasound guidance.
• Measurement of glucose concentration in abdominal effusion in comparison with peripheral blood may aid in the diagnosis of septic abdomen. A blood-to-abdominal fluid glucose difference of > 20 mg/dL is consistent with septic effusion.
• Pancreatitis patients may have an abdominal effusion characterized as a non-septic (sterile) peritonitis.
• Creatinine concentration higher in abdominal fluid than in serum indicates urinary tract leakage.
• Similarly, higher bilirubin concentration in abdominal fluid than in serum indicates bile peritonitis.

Sedation and Abdominal Palpation
• Because of abdominal splinting associated with pain, thorough abdominal palpation is often not possible without sedation; this is particularly useful for detecting intestinal foreign bodies that do not appear on survey radiographs.

Exploratory Laparotomy
• Surgery may be useful diagnostically (as well as therapeutically) when ultrasonography (or other advanced imaging) is not available or when no definitive cause of the acute abdomen has been established with appropriate diagnostics.

TREATMENT
APPROPRIATE HEALTH CARE
• Inpatient management with supportive care until decision about whether the problem is to be treated medically or surgically. Early intervention with surgery is important when indicated.
• Aggressive therapy and prompt identification of the underlying cause is very important.
• Many causes of acute abdominal pain require emergency surgical intervention.
• Keep patient NPO if vomiting, until a definitive cause is determined and addressed.
• Intravenous fluid therapy is usually required because of the large fluid loss associated with an acute abdomen; the goal is to restore the normal circulating blood volume.
• If severe circulatory compromise (shock) exists, supplement initially with isotonic crystalloid fluids (90 mL/kg, dogs; 70 mL/kg, cats) over 1–2 hours; hypertonic fluids or colloids may also be beneficial if refractory to isotonic crystalloids or hypoproteinemic.
• Evaluate hydration and electrolytes (with appropriate treatment adjustments) frequently after commencement of treatment.

DIET
Early nutritional support important, especially in order to maintain GI mucosal barrier. Nutritional support can be enteral (oral, nasoesophageal, esophageal tube, gastrostomy tube, enterostomy tube) or parenteral.

SURGICAL CONSIDERATIONS
• Many different causes of an acute abdomen (with both medical and surgical treatments) exist; make a definitive diagnosis whenever possible prior to surgical intervention.
• This can prevent both potentially unnecessary and expensive surgical procedures and associated morbidity and mortality.
• It will also allow the surgeon to prepare for the task and to educate the owner on the prognosis and financial investment.

MEDICATIONS
DRUG(S)
Analgesics
• Pain medication may be indicated for control of abdominal discomfort.
• Opioids, such as hydromorphone or fentanyl, are often good choices.

Histamine H_2 Antagonists
• Reduce gastric acid production.
• Famotidine 0.5–1.0 mg/kg IV, SC or IM q12h.
• Ranitidine 2 mg/kg IV q12h

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ACUTE ABDOMEN (CONTINUED)

Proton Pump Inhibitor
Pantoprazole 1–1.5 mg/kg IV as a CRI over 24 hours.

Protectants
Sucralfate 0.25–1 g PO q8h.

Antiemetics
- Metoclopramide 0.2–0.4 mg/kg IV q6–8h (or 24-hour continuous rate infusion (1–2 mg/kg/24h).
- Maropitant: dogs, 1–2 mg/kg SC; cats, 1 mg/kg SC
- Ondansetron 0.5–1 mg/kg IV slowly q6–12h.
- Dolasetron 1 mg/kg IV q24h.

Antibiotics
- Antibiotics may be indicated if signs of infection (fever, elevated white blood cell count, positive culture) are seen or hemorrhagic diarrhea is present.
- Broad spectrum for Gram-positive, Gram-negative, and anaerobic bacteria.
- Gram stain and cultures prior to treatment if possible, but do not delay intervention pending results.

CONTRAINDICATIONS
Do not use metoclopramide if GI obstruction is suspected. Do not use barium if gastrointestinal perforation is suspected. Use iodinated contrast agent instead.

PRECAUTIONS
Gentamicin and most NSAIDs can be nephrotoxic and should be used with caution in hypovolemic patients and those with renal impairment. Opiates are preferred to NSAIDs for pain management as NSAIDs may cause GI complications.

FOLLOW-UP

PATIENT MONITORING
Patients usually require intensive medical care and frequent evaluation of vital signs and laboratory parameters.

MISCELLANEOUS

SYNONYM
Colic

SEE ALSO
- Gastric Dilation and Volvulus Syndrome
- Gastroduodenal Ulceration/Erosion (GUE)
- Gastrointestinal Obstruction
- Intussusception
- Pancreatitis
- Pyelonephritis
- Prostatitis and Prostatic Abscess
- Urinary Tract Obstruction

ABBREVIATIONS
- GI = gastrointestinal
- NSAID = nonsteroidal anti-inflammatory drug

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Consulting Editor Stanley L. Marks

ACUTE RESPIRATORY DISTRESS SYNDROME

BASICS

DEFINITION

• Acute respiratory distress syndrome (ARDS) is a syndrome of acute onset of respiratory failure typified by diffuse bilateral pulmonary infiltrates on a dorsoventral thoracic radiograph with no clinical evidence of left atrial hypertension or volume overload. ARDS results from an overwhelming inflammatory reaction in the alveolocapillary membrane in response to a systemic or pulmonary inflammatory insult. The end result is increased vascular permeability leading to edema. • The 2012 Berlin Definition of ARDS defines three categories of severity based on PaO_2/FiO_2 ratio and level of PEEP employed during ventilation, with mild ARDS defined by a PF ratio of 200–300 mmHg with PEEP ≥ 5 mmHg, moderate ARDS as a PF ratio of 100–200 mmHg with PEEP ≥ 5 mmHg, and severe ARDS as a PF ratio < 100 mmHg with PEEP ≥ 5 mmHg.

PATHOPHYSIOLOGY

• ARDS is due to a diffuse inflammatory insult that causes widespread damage to alveolar endothelial and epithelial cells resulting in thickening of the membrane and impaired gas exchange. This inflammatory insult can be triggered by primary pulmonary disease or it can be of non-pulmonary origin, and leads to exudative, proliferative, and fibrotic changes within the lung: • First, excessive accumulation and activation of neutrophils, monocytes, and platelets in the pulmonary microvasculature leads to increased alveolar endothelial permeability. This causes protein-rich edema fluid and inflammatory cells to leak into the interstitial and alveolar spaces. • Alveolar epithelial injury results from release of cytokines and other inflammatory mediators from leukocytes and platelets. • Epithelial injury involves both type I and type II alveolar epithelial cells, and results in alveolar flooding and surfactant dysfunction. This causes collapse and consolidation of alveoli with development of severe hypoxemia, and hyaline membrane formation in the alveolar spaces. • Microthrombi in the pulmonary vasculature, hypoxic pulmonary vasoconstriction, and release of endogenous vasoconstrictors lead to pulmonary arterial hypertension, which can lead to right-sided heart failure. • Proliferation of type 2 alveolar epithelial cells and pulmonary fibrosis occurs in the late stages of ARDS.

SYSTEMS AFFECTED

• Respiratory. • Cardiovascular—right-sided heart failure secondary to pulmonary hypertension; hemodynamic compromise may be associated with aggressive mechanical ventilator settings.

GENETICS

Certain humans are more prone to developing ARDS than others due to specific gene polymorphisms. This has not been investigated in the veterinary population.

INCIDENCE/PREVALENCE

Unknown

SIGNALMENT

Species

Dog and cat

Breed Predilections

A familial form of ARDS has been reported in a group of related Dalmatian dogs; it is clinically indistinguishable from ARDS.

Mean Age and Range

Unknown

SIGNS

Historical Findings

• Acute onset of respiratory distress in a patient with a significant underlying disease or exposure to known risk factors. • The patient is often hospitalized for its primary disease when it develops ARDS.

Physical Examination Findings

• Severe respiratory distress • Crackles (if present) heard bilaterally on auscultation • Fever—depends on underlying disease • Cyanosis in more severe cases • Signs relevant to the primary disease process.

CAUSES

Primary Pulmonary Causes

• Aspiration pneumonia • Pneumonia • Pulmonary contusion • Near drowning • Smoke inhalation • An idiopathic form of ARDS associated with acute interstitial pneumonia or idiopathic pulmonary fibrosis has been reported in humans and dogs.

Non-pulmonary Causes

• SIRS • Sepsis • Neoplasia • Pancreatitis • Severe trauma and shock • Severe bee sting envenomation

RISK FACTORS

• SIRS • Sepsis • Severity of illness • Multiple transfusions

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Left-sided congestive heart failure • Fluid overload • Diffuse pneumonia • Pulmonary hemorrhage

CBC/BIOCHEMISTRY/URINALYSIS

• Leukocytosis or leukopenia • Other changes dependent on the underlying disease process

OTHER LABORATORY TESTS

• Arterial blood gases—low PaO_2/FiO_2 ratio (where PaO_2 is measured in mmHg and FiO_2 is 0.21–1.0). Normal PaO_2/FiO_2 ratio = 500; comparison of this ratio allows evaluation of severity of lung disease and allows direct comparison of blood gases taken at different FiO_2. $PaCO_2$ is often low; hypercapnia tends to be a late (preterminal) development. • Total protein of airway edema fluid compared with serum total protein—ratio of edema fluid to serum total protein < 0.5 is supportive of low-protein hydrostatic pressure pulmonary edema (e.g., heart failure, fluid overload); edema fluid/serum total protein ratio > 0.7 suggests a high-protein, increased permeability pulmonary edema such as ARDS and pneumonia. • Coagulation panel may reveal hypocoagulable state supportive of DIC or cause of pulmonary hemorrhage.

IMAGING

Thoracic Radiographs

• Bilateral/diffuse pulmonary infiltrates. • Severity of radiographic signs can lag behind clinical disease by 12–24 hours. • Can be difficult to distinguish from cardiogenic edema. Cardiac silhouette and pulmonary vascular size is usually normal in ARDS.

Echocardiography

• Attempt to rule out cardiogenic cause for pulmonary edema. • May be able to estimate degree of pulmonary hypertension.

DIAGNOSTIC PROCEDURES

Pulmonary artery catheter to measure pulmonary artery occlusion pressure can be used to rule out cardiogenic cause for edema; by definition, ARDS is associated with PAOP ≤ 18 mmHg.

PATHOLOGIC FINDINGS

Gross Pathology

Lungs are dark, heavy, and ooze fluid when cut.

Histopathology

• Acute phase—pulmonary vascular congestion with edema fluid and inflammatory cell accumulation in the interstitium and alveoli; epithelial cell damage, hyaline membrane formation, microthrombi, microatelectasis. • Proliferative phase—hyperplasia of type 2 pneumocytes, interstitial mononuclear infiltration, organization of hyaline membranes, and fibroproliferation.

TREATMENT

APPROPRIATE HEALTH CARE

• There is no specific therapy. General aims are to maintain tissue oxygenation and to minimize iatrogenic lung injury while treating the underlying disease. • Oxygen therapy—no more than is required to maintain PaO_2 > 60–80 mmHg to minimize oxygen toxicity. • Positive-pressure ventilation is essential in the management of ARDS patients. It is indicated in patients that are hypoxemic despite oxygen therapy, patients requiring high levels of inspired oxygen for

A

ACUTE RESPIRATORY DISTRESS SYNDROME (CONTINUED)

prolonged periods, or patients working so hard to breathe that they are at risk of exhaustion. • ARDS is thought to be exacerbated by ventilator-induced lung injury associated with alveolar overdistension compounded by cyclic opening and collapse of atelectatic alveoli. Therefore, lung-protective strategies of positive-pressure ventilation with moderate to high PEEP, low tidal volumes, and permissive hypercapnia are recommended to minimize ventilator-induced lung injury. Tidal volumes of 6 mL/kg have been found to increase survival significantly in human ARDS patients compared to tidal volumes of 12 mL/kg. • Recruitment maneuvers and high levels of PEEP can both cause significant hemodynamic compromise and patients should have constant direct arterial blood pressure monitoring.
• Intensive supportive care of the cardiovascular system and other organ systems is vital, as these patients are at high risk for development of multiple organ dysfunction.

NURSING CARE
• Monitor temperature closely, especially if using an oxygen cage, as animals with excessive work of breathing can easily become hyperthermic. • Ventilator patients require frequent position changes and physical therapy; regular oral care with a dilute chlorhexidine solution is important to reduce oral colonization with bacteria as a source of sepsis, and frequent endotracheal tube suctioning is needed to prevent occlusion. Inflate cuff carefully and change endotracheal cuff position regularly to prevent tracheal damage. • Blood pressure monitoring, as septic patients are prone to hypotension.
• Fluid therapy is important to support the cardiovascular system and to maintain normovolemia while avoiding fluid overload, as this will negatively affect lung function.

ACTIVITY
If not anesthetized for ventilation, strict cage confinement.

DIET
Nutritional support is important but challenging. Enteral feeding is desired over parenteral nutrition, but must consider high risk of regurgitation and aspiration in a recumbent patient.

CLIENT EDUCATION
Clients need to be aware of the guarded prognosis and high costs of therapy.

SURGICAL CONSIDERATIONS
The underlying disease may require surgery.

MEDICATIONS

DRUG(S) OF CHOICE
• No specific drug therapy.
• Antibiotics for the underlying disease where indicated.
• Vasoactive drugs to maintain blood pressure.
• Anesthetic drugs to allow positive-pressure ventilation.
• Analgesia as appropriate.
• Low-dose corticosteroid—use remains controversial with conflicting reports of efficacy for low-dose steroids in early or late ARDS.

ALTERNATIVE DRUG(S)
Furosemide may produce pulmonary venous dilation and improve lung function, as an intermittent bolus of 1 mg/kg IV q6–12h or as a CRI of 0.2 mg/kg/h IV. Beware dehydration and effects on organ function.

FOLLOW-UP

PATIENT MONITORING
Arterial blood gases, pulse oximetry, end-tidal carbon dioxide, thoracic radiographs, arterial blood pressure, ECG, temperature, urine output, CBC, coagulation profiles, serum chemistry, blood cultures, monitoring for other organ dysfunction.

PREVENTION/AVOIDANCE
• Aggressive therapy of primary disease processes to reduce the inflammatory insult to the lung. • Intensive cardiovascular monitoring and support of critically ill animals to ensure adequate tissue perfusion.
• Careful management of recumbent animals to reduce the chance of aspiration, especially if patient has neurologic disease or upper airway disorders that reduce the ability to protect the airway. • Judicious use of blood products in patients with inflammatory or severe systemic disease.

POSSIBLE COMPLICATIONS
• Multiorgan dysfunction syndrome—acute kidney injury, DIC, and gastrointestinal disease are the more common forms of organ dysfunction seen. • Barotrauma—can result in pneumothorax. Incidence is thought to be less with lower tidal volume ventilation strategies. • Ventilator-associated pneumonia—patients on PPV have increased risk of pneumonia that may be difficult to differentiate from worsening of the initial lung injury. Airway cultures should be considered in deteriorating patients.
• Oxygen toxicity may be unavoidable due to severity of hypoxemia in spite of PPV. Oxygen toxicity is indistinguishable from ARDS on histopathology making the incidence of this problem impossible to determine.

EXPECTED COURSE AND PROGNOSIS
• Mortality in human patients remains at 40–60%. • Mortality in veterinary patients likely approaches 100%.

MISCELLANEOUS

ASSOCIATED CONDITIONS
Systemic inflammatory response syndrome, multiple organ dysfunction syndrome, sepsis.

SYNONYMS
• Acute hypoxemic respiratory failure • Acute interstitial pneumonia • Adult respiratory distress syndrome • High-protein pulmonary edema • Shock lung

SEE ALSO
• Dyspnea and Respiratory Distress • Panting and Tachypnea • Pulmonary Edema, Noncardiogenic • Sepsis and Bacteremia

ABBREVIATIONS
• ARDS = acute respiratory distress syndrome • CRI = constant rate infusion • DIC = disseminated intravascular coagulation • PAOP = pulmonary artery occlusion pressure (formerly pulmonary capillary wedge pressure [PCWP]) • PEEP = positive end-expiratory pressure • PF ratio = PaO_2/FiO_2 ratio • PPV = positive-pressure ventilation • SIRS = systemic inflammatory response syndrome

INTERNET RESOURCES
http://www.ardsnet.org

Suggested Reading
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ADENOCARCINOMA, ANAL SAC

BASICS

OVERVIEW
• Malignant neoplasm derived from apocrine glands of the anal sac. • Locally invasive. • High metastatic rate, often to sublumbar lymph nodes. • Frequently associated with hypercalcemia, secondary to parathyroid hormone–related peptide secretion. • Prognosis guarded to fair.

SIGNALMENT
• Older dogs; extremely rare in cats. • Females overrepresented in some studies. • English cocker spaniels significantly overrepresented, springer and Cavalier King Charles spaniels also overrepresented.

SIGNS
Historical Findings
Signs may be due to physical obstructive nature of primary tumor (rectal mass, tenesmus) or enlarged local lymph node metastasis (tenesmus, constipation, stranguria), or systemic manifestations due to hypercalcemia (anorexia, polyuria/polydipsia, lethargy).

Physical Examination Findings
• Mass associated with anal sac; may be quite small despite massive metastatic disease. • Sublumbar lymphadenopathy—on rectal or abdominal palpation.

CAUSES & RISK FACTORS
None definitively identified

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Anal sac abscess • Perianal adenoma/adenocarcinoma • Mast cell tumor • Lymphoma • Squamous cell carcinoma • Perineal hernias

CBC/BIOCHEMISTRY/URINALYSIS
• Hypercalcemia—25–50% of cases. • Secondary renal failure may develop.

OTHER LABORATORY TESTS
If hypercalcemia is present, and tumor cannot be identified, parathyroid hormone and PTHrP levels can be assessed—high PTHrP support neoplasia as the cause of hypercalcemia.

IMAGING
• Abdominal radiography—to evaluate sublumbar lymph nodes and lumbar and pelvic bones. • Thoracic radiography—to evaluate for pulmonary metastasis. • Abdominal ultrasonography—may identify mildly enlarged sublumbar lymph nodes not visible radiographically, also nodules in liver/spleen. • MRI—recently shown to identify lymphadenopathy with greater sensitivity than ultrasound.

DIAGNOSTIC PROCEDURES
• Fine-needle aspiration of anal sac mass to rule out conditions other than adenocarcinoma; while differentiation of benign versus malignant neoplasm of perianal masses is difficult, apocrine gland adenocarcinoma of the anal sac will have a neuroendocrine appearance and can be differentiated from perianal gland tumors. • Fine-needle aspiration of enlarged lymph nodes, liver, or splenic nodules to confirm metastasis. • Incisional biopsy for histopathology required for definitive diagnosis, although excisional biopsy may be appropriate if location of mass and cytology are supportive of anal gland neoplasia.

TREATMENT

• Surgical resection—treatment of choice. • Resection of primary tumor and enlarged lymph nodes may prolong survival. • If mass is large and regionally invasive at diagnosis, surgery often palliative, not curative. • Debulking all disease present may control hypercalcemia until tumor recurrence. • Saline diuresis (200–300 mL/kg/day) preoperatively if hypercalcemia is severe. • Radiation may help delay local recurrence and control growth of sublumbar metastases.

MEDICATIONS

DRUG(S)
• Limited reports of partial responses to platinum compounds in dogs—cisplatin (70 mg/m^2 IV with 6-hour saline diuresis—18.3 mL/kg/h), carboplatin (300 mg/m^2 IV as a slow bolus) every 3 weeks. • Mitoxantrone (5 mg/m^2 IV every 3 weeks for five treatments) in combination with radiation therapy used in one small case series. • Possible role for melphalan after debulking surgery (7 mg/m^2 PO q24h for 5 days every 3 weeks). • Toceranib phosphate reported to have some benefit (partial response or stable disease) in 28 dogs with measurable tumor.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
• Avoid platinum chemotherapeutic agents in dogs with renal insufficiency. • Do not use cisplatin in cats.

FOLLOW-UP

PATIENT MONITORING
• Complete resection—physical examination, thoracic radiography, abdominal ultrasonography, and serum biochemistry at 1, 3, 6, 9, and 12 months postoperatively, then every 6 months thereafter. • Incomplete resection—monitor tumor size and blood calcium and renal values.

EXPECTED COURSE AND PROGNOSIS
• Guarded prognosis with both local progression and metastasis occurring. • Cures may occur if tumor is found early and treated aggressively. • Growth of the tumor may be slow and debulking lymph node metastatic disease may significantly prolong survival. • Hypercalcemia is variably associated with a poor prognosis. • Four papers (involving 200 dogs) showed median survival times of 6 to 20 months, depending on stage and treatment. • A recent report on 16 dogs without metastasis showed a median survival time not met with a follow-up of 33 months. • Dogs with lymph node metastasis lived significantly longer if the nodes were extirpated. • Ultimately, dogs that cannot have their tumors excised completely succumb to hypercalcemia-related complications or mass effect from primary tumor or sublumbar nodal metastases.

MISCELLANEOUS

ASSOCIATED CONDITIONS
Hypercalcemia as a paraneoplastic syndrome

ABBREVIATION
PTHrP = parathyroid hormone-related peptide

Suggested Reading

Anderson CL, Mackay CS, Roberts GD, Fidel J. Comparison of abdominal ultrasound and magnetic resonance imaging for detection of abdominal lymphadenopathy in dogs with metastatic apocrine gland adenocarcinoma of the anal sac. Vet Comp Oncol 2013, doi: 10.1111/vco.12022.

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Author Laura D. Garrett
Consulting Editor Timothy M. Fan

Client Education Handout available online

JWST589-A26-15 JWST589-Tilley Printer: Yet to Come August 1, 2015 10:58 279mm×216mm

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ADENOCARCINOMA, LUNG

BASICS

OVERVIEW
• Comprises 75% of primary pulmonary tumors in dogs and cats. • Strongest predictors of outcome are tumor grade, node involvement, and clinical signs. • May metastasize. • May be associated with hypertrophic osteopathy.

SIGNALMENT
Dogs
• 1% of all tumors • Mean age of affected animals 10 years • No sex predilection, though more females in some reports
• Medium to large breeds overrepresented

Cats
• Rarer than in dogs • Mean age of affected animals 11 years • No breed predilection

SIGNS
Historical Findings
• Related to presence of a lung mass:
◦ Nonproductive cough (> 50% of dogs)
◦ Dyspnea (may be related to pneumothorax)
◦ Tachypnea ◦ Hemoptysis • Paraneoplastic signs: ◦ Lameness—bone metastasis or hypertrophic osteopathy (dogs or cats), weight-bearing lytic digit metastasis (cats)
◦ Polyuria or polydipsia—hypercalcemia or hyperadrenocorticism from ectopic production of ACTH ◦ Fever

Physical Examination Findings
• May be asymptomatic or lack respiratory signs • Tachypnea and dyspnea • Fever
• Limb swelling • Ascites, pleural effusion
• Caval syndrome

CAUSES & RISK FACTORS
Some evidence correlates risk to urban environment; controversial

DIAGNOSIS

• Fine-needle aspirate cytology • Tissue biopsy or definitive resection

DIFFERENTIAL DIAGNOSIS
• Granulomatous lesion (fungal, foreign body, parasitic) • Pulmonary abscess • Other primary lung tumor: ◦ Squamous cell carcinoma ◦ Sarcomas (osteo-, chondro-, lipo-) • Metastatic lung tumor • Pneumonia
• Asthma • Pulmonary thromboembolism
• Congenital cyst • Lung torsion or hematoma

CBC/BIOCHEMISTRY/URINALYSIS
No specific abnormalities

OTHER LABORATORY TESTS
Coagulation tests

IMAGING
• Thoracic radiography—usually demonstrates a focal, solitary, well-circumscribed mass; must be performed in cats presenting with multiple digit tumors to screen for primary lung tumor (lung-digit syndrome). • Ultrasonography—may help with obtaining an aspirate or biopsy specimen from lung, or to evaluate abdomen.
• CT—most accurate assessment of surgical feasibility, lymphadenopathy (93% accuracy), metastatic disease. • Dogs—most common in right caudal lung lobe and accessory lobe; cats—most common in left caudal lung lobe.

DIAGNOSTIC PROCEDURES
• Thoracocentesis with cytologic examination (for pleural effusion). • Cytology—transthoracic fine-needle aspiration (83% agreement with histopathology).
• Percutaneous tissue biopsy—use Tru-Cut instrument. • Open lung biopsy—specimen via thoracotomy, or minimally invasive thoracoscopy.

PATHOLOGIC FINDINGS
• Adenocarcinoma—classified according to location (bronchial, bronchiolar, bronchiolar-alveolar, or alveolar) and degree of differentiation. • Thyroid transcription factor-1 positivity may distinguish primary from metastatic carcinoma. • Cats tend to have less differentiated tumors, corresponding to more aggressive behavior.

TREATMENT

• Surgery—mainstay of treatment: partial or complete lobectomy with tracheobronchial lymph node biopsy or removal; thoracoscopic removal possible at limited centers and offers less postoperative morbidity.
• Radiotherapy—reports are anecdotal, but certain patients may benefit. • Chemotherapy should be considered following surgery for tumors that are high grade, undifferentiated, and/or have nodal involvement. Intracavitary chemotherapy can be used to treat malignant pleural effusion.

MEDICATIONS

DRUG(S)
• Chemotherapy—vinorelbine concentrates in lungs and responses have been seen.
◦ Doxorubicin, cisplatin, carboplatin, mitoxantrone, vinorelbine, and/or vindesine—rational choices for palliation
◦ Platinum based or gemcitabine chemotherapy may be superior
◦ Toceranib Phosphate (Palladia) has shown some anecdotal success
• Chemotherapy can be toxic; seek advice if unfamiliar with cytotoxic drugs.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
• Doxorubicin—monitor patients with underlying cardiac disease carefully; consider pretreatment with diphenhydramine and serial echocardiograms and ECGs.
• Cisplatin—do not give to cats (fatal); do not use in dogs with pre-existing renal disease; never use without appropriate and concurrent diuresis.

FOLLOW-UP

PATIENT MONITORING
• Serial thoracic radiographs—consider every 3 months; administer a minimum of two cycles of chemotherapy before evaluating response to treatment. • Perform CBC (with any chemotherapy), biochemical analysis (cisplatin), and urinalysis (cisplatin) before each chemotherapy treatment.

POSSIBLE COMPLICATIONS
• Following diagnostic procedures or thoracotomy: pneumo- or hemothorax
• Resulting from chemotherapy: myelosuppression, fever, sepsis, nausea

EXPECTED COURSE AND PROGNOSIS
• Metastasis to the tracheobronchial lymph nodes—single best prognostic indicator; median survival without metastasis approaches 1 year and with metastasis, 60 days. More common (75%) in cats.
• Postoperative survival in dogs (~1 yr) is better than in cats (~4 mo), but around 2 years in either species if positive prognostic factors are present. • Other patient, tumor, and treatment factors influencing prognosis—complete surgical excision; size of the primary tumor (< 5 cm better); metastasis (better if none); degree of cell differentiation (histologic score, better if well differentiated), lack of clinical signs prior to surgery.

MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING
Chemotherapy is not advised in pregnant animals.

ABBREVIATIONS
ACTH = adrenocorticotrophic hormone

Suggested Reading
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Author Kim A. Selting
Consulting Editor Timothy M. Fan
Acknowledgments The author and editors acknowledge the prior contribution of Renee Al-Saraff.

ADENOCARCINOMA, NASAL

BASICS

DEFINITION
Malignant neoplasm involving the nasal cavity and paranasal sinuses.

PATHOPHYSIOLOGY
Progressive local and regional invasion of the nasal cavity, paranasal sinuses, and surrounding tissues by neoplastic epithelial and glandular epithelial cells.

SYSTEMS AFFECTED
• Respiratory—congestion, obstruction, dyspnea, epistaxis, mucopurulent nasal discharge
• Nervous—seizures, altered mentation
• Ophthalmic—exophthalmos, epiphora

INCIDENCE/PREVALENCE
• In dogs, less than 2% of all tumors are nasal tumors.
• In dogs, adenocarcinoma is more common than squamous cell carcinoma, chondrosarcoma, and other histologies, comprising 31.5% of all nasal tumors.
• In cats, nasal tumors comprise < 1% of all tumors. In cats, adenocarcinoma and lymphoma are most common.

GEOGRAPHIC DISTRIBUTION
Nasal adenocarcinomas are more commonly reported in urban areas.

SIGNALMENT
• Dog and cat.
• Median age in dogs is 10 years and 13 years in cats.
• In dogs, medium to large breeds affected more commonly with a possible overrepresentation of mesocephalic and dolichocephalic breeds.

SIGNS
Historical Findings
• Intermittent and progressive history of unilateral to bilateral epistaxis and/or mucopurulent discharge that initially responds to antibiotic therapy (median duration, 3 months).
• Sneezing and increased upper respiratory noises including reverse sneezing.
• Open-mouth breathing.
• Halitosis.
• Anorexia (more frequent in cats).
• Seizures (secondary to invasion of cranial vault).

Physical Examination Findings
• Nasal discharge (blood, mucopurulent)
• Decreased or absent airflow in the nasal passages (unilateral or bilateral)
• Facial deformity, exophthalmos, epiphora
• Pain upon nasal or paranasal sinus palpation or upon opening the mouth
• Regional lymphadenomegaly (rare)
• Abnormal mentation or other neurologic findings (rare)

CAUSES
Dolichocephalic morphology, p53 mutations, and COX-2 overexpression may all play a role.

RISK FACTORS
Urban environment and second-hand smoke may be risk factors.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Other sinonasal tumors (e.g., squamous cell carcinoma, lymphoma, sarcomas, olfactory neuroblastoma)
• Intracranial neoplasia
• Viral infection—cats
• Fungal infections including aspergillosis (dogs) and cryptococcosis (cats)
• Bacterial sinusitis
• Parasites (e.g., nasal mites)
• Foreign body
• Trauma
• Tooth root abscess and oronasal fistula
• Coagulopathies
• Ehrlichiosis, leishmaniasis
• Systemic hypertension

CBC/BIOCHEMISTRY/URINALYSIS
• Usually normal
• Occasional blood loss anemia

OTHER LABORATORY TESTS
• Cytologic examination: occasionally helpful (e.g., aspirates of the subcutaneous mass if facial deformity)
• Coagulation profile

IMAGING
• Survey skull radiography—not sensitive; may show asymmetrical destruction of turbinates accompanied by a soft tissue mass effect; may see fluid density in the frontal sinuses secondary to outflow obstruction.
• Thoracic radiography—evaluate for lung metastasis (uncommon).
• CT or MRI best imaging method for local staging and observing integrity of cribriform plate or orbital invasion, and also used for therapeutic planning.

DIAGNOSTIC PROCEDURES
• Blood pressure.
• Oral exam under anesthesia.
• Rhinoscopy may permit visual observation of the mass and aid biopsy..
• Tissue biopsy necessary for definitive diagnosis. Biopsies may be performed blind, following advanced imaging, using pinch biopsy instrument including retroflex rhinoscopic biopsy of nasopharynx, cannula (closed suction), or hydropulsion techniques.
• Cytologic evaluation of regional lymph nodes to detect regional metastatic disease.

PATHOLOGIC FINDINGS
• Bilateral involvement and osteolysis common.
• Regional lymph node metastasis < 10% at time of diagnosis but up to 45% at necropsy.

TREATMENT

APPROPRIATE HEALTHCARE
• Radiation therapy is the standard of care.
• Radiation therapy can be administered with curative intent (definitive) or for palliation of clinical signs.
• Definitive radiation involves multiple fractions for a high total dose.
• Palliative radiation uses a low total dose to minimize toxicity while improving the quality of life through reduction of tumor size.
• Novel radiation techniques including IMRT and stereotactic radiation therapy may decrease risk of late toxicity while improving tumor control.
• Combining radiation therapy with novel drug therapy (toceranib phosphate (Palladia), others) appears safe and well tolerated.
• Radiation therapy followed by surgery to debulk residual mass may improve local control time but results in higher risk of late toxicity.
• Surgery alone considered ineffective with most tumors relapsing within 6 months.

NURSING CARE
• During radiation therapy, supportive care for radiation related mucositis may involve softening food, rinsing mouth with saline, dilute black tea, and administration of medications to control discomfort.
• These side effects are temporary but may cause discomfort for 10–14 days.

ACTIVITY
• Limit activity to minimize risk of epistaxis and dyspnea.
• Using a harness instead of a collar during walks may help minimize epistaxis.

DIET
• Soften food if needed during radiation therapy.
• Avoid extremes of temperatures and salty foods with radiation therapy-related mucositis.

CLIENT EDUCATION
Nasal adenocarcinoma may be painful even though the pet is not showing visible signs of pain.
• Consider the use of medications for discomfort and congestion.
• Radiation therapy is the most effective option and is well-tolerated using modern radiotherapy techniques.
• Radiation side effects may impact the patient's quality of life during treatment, but most pets enjoy a relatively normal quality of life following treatment.

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ADENOCARCINOMA, NASAL (CONTINUED)

• Intermittent congestion and sneezing may occur post therapy due to increased sensitivity from the tumors' destruction of the nasal turbinates.

SURGICAL/ANESTHETIC CONSIDERATIONS

Anesthetic recovery—ensure airway is maintained until animal is sternal to prevent apnea in patients with bilateral nasal obstruction.

MEDICATIONS

DRUG(S) OF CHOICE

• Chemotherapy is considered ineffective for durable tumor control, but may benefit some patients if radiation therapy is not a viable option. Various drugs have been described including cisplatin (dogs only), carboplatin, doxorubicin, and piroxicam. Toceranib phosphate (Palladia) exerts therapeutic activity against nasal carcinoma.
• Consult with an oncologist for more details.
• Adequate analgesic therapy should be employed as needed in patients suffering from invasive disease with bone destruction, signs of pain, and radiation therapy side effects.

CONTRAINDICATIONS

Cisplatin—never use in cats.

PRECAUTIONS

• Most chemotherapeutics have gastrointestinal, hematologic, and other potential side effects and should be administered and monitored by an oncologist.
• Piroxicam can cause gastric ulceration so careful monitoring of appetite, vomiting, and stool color (melena) is recommended.

POSSIBLE INTERACTIONS

Concurrent radiation therapy and chemotherapy will increase the risk of side effects but have not shown to significantly improve tumor control.

ALTERNATIVE DRUGS

• Palladia, a tyrosine kinase inhibitor, may have anticancer activity in some carcinomas including nasal adenocarcinomas. It is currently being investigated at the labeled dose alone and in combination with radiation therapy.
• Objective responses have been documented with use of Palladia alone.

FOLLOW-UP

PATIENT MONITORING

• CT or MRI are needed to assess response to therapy and are recommended 2–3 months post radiation treatment.
• Other staging tests including thoracic radiography or CT and lymph node evaluation are generally recommended in 3-month intervals during/following therapy.
• Routine staging with CT/MRI and monitoring of recurrent clinical signs can detect early recurrence.

POSSIBLE COMPLICATIONS

• Dyspnea
• Epistaxis
• Secondary infections
• Weight loss
• Anorexia
• Chemotherapy or radiation toxicity

EXPECTED COURSE AND PROGNOSIS

• Untreated—median survival around 2–6 months.
• Radiation therapy—median survival times around 12–18 months in dogs and 12–20 months in cats; 1-year survival rate 20–57% (dogs and cats); 2-year survival rate 20–48% (dogs and cats).
• Presence of cribriform lysis, brain involvement or metastatic disease (advanced stage) are poor prognostic indicators.
• Ophthalmic complications of radiation therapy—more likely in dogs than cats.
• Incidence and severity of ophthalmic toxicity are decreasing with advanced radiation therapy techniques now commonly used.
• Chronic rhinitis is possible following radiation therapy for sinonasal tumors and may require periodic symptomatic therapy.

MISCELLANEOUS

AGE-RELATED FACTORS

None

PREGNANCY/FERTILITY/BREEDING

Chemotherapeutic drugs and general anesthesia are a risk to the fetus and would not be recommended in pregnant animals.

SYNONYMS

• Nasal carcinoma
• Nasal tumor

SEE ALSO

• Squamous cell carcinoma, nasal
• Chondrosarcoma, nasal
• Lymphoma, nasal

ABBREVIATIONS

• CT = computed tomography
• MRI = magnetic resonance imaging

INTERNET RESOURCES

• http://veterinarymedicine.dvm360.com/vetmed/Medicine/Canine-and-feline-nasal-tumors/ArticleStandard/Article/detail/735167
• http://smallanimal.vethospital.ufl.edu/clinical-services/oncology/types-of-cancer-and-treatment/nasal-tumors-dogs/
• http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2643460/

Suggested Reading

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ADENOCARCINOMA, PANCREAS

BASICS

OVERVIEW
• Malignant tumor of ductal or acinar origin arising from the exocrine pancreas.
• Usually metastatic by the time of diagnosis, affecting regional lymph nodes and visceral abdominal organs (liver) and associated peritoneal cavity.

SIGNALMENT
• Rare in dogs—0.5–1.8% of all tumors
• Rare in cats—2.8% of all tumors
• Older female dogs and Airedale terriers at higher risk than others
• Median age (dogs)—9.2 years
• Mean age (cats)—11.6 years

SIGNS
• Nonspecific—fever; vomiting; weakness; anorexia; icterus; malabsorption syndrome; weight loss.
• Abdominal pain—variable.
• Abdominal effusion—malignant.
• Metastasis to bone and soft tissue common.
• Pathologic fractures secondary to metastasis reported.
• Palpable abdominal mass (cats).
• Paraneoplastic syndromes of epidermal necrosis, hyperinsulinemia, and hyperglucagonemia may be present.
• Average duration of clinical signs (cats): 41 days, range 2–180 days.

CAUSES & RISK FACTORS
Unknown

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Primary pancreatitis; may be concurrent and complicate or delay early diagnosis
• Pancreatic pseudocyst
• Pancreatic nodular hyperplasia
• Hepatic neoplasia
• Other causes of vomiting and icterus
• Peritoneal carcinomatosis
• Other causes of abdominal effusion in cats

CBC/BIOCHEMISTRY/URINALYSIS
• Usually nonspecific changes (e.g., mild anemia and neutrophilia).
• Hyperamylasemia less reliable than hyperlipasemia.
• Lipase concentrations are often markedly elevated and may serve as a non-invasive biochemical marker of neoplasia in dogs.

OTHER LABORATORY TESTS
Rarely there may be significant metabolic alterations that affect glucagon, insulin, and amino acid concentrations.

IMAGING
• Abdominal radiographs may reveal a mass or loss of serosal detail associated with concurrent pancreatitis or peritoneal effusion.
• Ultrasonography may reveal one or more masses or concurrent pancreatitis (mixed echogenicity, large pancreas, hyperechoic peripancreatic fat). Pancreatic thickening, abdominal effusion, and single to multiple nodules of varying size may be identified. Sonographic findings may be impossible to distinguish from pancreatic nodular hyperplasia. Rarely the ultrasound of the pancreas may appear normal except for dilation of the pancreatic duct.

DIAGNOSTIC PROCEDURES
• Surgical biopsy—definitive.
• Fine-needle aspirate cytology—supportive. In many cases, where the tumor is not resectable, the fine-needle aspirates may provide strong enough evidence to start medical treatment.

TREATMENT
• None reported curative.
• Palliation of pain with aggressive analgesic combinations is necessary.
• Surgical intervention to alleviate intestinal and biliary obstruction, if necessary.
• Surgery is typically not a good option in many cases, due to the extent of the disease at the time of diagnosis.
• If surgery is an option, partial or total pancreatectomy may prolong survival.
• Treat concurrent pancreatitis.
• Antiemetics and supportive care (hydration and caloric requirements).

MEDICATIONS

DRUG(S)
• Gemcitabine is used in humans for the treatment of pancreatic carcinoma, and while used in dogs with cancer, it has not been established as the standard of care for dogs with pancreatic adenocarcinoma.
• Always consult a veterinary oncologist for updates in treating this rare neoplasm.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
N/A

FOLLOW-UP

POSSIBLE COMPLICATIONS
• Intestinal obstruction
• Biliary obstruction
• Pancreatic abscess
• Peritonitis
• Metastasis

EXPECTED COURSE AND PROGNOSIS
Progression to death is often rapid given that there is no successful curative treatment available. Despite the grave prognosis, individual patients treated with complete resection of their tumor and chemotherapy, in the absence of systemic metastasis, may have prolonged survival.

MISCELLANEOUS

ASSOCIATED CONDITIONS
Gastrin-secreting pancreatic carcinoma (gastrinoma) has been reported in dogs and cats. Clinical signs are associated with hypergastrinemia, which results in inappropriate hydrochloric acid secretion by the stomach, leading to gastroduodenitis.

Suggested Reading

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Consulting Editor Timothy M. Fan
Acknowledgment The author and editors acknowledge the prior contribution of Wallace B. Morrison.

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ADENOCARCINOMA, PROSTATE

BASICS

OVERVIEW
• Prostatic adenocarcinoma is a malignant tumor that occurs in both neutered and intact male dogs.
• Although this neoplasm represents < 1% of all canine malignancies, it is the most common prostatic disorder in neutered male dogs.
• Metastases to regional lymph nodes, lungs, and the lumbosacral skeleton are common. Skeletal metastases can adopt an osteoblastic appearance.

SIGNALMENT
• Dog and rarely cat
• Medium- to large-breed intact or neutered male dogs
• Median age of 9–10 years

SIGNS
Historical Findings
• Tenesmus (with the production of ribbon-like stool)
• Weight loss
• Stranguria and dysuria
• Rear limb lameness or neurologic weakness
• Lethargy
• Exercise intolerance

Physical Examination Findings
• A firm, asymmetrical, and immobile prostate gland.
• Prostatomegaly is common, but is not always present.
• Pain may be elicited in response to abdominal or rectal palpation.
• Caudal abdominal mass, cachexia, pyrexia, and dyspnea may also be identified in advanced cases of disease.

CAUSES & RISK FACTORS
Neutered males are at increased risk for prostatic neoplasia

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Other primary neoplasia (i.e., squamous cell carcinoma, transitional cell carcinoma).
• Metastatic or locally invasive neoplasia (i.e., transitional cell carcinoma).
• Acute or chronic prostatitis, benign prostatic hypertrophy, prostatic abscess, and prostatic cysts are possible differentials in intact male dogs but are highly unlikely in neutered dogs.

CBC/BIOCHEMISTRY/URINALYSIS
• Inflammatory leukogram possible.
• Alkaline phosphatase may be high if skeletal metastases exist.
• Post-renal azotemia may be present if urethral obstruction exists.
• It is prudent to evaluate urine samples via cystocentesis and free-catch techniques, as hematuria, pyuria, and malignant epithelial cells may be observed in free-catch samples but are unusual in samples obtained by cystocentesis.

OTHER LABORATORY TESTS
Serum and seminal plasma markers such as acid phosphatase, prostate specific antigen, and canine prostate specific esterase are not elevated in dogs with PAC.

IMAGING
• Thoracic radiography—metastases may appear as pulmonary nodules or increased interstitial markings.
• Abdominal radiography—sublumbar lymphadenomegaly, mineralization of the prostate, lytic lesions to the lumbar vertebrae or pelvis as a consequence of direct tumor extension from regionally infiltrated lumbar lymph nodes may be seen.
• Abdominal ultrasonography—focal to multifocal hyperechogenicity with asymmetry and irregular prostatic outline, ± prostatic mineralization.
• Contrast cystography may help differentiate prostatic from urinary bladder disease.

DIAGNOSTIC PROCEDURES
• Prostatic aspirate (percutaneous or transrectal).
• Prostatic wash.
• Prostatic biopsy performed percutaneously or surgically.
• Percutaneous biopsy has been associated with tumor seeding along the biopsy tract.

TREATMENT
• Prostatectomy if local disease (success of this procedure depends on the skill of the surgeon and extent of disease).
• Radiation therapy may palliate signs and prolong survival.
• Prostatic urethral stenting can alleviate urethral obstruction.
• Neutering—however, most tumors are not androgen responsive.

MEDICATIONS

DRUG(S)
• Chemotherapy—carboplatin, mitoxantrone, or doxorubicin; may offer short-term benefit.
• Pain relief with NSAIDs, morphine-derived drugs.
• Aminobisphosphonates for the relief of painful skeletal metastases.
• Stool softeners to relieve tenesmus.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
N/A

FOLLOW-UP

PATIENT MONITORING
Ability to urinate and defecate, pain secondary to skeletal metastases, quality of life.

PREVENTION/AVOIDANCE
Keeping dogs sexually intact may decrease risk.

POSSIBLE COMPLICATIONS
• Urethral obstruction
• Metastasis to regional lymph nodes, skeleton, and lungs

EXPECTED COURSE AND PROGNOSIS
Guarded to poor, survival of 2–6 months depending upon presenting clinical symptoms. Treatment early in the course of disease with curative-intent radiation and systemic chemotherapy can extend survival times to 12 months.

MISCELLANEOUS

ASSOCIATED CONDITIONS
None

AGE-RELATED FACTORS
None

ABBREVIATIONS
• NSAID = nonsteroidal anti-inflammatory drug
• PAC = prostatic adenocarcinoma

Suggested Reading
Bryan JN, et al. A population study of neutering status as a risk factor for canine prostate cancer. Prostate 2007, 67:1174–1181.

Author Ruthanne Chun
Consulting Editor Timothy M. Fan

ADENOCARCINOMA, RENAL

BASICS

OVERVIEW
• Accounts for < 1% of all reported neoplasms in dogs.
• Renal tumors tend to be highly metastatic via hematogenous dissemination, locally invasive, and often bilateral.
• Renal cystadenocarcinoma, a rare heritable syndrome with a less aggressive behavior and better long-term prognosis than renal adenocarcinoma, has been described in German shepherd dogs.

SIGNALMENT
• Adenocarcinoma—older (8–9 years) dogs, 1.6:1 male-to-female ratio, no breed predilection.
• Cystadenocarcinoma—German shepherd dogs, often female.

SIGNS
• Adenocarcinoma—insidious, non-specific signs such as weight loss, inappetance, lethargy, hematuria, and pale mucous membranes. Possibility for paraneoplastic polycythemia.
• Cystadenocarcinoma—may present for nodular dermatofibrosis, a syndrome of painless, firm, fibrous lesions of the skin and subcutaneous tissues.

CAUSES & RISK FACTORS
• Adenocarcinoma—unknown.
• Cystadenocarcinoma—heritable in German shepherd dogs.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Other primary neoplasia (i.e., lymphoma, nephroblastoma)
• Metastatic neoplasia (i.e., hemangiosarcoma)
• Renal adenoma or cyst
• Pyelonephritis

CBC/BIOCHEMISTRY/URINALYSIS
• CBC may show paraneoplastic polycythemia or leukocytosis, or anemia.
• Biochemistry may be normal, or may reveal azotemia.
• Urinalysis may show hematuria, proteinuria, bacteriuria, or casts.

OTHER LABORATORY TESTS
Urine culture and sensitivity

IMAGING
• Thoracic radiographs—metastatic disease reported in up to 16% of patients.
• Abdominal radiographs—mass visualized in 81% of patients.
• Abdominal ultrasonography, CT, or contrast radiography—useful in identifying and staging the disease. Advanced imaging can guide decisions regarding surgical resectability.

DIAGNOSTIC PROCEDURES
• Renal biopsy (ultrasound-guided or surgical) for definitive diagnosis.
• Percutaneous fine-needle aspirate can be used for supportive diagnosis.

TREATMENT

• Aggressive surgical excision is the treatment of choice for unilateral disease.
• Successful chemotherapeutic management of either disease has not been described.
• Supportive management for patients in renal failure may be necessary.

MEDICATIONS

DRUG(S)
None

FOLLOW-UP

PATIENT MONITORING
• Renal failure—measure serum urea nitrogen and creatinine; urinalysis.
• Quality of life if bilateral or otherwise non-surgical disease.

PREVENTION/AVOIDANCE
N/A

POSSIBLE COMPLICATIONS
• Renal failure
• Metastatic disease
• Invasion of local vital structures (vena cava, aorta)

EXPECTED COURSE AND PROGNOSIS
• Adenocarcinoma—median reported survival of 49 dogs was 16 months (range 0–59 months).
• Cystadenocarcinoma—few large studies of this rare disease, reported median survival of 12+ months with no definitive therapy.

MISCELLANEOUS

ASSOCIATED CONDITIONS
• The paraneoplastic syndromes of hypertrophic osteopathy, polycythemia, and a neutrophilic leukocytosis have been reported in isolated cases.
• Renal failure.
• Nodular dermatofibrosis and uterine leiomyomas are commonly associated with cystadenocarcinoma.

ABBREVIATION
• CT = computed tomography

Suggested Reading

Bryan JN, et al. Primary renal neoplasia of dogs. J Vet Intern Med 2006, 20:1155–1160.
Knapp DW. Tumors of the urinary system. In: Withrow SJ, Vail DM, eds., Small Animal Clinical Oncology, 4th ed. Philadelphia: Saunders, 2007, pp. 649–658.

Author Ruthanne Chun
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A

ADENOCARCINOMA, SALIVARY GLAND

BASICS

OVERVIEW
• Tumor arising from major (e.g., parotid, mandibular, sublingual, or zygomatic) or minor salivary glands.
• Mandibular or parotid glands constitute 80% of cases.
• Mandibular gland most frequently affected in dogs.
• Parotid gland most frequently affected in cats.
• Locally invasive and regionally metastatic.
• Cats typically have more advanced disease than dogs at time of diagnosis.
• Metastasis—regional lymph node involvement in 39% of cats and 17% of dogs at diagnosis; distant metastasis reported in 16% of cats and 8% of dogs at diagnosis but may be slow to develop.
• Other salivary gland neoplasms—carcinoma; squamous cell carcinoma; mixed neoplasia.
• Epithelial malignancies—constitute roughly 85% of salivary gland tumors.
• Fibrosarcomas, lipomas, mast cell tumors, and lymphomas have involved the salivary glands by direct extension and invasion. A concurrent malignant fibrous histiocytoma (giant cell type) and malignant mixed tumor (likely of ductal origin) within the salivary gland has also been described.
• Adenomas comprise only 5% of salivary tumors.

SIGNALMENT
• Dog and cat.
• Mean age, 10–12 years.
• Siamese cats—may be at relatively higher risk.
• Male cats affected twice as often as female cats.
• No other breed or sex predilection has been determined.

SIGNS
• Unilateral, firm, painless swelling of the upper neck (mandibular and sublingual), ear base (parotid), upper lip or maxilla (zygomatic), or mucous membrane of lip (accessory or minor salivary tissue).
• Other signs may include halitosis, weight loss, anorexia, dysphagia, exophthalmus, Horner's syndrome, sneezing, and dysphonia.

CAUSES & RISK FACTORS
Unknown

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Squamous cell carcinoma
• Mucocele
• Abscess
• Soft tissue sarcoma, e.g., fibrosarcoma
• Lymphoma
• Sialadenosis

CBC/BIOCHEMISTRY/URINALYSIS
Results often normal

IMAGING
• Regional radiographs usually are normal; may see periosteal reaction on adjacent bones or displacement of surrounding structures.
• MRI or CT imaging allows superior discrimination of tumor for surgery and/or radiation treatment planning.
• Thoracic radiographs indicated to check for lung metastases.

DIAGNOSTIC PROCEDURES
• Cytologic examination of aspirate may differentiate salivary adenocarcinoma from mucocele and abscess.
• Needle core or wedge biopsy for histopathology—definitive diagnosis.

TREATMENT

• Aggressive surgical resection—when possible; most are invasive and difficult to excise completely.
• Radiotherapy—good local control and prolonged survival in three reported cases.
• Aggressive local resection (usually histologically incomplete) followed by adjuvant radiation can achieve local control and long-term survival, but further studies are needed to determine the most effective treatment, including the possible role for chemotherapy.

MEDICATIONS

DRUG(S)
Chemotherapy (mitoxantrone or carboplatin) efficacy is largely unreported; however, may be indicated for treatment/palliation of metastatic disease.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
N/A

FOLLOW-UP

PATIENT MONITORING
Evaluations—physical examination and thoracic radiographs every 3 months reasonable if aggressive surgery and/or radiation therapy employed.

POSSIBLE COMPLICATIONS
Temporary acute side effects (e.g., moist dermatitis and alopecia) expected with definitive radiation therapy in dogs, but uncommon in cats. Consultation with a radiation oncologist is recommended regarding specific, anatomic site-related side effects associated with planned dose and field size.

EXPECTED COURSE AND PROGNOSIS
• Improved survival time in dogs without evidence of nodal or distant metastasis at diagnosis; clinical stage not prognostic for cats.
• Median survival 550 days for dogs and 516 days for cats in retrospective study.
• Local control obtained through radiation and/or surgery remains critical.

MISCELLANEOUS

ABBREVIATIONS
• CT = computed tomography
• MRI = magnetic resonance imaging

Suggested Reading

Hammer A, Getzy D, Ogilvie G, et al. Salivary gland neoplasia in the dog and cat: Survival times and prognostic factors. J Am Anim Hosp Assoc 2001, 37:478–482.

Author Anthony J. Mutsaers
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ADENOCARCINOMA, SKIN (SWEAT GLAND, SEBACEOUS)

BASICS

OVERVIEW
Malignant growth originating from sebaceous or apocrine sweat glands of the skin.

SIGNALMENT
• Apocrine sweat gland—rare in dogs, uncommon in cats.
• Sebaceous gland—rare in both dogs and cats.
• Middle-aged to older pets.
• Female dogs overrepresented for apocrine adenocarcinoma in one study.

SIGNS
• May appear as solid, firm, raised, superficial skin lesions.
• May be ulcerated and bleeding and accompanied by inflammation of the surrounding tissue.
• Apocrine sweat gland—often poorly circumscribed, ulcerated; very invasive into underlying tissue; may occur anywhere on the body, frequently affecting the trunk in dogs.
• Sebaceous gland—often ulcerated and inflamed, moderate risk of lymph node involvement.
• Dermal and lymphatic tracking can be observed early in disease course.

CAUSES & RISK FACTORS
Unknown

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Other more frequent skin tumors
• Cutaneous histiocytic diseases
• Immune-mediated skin diseases
• Bacterial/fungal infections

CBC/BIOCHEMISTRY/URINALYSIS
Normal

OTHER LABORATORY TESTS
N/A

IMAGING
Thoracic radiographs recommended at the time of diagnosis to assess for distant metastases.

DIAGNOSTIC PROCEDURES
• Biopsy for histopathology and definitive diagnosis
• Cytologic examination or biopsy of draining lymph nodes

PATHOLOGIC FINDINGS
• Apocrine gland adenocarcinomas are typically invasive into the underlying stroma and blood vessels, and often show poorly demarcated borders and a high mitotic index.
• Sebaceous gland adenocarcinomas often reveal lymphatic vessel invasion.

TREATMENT

• Aggressive *en bloc* surgical excision, including resection of draining lymph node, recommended for both types. Histopathologic analysis of lymph nodes assists with determining prognosis and establishing adjuvant treatment plan.
• Margins of entire tissue specimen must be evaluated histologically to assess completeness of resection.
• Radiation therapy may be recommended for treatment of draining lymph nodes after resection to prevent recurrence and development of regional metastasis; radiation therapy of primary tumor site recommended when wide and complete resection not possible.

MEDICATIONS

DRUG(S)
• Chemotherapy has been used anecdotally for the treatment of both tumor types, in both species.
• Contact a veterinary oncologist for any updated treatments that may be available.
• Nonsteroidal anti-inflammatory drugs and other analgesics are recommended, as indicated, for pain control.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
None

FOLLOW-UP

• Sebaceous gland adenocarcinoma—little is known about the metastatic potential of this malignancy, but may be rapidly metastatic to regional lymph nodes in some patients; long-term prognosis is anecdotally good with multimodal therapy combining aggressive surgery, chemotherapy, and radiation therapy.
• Apocrine gland adenocarcinoma—fair to good long-term prognosis; the histologic finding of vascular invasion is a negative prognostic factor predicting systemic metastases; aggressive surgical resection (local and regional tumor control) followed by adjuvant chemotherapy is recommended to improve survival. A study reported a post-excisional median survival time of 30 months in dogs.

MISCELLANEOUS

Suggested Reading

Carpenter JL, Andrews LK, Holzworth J. Tumors and tumor like lesions. In: Holzworth J, ed., Diseases of the Cat: Medicine and Surgery. Philadelphia: Saunders, 1987, pp. 406–596.
Pakhrin B, Kang MS, Bae IH, et al. Retrospective study of canine cutaneous tumors in Korea. J Vet Sci 2007, 8:229–236.
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Haziroglu R, Haligur M, Keles H. Histopathological and immunohistochemical studies of apocrine sweat gland adenocarcinomas in cats. Vet Comp Oncol 2014, 12(1):85–90.

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A

ADENOCARCINOMA, STOMACH, SMALL AND LARGE INTESTINE, RECTAL

BASICS

OVERVIEW
• Uncommon tumor arising from the epithelial lining of the gastrointestinal tract.
• Prognosis guarded to poor.

SIGNALMENT
• Dog more commonly affected than cat.
• Middle-aged to older (> 6 years) animals; age range 3–13 years.
• No breed predisposition.
• More common in males than females.

SIGNS
Historical Findings
• Stomach—vomiting, anorexia, weight loss, hematemesis, and melena.
• Small intestine—vomiting, weight loss, borborygmus, flatulence, and melena.
• Large intestine and rectum—mucus and blood-tinged feces and tenesmus.

Physical Examination Findings
• Stomach—nonspecific.
• Small intestine—may feel mid-abdominal mass; distended, painful loops of small bowel; melena on rectal exam.
• Large intestine and rectum—palpable mass per rectum, may form annular ring, or multiple nodular lesions protruding into the colon; bright red blood on feces.

CAUSES & RISK FACTORS
• Unknown.
• Nitrosamines—reported as causative agent in experimental literature.
• Possible genetic cause—gastric adenocarcinomas in related Belgian shepherds and Dutch Tervuren shepherds.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Foreign body
• Inflammatory bowel disease
• Lymphoma
• Parasites
• Leiomyoma
• Leiomyosarcoma
• Pancreatitis

CBC/BIOCHEMISTRY/URINALYSIS
• Stomach and small intestine—may see microcytic, hypochromic anemia (iron-deficiency anemia). Mild and persistent elevations in blood urea nitrogen in the face of normal creatinine can support intestinal blood loss.
• Large intestine and rectum—no characteristic changes.

OTHER LABORATORY TESTS
Fecal occult blood may be positive; diet may affect results—can recheck to confirm after feeding non-meat diet for 3 days.

IMAGING
• Ultrasound—may reveal a thickened stomach or bowel wall; may see mass in the gastrointestinal tract, enlarged lymph nodes.
• Positive contrast radiography—filling defect (stomach); intraluminal space-occupying or annular constriction (small bowel); gastric neoplasm most often found in distal two-thirds of stomach.
• Double contrast radiography—large intestine and rectum; polypoid or annular space-occupying masses.
• Advanced imaging with contrast CT or MRI can provide highest quality images of gastrointestinal tract.

DIAGNOSTIC PROCEDURES
• Ultrasound-guided fine-needle aspirate of bowel mass or enlarged lymph node may reveal carcinoma cells on cytology, which can be useful to rule out lymphoma.
• Endoscopic biopsy may be non-diagnostic because tumors are frequently deep to the mucosal surface; thus surgical biopsy frequently required.

TREATMENT

• Surgical resection—treatment of choice; seldom curative.
• Gastric—usually non-resectable.
• Small intestine—remove by resection and anastomosis; metastasis to regional lymph nodes and the liver common.
• Large intestine and rectal—may occasionally be resected by a pull-through surgical procedure; metastasis common; transcolonic debulking may provide palliation of obstruction.

MEDICATIONS

DRUG(S)
• Chemotherapy—only anecdotal reports, usually unsuccessful.
• Piroxicam 0.3 mg/kg PO q24 h can provide palliation for large intestinal and rectal tumors.
• Aggressive combination analgesics should be instituted.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
Seek advice before initiating treatment with cytotoxic drugs.

FOLLOW-UP

Physical examination, thoracic radiographs, and abdominal ultrasound—at 1, 3, 6, 9, and 12 months post-surgery.

EXPECTED COURSE AND PROGNOSIS
Dogs
• Overall poor; pedunculated rectal tumors do best; most cases recur locally, develop metastasis, or both rapidly.
• Median survival gastric—2 months.
• Median survival small intestinal—10 months.
• Mean survival large intestinal—annular 1.6 months versus pedunculated 32 months.

Cats
• Guarded.
• Few reported cases, but may have prolonged survival (> 1 year).

MISCELLANEOUS

ABBREVIATIONS
• CT = computed tomography
• MRI = magnetic resonance imaging

Suggested Reading
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Author Laura D. Garrett
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ADENOCARCINOMA, THYROID—DOGS

BASICS

DEFINITION
A malignant tumor arising from the follicular or parafollicular cells (medullary/C-cells) of the thyroid gland.

PATHOPHYSIOLOGY
• About 60% of patients are euthyroid, 30% hypothyroid, and 10% hyperthyroid.
• Typically very invasive tumors with high rate of metastasis (lungs, retropharyngeal lymph nodes, liver), with up to 35–40% of dogs having metastasis at the time of diagnosis.
• Animals with bilateral tumors have a sixteen times greater risk of developing metastatic disease than animal with unilateral tumors.

SYSTEMS AFFECTED
• Cardiovascular—hyperthyroid dogs are usually tachycardic and may have systemic hypertension; may see anemia and DIC in advanced disease.
• Endocrine/Metabolic—affected dogs may be hypothyroid, euthyroid, or hyperthyroid; hypercalcemia may be seen as a paraneoplastic syndrome or secondary to concurrent parathyroid hyperplasia or parathyroid adenocarcinoma.
• Respiratory—dogs may be dyspneic owing to a space-occupying mass adjacent to the trachea; metastasis to the lungs common. Large compressive masses can result in caval syndrome manifested as facial edema.

GENETICS
Unknown

INCIDENCE/PREVALENCE
Accounts for 1.2–3.8% of all canine tumors and represents 10–15% of all primary head and neck tumors.

GEOGRAPHIC DISTRIBUTION
May be more common in iodine-deficient areas.

SIGNALMENT
Species
Dog

Breed Predilections
Boxers, golden retrievers, Siberian huskies, and beagles at increased risk but seen in any breed.

Mean Age and Range
Older dogs (median 9–15 years; range 4–18 years)

Predominant Sex
No gender predilection.

SIGNS
General Comments
• Usually not diagnosed until a large mass is palpable.
• Approximately 65% are unilateral, 35% are bilateral.

Historical Findings
• Palpable mass/swelling in cervical neck, coughing, dyspnea, dysphagia, dysphonia, facial edema, neck pain.
• If functional thyroid tumor—may see polyuria, polydypsia, polyphagia, weight loss, restless behavior, diarrhea.
• If hypothyroid—may see poor hair coat, weight gain, lethargy.

Physical Examination Findings
• Freely movable or fixed cervical mass, unilateral or bilateral.
• Rarely may see Horner's syndrome, or cranial vena cava syndrome.
• If hyperthyroid—cardiac arrhythmias or murmurs.

CAUSES
Unknown

RISK FACTORS
• Untreated hypothyroidism has been shown to be a risk factor in a colony of beagles.
• Breed predilection.
• Iodine deficiency.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Other primary neoplasms—lymphoma; soft tissue sarcoma; salivary gland adenocarcinoma; parathyroid carcinoma; carotid body tumor.
• Secondary tumors—metastatic oral squamous cell carcinoma; oral melanoma.
• Inflammatory—abscess or granuloma.
• Salivary mucocele.

CBC/BIOCHEMISTRY/URINALYSIS
• Usually normal.
• May see non-regenerative normocytic normochromic anemia of chronic disease, leukocytosis.
• Rare—hypercalcemia; isosthenuria; DIC.

OTHER LABORATORY TESTS
Thyroid hormone (T_4 and/or free T_4 levels) and endogenous TSH levels.

IMAGING
• Thoracic radiography (3 view)—evaluation of lungs and other thoracic structures for metastasis.
• Cervical ultrasonography, computed tomography, and magnetic resonance imaging—evaluation of tissue of origin, vascularity, invasion, and cervical lymph nodes.
• Technetium-99 m scintigraphy to evaluate for ectopic thyroid tissue or metastatic lesions.
• Radioiodine studies—may provide information about the tumor's ability to produce thyroid hormone.

DIAGNOSTIC PROCEDURES
Biopsy
Tru-Cut not recommended owing to high risk of severe hemorrhage; open biopsy usually required and allows for controlled hemostasis in the event of bleeding.

Cytology
• Examination of fine-needle aspirates from tumor and palpable regional lymph nodes.
• Specimen almost always heavily contaminated with blood owing to highly vascular nature of tumor.
• Homogeneous population of epithelial cells, sometimes with colloid and/or tyrosine-containing granules.
• Unable to differentiate malignant from benign thyroid cells; but almost all thyroid neoplasms in dogs are malignant.

PATHOLOGIC FINDINGS
Gross
• Characterized by high vascularity with areas of hemorrhage and necrosis.
• Usually poorly encapsulated; often invade adjacent tissues (e.g., trachea and esophagus, and surrounding vasculature); may adhere to the jugular vein, carotid artery, and vagosympathetic trunk.

Histopathology
• Three main types—follicular, papillary, and compact (solid); mixed follicular and solid tumors most common in dogs.
• C-cell (e.g., parafollicular, medullary) carcinomas less common.

TREATMENT

APPROPRIATE HEALTH CARE
• Definitive treatment is dependent on tumor stage (tumor size, mobility, and evidence of metastatic disease).
• Complete surgical excision recommended for freely movable thyroid tumors.
• Full course external beam radiation therapy recommended preoperatively for large tumors, as a sole therapy for non-resectable tumors, or postoperatively for incompletely surgically removed tumors.
• Palliative radiation and/or chemotherapy recommended for tumors that are metastatic at presentation.
• Also can use iodine-131 but doses are very large (60–100 mCi) and therefore there are limited facilities that offer this therapy.
• Toceranib phosphate (Palladia) can exert cytoreductive activity.

NURSING CARE
Varies with signs on examination.

ACTIVITY
Restrict activity if dyspneic.

DIET
N/A

CLIENT EDUCATION
• Warn owners of the importance of controlling heart rate and rhythm in hyperthyroid patients and of the possibility of episodes of collapse.

A

ADENOCARCINOMA, THYROID—DOGS (CONTINUED)

• Warn owners of possible postoperative laryngeal paralysis and intraoperative hemorrhage.
• Warn owners of acute radiation therapy toxicities—moist desquamation, laryngitis, tracheitis, esophagitis.

SURGICAL CONSIDERATIONS
See "Appropriate Health Care"

Risks
• Marked hemorrhage—tumors highly vascular and invasive into surrounding structures including vasculature; may need blood transfusion and intensive postoperative care.
• Laryngeal paralysis—owing to trauma to recurrent laryngeal nerve.
• Damaged parathyroid glands—may occur during surgery.

MEDICATIONS

DRUG(S) OF CHOICE
• Chemotherapeutic agents:
  ◦ Chemotherapy is recommended as a sole therapy, or possibly in combination with surgery and/or radiation therapy.
  ◦ Cisplatin (60 mg/m^2 every 3 weeks), carboplatin (300 mg/m^2 every 3 weeks), or doxorubicin (30 mg/m^2 every 3 weeks)—reported to effect partial remission in approximately 50% of cases.
  ◦ Toceranib (2.5–3 mg/kg 3 times a week)—had biologic activity in 80% of cases (26% partial remission, 53% stable disease).
  ◦ Cisplatin—nephrotoxic; must use with saline diuresis (18.3 mL/kg/hour IV over 6 hours; give cisplatin after 4 hours).
• Antiemetics for cisplatin therapy:
  ◦ Maropitant 1 mg/kg SC before cisplatin, or
  ◦ Dolasetron 0.6–1 mg/kg IV or PO q24 h, or
  ◦ Butorphanol 0.4 mg/kg IM before and after cisplatin.
• Thyroid management:
  ◦ Thyroxine—maintenance doses to decrease TSH production have been recommended; some tumors contain TSH receptors; value of hormone replacement therapy in affected dogs not determined.
  ◦ Methimazole 5 mg PO q8 h for medium to large dogs; may be beneficial for hyperthyroid patients.
  ◦ β-blockers—may be indicated for tachycardia or hypertension in hyperthyroid patients.

CONTRAINDICATIONS
• Doxorubicin is cumulatively toxic to cardiac myocytes causing decreased myocardial function. Do not give to animals with poor cardiac function or dilated cardiomyopathy.
• Cisplatin is nephrotoxic; do not give to animals with renal disease.

PRECAUTIONS
Chemotherapy can cause gastrointestinal, bone marrow, cardiac, and other toxicities—seek advice from a medical oncologist if unfamiliar with cytotoxic drugs.

POSSIBLE INTERACTIONS
Verapamil—may potentiate doxorubicin-induced cardiotoxicity.

ALTERNATIVE DRUG(S)
N/A

FOLLOW-UP

PATIENT MONITORING
• Serum calcium concentration—if bilateral thyroidectomy was performed; signs of hypocalcemia (agitation, panting, muscle tremors, tetany, and seizures) may be observed.
  ◦ Treat with 10% calcium gluconate (1–1.5 mL/kg IV over 10–20 minutes).
  ◦ Maintain serum calcium with dihydrotachysterol (vitamin D) orally.
• Thyroid hormone—supplementation with thyroxine may be necessary after bilateral thyroidectomy.
• TSH concentration—a goal of thyroxin supplementation is to downregulate the body's secretion of TSH.
• Site of primary tumor—physical examination and cervical ultrasound; thoracic radiographs every 3 months to detect pulmonary metastasis.

PREVENTION/AVOIDANCE
Unknown

POSSIBLE COMPLICATIONS
• Tumor—anemia; thrombocytopenia; hypercalcemia; DIC; respiratory distress.
• Chemotherapy—dilated cardiomyopathy; renal failure; pancreatitis; sepsis; gastrointestinal upset.
• Surgery—hemorrhage; hypothyroidism; hypoparathyroidism leading to hypocalcemia; laryngeal paralysis.
• Radiotherapy—acute side effects—moist desquamation, pharyngeal mucositis; esophagitis; tracheitis; late side effects—alopecia, and skin or coat color change (at radiation site).

EXPECTED COURSE AND PROGNOSIS
• Prognosis—related to stage of disease (tumor size, mobility and evidence of metastatic disease) with small, non-attached unilateral, non-metastatic tumors having best prognosis.
• MST after surgical removal of unilateral thyroid tumors is 1462 days vs. 365 days for patients undergoing bilateral thyroidectomy.
• For animals treated with full course external beam radiation therapy—progression-free survival at 1 year—80%, and 72% at 3 years in one study and in another study MST 24.5 months.
• Palliative radiation therapy in 13 dogs—MST 24 months.
• ^{131}I therapy in combination with surgery—MST 34 months, or ^{131}I alone MST 30 months.
• Animals treated with cisplatin alone (13 dogs)—overall response rate was 53%, median progression-free interval for responders was 202 days and overall MST was 98 days.

MISCELLANEOUS

ASSOCIATED CONDITIONS
• Non-thyroidal malignancies common
• Multiple endocrine neoplasia reported

AGE-RELATED FACTORS
None

PREGNANCY/FERTILITY/BREEDING
It is not recommended to breed animals with cancer. Chemotherapy is teratogenic—do not give to pregnant animals.

SYNONYMS
Thyroid carcinoma

ABBREVIATIONS
• DIC = disseminated intravascular coagulation
• MST = median survival time
• TSH = thyroid stimulating hormone

Suggested Reading

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Acknowledgment The author and editors acknowledge the prior contribution of Linda S. Fineman.

AGGRESSION TO UNFAMILIAR PEOPLE AND UNFAMILIAR DOGS

BASICS

OVERVIEW
A variety of different motivations exist, including fear, territoriality, conflict and possessiveness. Aggression is directed toward a person or dog that does not live in the household. Regular visitors may also be targets. May be within the range of normal behavior, but may be compounded by fearfulness.

SYSTEMS AFFECTED
• Behavioral. • Sympathetic stimulation (e.g., tachypnea, tachycardia).

INCIDENCE/PREVALENCE
Stranger-directed aggression represents 32.5% of canine behavioral referral caseload.

SIGNALMENT
• Can occur at any age. Signs may begin to emerge as primary socialization wanes (approximately 12–16 weeks of age) or may arise or intensify at social maturity (approximately 18–36 months). Genetic concerns and poor prognosis if signs arise before 12 weeks. • Territorial aggression more common in intact males—initial signs usually present by 1 year. • Aggression toward unfamiliar people and dogs overrepresented in males. • Breed predilection for inter-dog aggression in "fighting breeds" (e.g., pit bull terriers) and terriers.

SIGNS
• Aggression (barking, growling, lip-lifting, snarling, snapping, lunging, biting) toward unfamiliar people and dogs. May be accompanied by fearful or submissive body postures/facial expressions (head down, crouching, backing away, ears back, tail tucked, looking away, lip licking) or confident body postures (standing straight up, approach with tail up, ears forward). • Territorial aggression arises in familiar locations or spaces (e.g., home, yard, car). • May be confident, fearful or conflict. • Fear aggression more likely when dog is cornered or cannot escape. • May be more frequent or severe on- than off-leash.

CAUSES & RISK FACTORS
• May be a normal canine behavior.
• Strongly influenced by previous experience (e.g., early socialization, painful conditions, rough handling, inappropriate punishment, previous fear-evoking experience with unfamiliar people or dogs). • Underlying medical conditions, especially pain.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Fear aggression • Territorial aggression
• Possessive aggression • Conflict aggression
• Generalized anxiety disorder

CBC/BIOCHEMISTRY/URINALYSIS
Usually unremarkable. Abnormalities suggest an underlying medical condition.

OTHER LABORATORY TESTS
Usually unremarkable

IMAGING
MRI if CNS disease suspected. Other imaging as needed to rule out underlying medical conditions.

TREATMENT

CLIENT EDUCATION
Treatment is aimed at controlling the problem, not at achieving a "cure." Successful treatment, resulting in a decrease in aggressive incidents, depends on owner understanding of basic canine social behavior, risks involved, how to follow safety and management recommendations, correct identification of the aggression-eliciting stimuli, and effective implantation of reward-based behavior modification.

Safety Recommendations
• Owners' main responsibility is safety by avoiding situations that may evoke a fearful or aggressive reaction. Avoidance is also necessary to insure the pet's welfare and prevent further learning of aggressive behaviors. • Owners should be advised that dog owners may be liable for bites and could face civil/criminal prosecutions should a person be injured. • Successful treatment is more likely if a period of preventing exposure to aggression-provoking stimuli is instituted prior to behavior modification. • Confine dog away from potential victims, avoid walks or parks where stimulus exposure might occur, or have dog under direct physical control of a responsible adult whenever an aggression-provoking situation could arise (e.g., public location, when visitors are at the house).
• Confine territorial dogs to where they cannot see/hear visitors approaching territory before they become aggressively aroused.
• Introduce a head halter (e.g., Gentle Leader) and basket muzzle for easier and safer control.
• Owners should be advised that punishment/dominance-based training can lead to increased aggression, fear, agitation, and/or injuries and should be avoided. If safety cannot be insured, dogs should be removed from the household.

Behavior Therapy
• Structured interactions (also known as learn to earn or say please by sitting) where the dog is consistently taught to sit for anything it values (before feeding, petting, play, going for a walk) gives the dog control of its resources by sitting calmly, provides structure and predictability in all interactions, teaches impulse control and trains the dog that good things happen by sitting calmly.
• Commands: teach the dog to focus on the owner for guidance using eye contact and hand target (e.g., dog touch nose to owner's hand). • Teach the dog to sit and relax on verbal cue in neutral situations using food rewards; teach to go to mat, bed or crate to settle; teach to walk on loose leash. Train with head halter or muzzle if needed to insure safety. Private session with a force-free trainer should be considered to achieve basics before any exposure.

Behavior Modification: Systematic Desensitization and Counter-conditioning (DS/CC)
• When owner can effectively control and calm in the absence of stimuli, begin exposure by determining the limit (distance, location, person, dog) at which the dog will orient but not yet react. Have the dog focus on the owner or continue walking calmly (heel) and give favored (highest value) rewards to make positive associations with each stimulus exposure. • Gradually (baby steps) increase stimulus intensity, staying below the threshold that would result in fear and/or aggression by decreasing distance, increasing distractions, or moving to more challenging environments.
• Progress is slow (typically months). Carefully monitor body language to avoid setbacks. • If the dog is not calm, shows aggression or precursors to aggression (e.g., fixating on the stimulus) reduce the level of stimulation by moving farther away or taking the dog out of the situation. Future sessions should be at greater distances, or in locations or with stimuli where success can be achieved. For example, if the dog is calm when unfamiliar people pass on a walk, but when strangers pass the house the dog barks, revert to practicing DS/CC with the dog on walks and work up more slowly to practicing around the house. • Owners must always be vigilant for the approach of stimuli that might incite fear or aggression.

SURGICAL CONSIDERATIONS
• Castration reduced aggression by at least 50% toward unfamiliar dogs in < 20% of

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AGGRESSION TO UNFAMILIAR PEOPLE AND UNFAMILIAR DOGS (CONTINUED)

dogs studied and toward human territorial intruders in < 10% of dogs studied. Castration reduced inter-male aggression in 62% of dogs. • Military working German shepherds spayed at 5–10 months of age were more reactive 4–5 months post-surgery to approach by an unfamiliar person walking with an unfamiliar dog than intact dogs.

MEDICATIONS

SUPPLEMENTS

• Consider for mild fear or as an adjunct to drug therapy.
• Supplements are not a substitute for and should only be used to facilitate behavior modification.

L-theanine (Anxitane®)

• 2.5–5 mg/kg q12h.
• Active ingredient in green tea purported to increase serotonin, dopamine and GABA.
• Side effects: none reported.

Alpha-casozepine (Zylkene®)

• 15 mg/kg PO q24h (canine). Discontinue if no effect after 10 days.
• Purported to increase GABA.
• Side effects: none reported.
• Alpha-casozepine also in Royal Canin Calm Canine.

DRUG(S)

• There are no medications licensed for treatment of canine aggression. Owners must be aware that the use of medications is off-label. Note in the patient's record that owners were informed of potential risks and side effects. A signed informed consent form is advisable. NEVER use medications without concurrent behavior modification. Before prescribing medication, be sure that owners understand the risks and liability in owning an aggressive dog, will follow safety procedures, and do not expect medications to insure safety. In fact, medication may not be appropriate in all situations (e.g., households with small children, or individuals that have disabilities).
• There is a strong placebo effect when using drugs for behavior therapy in dogs. Studies have not shown a robust effect of drug treatment on aggression.

Selective Serotonin Reuptake Inhibitors

• Fluoxetine 0.5–2 mg/kg PO q24h.
• Paroxetine 0.5–1 mg/kg PO q24h.
• Sertraline 1–3 mg/kg PO q24h.
• Side effects: sedation, irritability, GIT effects, increased aggression; anorexia is common and usually transient.

Tricyclic Antidepressants

• Clomipramine 1–3 mg/kg q12h (label-restricted for aggression).
• Side effects: sedation, GIT effects, anticholinergic effects, cardiac conduction disturbances if predisposed, and increased aggression.

Alpha-2 agonists

• Clonidine 0.01–0.05 mg/kg PO PRN 1.5–2 hours before eliciting trigger, up to q12h.
• Side effects: transient hyperglycemia, hypotension, collapse, and bradycardia (responsive to atropine), and increased aggression.

Serotonin 2α antagonist/reuptake inhibitors

• Trazodone 2–5 mg/kg PRN prior to eliciting trigger up to q8h. Titrate to 8–10 mg/kg if no adverse effects.
• Side effects: sedation, anorexia, ataxia, GIT effects, cardiac conduction disturbances, and increased aggression.

PRECAUTIONS

• Use caution as any psychotropic medication may disinhibit, resulting in an increase rather than decrease in aggression. • Do not combine SSRIs, SARIs, TCAs, MAO inhibitors (e.g., amitraz, selegiline), opiods (e.g., tramadol) or other medications that increase serotonin—can result in potentially fatal serotonin syndrome.

FOLLOW-UP

PATIENT MONITORING

• Clients need ongoing assistance and should receive at least one follow-up call within the first 1–4 weeks after consultation. Provisions for further follow-up should be made. Ongoing communication improves client compliance.

PREVENTION/AVOIDANCE

• Treatment recommendations are life-long—aggression may recur with treatment lapses and continued exposure to fear- and aggression-producing stimuli. Owners must always be vigilant and in control of the dog's behavior. • Appropriate early socialization and habituation may help prevent fear-based behaviors later in life. Puppies that are not socialized during the first three months of life are more likely to be fearful, defensive, and possibly aggressive later in life. Socialization may include attending well-structured, positive reinforcement puppy classes starting during the sensitive period for socialization from 7–12 weeks (perhaps up to 14–16 weeks). One study found that vaccinated puppies that attended puppy socialization classes were at no increased risk of parvovirus.

POSSIBLE COMPLICATIONS

Human injuries; euthanasia or relinquishment of patient

EXPECTED COURSE AND PROGNOSIS

There is no cure. Prognosis is more favorable if aggression is motivated by fear, at a low intensity, and occurs only in a few predictable situations. Prognosis is highly dependent on owner compliance.

MISCELLANEOUS

ASSOCIATED CONDITIONS

Other fear- or anxiety-based conditions (e.g., noise phobias, separation anxiety) Aggression to other stimuli

ZOONOTIC POTENTIAL

Human injury from bite wounds

PREGNANCY/FERTILITY/BREEDING

Do not breed dogs with extremely fearful behavior or fear/aggression.

SEE ALSO

• Aggression toward Familiar People—Dogs • Aggression, Food and Resource Guarding—Dogs • Aggression—Between Dogs in the Household • Fear and Aggression in Veterinary Visits

ABBREVIATIONS

• CNS = central nervous system • DS/CC = desensitization and counter-conditioning • GABA = gamma-aminobutyric acid • GIT = gastrointestinal tract • MAO = monoamine oxidase • MRI = magnetic resonance imaging • SSRI = selective serotonin reuptake inhibitor • SARI = Serotonin 2a antagonist/reuptake inhibitor • TCA = tricyclic antidepressant

Suggested Reading

Herron ME, Shofer SS, Reisner IR. Survey of the use and outcome of confrontational and non-confrontational training methods in client-owned dogs showing undesired behaviors. Appl Anim Behav Sci 2009, 177:47–54.

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AGGRESSION TOWARD CHILDREN—DOGS

BASICS

OVERVIEW
Children are the most frequent victims of reported dog bites and tend to be injured more severely than adults.

SIGNALMENT
Any breed, age, gender, and neuter status.

Breed
• Breed reports vary with demographics. Breed identification may be unreliable. • Breeds most commonly presenting to a behavior referral service that had bitten a child include English springer spaniel, German shepherd, Labrador retriever, golden retriever, and American cocker spaniel. • Most fatal attacks (uncommon) are attributed to rottweilers, pit bulls, and their mixes. • Larger breeds and mixed breeds may be more likely to inflict severe injury. • Smaller breeds can also be dangerous.

Sex
• More frequent in males than females. • Neutering will not significantly reduce the risk.

Age
• Any age, but more frequent in socially mature dogs (2+ years old). • Risk may increase in geriatric dogs because of pain, sensory impairment, or irritability.

CAUSES & RISK FACTORS

Clinical Categories/Motivation for Aggression
• Fear-related • Pain-related • Play-related • Conflict-related • Predatory • Territorial • Resource (food/toy/bed) guarding

Dog-Associated Risk Factors
• Disease and associated irritability. • Pain-related aggression and resource guarding are the most common reasons for bites to familiar children < 6 years old. Generalized anxiety. • Fearful behavior. • Dog lying down, particularly under or on furniture. • Parent/littermate aggression.

Environmental/Social Risk Factors
• Younger children most likely bitten by the family pet or other familiar dogs. • Presence of infants (risk of predatory attacks). • Presence of young children. • Presence of food, edible toys. • Punishment-based training. • Inadequate supervision by parents/caregivers. • History of growling, snapping, biting. • Hugging, kissing, bending over anxious, fearful, or conflict-aggressive dog.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
See "Clinical Categories/Motivations for Aggression"

CBC/BIOCHEMISTRY/URINALYSIS
Baseline profile to rule out medical contributing factors.

OTHER LABORATORY TESTS
• Anecdotal evidence (only) correlates canine hypothyroidism with increased aggression; however, no data-based evidence. • Unnecessary supplementation with thyroid hormone may predispose to agitation or aggression.

DIAGNOSTIC PROCEDURES
Thorough physical examination. A detailed history of the bite event and the behavior of both dog and child to determine motivation.

TREATMENT

SAFETY WITH FAMILIAR DOGS
• Never leave infants or young children unsupervised with dogs. Securely separate infants from dogs when alone, if both asleep. • If one adult is present, separate dog from young children. • If more than one adult is present, assign responsibility for one adult to dog, and one to child. • Do not allow child to approach or interact with dog when dog is lying down. • Do not allow child to remove any object from dog. • Do not allow child to hug, kiss, bend over, or lie down beside dog. • Separate dog when eating or chewing valued items.

SAFETY WITH UNFAMILIAR DOGS
• Do not tether unsupervised. • Do not allow young children to interact with unfamiliar dogs. • Securely lock gates in yards. • Avoid underground electric fences, which do not prevent entry of children into yard.

BEHAVIOR MODIFICATION THROUGH LEARNING/TRAINING
• Redirect dog's attention: teach "look" or "touch" cues. • Establish secure, separate "safe haven" for dog. • Restrict fearful or reactive dog on lead and offer food at safe distance from children, to turn a negative situation into a positive one. • Do not rely on training alone; safe practices require prevention.

MEDICATIONS

DRUGS
Anxiolytic drug may be indicated for dogs with generalized or situational anxiety or fearful behavior.

Selective Serotonin Reuptake Inhibitors
• Fluoxetine 0.5–2.0 mg/kg q24 h
• Sertraline 0.5–3 mg/kg q24 h

Tricyclic Antidepressants
Clomipramine 1–3 mg/kg q12 h

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
• Psychotropic medication can increase agitation and anxiety or disinhibit aggression. Use with safety recommendations to prevent bites. • Avoid the following combinations:
◦ SSRI + TCA ◦ SSRI or TCA + tramadol
◦ SSRI or TCA + MAOI including amitraz
◦ SSRI + NSAID (caution, due to increased risk of GI or other hemorrhage).

FOLLOW-UP

PREVENTION/AVOIDANCE
• Do not rely on training alone to eliminate aggression. • Preventive measures are most important in management of canine aggression to children. • Even well-trained, socialized dogs may bite.

POSSIBLE COMPLICATIONS
• Family may not acknowledge risks. • Disease may aggravate aggression. • Family may not be compliant. • Psychotropic drug may be unrealistically relied upon or ineffective. • Young children may be impulsive and difficult to control.

EXPECTED COURSE AND PROGNOSIS
• Aggressive behavior can often be reduced and controlled. However, lifetime compliance is needed. • Prognosis is poor if social/physical environment cannot be controlled. • In some cases it may be necessary to rehome or euthanize dog, while in others the dog's behavior may improve as the child grows older.

MISCELLANEOUS

ABBREVIATIONS
• GI = gastrointestinal • MAOI = monoamine oxidase inhibitor • NSAID = nonsteroidal anti-inflammatory drug • SSRI = selective serotonin reuptake inhibitor • TCA = tricyclic antidepressant

Suggested Reading
Herron ME, Shofer FS, Reisner IR. Survey of the use and outcome of confrontational and non-confrontational training methods in client-owned dogs showing undesired behaviors. Appl Anim Behav Sci 2009, 117:47–54.
Reisner IR, Shofer FS, Nance ML. Behavioral assessment of child-directed canine aggression. Inj Prev 2007, 13:348–351.

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AGGRESSION TOWARD FAMILIAR PEOPLE—DOGS

BASICS

DEFINITION
Aggression, directed toward household members or people with an established relationship with the dog, often in situations involving access to resources. May be status-related/dominance, conflict, impulsive, competitive or possessive aggression.

PATHOPHYSIOLOGY
These dogs may show anxiety or be impulsive and unpredictable. When the aggression is guarding of resources, or in response to fear eliciting stimuli (e.g., threats, punishment, possibly handling) might be normal.

SYSTEMS AFFECTED
Behavioral

GENETICS
Pedigree analyses have shown increased occurrence in related dogs. May be genetic factors associated with impulse dyscontrol in English springer spaniel and English cocker spaniel. May be more common in show than field lines.

INCIDENCE/PREVALENCE
20–44% of behavioral referral caseloads.

GEOGRAPHIC DISTRIBUTION
Regional breed differences exist.

SIGNALMENT
Species
Dog

Breed Predilections
Spaniel (English springer and cocker), terrier, but may be exhibited by any breed.

Mean Age and Range
Usually manifested by social maturity (12–36 months of age). May be seen in younger dogs.

Predominant Sex
Males (castrated and intact).

SIGNS
General Comments
Detailed history-taking is needed to make a diagnosis, assess risks, and devise a safe and realistic treatment plan. Mild signs of aggression (e.g. staring, growling, baring teeth) often precede bites. Details of early aggressive episodes are vital to establish the diagnosis and prognosis. Often anxiety or fear based but may be motivated by desire to control, e.g., personal space, resources.

Historical Findings
• Aggression (barking, growling, lip-lifting, snarling, snapping, lunging, biting) directed toward family members. Aggression may occur around resources such as resting areas, food, or toys, handling (e.g., petting and reaching toward), or favored possessions (including resting with one family member when another approaches). Aggression may be seen in other contexts, e.g., denied access to items or activities, when resting, when confronted or punished, or during uncomfortable or fear-evoking interactions (e.g., ear cleaning, grooming, bathing). History-taking should attempt to establish triggers and frequency/severity of aggressive episodes. • Aggression may not be directed uniformly toward each household member. • Confident/dominant body postures (stiffening, staring, standing straight up, ears forward, tail up, and/or approaching/direct contact with the person) may be associated with aggressive behavior, or the motivation may be fear (tensing, head down, crouching, backing away, ears back, tail tucked, looking away, lip licking). Owners may report a combination of confident and submissive postures representing uncertainty (conflict). • Owners may describe dog as "moody" and may be able to predict when aggression is likely to occur. Early on the dog may show fear (e.g., eye aversion, tail tucked, avoidance) that may diminish and the dog may give less warning as it becomes more confident that aggression will be effective (negative reinforcement). • Anxiety may be noted in pet-owner interactions and other situations.

Physical Examination Findings
• Usually unremarkable. • Medical conditions, especially pain, may contribute to the expression of aggression.

CAUSES
• May be part of normal canine social behavioral repertoire, but its expression is influenced by environment, learning, and genetics. • Display of aggression may be influenced by underlying medical conditions (especially pain), early experiences (learning that aggression is effective to control situations), and inconsistent or lack of clear rules and routines in the household and in human-pet interactions.

RISK FACTORS
Inconsistent or inappropriate physical punishment and inconsistent owner interactions.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Fear-based aggression • Conflict aggression • Anxiety conditions • Disease conditions associated with aggression (e.g., painful conditions, endocrinopathies)

CBC/BIOCHEMISTRY/URINALYSIS
Usually unremarkable. Abnormalities may indicate an underlying or contributing medical condition.

OTHER LABORATORY TESTS
As indicated to rule out underlying diseases. Rule out hypothyroidism.

IMAGING
MRI if CNS disease is suspected; other imaging may be needed to rule out other medical conditions.

TREATMENT

ACTIVITY
Insure behavioral needs are being met.

DIET
Low-protein/tryptophan-supplemented diets may help reduce aggression.

CLIENT EDUCATION
General Comments
• Treatment is aimed at controlling the problem, not achieving a "cure." • Successful treatment, resulting in a decrease in aggressive incidents, depends on owner understanding of basic canine social behavior and communication, risks involved in living with an aggressive dog, and how to implement safety and management recommendations. • Owners must be aware that the only certain way to prevent future injuries is euthanasia. • Owners must be educated about the risks of using physical punishment and training techniques that rely on "dominating" their dogs. Improper and inappropriate use of physical punishment/dominance techniques such as alpha rolls, corrections with choke chains or prong collars, or even yelling "no" can lead to human injury, increased aggression and anxiety, and disruption of the human-animal bond.

Safety Recommendations
• If owners elect not to euthanize, they must be aware that their main responsibility is preventing human injury by diligently avoiding all situations that might evoke an aggressive response including situations that incite fear even if not aggression. • Treatment must begin with prevention of exposure to all aggression-provoking stimuli prior to any behavior modification. • Use patient history to identify each situation or trigger for owners to avoid. This may include not allowing on furniture or beds where aggression might arise, not giving valuable treats or toys (e.g., rawhides) except when confined away from family members, and limiting physical contact with the dog including petting in any place or situation where the dog might resist or bite. Instead provide the dog with opportunities (control) to avoid undesirable interactions (e.g., safe haven, crate). Reward the dog for entering the safe haven and for leaving (coming out). • Do not physically punish or reprimand the dog. • Introducing a head halter (e.g., Gentle Leader) with a lightweight 8- to 10-foot leash attached or a basket muzzle whenever in contact with people or in any situation where problems might arise, makes controlling potentially dangerous situations

(CONTINUED) AGGRESSION TOWARD FAMILIAR PEOPLE—DOGS

easier and safer. • Use the long leash to safely remove the dog from situations that may elicit aggression; do not reach for the dog directly.

Behavioral Therapy

• Behavior modification—use non-confrontational methods and reward-based training to achieve desirable outcomes and teach the dog behaviors without experiencing fear or becoming aggressive. • Structured interactions (also known as learn to earn or say please by sitting) where the dog is consistently taught to sit for anything it values (before feeding, petting, play, going for a walk) gives the dog control of its resources by sitting calmly, provides structure and predictability in all interactions, teaches impulse control and trains the dog that good things happen by sitting calmly. Owners must ignore the dog until it sits or train "sit", whenever soliciting attention. • Use positive reinforcement (e.g., food, toys, play, petting) for response substitution (or counter commanding) to teach behaviors that are incompatible with those that have resulted in aggression.

Desensitization and Counter-Conditioning

• Decreasing reactivity to situations that have resulted in aggression by making positive associations with each interaction. Do not begin until owner can insure success with reward-based training and sit for all interactions. • Teach the dog strategies to relax (sit, down, go to your bed) on verbal cue in neutral situations using food rewards. • Expose the dog to a sufficiently reduced stimulus where no fearful or aggressive reaction is elicited (e.g., owner passing by resting dog at sufficient distance). • Reward calm, non-fearful/aggressive behavior (e.g., verbal praise, tossing favored treats). • Gradually increase the level of stimulation, staying below the threshold that would result in fear and/or aggression. • Progress is slow (typically months) and careful monitoring is essential to understand and respect the dog's limits. • Train on cue those behaviors needed to manage specific problems, e.g., go to your bed (for dogs that are protective of resting areas) or "drop it" (for resource guarding).

SURGICAL CONSIDERATIONS

• Castration reduced aggression by at least 50% toward family members in approximately 30% of dogs studied. • Females that start to show dominance aggression at less than 6 months of age may be less aggressive if spaying delayed until mature.

MEDICATIONS

DRUG(S)

• There are no medications licensed for treatment of canine aggression. Owners must be aware that the use of medications is off-label. Note in the patient's record that owners were informed of potential risks and side effects. A signed informed consent form is advisable. NEVER use medications without concurrent behavior modification. Before prescribing medication, be sure that owners understand the risks and liability in owning an aggressive dog, will follow safety procedures, and do not expect medications to insure safety. In fact, medication may not be appropriate in all situations (e.g., households with small children or individuals with disabilities). • There is a strong placebo effect when using drugs for behavior therapy in dogs. Studies have not shown a robust effect of drug treatment on aggression.

Selective Serotonin Reuptake Inhibitors

• Fluoxetine 0.5–2 mg/kg PO q24 h. • Paroxetine 0.5–2 mg/kg PO q24 h. • Sertraline 1–3 mg/kg PO q24 h. • Side effects: sedation, irritability, GIT effects, increased aggression; anorexia is common and usually transient.

Tricyclic Antidepressants

• Clomipramine 1–3 mg/kg q12 h in dogs (label restriction for aggression) • Side effects: sedation, GIT effects, anticholinergic effects, cardiac conduction disturbances if predisposed, and increased aggression.

CONTRAINDICATIONS

Use caution as any psychotropic medication may reduce fear-based inhibition resulting in an increase rather than decrease in aggression.

PRECAUTIONS

Any psychotropic medication may increase rather than decrease aggression. Corticosteroids are contraindicated in food-aggressive dogs; polyphagia can lead to increased frequency/intensity of aggression.

POSSIBLE INTERACTIONS

Do not combine SSRIs, TCAs, MAO inhibitors (e.g., amitraz, selegiline), opioids (e.g., tramadol), and other medications that increase serotonin—can result in potentially fatal serotonin syndrome.

FOLLOW-UP

PATIENT MONITORING

Clients need ongoing assistance and should receive first follow-up call within the first 1–4 weeks after consultation. Provisions for further follow-up (by phone or in person) should then be made.

PREVENTION/AVOIDANCE

Treatment, including safety recommendations, are life-long—aggression may recur if preventive strategies not maintained.

POSSIBLE COMPLICATIONS

Human injuries; euthanasia or relinquishment of patient.

EXPECTED COURSE AND PROGNOSIS

There is no cure. Prognosis is more favorable if aggression is at a low intensity and occurs in relatively few predictable situations. Prognosis is highly dependent on owner compliance.

MISCELLANEOUS

ASSOCIATED CONDITIONS

Other forms of aggression, including interdog aggression, resource guarding, and aggression to unfamiliar people or dogs. Aggressive dogs often have underlying anxiety.

ZOONOTIC POTENTIAL

Human injury.

PREGNANCY/FERTILITY/BREEDING

Do not breed aggressive dogs.

SYNONYMS

• Competitive aggression • Conflict aggression • Dominance-related aggression • Rage syndrome • Status-related aggression

ABBREVIATIONS

• CNS = central nervous system • GIT = gastrointestinal tract • MAO = monoamine oxidase • MRI = magnetic resonance imaging • SSRI = selective serotonin reuptake inhibitor • TCA = tricyclic antidepressant

SEE ALSO

• Aggression Toward Unfamiliar People and Unfamiliar Dogs—Dogs • Aggression, Food and Resource Guarding—Dogs • Aggression—Between Dogs in the Household

Suggested Reading

Herron ME, Shofer SS, Reisner IR. Survey of the use and outcome of confrontational and non-confrontational training methods in client-owned dogs showing undesired behaviors. Appl Anim Behav Sci 2009, 177:47–54.

Sueda KL, Malamed R. Aggression toward people—a guide for practitioners. Vet Clin N Am 2014, 14:599–628.

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Consulting Editor Gary M. Landsberg

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Client Education Handout available online

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AGGRESSION TOWARD HUMANS—CATS

BASICS

DEFINITION
Human-directed aggression in cats

PATHOPHYSIOLGY
The more common causes for human-directed aggression in cats include play, fear/pain-related, redirected, maternal, and petting intolerance. Context is going to contribute greatly when making the correct diagnosis. For example, play aggression is likely to be seen in a young, solitary cat, while pain-related/fear aggression is a common behavior seen in the clinic setting.

SYSTEMS AFFECTED
• Behavioral
• Gastrointestinal—decreased appetite if fear and/or pain-related
• Hemic/Lymphatic/Immune—chronic stress effects on immune function
• Ophthalmic—dilated pupils in response to autonomic nervous system stimulation
• Skin/Exocrine—may show displacement behaviors such as overgrooming

GENETICS
There is no known genetic basis for human-directed aggression in cats.

INCIDENCE/PREVALENCE
Aggression is second only to inappropriate elimination for feline cases seen by veterinary behavior specialists.

GEOGRAPHIC DISTRIBUTION
None

SIGNALMENT
Cats of any age, gender/ neuter status, breed can be affected. Play-motivated aggression more likely in juvenile, solitary cat.

SIGNS
• Play-motivated: cat approaches its "victim," crouches in wait, stalks and chases; tail is twitching and ears are forward. Typically will attack moving target.
• Fear/Pain-related: ears back, body and tail lowered, piloerection, pupils dilated; may hiss and growl. Avoidance of person(s) who elicit the aggression. Attacks possible if approached and/or cornered. Extreme cases: expression of anal glands, urination, and/or defecation. Hiding behavior.
• Redirected: cat is highly aroused by stimulus and seeks out less appropriate target. Aggression can be very severe given the cat's level of arousal.
• Maternal: usually predictable and self-limiting. Queen will act to protect her kittens.
• Petting intolerance: cat signals its "displeasure" by twitching its tail and skin when being petted in an undesired location and/or for too long. Ears are usually back; mydriasis; may hiss and growl before turning to bite person.

CAUSES & RISK FACTORS
• Play-motivated: lacking in opportunities for normal play—no other cats, insufficient and/or inappropriate toys; history of owner using hands/feet to play with kitten and/or playing roughly with the kitten.
• Fear: poor socialization with humans and/or feral living, an aversive event associated with a person, or people in general.
• Pain-related: obvious medical/physical condition.
• Redirected: occurs during interference in, or interruption of, situations that have caused the cat to become aggressively aroused—such as a cat fight (between familiar household cats), the presence of a cat outside or noise.
• Maternal: recent birth of litter.
• Petting intolerance: exact etiology unknown. Cats tend to groom each other on head/neck so human grooming of cat in other locations may contribute to aggressive reaction.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
See causes above

CBC/BIOCHEMISTRY/URINALYSIS
Rule out contributing medical conditions based on presentation.

OTHER LABORATORY TESTS
• Senior cats: a complete thyroid panel.
• Urinalysis if inappropriate elimination and/or urine marking is presented as part of the aggression.

IMAGING
Based on clinical examination and/or suspected pain component

DIAGNOSTIC PROCEDURES
Thorough behavioral history including a description of the cat's postures during aggression and injuries inflicted, context, presence of outside cats, early historical information, litter box use, food consumption, and hiding behaviors.

PATHOLOGIC FINDINGS
N/A

TREATMENT

APPROPRIATE HEALTH CARE
Applicable only if health/medical issue diagnosed.

NURSING CARE
Applicable only if health/medical issue diagnosed.

ACTIVITY
• Play-motivated: cat should be provided with increased opportunity for appropriate play—either in the form of toys, human interaction, or additional housemate.
• Redirected: cat should be denied access to windows where outside cats can be seen.

DIET
• Hill's Science Diet c/d Multicare Feline Urinary Stress
• Royal Canin Feline Calm
• Either may be beneficial in helping to decrease anxiety.

CLIENT EDUCATION
• Play-motivated: normal play behavior and the importance for opportunities for appropriate play.
• Fear: avoidance of fear-inducing situations—ongoing exposure may worsen signs, cause severe stress, and compromise animal welfare.
• Redirected: importance in addressing primary stimuli—such as outside cats.
• Maternal: normal maternal and kitten-protective behavior—same as for fear-motivated aggression.
• Petting intolerance: normal feline grooming patterns; observation of cat's warnings so that behavior does not escalate.

Behavior Modification Exercises

Desensitization and Counter-Conditioning (DS & CC)
• Desensitization: exposing cat to the fear-inducing stimulus (scary person) at a low level so the cat does NOT react fearfully or aggressively. Over time, the intensity of the stimulus is increased (i.e., the distance between the cat and stimulus is decreased) without causing fearful responses.
• Counter-conditioning: rewarding the cat with a special treat, toy, grooming, petting, for relaxation.

Classical Conditioning (CC)
Classical conditioning: pairing the stimulus (person threatening to the cat) with a tasty treat, toy, petting. Example: scary person = tuna fish.

MEDICATIONS

The short-term use of medication may be necessary to decrease overall levels of anxiety and reactivity in more severe cases.

DRUG(S) OF CHOICE

Azapirones
Buspirone 0.5–1.0 mg/kg PO q12h. Most useful for fearful and withdrawn cats. Decreases anxiety and may increase "self-confidence." Anecdotal reports of "increase in affection"; therefore might be useful in severe cases of petting intolerance. Response noted in 1–2 weeks.

(CONTINUED)

AGGRESSION TOWARD HUMANS—CATS

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Selective Serotonin Reuptake Inhibitors (SSRIs)
• Fluoxetine, paroxetine, sertraline 0.5–1.5 mg/kg PO q24h.
• SSRIs must be given daily. May take 4–8 weeks to reach peak effects.

Tricyclic Antidepressants (TCAs)
• Amitriptyline 0.5–2.0 mg/kg PO q12–24h.
• Clomipramine 0.25–1.3 mg/kg PO q24h.
• TCAs must be given daily. May take 4–8 weeks to reach peak effects.

Benzodiazepines
• Alprazolam 0.125–0.25 mg/cat PO q8–24h.
• Diazepam 0.1–1.0 mg/kg PO q12–24h (rarely used due to potential hepatopathies).
• Can be given "as needed" for specific encounters with people inducing the fear response and during desensitization, counter-conditioning and classical conditioning sessions.
• Can be used in conjunction with azapirones, SSRIs, and TCAs.

CONTRAINDICATIONS/ PRECAUTIONS/POSSIBLE INTERACTIONS

• None of the drugs listed are approved for use in cats.
• All of the medications are to be administered orally, as they have not been shown to be effective through transdermal dosing.
• Azapirones: side effects are uncommon but occasional excitement is noted. Should not be given in combination with an MAOI. Avoid use in the aggressor cat; may increase any "bully" behavior.
• Neither SSRIs nor TCAs should be given with each other, nor in combination with MAOIs.
• SSRIs: side effects include mild sedation and decreased appetite, constipation, and urinary retention. Competitive inhibition of cytochrome P450 liver enzymes; when administered concurrently with medication utilizing the P450 enzymes, elevated plasma levels of the medications may increase, causing toxic levels.
• TCAs: side effects include sedation, constipation, diarrhea, urinary retention, appetite changes, ataxia, decreased tear production, mydriasis, cardiac arrhythmias, tachycardia, and changes in blood pressure.
• Benzodiazepines: side effects include sedation, ataxia, muscle relaxation, increased appetite, paradoxical excitation, and increased friendliness. Idiopathic hepatic necrosis has been reported in cats.
• Specific recommendations for the use of diazepam: baseline physical exam, CBC, and blood chemistries to confirm good health. Repeat the blood chemistries at 3–5 days. Elevated ALT or AST, discontinue the medication.

ALTERNATIVE DRUGS

Pheromones
• Used alone or concurrently with drugs
• Feliway—available in diffuser, spray and wipes—facial pheromone
• NurtureCALM 24/7 collar—maternal pheromone

Supplements
• Used alone or concurrently with drugs
• Anxitane—contains L-theanine, a calming compound found in green tea
• Zylkene—contains alpha-casozepine, a GABA agonist

FOLLOW-UP

PATIENT MONITORING

Weekly follow-up is recommended in the early stages of treatment, especially when on medication(s). Monthly follow-up once stable. For cats on medication, follow-up blood testing recommended every 6–12 months.

PREVENTION/AVOIDANCE

• Play-motivated: provide opportunities for appropriate play.
• Fear: avoidance of the fear-inciting stimuli if at all possible. Early socialization to people and events may help prevent some occurrences of fear-related responses to people.
• Pain: treat underlying condition(s).
• Redirected: address possible arousing stimuli—indoors and outdoors.
• Maternal: as for fear.
• Petting intolerance: limit amount of time petting the cat; desensitization and counter-conditioning to increase petting time.

POSSIBLE COMPLICATIONS

Potential human injury in all of the above cases, especially if the cat is approached or cornered and/or when highly aroused.

EXPECTED COURSE AND PROGNOSIS

Progress occurs slowly. Relearning is a process and each case is individual. If medications are indicated, begin at a low dose and work up as necessary. To discontinue medication, wait until the new behavior is stable (8–12 weeks) and wean off slowly, usually over weeks. If aggressive behavior recurs, return to the last dose that controlled the anxiety/reactivity and continue treatment.

MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

Play-motivated: typically seen in young, solitary cat in household.

ZOONOTIC POTENTIAL

People injured during an aggressive attack should seek prompt medical attention. Infection by *Bartonella henselae* can result from a cat scratch or bite.

PREGNANCY/FERTILITY/BREEDING

Avoid medications in breeding/nursing cats.

SYNONYMS

N/A

SEE ALSO

• Aggression Overview—Cats
• Fears, Phobias, and Anxieties—Cats

ABBREVIATIONS

• CC = classical conditioning
• DS & CC = desensitization and counter-conditioning
• MAOI = monoamine oxidase inhibitor
• SSRI = selective serotonin reuptake inhibitor
• TCA = tricyclic antidepressant

Suggested Reading

Horwitz DF, Neilson JC. Blackwell's Five-Minute Veterinary Consult Clinical Companion Canine & Feline Behavior. Ames, IA: Blackwell, 2007, pp. 109–178.
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AGGRESSION, FOOD AND RESOURCE GUARDING—DOGS

BASICS

OVERVIEW
• Aggressively guarding food (e.g., in food bowl, rawhides, bones, stolen/found items) or objects (e.g., toys, stolen objects).
• Usually within the range of normal behavior; genetics, learning or early experience may contribute to excessive expression of aggression.

SYSTEMS AFFECTED
Behavioral

SIGNALMENT
No breed or sex predilections.

SIGNS
Aggression (barking, growling, lip-lifting, snarling, snapping, lunging, biting) toward people or other animals in the presence of valued food items or objects.

CAUSES & RISK FACTORS
• May be part of normal canine behavior. Strongly influenced by previous experiences of successfully defending food, or objects through aggression and by resource availability/novelty.
• Underlying medical conditions and medications, especially those causing polyphagia, or calorie-restricted diets may increase level of food aggression.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Fear aggression
• Social status/dominance or conflict aggression

CBC/BIOCHEMISTRY/URINALYSIS
Usually unremarkable. Abnormalities suggest an underlying or contributing medical condition.

OTHER LABORATORY TESTS
Usually unremarkable.

IMAGING
MRI if CNS disease suspected. Other imaging as needed to rule out underlying medical conditions.

DIAGNOSTIC PROCEDURES
N/A

TREATMENT

CLIENT EDUCATION
• Treatment is aimed at control, not achieving a "cure." Successful treatment resulting in a decrease in aggressive incidents, depends on owner understanding of basic canine social behavior, risks involved in living with an aggressive dog, and ability to follow safety and management recommendations.
• If safety cannot be insured, pet should be removed from the home.

Safety Recommendations
• The owner's main focus must be on preventing injury by diligently avoiding situations that may evoke an aggressive reaction.
• Owners may be more compliant with avoidance recommendations if they understand both the risk and the potential liability if the dog causes injury.
• Successful treatment is more likely if a period of preventing exposure to aggression-provoking stimuli is instituted prior to behavior modification.
• Always confine the dog away from potential victims or the dog must be under the direct physical control of a responsible adult whenever an aggression-provoking situation could arise.
• Give food and any other objects that the dog might guard in a confinement/safe haven location away from people and other animals; prevent access to items that may evoke aggression.
• Teach the dog to be comfortable wearing a head halter (e.g., Gentle Leader) and basket muzzle for safer control of potentially dangerous situations.
• Punishment/dominance-based training techniques are contraindicated as they cause further fear, agitation, defensive aggression, and further learning (fear of approach and negative reinforcement if successful).

Behavior Modification
• Command-response-reward program (say please by sitting): to increase owners' control of resources, make the dog more responsive to the owner, and create structure and predictability in the dog's life.
• Use positive reinforcement (e.g., food, toys, play) to teach behaviors that are incompatible to those that lead to aggression including a calm sit and watch before giving any food, chews or toys, and "drop it" to release toys for valued rewards.
• Prevent access to items that might be stolen or guarded by supervising with leash if necessary, dog proofing or confinement training.
• "Booby trap" items by applying an aversive substance such as hot sauce.
• Systematic desensitization and counter-conditioning to specific aggression-provoking stimuli if safety and owner compliance can be insured.
• Find the threshold (distance, location) at which the dog shows no anxiety or aggression when in possession of food or chews and make positive associations by tossing small food treats each time the owner walks by—the goal is for the dog to associate the owner's presence with positive outcomes. If successful, training can very gradually proceed to closer proximities—level of improvement will be limited by safety and the dog's motivation to retain the resource.

MEDICATIONS

DRUG(S)
Medications are generally not indicated in the treatment of resource guarding.

FOLLOW-UP

PATIENT MONITORING
Clients usually need ongoing assistance with at least one follow-up call within the first 1–3 weeks after the consultation. Provisions for further follow-up should be determined at that time.

PREVENTION/AVOIDANCE
Management recommendations (avoiding triggers) are life-long..

POSSIBLE COMPLICATIONS
Human injuries; euthanasia or relinquishment of patient.

(CONTINUED) AGGRESSION, FOOD AND RESOURCE GUARDING—DOGS

EXPECTED COURSE AND PROGNOSIS

There is no cure. Prognosis for improvement is more favorable if aggression is at a low intensity, occurs in only a few predictable situations, and can be effectively and practically prevented.

MISCELLANEOUS

ASSOCIATED CONDITIONS

Fear and dominance/conflict aggression

ZOONOTIC POTENTIAL

Human injury and bite wounds

PREGNANCY/FERTILITY/BREEDING

Do not breed dogs with extreme aggression.

SEE ALSO

- Aggression Toward Unfamiliar People and Unfamiliar Dogs—Dogs
- Aggression Toward Familiar People—Dogs
- Aggression Between Dogs in the Household—Dogs

ABBREVIATIONS

- CNS = central nervous system
- MRI = magnetic resonance imaging

Suggested Reading

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AGGRESSION, INTERCAT AGGRESSION

BASICS

DEFINITION
Intercat aggression—offensive or defensive aggression between cats consisting of staring, displacing, vocalizing (growling, yowling, shrieking), spitting, hissing, swatting, lunging, chasing/stalking, and/or biting other cats.

PATHOPHYSIOLOGY
• May be normal behavior or abnormal. • May be caused by underlying medical disease (e.g., CNS) or the indirect result of concurrent medical disease lowering the threshold for irritable responses (e.g., pain, hyperthyroid). • May be multiple motivations including predatory/play, disputes over territory, sexual, fear, anxiety, and redirected.

SYSTEMS AFFECTED
• Behavioral. • Skin/Exocrine—secondary to traumatic injury. • Immune—chronic stress may alter the immune response. • Secondary infection (cat bite abscesses) are not uncommon. • Nervous.

GENETICS
No specific genetic basis, although some evidence to suggest that friendliness is mostly genetic and related to paternal effects.

INCIDENCE/PREVALENCE
Unknown

GEOGRAPHIC DISTRIBUTION
None

SIGNALMENT
Breed Predilections
None

Mean Age and Range
• Can occur at any age when due to changes in social environment (e.g., addition of a new cat, return of a cat from the veterinarian) or redirected. • Previously stable cat relationships can deteriorate as cats reach social maturity (2–4 years of age).

Predominant Sex
• Intact males more likely to initiate intercat aggression (related to territory, and/or proximity to females). • Females will defend their young from unfamiliar individuals. • Male kittens are more likely to initiate intercat aggression related to the predatory components of play.

SIGNS
Historical Findings
• May arise spontaneously and vary in frequency and intensity. • Owners most likely to seek behavioral intervention if there are physical injuries, the welfare of the aggressor and /or victim is compromised, or fighting becomes sufficiently distressing. • Human intervention in an attempt to interrupt fighting may result in human-directed aggression/injury.

Aggressor (usually offensive)
• Covert signs: staring, displacing other cats, stiff body language/movements while approaching the other cat. • Overt signs: Growling, yowling, spitting, hissing, swatting, lunging, chasing/stalking, and/or biting other cats, dilated pupils, may be accompanied by body language of fear (e.g., the classic Halloween cat stance—piloerection, back arched, tail up) or more offensive body language (stiff muscles, tail head elevated but rest of tail down, back straight or slightly slanted toward the head, ears forward or to the side), excessive facial marking, and perhaps urine marking.

Victim (usually defensive)
• Covert: avoidance of aggressor, hiding, change in grooming and eating habits, hypervigilance, dilated pupils. • Overt: hissing, swatting, running, vocalizing (including growling), Halloween cat stance, may escalate to defensive attack if cornered.

Elimination Outside of the Litter Box
• Aggressor may block access to the litter box area, forcing victims to choose alternative elimination locations; secondary substrate and/or location preferences and aversions can develop. • Both victims and aggressors may urine mark. • Extremely fearful cats may urinate or defecate in midst of aggressive events.

Physical Examination Findings
• None except injury from fights or if underlying medical issues. • Stress may affect eating and self-grooming (increased or decreased).

CAUSES
• Lack of appropriate socialization to other cats prior to 7 weeks of age. • May be a component of normal social behavior. • Social and environmental instability such as the addition of a new cat, loss of a resident cat, odor stimuli (return of a cat from the veterinarian or giving one cat a bath), aging or illness of one or both cats, cats reaching social maturity. • Household change, e.g., moving, changing furniture or resting areas. • Genetically unrelated cats and cats that have recently moved in together are more likely to show aggressive behaviors toward each other. • Resident cats commonly need prolonged exposure to new cats before accepting them into group. • Resource limitation (not enough vertical and/or horizontal space, lack of appropriate hiding areas, and limited food, water, and litter boxes, etc.) in multi-cat households. • Exposure to arousing stimuli (cats in the yard, visitors, noises, scents, etc.) can cause redirected aggression after which aggression might persist. • Medical problems including CNS disorders, hyperthyroidism, or any disorder that causes pain and/or increased irritability.

RISK FACTORS
• Singleton and/or bottle-raised kittens. • Lack of social exposure and experience with conspecifics during the socialization period (2–7 weeks) and beyond. • Male intact cats in multi-cat households. • Postpartum females with kittens in multi-cat households. • Separating and returning housemate (e.g., following veterinary visit, groomer). • Changes in social group such as the addition of a "new" cat to a home of resident cats. • Scratching and biting during the first introduction risks future intercat aggression. • Access to the outdoors and/or intrusion of unfamiliar cats onto the territory. • Crowding or lack of adequate social space and access to resources (food, water, litter boxes, and resting stations).

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Behavioral Differentials
• Fear-related aggression—cat may hiss, spit, arch the back, display piloerection and attempt to flee unless escape is thwarted; pupil dilation will accompany a fear response. • Status-related aggression—may occur with change or instability of social hierarchy and the control of access to resources; it is undecided if cats have dominance hierarchies or if conflict is better explained by territorial defense. • Territorial aggression—in response to threat to the territory; boundaries are often delineated by marking with urine, feces, or scent glands. • Redirected aggression—exposure to agitating stimuli (cats in the yard, visitors, noises, scents, etc.) with aggression directed toward a target other than the agitating stimuli. • Failure of recognition—aggression between feline housemates after returning from separation (e.g., veterinary visit, grooming); most likely due to change in odor and visual cues of victim. • Maternal aggression—aggression during the periparturient period; females guard kittens and nesting sites from unfamiliar individuals. • Intermale aggression—between males in response to territorial disputes, hierarchical status, or mates; aggression may be more pronounced at social maturity. • Sexual aggression—male typical behavior of chasing, pouncing, biting on the nape of the neck, and mounting with or without intromission. • Predatory/play-related aggression—predatory components of play directed toward another cat; the recipient is often an older cat that is not interested in playing.

Medical Differentials
• Any illness causing malaise, pain, or increased irritability • Endocrine, e.g., hyperthyroidism • Neurologic: space-occupying lesions, e.g., meningioma, lymphoma, encephalitis, seizures, feline

(CONTINUED) AGGRESSION, INTERCAT AGGRESSION A

ischemic encephalopathy, trauma, sensory or cognitive decline • Infectious: rabies, toxoplasmosis, aberrant parasitic migrations (e.g., cuterebriasis), FIV, FeLV • Iatrogenic: medications that increase irritability or disinhibit aggression (e.g., mirtazapine, benzodiazepines, buspirone) • Toxins: lead, illicit substances

CBC/BIOCHEMISTRY/URINALYSIS
Baseline CBC, biochemistry, urine to rule out medical causes and as a baseline if drug therapy indicated.

OTHER LABORATORY TESTS
• FeLV/FIV • Cats > 6 years should have total T_4 measured

IMAGING
As indicated based on history and physical signs

DIAGNOSTIC PROCEDURES
• Obtain a detailed behavioral and medical history of the patients. • Identify if there is a clear aggressor and/or victim and if aggression is overt or covert. • If multiple cats determine which cats spend time together, mutually groom each other, and which cats physically avoid each other. • Identify the preferred core areas of each cat for feeding, play, and resting and locations of any house soiling or marking. • Identify: the number, location, types of litter boxes and their management. • Media in the form of video, photographs, and/or drawn floor plans can provide spatial details and information regarding body language during social interactions. • Note any other changes in demeanor, routine, eating, and grooming.

PATHOLOGIC FINDINGS
None unless concurrent medical diseases

TREATMENT

APPROPRIATE HEALTH CARE
• Treat as outpatients with behavior and environmental modification (± medication) • Current on routine vaccinations, including rabies

NURSING CARE
Supportive care if any injuries from fighting.

ACTIVITY
May need to be restricted if confinement required to prevent the perpetuation of aggression and negative emotional responses. Provide sufficient alternate outlets for each cat during confinement area and during release.

DIET
None (except possible therapeutic diet trial discussed below)

CLIENT EDUCATION
For chronic, severe cases or for aggression that does not respond to treatment, may require permanent separation either by rehoming one of the cats or by splitting up the residence.

For Cases that have a Low Frequency of Intense, Injurious Aggressive Outbursts
• Separate the cats when they cannot be supervised (create "safe zones"). • Either keep them separate in the same areas each day in an effort to form separate core territories for each cat, or "time share" the space between cats. • Confine the newly introduced cat or the aggressor to the smaller, less familiar area. • For multiple cats, separate by stability of relationship between cats. Any despotic/bully cats should be confined alone. • Consider "artificial allomarking" to form a communal scent between the cats that are fighting; a towel (facecloth) may be rubbed (cephalocaudally) to obtain the scent of one cat and then rubbed onto the other cat and vice versa. • Towels should be left in the environment to allow for habituation to each other's scent especially if the cats are kept separated. • Reward cats with food, play, and/or attention for being in the same room together without having aggressive events. Cats should stay at a distance that allows for calm participation. • Engage cats in daily sessions of pleasurable activities (e.g., play, training, eating delectable food treats) at distances that do not incite aggression. Gradually move the fun sessions closer to each other, making sure to stay at a distance that does not trigger overt/covert aggression. • Teach the cats a "come and/or go to place" cue using positive reinforcement at times, in situations, and with sufficient rewards that the cats are most able to learn. • Interrupt or redirect the cats by cueing to come or go to its place, or by luring one or both cats to their safe zones with food and treats, wand toys, tossed toys, or laser pointers before aggression starts or as initial signs are seen (e.g., staring, tail twitching, pupil dilation). • Aversives and/or punishers can increase aggressive behavior and increase negative associations with other cats, so must be avoided or used cautiously. • The goal of management and safety is to prevent aggressive events. In an emergency, use of a laundry basket or blanket placed between or over the cats, can stop aggression, and direct the cat to its safe area until calm, but should not be considered as a treatment. • Bell the aggressor (using a quick release or safety collar) so both the owners and victim can quickly identify his/her location. • Increase the number of resources and locations (e.g., food, water, scratching, perching, bedding, play and feeding toys) throughout the residence including each cat's core area. The efficacy of multimodal environmental enrichment should not be underestimated. • Increase litter boxes to the number of cats plus one divided among multiple locations so that one cat cannot keep another from accessing the boxes; locations with more than one exit/entry are ideal. • Increase the number of hiding places and resting areas; especially concentrate on increasing vertical space (e.g.,. resting areas on shelves, window sills). • No new cats should be added to the house.

For Cases where the Cats Cannot be in the Same Room without Immediately Becoming Agitated
• Separate cats completely when unsupervised. • Meet each cat's needs for play, litter boxes, food, water, perching, resting, and attention. • A large wire dog kennel or vertical orientated wire cat cage (with shelving) may be better tolerated than smaller cat kennels and can be used for controlled exposure. • Cats may be taught to tolerate harnesses and leashes so that they can be used during training and controlled reintroduction. This is especially valuable for the aggressor. • Set up desensitization and counter-conditioning sessions daily; initially utilize physical and visual barriers. • Introduce the cats (in their kennels or on leash and harness) at a distance from each other that prevents overt/covert aggression. Feed the cats or engage in play for classical counterconditioning. • Over many sessions gradually reduce the distance between the cats, being careful to stay far enough apart during each session that no overt or covert behavioral signs of aggression and/or fear are seen. Start and end all sessions on a successful note. • Teach the cats a "come and/or go to place" cue using operant counterconditioning and positive reinforcement. Practice these cues several times daily so each cat learns to respond reliably. Behavioral cues are best taught when animals are not stressed. • When ready to allow the cats more freedom with each other, follow the instructions for less severe interact aggression (above).

SURGICAL CONSIDERATIONS
Neutering intact males is approximately 90% effective in reducing roaming, intercat aggression, and urine spraying. Neutering/spaying is effective in reducing mounting/sexual behavior.

MEDICATIONS

DRUG(S) OF CHOICE
As all medications are extra-label, insure that the client is informed, and review target desirable outcomes and potential adverse effects.

For the Aggressor and/or Victim
Selective Serotonin Reuptake Inhibitors (SSRI)
• Fluoxetine or paroxetine 0.5–1 mg/kg PO q24 h.
• Drugs of choice for aggression, anxiety, and/or urine marking, may decrease impulsivity.
• Side effects may include gastrointestinal upset, decreased appetite, sedation, urinary

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AGGRESSION, INTERCAT AGGRESSION (CONTINUED)

retention (paroxetine), and increased agitation/irritability.

Tricyclic Antidepressant (TCA)

• Clomipramine 0.3–0.5 mg/kg PO q24 h: serotonin selective tricyclic: for anxiety and aggression

• Side effects include gastrointestinal upset, sedation, urinary retention, constipation, and lowered seizure threshold. Do not use in patients with arrhythmias or cardiomyopathies.

Pheromones

Feliway and Feliway Multicat (CEVA) and Felifriend (CEVA, presently available in Europe) are feline facial pheromones that may be helpful in cases of intercat aggression when used with a multimodal plan.

For the Victim

Azapirone

Buspirone 0.5–1 mg/kg PO q8–24 h (feline dose): reserved for victims to increase social confidence.

• Side effects rare; may include decreased sociability and increased agitation/irritability. May increase intercat aggression as victim may be more confident and fight back."

Benzodiazepines

• Lorazepam 0.125–0.25 mg/cat PO up to q12–24 h or oxazepam 0.2–0.5 mg/kg PO q12–24 h for anxious or fearfully aggressive cats and as an appetite stimulant helping to facilitate classical counter conditioning. May be used as needed with peak effects seen within 1 hour.

• Side effects may include increased appetite, ataxia, inhibited learning, and disinhibition of aggression.

• Note: controlled substance; dependence can develop; Medication should be gradually weaned if used consistently for longer than 2 weeks.

CONTRAINDICATIONS

• Benzodiazepines should be used cautiously or avoided in cats with hepatopathies.

• Paroxetine and TCAs may produce anticholinergic side effects. Fluoxetine also occasionally reported to cause urine retention.

• SSRIs and TCAs should be used with caution in patients with histories of cardiac abnormalities, seizures, and liver disease.

PRECAUTIONS

• Any behavioral drug has the potential to produce paradoxical reactions, including fear, anxiety, hyperexcitability and/or aggression.

• Medications that alter serotonin levels have the potential to produce serotonin syndrome.

POSSIBLE INTERACTIONS

• Avoid concurrent use of SSRIs and TCAs or MAO inhibitors such as selegiline and use cautiously or avoid with buspirone, tramadol, and tryptophan due to possible serotonin syndrome. • Caution with concurrent medications considered substrates of P450.

ALTERNATIVE DRUGS

• Amitriptyline (TCA) 0.5–1 mg/kg PO q12–24 h: for anxious cats especially if comorbid recurrent FIC/FLUTD; not selective for serotonin reuptake inhibition and likely less effective for the aggressor. • Dietary supplementation with alpha-casozepine (Zylkene: Veotquinol), ROYAL CANIN Veterinary Diet CALM (contains alpha-casezopine, l-tryptophan, and nicotinamide) or Hill's Prescription Diet Multicare Feline Urinary Stress (contains l-tryptophan and milk protein hydrolysate).

FOLLOW-UP

PATIENT MONITORING

• Clinicians should monitor patients 2 weeks after treatment initiation and monthly for the first few months by phone or email; a follow-up visit should be scheduled 4–8 weeks into treatment if drugs dispensed to assess response and adjust dose if necessary.

• Benzodiazepines may rarely cause cases of fatal hepatopathies; patients should be rechecked immediately if any adverse events, including anorexia. • Medication should be used for at least 4–6 weeks after resolution of signs, then gradually weaned by reducing the dosage no faster than 25% per day on a weekly basis. • Some patients require long-term medication; recheck laboratory work every 6 months to 1 year depending on health and age..

PREVENTION/AVOIDANCE

• Proper socialization 2–7 weeks and ongoing. Gradual introduction more closely resembles the natural process through which new cats enter an existing group at the periphery and may be accepted over time. Intercat aggression may be more common when unfamiliar cats are suddenly placed together. A negative initial encounter is often associated with future intercat aggression. Related and familiar cats are less likely to have intense intercat aggression. In stable multi-cat households, avoid adding additional cats.

POSSIBLE COMPLICATIONS

Abrupt withdrawal of behavioral medications may result in aggression and rebound anxiety.

EXPECTED COURSE AND PROGNOSIS

• The prognosis for most cases is fair; it is complicated by prolonged duration, high intensity, underlying medical conditions, and incomplete owner compliance. In one study 62% (30/48) were considered cured and 37% (17/48) not cured (cat given away, euthanized or permanently separated). • Recent and mild (low-intensity, low-frequency) cases may have better long-term outcomes.

MISCELLANEOUS

ASSOCIATED CONDITIONS

• Urine marking/spraying • House soiling • Excessive grooming • Fearful/anxiety-related behavior • Human-directed or interspecies aggression

AGE-RELATED FACTORS

Predatory/Play-related aggression more common in young active and playful cats housed indoors with more sedentary or aged individuals.

ZOONOTIC POTENTIAL

Humans intervening while cats are fighting may be injured and contract infections through cat bites and/or scratches.

PREGNANCY/FERTILITY/BREEDING

Most behavioral medications are contraindicated in breeding animals.

SYNONYM

Feline intraspecies aggression

ABBREVIATIONS

• FeLV = feline leukemia virus

• FIC/FLUTD = feline idiopathic cystitis/feline lower urinary tract disease

• FIV = feline immunodeficiency virus

• MAOI = monoamine oxidase inhibitor

• SSRI = selective serotonin reuptake inhibitor • T_4 = thyroxine • TCA = tricyclic antidepressant

SEE ALSO

• Aggression, Overview—Cats • Pediatric Behavior Problems—Cats

INTERNET RESOURCES

http://indoorpet.osu.edu/cats/

Suggested Reading

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Consulting Editor Gary M. Landsberg

AGGRESSION, OVERVIEW—CATS

BASICS

DEFINITION

• Aggression is a behavioral strategy used to manage aversive situations. • May be normal and appropriate in certain contexts. • May be abnormal with serious deleterious effects on the cat's physical and emotional well-being. • Aggressivity: describes both mood and temperament traits relating to the propensity to show aggression when environmental circumstances dictate it might be used.

OVERVIEW OF TYPES

Play Aggression (Toward People)

• Typically refers to a cat who scratches and bites the owners during play. • Not true aggression but overzealous play without proper impulse control due to lack of training or proper intraspecific social feedback. • The cat's intent is not to harm the person. • Behavior encouraged and rewarded by owners through rough play with a kitten; when larger and stronger, becomes perceived as aggression rather than overzealous play.

Predatory Aggression (Toward People or Other Animals)

• Cats have an innate drive to "hunt" or show predation behavior, which includes stalk, hide, and pounce. • Predation is not a direct function of hunger. • Typically stimulated by fast movements and can progress to the cat hiding and waiting for an animal or person to walk by. • Play is a common way for young cats to perfect predation skills; play aggression and predatory aggression may overlap.

Redirected Aggression (Toward People or Other Animals)

• Cats who see, hear, or smell a trigger and direct aggressive behavior toward the closest bystander. • In some cases, one person or animal in the home becomes the designated victim, and the cat may bypass a nearby individual and look for the preferred victim. • Some cats may stay aroused for 24–72 hours after a triggered event. • Common triggers inciting redirected aggression are seeing another cat or wildlife outside or loud noises.

Fear/Defensive Aggression (Toward People or Other Animals)

• The cat will show body postures indicative of fear/anxiety and may use aggression as a strategy to manage that aversive situation. • Typical behaviors shown include a combination of any of the following: hissing, spitting, piloerection, arched back, turning away, running away, cowering, rolling on its back and pawing (defensive position, not submissive position) if cornered.

Territorial Aggression (Toward People or Other Animals)

• Some cats, particularly male cats, show territorial behaviors in domestic home settings due to size and the presence of more resources (e.g., people, food, resting areas, feeding areas, elimination sites, etc.) to defend in a smaller area. • Territorial behaviors include marking with urine, feces, or bunting (the rubbing of the cheeks on surfaces to deposit pheromones) and scratching (also deposits pheromones and leaves visual marker) and may be associated with aggression. • In severe cases, the aggressor may seek out the other individuals and attack. • Body posture with territorial aggression is assertive and confident.

Pain Aggression (Toward People and Animals)

Cats who are in pain may show aggression (hiss, growl, scratch, bite) when they are physically handled or prior to or after movements such as jumping onto or off a piece of furniture.

Maternal Aggression

A female cat may show aggressive behaviors toward individuals approaching her kittens.

Impulse Control Aggression

Cats who show intense aggressive responses to mild stimuli without much or any warning may have an impulse control disorder arising from dysfunctional serotonin neural circuits.

Frustration-Induced Aggression (To People and Other Animals)

Some cats have very outgoing, social personalities and exhibit aggression if the captive life indoors does not meet their behavioral needs.

Contact-Induced/Petting Aggression (Toward People)

• Cats will show early signs of aversion when people stroke their cats, with their ears going back and tail swishing. • If physical contact continues, they typically bite. • Owners often miss the early warning signs. • When cats groom one another, they typically limit the grooming to the head region. • Some cats appear to be particularly sensitive to being stroked along the dorsum, the common method used by owners.

Intercat Aggression within a Home

• Fifty percent of cat owners report fighting (scratching and biting) after introducing a new cat to the home. • The number of cats, gender, and age are not significant factors in predicting which cats will show aggression. • Any of the above categories of aggression are all possibilities for fights between or among cats. • Fear/anxiety is the most common cause of intraspecific aggression.

CONTRIBUTING FACTORS TO THE PATHOPHYSIOLOGY

Behavior problems are typically multifactorial in cause, and Figure 1 is a diagram illustrating some of the more common components that need to be evaluated to accurately diagnose and treat aggression cases.

SYSTEMS AFFECTED

• Behavioral—vary with type of aggression, occur alone or in combination: tail swishing/twitching, ears turned sideways or flattened, stiffening of shoulders/legs, crouching, dilation of pupils, hissing, spitting, growling, piloerection, staring, chasing, stalking, pawing, lunging. • Cardiovascular—signs associated with sympathetic activation and HPA activation. • Endocrine and Metabolic—long-term aggression associated with fear/stress/anxiety, symptoms associated with long-term activation of the HPA system. • Gastrointestinal—with chronic HPA stimulation may see a cat more prone to anorexia and GI ulcers. With acute fear aggression: evacuation of the bowel and possible diarrhea. IBD possible in chronic stress. • Hemic/Lymphatic/Immune—decreased immune response with chronic HPA stimulation; stress leukogram. • Musculoskeletal—an outcome of the aggression may result in damage to the muscles from damage by the nails and teeth. • Both the victim and the aggressor may suffer injuries. With chronic activation of the HPA, may see muscle wasting. • Nervous—increased reactivity for up to 72 hours following an aggressive outburst. May see an increase in aggression with decreased provocation as the synapses in the amygdala become sensitized. Some animals may have decreased serotonin, causing aggressive outbursts. Depending on the type of aggression, may see ritualized motor patterns, shaking, or trembling. • Ophthalmic—dilated pupils with sympathetic stimulation. • Renal/Urologic—may see associated spraying or small amounts of urine on horizontal surfaces. May exhibit signs consistent with FLUTD with aggression that is due to stress/anxiety/fear. • Respiratory—tachypnea in acute cases or when stressed. • Skin/Exocrine—damage due to fights. Damage due to excessive grooming associated with fear-based aggression/anxiety/distress.

SIGNALMENT

• There is preliminary evidence that behavioral traits in cats vary by breed and gender. • Males were more likely to show aggression to cats than females. • Abyssinian, Russian blue, Somali, Siamese, and chinchilla breeds showed more aggression. • Maine Coon, ragdoll, and Scottish folds showed the least aggressiveness.

SIGNS

• May appear at social maturity (2–4 years of age) except for play-related and should occur in specific social contexts/interactions. If onset occurs in an older cat, medical causes should be ruled out first. • General comments: most owners are able to detect overt signs of aggression (biting, hissing, growling) but may

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AGGRESSION, OVERVIEW—CATS (CONTINUED)

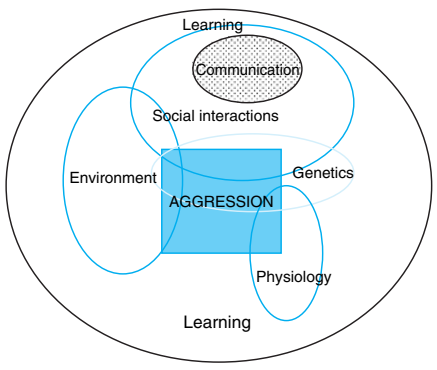

Figure 1.

miss more subtle signs of aggression that typically occur between cats (staring) and the resulting anxious behaviors that can result in aggression (meatloaf position, averting gaze, etc.). Videotapes of intercat interactions allow the clinician to assess the behavior.

CAUSES

• Underlying medical issues can cause aggression. • Temperament/behavior is influenced by genetics, rearing, socialization, environment in which the cat lives, and types of interactions the cat has with people.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• CNS diseases (e.g., infections, toxins, tumors, partial seizures, focal seizures) • Hyperthyroid • Hepatic encephalopathy • Any condition causing pain (e.g., arthritis, pancreatitis, dental disease, anal sacculitis) • Lead poisoning • Rabies • Diabetic neuropathy (pain-induced aggression when paws touched)

CBC/CHEMISTRY/URINALYSIS

Physical examination, baseline blood and urine screening followed by additional diagnostics as indicated based on history, examination and laboratory results.

OTHER LABORATORY TESTS

• Discuss *Bartonella* testing in any cat that bites or scratches people. • Thyroid levels. • Urinalysis ± culture if housesoiling is part of the aggression issue. • Feline serology (FCV, FeLV, FIV).

TREATMENT

• Never use physical correction/punishment; may escalate the aggression. • Never try to physically handle or manipulate a cat in an aggressive state. • Avoid known triggers. • Identify triggers and desensitize and counter-condition the cat to the triggers. • Implement safety measures (nail caps, wearing long pants/long sleeves, keep flattened cardboard boxes around home to place between yourself and your cat, redirect the behavior in early arousal phase). • Behavior modifications to redirect the cat and reduce arousal (specific plans are dependent upon the specifics of each case). • Train your cat to commands such as "sit," "go to place," etc. • Implement environmental enrichment. • Teach owners to identify early signs of arousal so the cat can be redirected or so they can avoid the cat. • After a very aggressive outburst, keep aggressor isolated in a room for at least 24 hours (as long as the cat remains aroused after an attack). • Pheromones. • Medications.

MEDICATIONS

DRUGS OF CHOICE

• SSRIs: fluoxetine or paroxetine 0.5 mg/kg PO q24h.
• TCAs: clomipramine 0.5 mg/kg PO q24h.
• Buspirone at 0.5–1.0 mg/kg q8–24h or benzodiazepines such as oxazepam at 0.2–0.5 mg/kg q12–24h might reduce fear and build confidence in the fearful cat that does not retaliate or fight back.

CONTRAINDICATIONS

• Cats with renal or hepatic disease • Caution with TCAs and SSRIs in diabetics • TCAs in patients with cardiac abnormalities

POSSIBLE INTERACTIONS

• TCAs and SSRIs should not be used together. • Mirtazapine should not be used in combination with a TCA or SSRI. • Any other medication the cat is on, the practitioner should look up which liver enzyme system is utilized in metabolism to maximize safety in combining medications.

ALTERNATIVE DRUGS

• Amitryptiline 0.5–1.0 mg/kg PO q12–24h • SAMe: 100 mg PO q24h • Zylkene 75 mg (15 mg/kg or greater) PO q24h • Feliway Multicat diffuser l-theanine 25 mg PO q24h • Zylkene 75 mg PO SID

FOLLOW-UP

PATIENT MONITORING

• Call owners once every 1–2 weeks for the first 2 months after a treatment plan has been recommended. Determine implementation of safety recommendations and the behavioral plan. • If medications are involved, the medication dose should be reevaluated every 3–4 weeks. • Frequency of follow-up will be dictated by the severity of the case and owner compliance. • CBC, chemistry, T_4 prior to medication. Recheck liver and kidney values 2–3 weeks after starting medication. Recheck bloodwork annually in young healthy patients, semiannually in older patients. • Repeat physical exams in older patients semiannually, as painful conditions may start to contribute to/exacerbate the pain.

EXPECTED COURSE AND PROGNOSIS

• Ultimately depends on the specific kind of aggression and the compliance of clients with the suggested treatment plan. • Most cases of aggression need a combination of behavioral modification, environmental modification, training, and, when necessary, medication to maximize chances of improvement. • Some types of aggression can resolve or improve within a few weeks, whereas others may take several months or longer. • Some forms of aggression have a poor prognosis.

MISCELLANEOUS

AGE-RELATED FACTORS

• Older cats—cognitive decline, CNS disease, arthritis, meningioma, other medical conditions. • Age 2–4—social maturity, when cats may start to show certain kinds of aggression.

ABBREVIATIONS

• CNS = central nervous system • FCV = feline calicivirus • FeLV = feline leukemia virus • FIV = feline immunodeficiency virus • FLUTD = feline lower urinary tract disease • GI = gastrointestinal • HPA = hypothalamic-pituitary-adrenal • IBD = inflammatory bowel disease • SAMe = S-adenosyl-L-methionine-tosylate disulfate • SSRI = selective serotonin reuptake inhibitor • TCA = tricyclic antidepressant

SEE ALSO

• Aggression—Intercat Aggression
• Aggression Toward Humans—Cats

Suggested Reading

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Consulting Editor Gary M. Landsberg
Acknowledgment Karen L. Overall

Client Education Handout available online

AGGRESSION, OVERVIEW—DOGS

BASICS

DEFINITION

• Action by one dog directed against another organism with the result of, limiting, depriving, or harming that organism. Aggression refers to any behavior along an aggression continuum, from a stare, to immobility (freeze), growl, snarl, lunge, air snap, single bit, multiple bite, multiple attacks, and chase and attack.
• Numerous functional types have been posited. Here, aggression is classified on the basis of (1) affective aggression, (2) predatory aggression, and (3) play-related aggression. Affective (emotional) aggression is the focus of this chapter. Affective states, such as fear and arousal, and motivational factors, such as hunger and sexual drive, influence the probability of overt aggression, such as biting. Affective aggression may be human-directed or dog-directed. Within these contexts, there may be additional specificity, such as human-directed aggression toward unfamiliar persons, or human-directed aggression directed toward familiar persons. Often dogs display aggression in a single context.
• Human-directed aggression toward familiar persons in response to controlling gestures is historically called dominance aggression, although newer terminology, such as conflict aggression, may be used to avoid often-erroneous semantic assumptions inherent in the term "dominance."
• Human-directed aggression toward unfamiliar persons specific to home location is called territorial aggression.
• Predatory aggression refers to behaviors associated with chasing and hunting prey. It is often considered nonaffective and may be socially facilitated by other dogs. Predatory behaviors may be triggered by movement or high-pitched sounds and may be misdirected to humans or objects.
• Play-related aggression involves aggressive gestures, such as growling and biting, in the context of play and is commonly displayed toward other dogs or humans. It is often initiated by signs of play, such as the play bow.
• In all cases, medical factors that might contribute to aggression (including pain) must be evaluated.

PATHOPHYSIOLOGY

• Affective aggression involves arousal of the sympathetic nervous system. Some pathologic conditions are associated with an increase in aggression because of CNS effects such as pain or irritability.
• Abnormalities in the CNS serotonin neurotransmitter system have been implicated in one type of impulsive human-directed aggression, colloquially called "rage," directed toward familiar persons over controlling gestures.
• Aggression often has a learned component whereby dogs learn to use aggression to manage distance from fearful stimuli or control resources.

SYSTEMS AFFECTED

• Behavior.
• Other, if there is an underlying medical etiology.

GENETICS

• In some breeding programs, aggressive tendencies and bite styles have been selected for (or against).
• One study in the United States linked English springer spaniels that display human-directed dominance aggression to one breeding sire, implicating a heritable component.
• One study of human-directed dominance aggression among English cocker spaniels reported that males were more aggressive than females, and dogs with solid coat color were more aggressive than those with parti coat color.

INCIDENCE/PREVALENCE

• Canine aggression is the most common diagnostic category seen by board-certified veterinary behaviorists in North America.
• According to the Centers for Disease Control and Prevention (2009), about 4.7 million people are bitten by dogs each year in the US, although this number is considered an underestimation as the majority of dog bites are not reported.
• In the US, it is estimated that one in five of those who are bitten require medical attention for dog bite–related injuries.
• Among children and adults, males are more likely than females to be bitten.
• Based on emergency room data in the US, the rate of dog bite–related injuries is highest for children aged 5–9 years.
• In the majority of cases, people are bitten by dogs that are known to them.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog

Breed Predispositions

• Any breed or breed mix.
• Pit bull, German shepherd dog, and rottweiler are the most common breed types implicated in fatal dog bites in the US.
• In the US, English springer spaniels appear to be at risk for human-directed "dominance" aggression.

Mean Age and Range

Any age

Predominant Sex

• Any sex.
• Males—intact or castrated are most commonly implicated in cases of human-directed "dominance" type aggression. Intact males are overrepresented in dog-bite fatalities.
• Females—spayed are most commonly implicated in aggression to other female dogs in the home. In some studies, spayed females are less likely than males to display human directed aggression.

SIGNS

General Comments

• Any dog can display aggression. Many factors, including individual dog temperament and experience, influence the propensity to bite.
• Dogs may display warning signs—including immobility, growls, snarls, or air snaps that may provide time to avoid overt aggression. These signs should not be punished, as this might decrease the probability of warning signs without affecting the underlying risk, or may further intensify the aggressive (defensive) response. Instead, the animal should be safely removed from the situation and the underlying triggers for the affective state should be addressed.

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AGGRESSION, OVERVIEW—DOGS (CONTINUED)

Historical Findings
• Variable.
• Basis for risk analysis and details of treatment program. Important questions: Who is the target? Who was present to manage the dog? How severe were the resulting injuries? What are the circumstances (including location, time) in which aggression occurred? Are there any reliable triggers for the aggressive behavior? Abnormalities in mentation or awareness might indicate a medical cause

Physical Examination Findings
• Usually unremarkable.
• Use extreme care when handling aggressive dogs.
• A comfortable, well-fitting basket muzzle is recommended prior to examination of any dog with a history of human-directed aggression. Basket-style muzzles allow dogs to pant.
• Abnormalities on the neurologic examination may suggest an organic disease process (e.g., rabies, pain, blindness). Dogs can display aggression preictal, postictal or ictal period.

CAUSES
• Part of the normal range of behavior; strongly influenced by individual temperament, experience, early socialization (before 12 weeks), and other variables.
• Harsh handling and confrontational responses can escalate aggression and should be avoided.
• May be a manifestation of an organic condition, such as hepatic encephalopathy or pain.
• In all cases, evaluate medical causes of aggression.

RISK FACTORS
• Inadequate socialization during the canine critical period (3–12 weeks).
• Traumatic/fearful/negative experience(s).
• Predisposing environmental conditions—lack of training, inadequate restraint, harsh handling.
• Inability of owner to safely confine or manage the dog in order to prevent future incidents. Helpful devices include a barrier fence, a muzzle, a collar or head halter, a leash.
• Previous aggression/bite history (number of incidents, number of bites per incident, target, severity of injury); legal citation for biting.
• Unpredictability of aggressive behaviors, lack of warning signals.
• Presence of children, elderly people, or other humans or animals at high risk living in or visiting household.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• A thorough medical evaluation should be conducted on all cases of aggression.
• Identify pathologic conditions associated with aggression before making a purely behavioral diagnosis.
• Rule out developmental abnormalities (hydrocephaly, lissencephaly, hepatic shunts), metabolic disorders (hypoglycemia, hepatic encephalopathy, diabetes), neuroendocrinopathies (hypothyroidism, hyperadrenocorticism), dermatopathy, neurologic conditions (intracranial neoplasm, seizures), toxins, inflammatory diseases (encephalitis, rabies), cognitive dysfunction, acute or chronic pain, and iatrogenic causes, such as glucocorticoid administration.

CBC/BIOCHEMISTRY/URINALYSIS
• May be indicated to evaluate dog as candidate for behavioral medications.
• Abnormalities may suggest underlying metabolic, endocrine causes, or other medical conditions.
• Usually no significant findings outside laboratory range unless an underlying medical etiology is detected.

OTHER LABORATORY TESTS
• Thyroid testing.
• Others as indicated by history and physical exam.

IMAGING
• May be indicated to identify sources of pain or disease.
• MRI or CT—particularly if cerebral disease/neoplasia suspected.

DIAGNOSTIC PROCEDURES
• Collection of thorough behavioral history and evaluation of medical concerns.
• Postmortem fluorescent antibody test is indicated for any aggressive dog for which rabies is a differential diagnosis, including any dog not quarantined for 10 days after a bite injury to a human or other animal.

PATHOLOGIC FINDINGS
None

TREATMENT

APPROPRIATE HEALTH CARE
• Manage any underlying medical conditions.
• Management success—combination of multiple modalities: safe environmental control, behavior modification to teach animals appropriate behavior, and pharmacotherapy.
• Consult a veterinarian with experience and training in aggression management.
• Euthanasia should be discussed or recommended when the risk of injury is high. Note recommendation in medical record.
• Rehoming aggressive dogs may put those involved at liability risk.

NURSING CARE
A boarding facility able to safely manage the dog might be used until a safe management plan can be implemented, or until an outcome decision can be made.

ACTIVITY
Since frustration and arousal may increase the incidence of aggression, an appropriate and safe exercise regime should be incorporated into the treatment program.

DIET
There is modest evidence that a low-protein diet may reduce territorial aggression in dogs, an effect that might be enhanced with tryptophan supplementation.

CLIENT EDUCATION
• Safe practices should dictate all decisions. These practices include safe confinement, physical barriers, head halters, leash control, muzzle use, and supervision by a competent adult.
• Situations that have led to aggression in the past should be listed and a specific plan developed to avoid these situations and associated locations in the future, and a long-term management plan developed.
• The dog should calmly be removed from aggression-provoking situations.
• Safe, non-confrontational techniques that manage resources and use positive reinforcement to teach the dog appropriate responses should be employed.

(CONTINUED) AGGRESSION, OVERVIEW—DOGS

• Confrontational management techniques, such as roll-overs, increase the probability of a defensive aggressive response, may lead to human injury, and should be strictly avoided.
• Management ("dominance") techniques including punishment are associated with defensive fear responses by the dog and an increased risk of human-directed aggression. These should be avoided and replaced with positive management techniques.
• The client should be advised to consider personal and legal liability risks of keeping the dog. Human injury, bite-related lawsuits, and homeowner's insurance claims can result from canine aggression. Such risk assessment may help the client objectively evaluate the situation.
• Euthanasia should be considered if safe management cannot be employed, or when the risk of injury is high.

SURGICAL CONSIDERATIONS
Castration of males may reduce the incidence of inter-male aggression.

MEDICATIONS

DRUG(S) OF CHOICE
• None approved by the FDA for the treatment of aggression.
• No drug will eliminate the probability of aggression.
• Use drugs only when a safe management plan has been implemented.
• Inform the client of the extra-label nature of medication and risk involved; document in the medical record, obtain signed informed consent.
• Drugs that increase serotonin may be helpful to reduce anxiety, arousal, and impulsivity.
• Treatment duration: minimum 4 months, maximum: lifetime.
• See Table 1 for drugs used to facilitate management of aggression in combination with a safe management plan.

CONTRAINDICATIONS
• Fluoxetine is generally contraindicated in cases of seizures.
• Clomipramine is contraindicated in cases of cardiac conduction disturbances or seizures; in one open trial, clomipramine was no more effective than control in cases of human-directed aggression.

PRECAUTIONS
Avoid the use of benzodiazepines (e.g., diazepam) in aggressive dogs because of the risk of behavioral disinhibition. Aggression may increase when dogs lose their fear of the repercussions of biting.

POSSIBLE INTERACTIONS
Do not use SSRIs or TCAs with monoamine oxidase inhibitors, including amitraz and selegiline, or with each other because of the risk of serotonin syndrome.

ALTERNATIVE DRUG(S)
• L-Tryptophan (10 mg/kg PO q12 h).
• Trazodone (4–8 mg/kg PO q12 h or PRN) may be used with the agents listed in Table 1 to reduce anxiety and arousal.
• Clonidine (0.01–0.05 mg/kg PO q12 h or PRN), may be used with the agents listed in Table 1 to reduce anxiety and arousal.

FOLLOW-UP

PATIENT MONITORING
Weekly to biweekly contact recommended in the initial phases to guide clients with behavior modification plans and medication management.

PREVENTION/AVOIDANCE
• To prevent aggressive incidents, avoid all situations that have led to aggression in the past, using safe confinement, gates, halters, collars, leashes, muzzles.
• Reduce the risk of aggression in young dogs (3–12 weeks) with a positive socialization program; avoid intimidation techniques and negative, fear-inducing situations.

POSSIBLE COMPLICATIONS
• Injury to humans or animals.
• Liability to client, veterinarian.
• In cases of dog-directed aggression, although not the intended target, humans who interfere are often seriously injured either by accident or by redirected aggression; owners should not reach for fighting dogs; pull apart with leashes.
• Aggressive dogs are at risk for relinquishment or euthanasia.

EXPECTED COURSE AND PROGNOSIS
• Aggressive dogs weighing over 18.5 kg are at increased risk for behavioral euthanasia.
• Aggressive dogs may be successfully managed, but should not be considered "cured."
• Prognosis is case-dependent due to risk factors and management features of each situation.

MISCELLANEOUS

ASSOCIATED CONDITIONS
N/A

AGE-RELATED FACTORS
Onset of aggression in mature dogs suggests a medical cause; carefully evaluate sensory acuity, sources of pain, endocrinopathy, cognitive function.

Table 1

Drugs and dosages used to manage canine aggression.

Drug	*Drug Class*	*Oral Dosage in Dogs*	*Frequency*	*Side Effects-usually transient*
Fluoxetine	SSRI	1.0–2.0 mg/kg	q24 h	Decreased appetite, sleepiness
Paroxetine	SSRI	1.0–2.0 mg/kg	q24 h	Constipation
Sertraline	SSRI	2.0–4.0 mg/kg	q24 h	Sleepiness
Clomipramine	TCA	1.0–3.0 mg/kg	q12 h	Sleepiness, vomiting

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AGGRESSION, OVERVIEW—DOGS (CONTINUED)

ZOONOTIC POTENTIAL

- Dog bites are significant public health risk.
- Rabies is a potential cause of aggression.

PREGNANCY/FERTILITY/BREEDING

Tricyclic antidepressants are contraindicated in breeding males and pregnant females.

SYNONYM

Biting

SEE ALSO

- Aggression—Between Dogs in the Household
- Aggression, Food and Resource Guarding—Dogs
- Aggression to Unfamiliar People and Unfamiliar Dogs
- Aggression Toward Children—Dogs
- Aggression Toward Familiar People—Dogs

ABBREVIATIONS

- CNS = central nervous system
- CT = computed tomography
- FDA = US Food and Drug Administration
- MRI = magnetic resonance imaging
- SSRI = selective serotonin reuptake inhibitor
- TCA = tricyclic antidepressant

INTERNET RESOURCES

- American Veterinary Medical Association Dog Bite Prevention:. https://www.avma.org/public/Pages/Dog-Bite-Prevention.aspx
- Centers for Disease Control and Prevention Dog Bites: http://www.cdc.gov/HomeandRecreationalSafety/Dog-Bites/
- ASPCA Aggression in Dogs: http://www.aspca.org/pet-care/virtual-pet-behaviorist/dog-behavior/aggression-dogs

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Client Education Handout available online

AGGRESSION—BETWEEN DOGS IN THE HOUSEHOLD

BASICS

OVERVIEW
Aggression toward other dog(s) within a household or those dogs that are otherwise familiar and spend time together regularly. Dogs can form stable social relationships quickly, sometimes within minutes of being introduced. Aggression usually revolves around resources (e.g., food, toys, owner attention, resting places), but may be fear-related or can occur at times of excitement/
arousal (e.g., visitors or other dogs on the property). Usually within the range of normal behavior, but may be abnormal or excessive due to learning, early environment, or genetics (dogs bred for fighting).

SYSTEMS AFFECTED
Behavioral

SIGNALMENT
Species
Dog

Breed Predilections
• More common in purebreds with 50% being the same breed. • Breed predilection in "fighting breeds" (e.g., pit bull terrier) and terrier.

Mean Age and Range
Signs usually develop at social maturity (approximately 18–36 months of age).

Predominant Sex
May be more common/intense between females.

SIGNS
• Aggression (barking, growling, lip-lifting, snarling, snapping, lunging, biting) toward other dogs in the home. This may be accompanied by fearful or submissive body postures/facial expressions (crouching, backing away, ears back, tail tucked, looking away, lip licking) or confident/dominant body postures (standing straight up, approaching/direct contact with the other dog, tail up, ears forward). • History prior to the onset of fights may include subtle signs of social/resource control/dominance (e.g., staring, lying across doorways to block the other dog's access to a room) and submission (e.g., turning away from the staring dog or not entering the same room as the other dog). • Dogs fighting in a household may get along well except in specific situations, especially over resources, access to passageways/doorways, times of arousal. Dogs that fight over owner attention often described as "jealous." • Aggression typically occurs when the owner is present.

CAUSES & RISK FACTORS
• May be a normal canine behavior; strongly influenced by previous experience (e.g., early socialization, previous aggressive encounters with other dogs, inappropriate punishment). • Breed predilections due to selective breeding for interdog aggression. • Aggression is likely to be more severe toward dogs of the same sex, especially two females. • Instigators are usually newer to the household and younger than recipients. • In cases of aggression within a household, there may be history of owners interfering in normal canine communication, especially when one dog appears to be denying another dog access to something that the owners think they should "share." This shift may actually support one dog in what would be considered inappropriate "canine" behavior and result in escalation of the interdog aggression. For example, an owner calling dog "A" into a room when the other dog "B" has blocked its access even though "A" was willing to remain outside of the room or the owner punishing dog "B" for blocking dog "A's" access. Both of these situations undermine dog "B" in its hierarchal position while it was subtly asserting control to which dog "A" was willing to defer. • Underlying medical conditions, especially pain, may increase the level of aggression. • If the aggressor initiates or continues its attack despite deference from the other dogs, or if the deferent dog is overly fearful or defensive, then these may indicate abnormal responses that might have a poor prognosis (unable to socially communicate) or require drug therapy to manage the abnormal behavior.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Play behavior/excited non-aggressive arousal
• Possessive aggression • Fear aggression
• Others depending on circumstances

CBC/BIOCHEMISTRY/URINALYSIS
Usually unremarkable. Rule out underlying medical contributing conditions with blood, urine and thyroid screening.

OTHER LABORATORY TESTS
As needed to rule out underlying medical conditions.

IMAGING
MRI if CNS disease suspected; as needed to rule out underlying medical conditions.

DIAGNOSTIC PROCEDURES
N/A

TREATMENT

CLIENT EDUCATION
General Comments
• Treatment is aimed at controlling the problem, not achieving a "cure." Successful treatment, as measured by a decrease in aggressive incidents, depends upon owner understanding of basic canine social behavior and communication, risks involved in living with an aggressive dog(s), and willingness and ability to follow safety and management recommendations. • Owners must be aware that the only way to absolutely prevent future injuries is to continually separate the dogs or remove one from the home.

Safety Recommendations
• The owner's primary responsibility is to insure safety by identifying and avoiding all situations that may evoke an aggressive response. Dogs within a household may initially need to be kept in separate housing areas to prevent fighting. • Owners should be advised that they may be liable if their dog bites and could face civil/criminal prosecutions should a person be injured. • If needed, owners must be instructed in methods of safely breaking up dog fights.
• Treatment is more likely to be successful if aggression-provoking stimuli can be effectively prevented prior to behavior modification. • The dogs must be confined away from each other or under the direct physical control of a responsible adult whenever an aggression-evoking situation could arise (e.g., around food/valued resources). • Teaching the dogs to be comfortable wearing a head halter (e.g., Gentle Leader) with a lightweight 8- to 10-foot leash attached or a basket muzzle makes controlling potentially dangerous situations easier and safer. If needed, use the long leash both for prevention and to safely remove the dog from situations that may elicit aggression; do not reach for the dog directly.
• The more dominant dog typically asserts control of resources (e.g., staring, growling) with confident body postures directed toward the more subordinate dog who relinquishes the resource by moving or looking away.
• When there is competition over resources, allow priority access to the more controlling/dominant individual and encourage and reinforce deference in the other dog(s).
• Priority access may vary between resources (individual motivation), and contexts (location, who accesses first)—separate (time out) any dog displaying an inappropriate response. • For some dogs problems may be resolved if additional resources and sufficient distribution are provided to reduce competition. • Alternately, dogs may need to be separated when given resources that are a source of repeated conflict.

Behavior Therapy
• Depending on the situation, supporting and reinforcing the hierarchal positions of the dogs will result in rapid (e.g., 1–2 weeks) resolution of the problem and a drastic decrease in aggressive incidents between dogs. Fighting is likely to recur if support of the hierarchy by humans is not continued.
• Separately, teach each dog those behaviors that will serve as a foundation for

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AGGRESSION—BETWEEN DOGS IN THE HOUSEHOLD (CONTINUED)

management and control when together including sit and relax, down-settle and teaching to go to mat, bed or crate to settle. • NEVER allow dogs to "fight it out" as serious injuries may occur. • During times together, use verbal cues or leave leash attached to train desirable and prevent or interrupt undesirable behavior. • Structured interactions (also known as learn to earn or say please by sitting) where each dog is consistently taught to sit for anything it values (before feeding, petting, play, going for a walk) provides structure and predictability in all interactions, teaches impulse control and gives the dog control of its resources by sitting calmly. • Systematic desensitization and counter-conditioning to fear-provoking stimuli.

MEDICATIONS

DRUG(S)

• There are no medications licensed for the treatment of canine aggression. Owners must be aware that the use of medication is off-label. • A signed informed consent form is advisable listing potential risks and side effects. • NEVER use medications without concurrent behavior modification. • Before prescribing medication, be sure that owners understand the risks in owning an aggressive dog, will follow safety procedures, and that they understand that medication will not insure safety. • Medication may not be appropriate in all situations (e.g., households with small children, individuals that are immunocompromised or have disabilities). • Studies have not shown a robust effect of drug treatment on aggression. Placebo effect may be strong. • Medications are most likely to be helpful in situations where there is a strong fear/anxiety component, or where one or both dogs are behaviorally abnormal (e.g., reactivity, impulsivity, intensity) as opposed to situations where closely ranked dogs use aggression to establish resource control.

Selective Serotonin Reuptake Inhibitors

• Fluoxetine 0.5–2 mg/kg PO q24h.
• Paroxetine 0.5–1 mg/kg PO q24h.
• Sertraline 1–3 mg/kg PO q24h. • Side effects: sedation, irritability, GIT effects, increased aggression; anorexia is common and usually transient.

Tricyclic Antidepressants

• Clomipramine 1–3 mg/kg PO q12h (caution: label restriction for aggression). • Side effects: sedation, GIT effects, anticholinergic effects, cardiac conduction disturbances if predisposed, and increased aggression.

Alpha-2 agonists

• Clonidine 0.01–0.05 mg/kg PO PRN 1.5–2 hours before eliciting trigger, up to q12h. • Side effects: transient hyperglycemia, anticholinergic, hypotension, collapse, and bradycardia (responsive to atropine), and increased aggression.

Serotonin 2a antagonist/reuptake inhibitors

• Trazodone 2–5 mg/kg PO PRN prior to eliciting trigger, up to q6h—may titrate up to 8–10 mg/kg if no adverse effects. • Side effects: sedation, anorexia, ataxia, GIT effects, cardiac conduction disturbances, increased aggression.

CONTRAINDICATIONS

Use caution as any psychotropic medication may reduce fear-based inhibition resulting in an increase rather than decrease in aggression.

PRECAUTIONS

Any psychotropic medication may increase irritability and aggression. Corticosteroids are contraindicated in food-aggressive dogs; polyphagia can lead to increased frequency/intensity of aggression.

POSSIBLE INTERACTIONS

Do not combine SSRIs, TCAs, MAO inhibitors (e.g., amitraz, selegiline), opioids (e.g., tramadol), and other medications that increase serotonin—can result in potentially fatal serotonin syndrome.

FOLLOW-UP

PATIENT MONITORING

Clients usually need ongoing assistance and should receive at least one follow-up call within the first 1–3 weeks after the consultation. Provisions for further follow-up should be made at that time.

PREVENTION/AVOIDANCE

Treatment recommendations are life-long.

POSSIBLE COMPLICATIONS

Injuries to dogs and humans; euthanasia or relinquishment of patient.

EXPECTED COURSE AND PROGNOSIS

There is no cure. Prognosis for improvement is more favorable if aggression is at a fairly low intensity and occurs in only a few predictable situations. Prognosis is highly dependent on owner compliance. Relationship issues may recur with changes in housing, health or age.

MISCELLANEOUS

ASSOCIATED CONDITIONS

Other fear- or anxiety-based conditions; territorial aggression.

ZOONOTIC POTENTIAL

Human injury and bite wounds when separating fighting dogs.

PREGNANCY/FERTILITY/BREEDING

Do not breed dogs with extreme interdog aggression.

SEE ALSO

• Aggression to Unfamiliar People and Unfamiliar Dogs • Aggression, Food and Resource Guarding—Dogs

ABBREVIATIONS

• CNS = central nervous system • GIT = gastrointestinal tract • MAO = monoamine oxidase • MRI = magnetic resonance imaging • SSRI = selective serotonin reuptake inhibitor • SARI = Serotonin 2a antagonist/reuptake inhibitor • TCA = tricyclic antidepressant

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ALKALOSIS, METABOLIC (TRADITIONAL APPROACH)

BASICS

DEFINITION

A process in the body that leads to an elevation in pH above the reference interval for that species. An elevation in blood pH is specifically termed Alkalemia. Associated with an increase in plasma bicarbonate concentration (HCO_3^-) (dogs, > 24 mEq/L; cats, > 22 mEq/L) and base excess (BE) (> 4 mmol/L) with a compensatory increase in carbon dioxide tension (PCO_2).

PATHOPHYSIOLOGY

• Metabolic alkalosis may develop from either a *gain in bicarbonate* or a *loss in acid.*
∘ *Bicarbonate gain* subsequent to: Contraction alkalosis due to free water deficit; iatrogenic administration of alkalinizing therapy (e.g., Na HCO_3^-); metabolism of organic ions (lactate, citrate, acetate, and ketones); hypokalemia; and renal ammoniagenesis. ∘ *Acid loss* subsequent to: gastric or renal acid loss (loop or thiazide diuretic); mineralocorticoid excess; presence of non-reabsorbable anions; decreased weak acids (hypoalbuminemia and hypophosphatemia). ∘ Renal HCO_3^- excretion is often very efficient in eliminating an excess HCO_3^- load, but is hindered by decreased effective circulating volume; hypokalemia, hypochloremia, and hyperaldosteronism. Metabolic alkalosis persists only if renal excretion of HCO_3^- is impaired. This primarily occurs from continued high rate of alkali administration, or some stimulus for the kidneys to retain sodium in the presence of a relative chloride deficit. • *Hypochloremic (corrected)* metabolic alkalosis results from loss of fluid rich in chloride and H^+ primarily from the alimentary tract or kidneys. Loss of chloride and H^+ is associated with an increase in plasma HCO_3^- concentration. With chloride loss and volume depletion, the kidneys reabsorb sodium with HCO_3^- instead of chloride, perpetuating the metabolic alkalosis. Hypochloremic alkalosis is divided into *chloride-responsive* and *chloride-resistant*.
∘ *Chloride-responsive* results primarily from the loss of chloride rich fluid and is characterized by decreased extracellular fluid volume, hypochloremia, and low urinary chloride levels. This type of alkalosis responds to administration of chloride salt.
∘ *Chloride-resistant* is characterized by excessive mineralocorticoid leading to increased effective circulating volume and is not responsive to chloride salt. • *Hypokalemia* may contribute to metabolic alkalosis by shifting H+ intracellularly; stimulating apical H+/K+ ATPase in the collecting duct; stimulating renal ammoniagenesis; impairing chloride ion reabsorption in the distal nephron; and reducing glomerular filtration rate (GFR) which decreases the filtered load of HCO_3^- and in the presence of volume depletion, impairs renal excretion of the excess HCO_3^-. • *Hypoalbuminemic* alkalosis is due to a decrease in the level of plasma albumin. Plasma albumin is a weak acid.
• *Compensatory* metabolic alkalosis occurs in response to respiratory acidosis. This is associated with a low pH and elevated PCO_2.

SYSTEMS AFFECTED

• Nervous—muscle twitching and seizures occur rarely in dogs. Metabolic alkalosis and associated hypokalemia may precipitate hepatic encephalopathy in patients with liver failure. • Urinary—the kidneys rapidly and effectively excrete excessive alkali. In patients with chloride deficiency (and less importantly, volume depletion), the kidneys cannot excrete the excess alkali. Therefore, metabolic alkalosis is maintained. In these patients, chloride administration is required for renal compensation to occur. Volume expansion will hasten compensation. Patients with mineralocorticoid excess have excessive chloride loss. Therefore, chloride administration does not lead to hyperchloremia and correction of metabolic alkalosis (so-called chloride-resistant metabolic alkalosis). • Respiratory—low $[H^+]$ (elevated pH) reduces alveolar ventilation. Hypoventilation increases PCO_2 and helps offset the effects of high plasma HCO_3^- on pH. In dogs, for each 1 mEq/L increase in plasma HCO_3^- there is an expected increase of approximately 0.7 mmHg in PCO_2. Limited data is available for cats, but the degree of respiratory compensation appears to be similar.

SIGNALMENT

Any breed, age, or sex of dog and cat

SIGNS

Historical Findings

• Administration of loop diuretics (e.g., furosemide) or thiazides • Vomiting

Physical Examination Findings

• Signs related to the underlying disease or accompanying potassium depletion (e.g., weakness, cardiac arrhythmias, ileus, etc.). • Muscle twitching caused by low ionized calcium concentration. • Dehydration in volume-depleted patients. • Muscle twitching and seizures in patients with neurologic involvement (rare).

CAUSES

• *Chloride-responsive*—gastrointestinal losses (e.g., gastric vomiting, nasogastric tube suctioning); renal losses (diuretic therapy); and rapid correction of chronic hypercapnia (respiratory acidosis). • *Chloride-resistant*—hyperadrenocorticism and primary hyperaldosteronism. • *Oral administration of alkalinizing* agents—sodium bicarbonate or other organic anions with sodium (e.g., lactate, acetate, gluconate); administration of cation-exchange resin with non-absorbable alkali (e.g., phosphorus binders).
• *Hypoalbuminemia*—liver disease, protein losing nephropathy or enteropathy, nephrotic syndrome. • *Free water deficit*—diabetes insipidus; water deprivation; post-obstructive diuresis; polyuric renal failure.
• *Hypokalemia*—see Hypokalemia.

RISK FACTORS

• Administration of loop or thiazide diuretics. • Vomiting. • Stomach drainage. • Diseases associated with hypoalbuminemia (e.g., nephrotic syndrome, liver failure).

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

High plasma HCO_3^- and hypochloremia may also occur in animals compensating for chronic respiratory acidosis, in which PCO_2 is high and pH is low despite high HCO_3^- and low chloride concentration; blood gas determination required to differentiate.

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

None

Disorders That May Alter Laboratory Results

• Too much heparin (> 10% of the sample) decreases pH, PCO_2 and HCO_3^-. • Blood samples stored at room temperature for more than 15 minutes have low pH because of increased PCO_2. • Exposure to room air decreases PCO_2. • Venous samples may have pH 0.5–1 unit lower and PCO2 5–10 mmHg higher than an arterial sample.

Valid if Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

• High total CO_2 (total CO_2 in samples handled aerobically closely approximates HCO_3^-). • Low blood ionized calcium concentration. • Serum electrolyte abnormalities vary with underlying cause.
• Hypochloremia—consider hypochloremic metabolic alkalosis, the most common reason for metabolic alkalosis in dogs and cats, which usually results from diuretic administration or vomiting of stomach contents. • High sodium but normal chloride concentration—consider chloride-resistant metabolic alkalosis (e.g., hyperadrenocorticism or primary hyperaldosteronism) or administration of alkali. • Hypoalbuminemia—consider hypoalbuminemic metabolic alkalosis (e.g., liver failure, protein-losing enteropathy, and protein-losing nephropathy). In vitro, a 1 g/dL decrease in albumin concentration is associated with an increase in pH of 0.093 in cats and 0.047 in dogs. • Hypokalemia—

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ALKALOSIS, METABOLIC (TRADITIONAL APPROACH) (CONTINUED)

hypokalemia likely results from intracellular potassium shifting due to metabolic alkalosis or the underlying problem (e.g., vomiting of stomach contents or loop diuretic administration). • Urinary chloride levels—chloride-responsive metabolic alkalosis has urine chloride levels < 10 mEq/L while chloride-resistant metabolic alkalosis involves urine chloride levels of > 20 mEq/L.

OTHER LABORATORY TESTS
Blood gas analysis reveals high HCO_3^-, PCO_2, pH and base excess (BE). Unlike HCO_3^-, BE is independent of changes in and is considered a more reliable measure of metabolic acid-base changes.

IMAGING
None

DIAGNOSTIC PROCEDURES
• Blood pressure—the combination of hypertension, hypernatremia, and hypokalemia with metabolic alkalosis may indicate the presence of hyperaldosteronism. • Diagnostic testing for hyperadrenocorticism or primary hyperaldosteronism (e.g., plasma renin and aldosterone levels).

TREATMENT

• Acid-base disturbances are secondary phenomena. Diagnosis and treatment of the underlying disease process is integral to the successful resolution of acid-base disorders. • Severe alkalemia is uncommon, but may be life-threatening. Patients with chronic respiratory disease and respiratory alkalosis are at risk of developing severe alkalemia if they start vomiting or receive diuretics. • Discontinue drugs that may cause metabolic alkalosis. • *Chloride-responsive*—the fluids of choice contain chloride; give patients with volume depletion an intravenous infusion of balanced, buffered isotonic electrolyte replacement fluid supplemented with KCl; patients with hypokalemia may require large doses of KCl (see Hypokalemia). • *Chloride-resistant* metabolic alkalosis can only be corrected by resolution of the underlying disease; metabolic alkalosis is usually mild in these patients. • If the metabolic alkalosis is associated with hypokalemia and total body potassium deficits, correcting the deficit with KCl is a particularly effective way to reverse the alkalosis.

NURSING CARE
Supportive care to maintain euhydration, euvolemia, adequate nutrition, etc.

MEDICATIONS

DRUG(S) OF CHOICE
Hypochloremic Alkalosis
• If chloride-responsive alkalosis occurs during an edematous state (e.g., congestive heart failure), oral compounds containing chloride without sodium are recommended to correct the alkalosis. If diuresis is needed due to volume overload, a carbonic anhydrase inhibitor (e.g., acetazolamide) or a potassium-sparing diuretic (e.g., spironolactone, amiloride) can be used to correct the alkalosis. • H2-blocking agents such as famotidine reduce gastric acid secretion and may be considered as adjunctive therapy if gastric losses are ongoing.
• Antiemetics may help prevent further gastric acid loss.

Hypoalbuminemic Alkalosis
• Treatment for hypoalbuminemic alkalosis should be directed at the underlying cause and the decreased colloid oncotic pressure.
• Foster enteral nutrition to increase endogenous albumin production.
• Consider species-specific plasma or albumin (canine albumin) therapy.

CONTRAINDICATIONS
• Avoid chloride-free fluids—they may correct volume depletion but will not correct hypochloremic alkalosis. • Avoid using salts of potassium without chloride (e.g., potassium phosphate)—potassium will be excreted in the urine and will correct neither the alkalosis nor the potassium deficit.

PRECAUTIONS
Do not use distal blocking agents (e.g., spironolactone) in volume-depleted patients.

POSSIBLE INTERACTIONS
None

ALTERNATIVE DRUG(S)
None

FOLLOW-UP

PATIENT MONITORING
Acid-base status—frequency dictated by the underlying disease and patient response to treatment.

POSSIBLE COMPLICATIONS
• Hypokalemia • Neurologic signs

MISCELLANEOUS

ASSOCIATED CONDITIONS
• Hypokalemia • Hypochloremia

AGE-RELATED FACTORS
None

PREGNANCY/FERTILITY/BREEDING
N/A

SYNONYMS
• Non-respiratory alkalosis.
• Chloride-responsive metabolic alkalosis—metabolic alkalosis that responds to chloride administration. • Chloride-resistant alkalosis—metabolic alkalosis secondary to increased mineralocorticoid activity that does not respond to chloride administration.
• Hypochloremic alkalosis—metabolic alkalosis caused by low chloride concentration. • Hypoalbuminemic alkalosis—metabolic alkalosis caused by low albumin concentration. • Concentration alkalosis—metabolic alkalosis resulting from decreased free water in plasma. • Contraction alkalosis—metabolic alkalosis formerly attributed to volume contraction, but now known to be caused by chloride depletion. Volume depletion is a common but not essential feature.

SEE ALSO
• Hypochloremia • Hypokalemia

ABBREVIATIONS
• BE = base excess • H^+ = hydrogen ion • HCO_3^- = bicarbonate • PCO_2 = carbon dioxide tension

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ALOPECIA—CATS

BASICS

DEFINITION
• Common problem • Pattern of hair loss—varied or symmetrical • Causes—multifactorial

PATHOPHYSIOLOGY
Specific and unique for each cause

SYSTEMS AFFECTED
• Endocrine/Metabolic • Hemic/Lymphatic/Immune • Skin/Exocrine

SIGNALMENT
• No specific age, breed, or sex predilection.
• Neoplastic and paraneoplastic associated alopecias—generally recognized in older cats.

SIGNS
Depends on specific diagnosis

CAUSES
• Neurologic/behavioral—compulsive disorder. • Endocrine—sex hormone alopecia, hyperthyroidism, hyperadrenocorticism, diabetes mellitus. • Immunologic—allergic dermatitis, alopecia areata, alopecia mucinosa, lymphocytic mural folliculitis, pseudopelade.
• Parasitic—demodicosis, cheyletiellosis.
• Infections—dermatophytosis.
• Physiologic/metabolic—sebaceous adenitis.
• Neoplastic—paraneoplastic dermatitis, squamous cell carcinoma in situ, epitheliotropic lymphoma, thymoma with exfoliative dermatitis. • Idiopathic/inherited—alopecia universalis, hypotrichosis, spontaneous pinnal alopecia, anagen and telogen defluxion. • Injection site reaction.
• Medication effect—corticosteroids.
• Viral—FeLV- and FIV-associated disease (giant cell dermatosis).

RISK FACTORS
FeLV/FIV—reported risk for demodicosis (not all cases associated with viral infection).

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Endocrine Alopecia/Sex Hormone
• Non-inflammatory alopecias are rarely hormonal in etiology; search for other causes before exploring endocrine etiology.
• Hormonal causes—primarily castrated males; alopecia along the caudal aspect of the hind limbs, which may extend along the perineum. • Excessive corticosteroid administration; may also cause curling of pinnal tips. • Megestrol acetate—may produce lesions similar to/associated with diabetes mellitus or hyperadrenocorticism.

Compulsive Disorder
• Uncommon as sole source of symptoms.
• Often misdiagnosed in cases of allergic dermatitis. • Often misdiagnosed as endocrine alopecia. • The pattern of alopecia is frequently symmetrical without associated inflammation.

Allergic Dermatitis
• Varies from mild partial alopecia with little inflammation to severe excoriation and ulceration. • Barbering of the hair coat often occurs clandestinely leading to a misdiagnosis of endocrine alopecia. • Distribution—varied; often the head and neck or ventral abdominal regions are most affected. • Food allergy, atopic dermatitis, contact allergy, and ectoparasite hypersensitivity.

Hyperthyroidism
• Partial to complete alopecia from self-barbering. • Varied pattern. • Middle-aged to old cats. • Often misdiagnosed in cases of allergic dermatoses, compulsive disorder, or other endocrine alopecia.

Diabetes Mellitus
• Partial alopecia with an unkempt or greasy hair coat and excessive scaling. • Poor wound healing. • Increased susceptibility to infections. • Rarely, cutaneous xanthomatosis secondary to hyperlipidemia (nodular to linear, yellow-pink alopecic plaques that tend to ulcerate).

Hyperadrenocorticism
• Rare; characterized by alopecia and extreme fragility of the skin. • Truncal alopecia, with or without a rattail and curling of the pinnal tips. • Extreme skin fragility noted in approximately 70% of cases. • Occurs secondary to pituitary or adrenal tumors.
• Iatrogenic form less common in cats than in dogs; associated with frequent repositol corticosteroid injections.

Paraneoplastic Alopecia
• Most cases associated with pancreatic exocrine adenocarcinomas, bile duct carcinomas, or exfoliative dermatitis with thymoma. • Middle-aged to old cats (9–16 years). • Pancreatic carcinoma/bile duct carcinoma: acute onset, progress rapidly, bilaterally symmetrical, ventrally distributed (also located along the bridge of the nose and periocular), hair epilates easily, rare pruritus, erythema with dry fissuring footpads, glistening appearance to alopecic skin, skin is often thin and hypotonic, rapid weight loss.
• Thymoma with exfoliative dermatitis: non-pruritic scaling dermatitis that starts on the head and neck. Brown waxy deposits accumulate around the eyes and nasal region. Surgical removal of the thymoma will cause resolution of the dermatitis within a few months (typically 4–5 months).

Sebaceous Adenitis
• Slowly progressive partial alopecia associated with scaling along the dorsum of the body and the extremities. • Sebaceous glands are, theoretically, selectively destroyed by toxic intermediate metabolites or immunologic mechanisms. • Possible dramatic pigment accumulation along the eyelid margins. • Questionable association with systemic disease or stressful event (e.g., inflammatory bowel disease, lupus-like syndromes, upper respiratory tract infections).

Squamous Cell Carcinoma In Situ
• Multicentric premalignant dermatosis in old cats. • Associated with papilloma virus; Bowenoid *in situ* carcinoma. • Slightly elevated, often pigmented, plaque-like or papillated lesions with scaling and partially alopecic surfaces. • Often misdiagnosed as seborrhea before distinct lesions develop.
• About 25% may convert to squamous cell carcinoma *in situ* lesions along the borders (histologically).

Epitheliotropic Lymphoma
• Early stages—varying degrees of alopecia associated with scaling and erythema. • Later stages—plaques and nodules. • Old cats.

Alopecia Areata/Pseudopelade/Lymphocytic Mural Folliculitis (Lymphocytic Invasion of the Hair Follicle)
• Often associated with an immunologic inciting cause; may occasionally be pre-neoplastic. • Alopecia areata—rare; complete alopecia in a patchy distribution with no inflammation; head, neck, ears; histologic lymphocytic accumulation around the hair bulb. • Lymphocytic mucinotic mural folliculitis—diffuse alopecia of the face, eyelids, muzzle; skin has a thick waxy feel; histologic lymphocytic invasion of the follicular outer root sheath and epidermis.
• Pseudopelade—well-circumscribed non-pruritic alopecia that often starts on the face; nails may slough; lymphocytic invasion of the isthmus region of the hair follicle.

Feline Cutaneous Lymphocytosis (Pseudolymphoma)
• Characterized by dermal lymphocytic infiltrate rather than follicular or epidermal.
• Older cats; often solitary lesions of partial alopecia with scaling ± erythema and pruritus.

Alopecia Universalis (Sphynx Cat)
• Hereditary. • Complete absence of primary hairs; decreased secondary hairs. • Thickened epidermis; normal dermis. • Sebaceous and apocrine ducts open directly onto the skin surface; oily feel to skin. • Wrinkled foreheads; gold eyes; no whiskers; downy fur on paws, tip of tail, and scrotum.
• Comedones with or without secondary folliculitis.

Feline Hypotrichosis
• Siamese and Devon Rex cats (autosomal recessive alopecia). • Poorly developed primary telogen hair follicles. • Born with a normal coat; becomes thin and sparse as young adult.

A

ALOPECIA—CATS (CONTINUED)

Spontaneous Pinnal Alopecia
• Siamese cats predisposed. • May represent a form of alopecia areata or pattern baldness.

Anagen and Telogen Defluxion
• Acute loss of hair due to interference with the growth cycle. • Causes—stress, infection, endocrine disorder, metabolic disorder, fever, surgery, anesthesia, pregnancy, drug therapy.

Demodicosis
• Rare. • Partial to complete multifocal alopecia of the eyelids, periocular region, head, and neck; can generalize. • Variable pruritus with erythema, scale, and crust, and ceruminous otitis externa. • *Demodex cati* (elongated shape) often associated with metabolic disease (e.g., FIV, systemic lupus erythematosus, diabetes mellitus).
• Short/blunted *D. gatoi* mite is rarely a marker for metabolic disease; this form may be transferable from cat to cat and has been associated with pruritus most often affecting the lateral thorax and abdomen.

Cheyletiellosis
• Variable pruritus with scaling. • Not all animals in the household may be affected.

Dermatophytosis
Numerous clinical manifestations; always associated with alopecia.

CBC/BIOCHEMISTRY/URINALYSIS
Abnormalities may be noted with diabetes mellitus, hyperadrenocorticism, and hyperthyroidism.

OTHER LABORATORY TESTS
• FeLV and FIV—risk factors for demodicosis. • Thyroid hormones—document hyperthyroidism. • ANA titer—look for systemic lupus erythematosus.
• ACTH-response test, LDDST, and HDDST—diagnose hyperadrenocorticism.

IMAGING
• Abdominal ultrasound—assess adrenals in hyperadrenocorticism and look for neoplasia in animals with paraneoplastic syndrome.
• Chest radiographs/ultrasound to rule out thymoma. • CT scan—look for pituitary or other neoplasia tumors in animals with hyperadrenocorticism.

DIAGNOSTIC PROCEDURES
• Skin biopsy • Skin scrapes • Dermatophyte culture • Shirts/collar to prove self-trauma
• Food elimination trials • Intradermal allergy test

TREATMENT
• Therapy is specific for many of these disorders. • Behavioral modification or protecting hair coat with a shirt may prevent self-barbering. • Removal of an offending dietary item may alleviate the symptoms of food allergy. • If the pet is compliant, shampoo and topical therapy may relieve secondary problems, such as hyperkeratosis in sebaceous adenitis, crusting in demodicosis, secondary bacterial infection, and malodor for greasy dermatoses.

MEDICATIONS
DRUG(S)
• Compulsive disorder—amitriptyline (10 mg/cat/day) as well as other behavior-modifying medications, such as gabapentin (5–10 mg/kg PO q12h).
• Endocrine alopecia (males)—testosterone supplementation.
• Allergic dermatitis—antihistamines, restricted-ingredient diet, corticosteroids, cyclosporine (7.3 mg/kg/day initially), allergen-specific immunotherapy, ectoparasite control.
• Hyperthyroidism—methimazole (tapazole) or radioactive iodine therapy.
• Diabetes mellitus—regulation of glucose levels (insulin).
• Hyperadrenocorticism—surgery; no known effective medical therapy.
• Paraneoplastic alopecia—no therapy or surgical excision of neoplasia; often fatal.
• Epitheliotropic lymphoma—retinoids (isotretinoin), corticosteroids, interferon, cyclosporine, lomustine.
• Sebaceous adenitis—retinoids, corticosteroids, cyclosporine.
• Squamous cell carcinoma in situ—surgical excision, retinoids (topical and oral), topical imiquimod cream.
• Alopecia areata—no therapy; possibly counterirritants.
• Demodicosis—lime sulfur dips at weekly intervals for four to six dips.
• Cheyletiellosis—topical parasiticides and environmental control.
• Dermatophytosis—griseofulvin (caution: idiosyncratic toxicity), itraconazole (hepatic toxicity, vasculitis), terbinafine.

PRECAUTIONS
Toxicity with griseofulvin and itraconazole (see Dermatophytosis).

POSSIBLE INTERACTIONS
N/A

ALTERNATIVE DRUG(S)
N/A

FOLLOW-UP
PATIENT MONITORING
Determined by specific diagnosis

PREVENTION/AVOIDANCE
Determined by specific diagnosis

POSSIBLE COMPLICATIONS
Determined by specific diagnosis

EXPECTED COURSE AND PROGNOSIS
Determined by specific diagnosis

MISCELLANEOUS
ZOONOTIC POTENTIAL
• Dermatophytosis—can cause skin lesions in humans. • Cheyletiellosis—can cause irritation in humans.

PREGNANCY/FERTILITY/BREEDING
Retinoids and griseofulvin should not be administered to pregnant animals.

SEE ALSO
• Cheyletiellosis • Demodicosis • Dermatophytosis • Diabetes Mellitus without Complication, Cats • Feline Paraneoplastic Alopecia • Hyperthyroidism • Sebaceous Adenitis, Granulomatous

ABBREVIATIONS
• ACTH = adrenocorticotropic hormone • ANA = antinuclear antibody • CT = computed tomography • FeLV = feline leukemia virus • FIV = feline immunodeficiency virus • HDDST = high-dose dexamethasone-suppression test • LDDST = low-dose dexamethasone-suppression test

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Author Karen Helton Rhodes
Consulting Editor Alexander H. Werner

Client Education Handout available online

ALOPECIA—DOGS

BASICS

DEFINITION
• Common disorder.
• Characterized by a complete or partial loss of hair in areas where it is normally present.
• May be associated with multiple causes, be the primary problem, or be secondary to an underlying cause.

PATHOPHYSIOLOGY
• Multiple causes.
• Represents removal of hair or disruption in the growth of the hair from hypersensitivity, infection, trauma, immunologic attack, mechanical "plugging," endocrine abnormalities, neoplasia, drug reaction and/or blockage of the receptor sites for stimulation of the hair growth cycle.

SYSTEMS AFFECTED
• Endocrine/Metabolic
• Hemic/Lymphatic/Immune
• Skin/Exocrine

SIGNALMENT
Breed predilection listed below

SIGNS
• May be acute in onset or slowly progressive.
• Multifocal patches of circular alopecia—most frequently associated with folliculitis from bacterial infection and multifocal areas of demodicosis.
• Large, more diffuse areas of alopecia—may indicate a follicular dysplasia or metabolic component.
• The pattern and degree of hair loss are important for establishing a differential diagnosis.

CAUSES

Multifocal
• Localized demodicosis—partial to complete alopecia with erythema comedones, and mild scaling; lesions may become inflamed and crusted.
• Dermatophytosis—partial to complete alopecia with scaling; with or without erythema; not always ring-like.
• Staphylococcal folliculitis—circular patterns of alopecia with epidermal collarettes, erythema, crusting, and hyperpigmented macules.
• Injection reactions—inflammation with alopecia and/or cutaneous atrophy from scarring.
• Rabies vaccine vasculitis—well-demarcated patch of alopecia observed 2–3 months post-vaccination.
• Localized scleroderma—well-demarcated, shiny, smooth, alopecic, thickened plaque; extremely rare; still considered a controversial diagnosis.
• Alopecia areata—non-inflammatory areas of complete alopecia.
• Sebaceous adenitis of short-coated breeds (now termed "idiopathic periadnexal pyogranulomatous dermatitis")—annular to polycyclic areas of alopecia and scaling.

Symmetrical
• Hyperadrenocorticism—truncal alopecia associated with atrophic skin, comedones, and pyoderma.
• Hypothyroidism—thinning of truncal haircoat; generalized alopecia is an uncommon presentation; alopecic "rat" tail.
• Non-inflammatory alopecia (alopecia X)—symmetrical truncal alopecia associated with hyperpigmentation; alopecia often starts along the collar area of the neck; Pomeranian, chow chow, Akita, Samoyed, Keeshonden, Alaskan malamute, and Siberian husky.
• Hyperestrogenism (females)—symmetrical alopecia of the flanks and perineal and inguinal regions with enlarged vulva and mammary glands; may also be associated with exogenous hormone exposure.
• Hypogonadism in intact females—perineal, flank, and truncal alopecia.
• Testosterone-responsive dermatosis in castrated males—slowly progressive truncal alopecia.
• Male feminization from Sertoli cell tumor—alopecia of the perineum and genital region with gynecomastia.
• Castration-responsive dermatosis—hair loss in the collar area, rump, perineum, and flanks.
• Estrogen-responsive dermatosis in spayed female dogs—alopecia of the perineum and genital regions.
• Seasonal/cyclic/canine flank alopecia—serpiginous flank alopecia with hyperpigmentation; boxer, English bulldog, Airedale terrier.

Patchy to Diffuse
• Demodicosis—often associated with erythema, folliculitis, and hyperpigmentation.
• Bacterial folliculitis—multifocal areas of circular alopecia to coalescing large patches of hair loss; epidermal collarettes.
• Dermatophytosis—often accompanied by scale, erythema, and hyperpigmentation.
• Sebaceous adenitis—alopecia with a thick adherent scale; predominantly on the dorsum of the body, including the head and extremities.
• Color mutant/dilution alopecia—brittle or coarse hair, thinning of the blue or fawn colored hair coat, and secondary folliculitis.
• Follicular dysplasia—slowly progressive alopecia.
• Anagen defluxion and telogen defluxion—acute onset of alopecia.
• Hypothyroidism—diffuse thinning of the hair coat.
• Hyperadrenocorticism—truncal alopecia with thin skin and formation of comedones.
• Epitheliotropic lymphoma—diffuse, generalized truncal alopecia with scaling and intense erythema, later nodule and plaque formation.
• Pemphigus foliaceus—hair loss associated with scale and crust formation.
• Keratinization disorders—alopecia associated with excessive scale and greasy surface texture.

Specific Locations
• Pinnal alopecia/pattern baldness—miniaturization of hairs and progressive alopecia; dachshund, greyhound, American water spaniel, Portuguese water spaniel, Boston terrier, Manchester terrier, whippet, Italian greyhound, Chihuahua.
• Traction alopecia—hair loss on the top and lateral aspect of the cranium secondary to having barrettes or rubber bands applied to the hair.
• Post-clipping alopecia—failure to regrow after clipping; may be associated with hair growth cycle disruption.
• Melanoderma (alopecia of Yorkshire terriers)—symmetrical alopecia of the pinnae, bridge of the nose, tail, and feet.
• Seasonal/cyclic/canine flank alopecia—serpiginous flank alopecia with hyperpigmentation; boxer, English bulldog, Airedale terrier.
• Black hair follicular dysplasia—alopecia of the black-haired areas only.
• Dermatomyositis—alopecia of the face, tip of ears, tail, and digits; associated with scale crusting and scarring.

Breed-Related Alopecia
• Alopecic breeds: Chinese crested, Mexican hairless, Inca hairless, Peruvian Inca Orchid, American hairless terrier (often associated with comedones, folliculitis, and furunculosis).
• Congenital hypotrichosis: cocker spaniel, Belgian shepherd, poodle, whippet, beagle, French bulldog, Yorkshire terrier, Labrador retriever, bichon frise, Lhasa apso, basset hound.
• Color dilution alopecia: blue or fawn Doberman pinscher, silver Labrador, cream chow chow, blond Irish setter, blue pit bull terrier, other breeds with dilute coat colors.
• Melanoderma with alopecia in Yorkshire terrier.
• Seasonal/cyclic/canine flank alopecia—serpiginous flank alopecia with hyperpigmentation; boxer, English bulldog, Airedale terrier.
• Pinnal alopecia/pattern baldness—miniaturization of hairs and progressive alopecia; dachshund, greyhound, American water spaniel, Portuguese water spaniel, Boston terrier, Manchester terrier, whippet, Italian greyhound, Chihuahua.
• Non-inflammatory alopecia (alopecia X)—symmetrical truncal alopecia associated with hyperpigmentation; alopecia often starts along the collar area of the neck; Pomeranian, chow chow, Akita, Samoyed, Keeshonden, Alaskan malamute, and Siberian husky.

ALOPECIA—DOGS (CONTINUED)

RISK FACTORS
N/A

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
- Pattern and degree—important features for formulating a differential diagnosis.
- Inflammation, scale, crust, and epidermal collarettes—important for determining diagnosis.

CBC/BIOCHEMISTRY/URINALYSIS
Rule out metabolic causes such as hyperadrenocorticism

OTHER LABORATORY TESTS
- Thyroid testing—diagnose hypothyroidism.
- ACTH-response test, LDDST, and HDDST—evaluate for hyperadrenocorticism.
- Sex hormone profiles (questionable validity).

IMAGING
Ultrasonography—evaluate adrenal glands for evidence of hyperadrenocorticism.

DIAGNOSTIC PROCEDURES
- Response to therapy as a trial
- Fungal culture
- Skin scraping
- Cytology
- Skin biopsy—very useful to evaluate status of follicle/hair growth as well as epidermal changes associated with specific conditions.

TREATMENT
- Demodicosis—amitraz, ivermectin, milbemycin.
- Dermatophytosis—griseofulvin, ketoconazole, itraconazole, lime sulfur dips, terbinafine.
- Staphylococcal folliculitis—shampoo and antibiotic therapy.
- Sebaceous adenitis—keratolytic shampoo, essential fatty acid supplementation, retinoids, cyclosporine.
- Keratinization disorders—shampoos, retinoids, vitamin D, cyclosporine.
- Endocrine—ovariohysterectomy, castration, Lysodren, trilostane, adrenalectomy.

MEDICATIONS

DRUG(S) OF CHOICE
Varies with specific cause; see "Treatment."

CONTRAINDICATIONS
N/A

PRECAUTIONS
Toxicity with griseofulvin, retinoids, ivermectin, trilostane, lysodren, cyclosporine.

POSSIBLE INTERACTIONS
None

ALTERNATIVE DRUG(S)
None

FOLLOW-UP

PATIENT MONITORING
Determined by cause

POSSIBLE COMPLICATIONS
N/A

MISCELLANEOUS

ASSOCIATED CONDITIONS
N/A

AGE-RELATED FACTORS
N/A

ZOONOTIC POTENTIAL
Dermatophytosis can cause skin lesions in people.

PREGNANCY/FERTILITY/BREEDING
Avoid retinoids and griseofulvin in pregnant animals.

SEE ALSO
- Alopecia, Non-inflammatory—Dogs
- Demodicosis
- Dermatomyositis
- Dermatophytosis
- Hyperadrenocorticism (Cushing's Syndrome)—Dogs
- Hypothyroidism
- Pemphigus
- Sebaceous Adenitis, Granulomatous
- Sertoli Cell Tumor

ABBREVIATIONS
- ACTH = adrenocorticotropic hormone
- HDDST = high-dose dexamethasone-suppression test
- LDDST = low-dose dexamethasone-suppression test

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Client Education Handout available online

ALOPECIA, NON-INFLAMMATORY—DOGS

BASICS

DEFINITION
• Uncommon alopecic disorders that are associated with abnormal hair follicle cycling.
• Both endocrine and non-endocrine diseases can be associated with alopecia.
• Definitive diagnosis often requires ruling out the more common endocrine alopecias.
• Alopecia X has also been called growth hormone-responsive alopecia, castration-responsive alopecia, adrenal hyperplasia-like syndrome, among others.

PATHOPHYSIOLOGY
• There are many factors that affect the hair cycle, both hormonal and non-hormonal.
• Increased sex hormones can affect the hair cycle. Estrogen is a known inhibitor of anagen, the growth phase of the hair follicle.
• The mechanism by which alopecia X influences the hair cycle is not known.
• Exposure to human exogenous hormone replacement therapy.

SYSTEMS AFFECTED
• Behavioral
• Endocrine/Metabolic
• Hemic/Lymphatic/Immune
• Skin/Exocrine

GENETICS
Breed predispositions exist for alopecia X; however, the mode of inheritance is unknown.

INCIDENCE/PREVALENCE
• Hyperestrogenism and hyperandrogenism are uncommon to rare causes of alopecia.
• Alopecia X is relatively common in predisposed breeds.

GEOGRAPHIC DISTRIBUTION
None

SIGNALMENT
Species
Dogs

Breed Predilections
• Hyperestrogenism and hyperandrogenism—no breed predilections.
• Alopecia X—miniature poodle and plush-coated breeds such as Pomeranian, chow chow, Akita, Samoyed, Keeshonden, Alaskan malamute, and Siberian husky.

Mean Age and Range
• Hyperestrogenism and hyperandrogenism—middle-aged to old intact dogs.
• Alopecia X—1–5 years of age; however, older dogs may develop the condition.

Predominant Sex
• Hyperandrogenism, primarily intact males.
• Hyperestrogenism, primarily intact females or males.
• Alopecia X, neutered or intact dogs of either sex.

SIGNS
Historical Findings
• Overall change in the hair coat—dry or bleached because the hairs are not being replaced; lack of normal shed.
• Males with hyperestrogenism may attract other male dogs.

Physical Examination Findings
• Alopecia—usually diffuse and bilaterally symmetrical truncal alopecia sparing the head and distal extremities. Uncommon with hyperandrogenism.
• Hair coat—may be dry or bleached.
• Secondary seborrhea, pruritus, pyoderma, comedones, ceruminous otitis externa, and hyperpigmentation—variable.
• Enlargement of nipples, mammary glands, vulva, prepuce—may be associated with hyperestrogenism.
• Macular melanosis and linear preputial dermatitis—may be associated with hyperestrogenism.
• Abnormal-sized or different-sized testicles—may be associated with hyperestrogenism or hyperandrogenism.
• Testicles may also appear normal in size.
• Tail gland hyperplasia and perianal gland hyperplasia—usually associated with hyperandrogenism.
• Systemic signs (PU/PD/polyphagia) are usually NOT present.

CAUSES
Hyperestrogenism—Females
• Estrogen excess associated with cystic ovaries, ovarian tumors (rare), or exogenous estrogen supplementation.
• Animals with normal serum estrogen concentrations may have increased numbers of estrogen receptors in the skin (undocumented).

Hyperestrogenism—Males
• Estrogen excess due to Sertoli cell tumor (most common), seminoma, or interstitial cell tumor (rare).
• Associated with male pseudohermaphrodism in miniature schnauzers.

Hyperandrogenism—Males
Androgen-producing testicular tumors (especially interstitial cell tumors).

Alopecia X
Hairs fail to cycle but an underlying endocrine cause has not been identified.

RISK FACTORS
• Intact male and female dogs are at increased risk for developing testicular tumors and ovarian cysts/tumors, respectively.
• Cryptorchid males are at increased risk for developing testicular tumors.
• Exogenous estrogen supplementation.
• Exposure to human exogenous hormone replacement therapy.
• There are no known risk factors for alopecia X other than breed predisposition.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Inflammatory causes of alopecia (pyoderma, demodicosis, and dermatophytosis)—should be ruled out; these diseases usually cause a patchy rather than diffuse pattern of alopecia.
• Sebaceous adenitis – inflammatory cause of alopecia that may affect specific breeds (Samoyed, Akita).
• Hypothyroidism and hyperadrenocorticism—critical to rule out as these diseases may cause a very similar pattern of diffuse alopecia associated with lack of hair follicle cycling.
• Follicular dysplasias including color-dilution alopecia and black hair follicular dysplasia—alopecia should be color-restricted.
• Patterned alopecia of various breeds (dachshund, Boston terrier, greyhound, water spaniel, and others)—breed-specific alopecias of unknown cause.
• Seasonal/cyclic/canine flank alopecia—alopecia of the flank and dorsum, often serpiginous patterns with hyperpigmentation, more often in short-coated breeds (boxer, English bulldog, Airedale) and may recur seasonally.
• Post-clipping alopecia—hair fails to regrow following clipping; however, hair regrowth occurs within a year.
• Telogen defluxion—alopecia occurs 1–2 months following an illness or severe stressful episode and is usually more sudden in onset with relative ease of epilation.

CBC/BIOCHEMISTRY/URINALYSIS
• Usually unremarkable.
• Anemia and/or bone marrow hypoplasia or aplasia can be associated with hyperestrogenism.

OTHER LABORATORY TESTS
• Serum sex hormone concentrations—often normal, treat according to suspected diagnosis based on clinical signs and ruling out other disorders.
• Serum estradiol concentrations—sometimes elevated in male dogs with testicular tumors or female dogs with cystic ovaries; however, normal fluctuation of estradiol occurs throughout the day, making interpretation of estradiol concentrations difficult.

IMAGING
Radiography, ultrasonography, and laparoscopy—identify cystic ovaries, ovarian tumors, testicular tumors (scrotal or abdominal), adrenal tumors, sublumbar lymphadenopathy, and possible thoracic metastases of malignant tumors.

DIAGNOSTIC PROCEDURES
• Preputial cytology—may demonstrate cornification of cells in males with hyperestrogenism (similar to a bitch in estrus).
• Skin biopsy.

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ALOPECIA, NON-INFLAMMATORY—DOGS (CONTINUED)

PATHOLOGIC FINDINGS
Histologic changes associated with endocrine dermatoses (telogen hairs, follicular keratoses, hyperkeratosis, excess trichilemmal keratinization [flame follicles], thin epidermis and thin dermis) may also be seen with non-inflammatory alopecias including hyperestrogenism and alopecia X. Histopathology will help rule out inflammatory causes of alopecia (pyoderma, demodicosis, dermatophytosis, sebaceous adenitis) and some of the other differentials listed above.

TREATMENT

APPROPRIATE HEALTH CARE
N/A

NURSING CARE
N/A

ACTIVITY
None

DIET
None

CLIENT EDUCATION
Alopecia X is a cosmetic condition resulting in coat loss only and there is no definitive cure for the hair loss. The risk of treatment should be emphasized. Hair regrowth will only occur in a portion of dogs regardless of treatment chosen and hair loss may recur months to years later in spite of continued treatment.

SURGICAL CONSIDERATIONS
Hyperestrogenism/Hyperandrogenism
• Castration—scrotal testicular tumors.
• Exploratory laparotomy—diagnosis and surgical removal (ovariohysterectomy and castration) for ovarian cysts and tumors and abdominal testicular tumors.

Alopecia X
Neuter intact animals—a certain number will regrow hair following neutering. Hair regrowth can take up to 3 months to become evident.

MEDICATIONS

DRUG(S) OF CHOICE
General Treatments
• Topical antiseborrheic shampoos—for comedones and seborrhea associated with alopecia.
• Antibiotics and topical antimicrobial shampoos—for secondary skin infections associated with alopecia.

Alopecia X
• Melatonin—3 mg q12h for small breeds and 6–12 mg q12h for large breeds; hair regrowth can take up to 3 months to become evident. This treatment works in approximately 40% of cases. Because this treatment is the most benign, it is considered the treatment of choice following neutering. Once hair regrowth has occurred, discontinue treatment.
• Medroxyprogesterone acetate – 5–10 mg/kg SC q4 weeks for 4 treatments. Hair regrowth can take up to 6 months. This treatment works in approximately 40–50% of cases.

CONTRAINDICATIONS
None

PRECAUTIONS
• Melatonin at high doses can cause insulin resistance; therefore, use caution in treating dogs with diabetes mellitus.
• Medroxyprogesterone acetate can cause mammary nodules and cystic endometrial hyperplasia with long term use. Diabetes mellitus has been reported in a few dogs.

POSSIBLE INTERACTIONS
None

ALTERNATIVE DRUG(S)
• Mitotane—15–25 mg/kg—once daily as induction for 5–7 days, followed by twice weekly maintenance; hair regrowth occurs in a portion of dogs treated and can take up to 3 months to become evident. Use of this drug can result in an Addisonian crisis and other side effects as for treatment of Cushing's syndrome. Electrolytes and cortisol with ACTH stimulation testing should be monitored regularly.
• Trilostane—dosages as described for treatment of Cushing's syndrome; hair regrowth occurs in a portion of dogs treated and can take up to 3 months to become evident. Use of this drug can result in an Addisonian crisis and other side effects as for treatment of Cushing's syndrome. Electrolytes and cortisol with ACTH stimulation testing should be monitored regularly.
• Growth hormone administration and methyltestosterone may result in hair regrowth. Growth hormone can cause diabetes mellitus. Methyltestosterone can result in increased aggression, cholangiohepatitis, and seborrhea oleosa. Therefore, these drugs are not recommended.

FOLLOW-UP

PATIENT MONITORING
• Medroxyprogesterone acetate—complete physical examination and chemistry panel regularly.
• Mitotane—electrolytes and cortisol with ACTH stimulation testing regularly.
• Trilostane—electrolytes and cortisol with ACTH stimulation testing regularly.

PREVENTION/AVOIDANCE
None

POSSIBLE COMPLICATIONS
None

EXPECTED COURSE AND PROGNOSIS
• Female hyperestrogenism—improvement should occur within 3–6 months after ovariohysterectomy.
• Estrogen- and androgen-secreting tumors—resolution of signs should occur within 3–6 months after castration.
• Alopecia X—hair regrowth will only occur in a portion of dogs regardless of treatment chosen and hair loss may recur in spite of continued treatment. Therefore, if hair regrowth occurs, discontinue treatment to preserve treatment for future recurrence of the alopecia. Risk of treatment should be weighed with the fact that this is a cosmetic disease.

MISCELLANEOUS

ASSOCIATED CONDITIONS
• Pyoderma, seborrhea, comedones may be associated with the alopecia.
• Behavioral changes associated with hyperestrogenism or hyperandrogenism.

AGE-RELATED FACTORS
None

ZOONOTIC POTENTIAL
None

PREGNANCY/FERTILITY/BREEDING
N/A—neutering is usually recommended for managing these conditions.

SYNONYMS
Alopecia X—growth hormone-responsive alopecia, castration-responsive alopecia, adrenal hyperplasia-like syndrome, among others.

ABBREVIATIONS
• ACTH = adrenocorticotropic hormone
• PU/PD = polyuria/polydipsia

INTERNET RESOURCES
http://www.vet.utk.edu/hairloss/

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Author Linda A. Frank
Consulting Editor Alexander H. Werner

Client Education Handout available online

AMEBIASIS

BASICS

OVERVIEW

• Facultative parasitic amoeba that infects people and non-human primates, including dogs and cats. • Found primarily in tropical areas throughout the world, including North America.

SIGNALMENT

• Dog and cat. • Mainly young and/or immunosuppressed animals are infected.

SIGNS

Dogs

• *Entamoeba histolytica* infections are usually asymptomatic. • Severe infections—result in ulcerative colitis to cause dysentery (may be fatal). • Hematogenous spread—results in failure states of the organs (invariably fatal). • Granulomatous amoebic meningoencephalitis (caused by *Acanthamoeba* spp.)—causes signs similar to distemper (anorexia, fever, lethargy, oculonasal discharge, respiratory distress, and diffuse neurologic abnormalities). • Syndrome of inappropriate secretion of antidiuretic hormone has been reported in a young dog with acanthamoebisis causing granulomatous meningoencephalitis with invasion of the hypothalamus.

Cats

• Colitis—causing chronic intractable diarrhea (as per dogs). • Systemic amebiasis or *Acanthamoeba*—not reported in cats.

CAUSES & RISK FACTORS

• *Entamoeba histolytica*—infection occurs by ingesting cysts from human feces. • Encystment of trophozoites seldom occurs in dogs or cats so they are not a source of infection. • One of the few organisms transmitted from man to pets but rarely from pets to man. • Trophozoites (the pathogenic stage)—inhabit the colonic lumen as commensals or invade the colonic wall but can disseminate to other organs (rare) including lungs, liver, brain, and skin. • Trophozoites damage intestinal epithelial cells by secreting enzymes that lyse cells and disrupt intercellular connections. • Certain bacteria and a diet deficient in protein increase the virulence of the amoeba. • The host's immune response to invasion exacerbates pathology. • Colonic ulceration results when trophozoites in the submucosa undermine the mucosa. • *Acanthamoeba castellani* and *A. culbertsoni*—free-living species found in freshwater, saltwater, soil, and sewage; can infect dogs. • *Acanthamoeba* spp.—infection thought to be by inhalation of organisms from contaminated water or colonization of the skin or cornea; hematogenous spread or direct spread from the nasal cavity through the cribiform plate to the central nervous system may occur, resulting in a granulomatous amoebic meningoencephalitis.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Dogs

• Causes of bloody diarrhea or tenesmus, including constipation; food intolerance/allergy; parasitism (whip worms, leishmaniasis, balantidiasis); HGE; foreign body; irritable bowel syndrome; inflammatory bowel disease; diverticula; infectious (parvovirus, clostridial enteritis, bacterial overgrowth and other bacterial causes, fungal such as histoplasmosis or blastomycosis); neoplasia; ulcerative colitis; endocrinopathy (Addison's disease); toxic (lead, fungal, or plant); occasionally major organ disease causing colonic ulceration such as renal failure. • Other causes of diffuse neurologic disease in young animals, including infectious (distemper, fungal such as *Cryptococcus*, *Blastomyces*, *Histoplasma*, bacteria, protozoa such as *Toxoplasma* and *Neospora*); toxic (lead, organophosphate); trauma; GME; extracranial (hypoglycemia; hepatic encephalopathy); inherited epilepsy; neoplasia.

Cats

• Other causes of diarrhea, including food intolerance/allergy; inflammatory bowel disease; parasitism (giardiasis, parasites such as hookworms, roundworms, tritrichomonas); infectious (panleukopenia, FIV, FeLV producing panleukopenia-like syndrome, bacterial including *Salmonella,* rarely *Campylobacter*); drug (acetaminophen); neoplasia; pancreatitis; and major organ dysfunction.

CBC/BIOCHEMISTRY/URINALYSIS

Normal; can reflect severe diarrhea.

OTHER LABORATORY TESTS

• Microscopic examination—colonic biopsies (H&E) obtained via endoscopy is the most reliable method. • Trophozoites in feces—very difficult to detect; methylene blue staining improves chances. • Trichrome and iron-hematoxyline—the ideal fecal stains but require a reference laboratory to perform. • Fecal concentration techniques—no help. • CSF—elevated WBC count (70% mononuclear cells), protein and xanthochromia in dogs with granulomatous amebic meningoencephalitis due to *Acanthamoeba.*

IMAGING

MRI—shows brain granulomas.

DIAGNOSTIC PROCEDURES

Brain biopsy—required to definitively diagnose neurologic forms antemortem.

TREATMENT

• Colitis (caused by *E. histolytica*)—responds to metronidazole, although dogs continue to shed organisms. • Systemic forms (particularly neurologic disease)—invariably fatal despite treatment.

MEDICATIONS

DRUG(S)

• Tinidazole (44 mg/kg PO q24h for 6 days) in dogs—found to be more effective than metronidazole in treating amebiasis in humans.
• Metronidazole (20 mg/kg PO q12h for 7 days).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

High doses of metronidazole (usually > 30 mg/kg) for extended periods may cause neurologic signs in dogs.

FOLLOW-UP

Pets usually acquire infections from the same source as their owners; veterinarians must warn owners of possible risk.

MISCELLANEOUS

ABBREVIATIONS

• CSF = cerebrospinal fluid • FeLV = feline leukemia virus • FIV = feline immunodeficiency virus • GME = granulomatous meningoencephalopathy • H&E = hematoxylin and eosin • HGE = hemorrhagic gastroenteritis • MRI = magnetic resonance imaging • WBC = white blood cell

Suggested Reading

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Fung HB, Doan TL. Tinidazole: A nitroimidazole antiprotozoal agent. Clin Ther 2005, 27:1859–1884.

Author Stephen C. Barr
Consulting Editor Stephen C. Barr

A

AMELOBLASTOMA

BASICS

OVERVIEW
• Common oral tumor of odontogenic (tooth structure) ectoderm origin.
• Biologically these tumors are benign histologically but possess locally invasive properties.
• Tumors may arise anywhere within the dental arcade.
• Several histologic subtypes exist with similar invasive behavior.

SIGNALMENT
• Middle-aged and old dogs
• Rare in cats

SIGNS
• Dogs may present with a smooth, firm, gingival mass that is usually non-ulcerated.
• It may be incidental finding during dental prophylaxis/procedures. If involving rostral dental arcade, incisor teeth can be displaced and enveloped by proliferative tissue.

CAUSES & RISK FACTORS
N/A

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Epulis
• Gingival hyperplasia
• Squamous cell carcinoma
• Amelanotic melanoma
• Plasma cell tumor
• Other tumors related to the odontogenic apparatus

CBC/BIOCHEMISTRY/URINALYSIS
Unaffected

OTHER LABORATORY TESTS
N/A

IMAGING
• Skull or dental radiographs may show bone lysis deep to the superficial mass. Not particularly useful for diagnostic or treatment planning.
• Regional and distant metastasis has not been described.
• Computed tomography is helpful for planning surgery or radiation therapy, especially in large or caudal tumors.

DIAGNOSTIC PROCEDURES
• Deep tissue biopsies are necessary and recommended for definitive diagnosis.
• Squamous cell carcinoma may be misdiagnosed as ameloblastoma.

TREATMENT

• Surgical excision such as hemi- or total mandibulectomy or maxillectomy with > 1–2 cm margins is recommended as a curative treatment option. Always submit resected tissue for histopathology, in order to confirm the original diagnosis, and evaluate soft tissue and bone margins.
• Radiation therapy may provide long-term control in large tumors, or when the owners decline surgery.
• Intralesional chemotherapy with bleomycin has been reported, but results are generally inferior to those of surgery or radiation.

MEDICATIONS

DRUG(S)
N/A

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
N/A

FOLLOW-UP

Careful oral examination at 1, 3, 6, 9, and 12 months after definitive treatment is recommended to monitor for local recurrence.

MISCELLANEOUS

Suggested Reading

Amory JT, Reetz JA, Sánchez MD et al. Computed tomographic characteristics of odontogenic neoplasms in dogs. Vet Radiol Ultrasound 2014, 55(2):147–158.
Fiani N, Verstraete FJ, Kass PH, Cox DP. Clinicopathologic characterization of odontogenic tumors and focal fibrous hyperplasia in dogs: 152 cases (1995–2005). J Am Vet Med Assoc 2011, 238(4):495–500.

Author Nick Dervisis
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AMITRAZ TOXICOSIS

A

BASICS

OVERVIEW

• Amitraz—formamidine acaricide; applied topically to control ticks, mites, and lice.
• Amitraz-containing products (for dogs)—formulated as a 19.9% emulsifiable concentrate in 10.6-mL bottles for dilution and sponge-on; as a 9% impregnated 25-inch 27.5-g collar and an 18-inch 18.5-g collar; as a 14.34% component of a 0.023 fl. oz., 0.045 fl. oz., 0.113 fl. oz., 0.180 fl. oz., or 0.225 fl. oz. spot-on (discontinued); and as a 7.6% component of a 0.036 fl. oz., 0.072 fl. oz.,0.145 fl. oz., 0.217 fl. oz. spot-on
• Systems affected—nervous; cardiovascular; endocrine/metabolic (β cells of the pancreas); gastrointestinal.
• Clinical signs—most associated with α_2-adrenoreceptor agonist.
• After high-dose oral administration (dogs)—peak plasma concentration reached at approximately 6 hours; elimination half-life as long as 24 hours; metabolites excreted in the urine.
• Ingestion of sustained-release- impregnated collars—constant release and continued systemic exposure until collar segments have passed in the stool.
• Toxicosis—generally occurs when pieces of impregnated collar are ingested, when concentrated or improperly diluted solutions are applied topically, or when solutions are ingested or applied to the wrong size animal.
• Idiosyncratic reactions may occur.

SIGNALMENT

• Thorough history—usually identifies topical or collar use; topically missing collar or pieces seen in dog's environment or in the stool.
• Dogs—common, owing to more common use.
• Cats—more sensitive than dogs although cats are less likely involved.
• Predilection for old and toy-breed animals.

SIGNS

Historical Findings

Develop acutely after exposure (topical or oral)

Physical Examination Findings

• Minor to severe depression/lethargy
• Weakness
• Ataxia
• Bradycardia
• Vomiting (pieces of collar)
• Hyperthermia/hypothermia
• Hyperglycemia; diabetic patients can show significant hyperglycemia following exposure
• Hypotension
• Polyuria
• Gastrointestinal stasis
• Mydriasis
• Death (prognosis is typically good with treatment)

CAUSES & RISK FACTORS

• Ingestion of impregnated collar or pieces of collar.
• Inappropriate direct dermal application.
• Ingestion of undiluted product.
• After application of properly diluted and applied solutions—less common.
• Elderly, sick, toy-breed, or debilitated animals—may be predisposed.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Recreational and prescription drugs—marijuana; opioids; barbiturates; benzodiazepines; phenothiazines; antihypertensive medications; skeletal muscle relaxants; antidepressants (tricyclic, SSRIs), and other depressant drugs or chemicals.
• Ivermectins, avermectins, milbemycins—generally very high dose or exceptionally sensitive breed.
• Macadamia nuts, tea tree oil, and albuterol inhaler toxicosis.
• Alcohols—ethanol; ethylene glycol (antifreeze); methanol (windshield washer fluid); isopropyl alcohol (rubbing alcohol).
• Tick bite paralysis, botulism, cranial trauma, diabetes, hyperadrenocorticism, hypothyroidism, severe anemia, cardiac failure, and anaphylactic shock—marked depression or weakness.
• Depends on clinical signs, history of exposure, or evidence of exposure and elimination of other causes.

CBC/BIOCHEMISTRY/URINALYSIS

• Hyperglycemia—common, related to insulin inhibition
• Elevated liver enzymes—uncommon

IMAGING

Abdominal radiography—may reveal a collar buckle in the gastrointestinal tract; collar itself is not radioopaque..

DIAGNOSTIC PROCEDURES

Identify amitraz on hair or in gastrointestinal contents—analytical methods described; useful only to prove exposure; no data available correlating concentration with clinical signs.

PATHOLOGIC FINDINGS

High-dose, prolonged exposure—increased liver weight; slight enlargement of hepatocytes; thinning of the zonae fasciculata and reticularis; slight hyperplasia of the zona glomerulosa of the adrenal glands.

TREATMENT

• Inpatient—severely affected patients.
• Mild sedation after correctly applied sponge-on solutions—often transient; may require no treatment.
• Mild signs after topical application—wearing gloves, scrub with a hand dishwashing detergent; rinse with copious amounts of warm water; institute non-specific supportive therapy (e.g., intravenous fluids, maintenance of blood pressure and normal body temperature, nutritional support); monitor 1–2 days until improvement is noted.
• Ingestion of collar possible—endoscopic retrieval of the collar—removal of large segments from the stomach may be beneficial; usually numerous small pieces are located throughout the gastrointestinal tract, making removal unrealistic.

MEDICATIONS

DRUG(S)

Collar Ingestion, Asymptomatic Patient

• Emetic—3% USP hydrogen peroxide (2.2 mL/kg PO; maximum 45 mL after feeding a moist meal); apomorphine and especially xylazine not recommended.
• Activated charcoal has not been shown to be effective.
• Bulk diet (whole wheat bread, lactulose, pumpkin, psyllium husk [Metamucil]).
• Warm tap water enema (5–10 mL/kg); will stimulate GI motility and help pass pieces of collar through the GI tract.

Marked Depression

• May require pharmacologic reversal of the α_2-adrenergic effects.
• Atipamezole (Antisedan) 0.05 mg/kg 1/4th IV 3/4th IM; reverse clinical signs within minutes; repeat as needed; preferred over yohimbine because of its higher alpha-2 activities.
• Yohimbine (Yobine) 0.11–0.2 mg/kg IV, administered slowly; reverses depression and bradycardia within minutes; improves GI motility; objective is to keep the patient in a state of low-level depression with normal heart rate, blood pressure, body temperature, and blood glucose concentrations.
• Collar ingestion—monitor for recurrence of symptoms; may need additional yohimbine until collar segments appear in the stool.
• Yohimbine and atipamezole—may require repeated administration (as needed) possibly every 2–8 hours, because their half-life in dogs is short and amitraz elimination half-life is longer.

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AMITRAZ TOXICOSIS (CONTINUED)

• Atropine contraindicated because of potentiation of GI stasis.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Yohimbine and atipamezole—excessive administration may result in apprehension, CNS stimulation, and rarely seizures.

FOLLOW-UP

• Body temperature, blood pressure, serum glucose, and heart rate—important parameters.
• Close observation for recurrence of clinical signs—required for 24–72 hours.
• Yohimbine and atipamezole—requires readministration in severe cases, because reversal effects subside before collar segments have passed or before amitraz has been eliminated from the body.
• No long-term adverse effects expected.

MISCELLANEOUS

AGE-RELATED FACTORS

• Elderly, sick, or debilitated animals may take longer to fully recover.

ABBREVIATIONS

• CNS = central nervous system
• GI = gastrointestinal
• SSRI = selective serotonin reuptake inhibitor

Suggested Reading

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Authors Steven R. Hansen and Safdar A. Khan
Consulting Editor Lynn R. Hovda

AMPHETAMINE AND ADD/ADHD MEDICATION TOXICOSIS

BASICS

DEFINITION
Acute gastrointestinal, neurologic, neuromuscular, and cardiac toxicosis as the result of excessive consumption of amphetamine or a derivative. May be due to ingestion of prescription medications or illegal drugs.

PATHOPHYSIOLOGY
• Amphetamine and its derivatives belong to the CNS stimulant class phenylethylamines. Various substitutions of the basic phenylethylamine structure account for many pharmaceutical and illicit compounds found today.
• Amphetamine is a sympathomimetic that is structurally related to norepinephrine.
• Central action—stimulates cortical centers including cerebral cortex, medullary respiratory center, and reticular activating systems.
• Peripheral action—directly stimulates alpha and beta receptors and stimulates the release of norepinephrine from stores in adrenergic nerve terminals.
• Amphetamine may slow catecholamine metabolism by inhibition of monoamine oxidase.
• Several different product formulations including immediate and extended release and topical patch.
• Amphetamines are well absorbed orally; peak plasma levels are generally reached in 1–3 hours; this may be delayed with extended release formulations.
• Metabolism is minimal.
• The half-life, which varies from 7–34 hours, and rate of excretion of unchanged amphetamine in the urine are both dependent upon urine pH, with shorter half-lives associated with more acidic urine.
• Clinical signs may be seen at doses below 1 mg/kg.
• Oral lethal dose in dogs for most amphetamines ranges from 10 mg/kg to 23 mg/kg and for methamphetamine sulfate it is 9–11 mg/kg. Oral lethal dose for amphetamine sulfate is 20–27 mg/kg.
• Amphetamine and its derivatives are used in humans to treat ADD/ADHD, narcolepsy, and obesity.
• Illicit use of amphetamines in humans is also prevalent.

SYSTEMS AFFECTED
• Cardiovascular—stimulation most common: tachycardia and hypertension.
• Nervous—stimulation most common, depression uncommon.
• Neuromuscular—stimulation: muscle tremors and seizures.
• Respiratory—stimulation, tachypnea.
• Ophthalmic—mydriasis.
• Gastrointestinal—anorexia, vomiting, diarrhea.

INCIDENCE/PREVALENCE
N/A

SIGNALMENT
Species
Dogs and cats, although more prevalent in dogs.

Breed Predilections
N/A

Mean Age and Range
N/A

Predominant Sex
N/A

SIGNS
Historical Findings
• Abnormal behavior—usually hyperactivity, anxiety or pacing, anorexia, fast heart rate, panting; observed or evidence of exposure by owner/caretaker.
• Onset of signs typically begins within 30 minutes to 6 hours post-ingestion; depends on product formulation.

Physical Examination Findings
• Nervous—hyperactivity, agitation, restlessness, head bobbing, pacing, circling, vocalization, disorientation, hyperesthesia, ataxia, lethargy or depression (less common).
• Cardiovascular—tachycardia or bradycardia (less common, may be reflexive), hypertension.
• Neuromuscular—muscle fasciculation or tremors, seizures.
• Gastrointestinal—vomiting, diarrhea, anorexia, excessive salivation.
• Respiratory—tachypnea.
• Ophthalmic—mydriasis with possibly poor to unresponsive pupillary light response.
• Other—hyperthermia.

CAUSES
Accidental ingestion or administration, malicious poisoning.

RISK FACTORS
Households with children or adults currently taking prescription or illicit amphetamine or derivative.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Strychnine
• Organochlorine insecticides
• Methylxanthine
• 4-aminopyridine
• Metaldehyde
• Phenylpropanolamine
• Albuterol
• Nicotine
• Tremorgenic mycotoxins
• Hypernatremia
• Pseudoephredrine, phenylephrine
• 5 fluorouracil
• Ma huang, guarana, or ephedra

CBC/BIOCHEMISTRY/URINALYSIS
• CBC—disseminated intravascular coagulopathy secondary to severe hyperthermia (rare).
• Chemistry—
• Azotemia: prerenal—secondary to dehydration; renal—secondary to rhabdomylosis and myoglobinuria (rare).
• Elevated liver enzymes—secondary to seizures and/or hyperthermia (rare).
• Hypoglycemia.
• Urinalysis—evidence of myoglobinuria, urine specific gravity (high—prerenal azotemia; isosthenuria—renal failure).

OTHER LABORATORY TESTS
• Electrolytes—imbalances secondary to GI effects.
• Acid-base status—acidosis may occur.
• Over-the-counter urine drug screens—watch for false positive or negative. Consult user handbook for further information.
• Amphetamines are present in blood, urine, and saliva; consult with local veterinary diagnostic lab or human hospital for availability and proper sample submission.

IMAGING
N/A

DIAGNOSTIC PROCEDURES
• EEG for presence of any tachyarrhythmia or less commonly bradyarrhythmia.
• Blood pressure—identification of hypertension.

PATHOLOGIC FINDINGS
On necropsy presence of amphetamines may be found in the gastric contents, urine, plasma, liver, kidney, or muscle.

TREATMENT

APPROPRIATE HEALTH CARE
Majority of cases require emergency inpatient intensive care management.

NURSING CARE
• Intravenous fluid therapy to correct dehydration and electrolyte imbalances as well as support renal function and promote excretion of amphetamines. Use blood pressure to help guide fluid rate.
• Cool intravenous fluids, fans, cool water baths for hyperthermia.

ACTIVITY
Minimize activity and stimuli.

DIET
Withhold food if moderately to severely affected. Bland diet for a few days post-exposure if significant gastrointestinal signs were noted.

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AMPHETAMINE AND ADD/ADHD MEDICATION TOXICOSIS (CONTINUED)

CLIENT EDUCATION
In case of an exposure, owner should contact local veterinarian or veterinary poison center immediately.

SURGICAL CONSIDERATIONS
N/A

MEDICATIONS

DRUG(S) OF CHOICE

Decontamination
• Induce emesis—if a recent exposure and pet is not already symptomatic.
• Apomorphine—0.04 mg/kg IV, subconjuctival.
• Hydrogen peroxide 3%—2.2 mL/kg, maximum dose 45 mL.
• Gastric lavage if extremely large ingestion or patient is already symptomatic.
• Activated charcoal with a cathartic.

CNS Signs of Stimulation
• Acepromazine 0.05–1.0 mg/kg IV or IM
• Chlorpromazine 0.5 mg/kg IV, titrate up as needed.
• Cyproheptadine (serotonin antagonist): dogs, 1.1 mg/kg orally or rectally, may be repeated q8h as needed for signs consistent with serotonin syndrome; cats, 2–4 mg/cat, may repeat q12h as needed for signs consistent with serotonin syndrome
Methocarbamol (for muscle tremors): 50–220 mg/kg IV, titrate to effect. Do not exceed 330 mg/kg/day.

Cardiovascular Signs
• Tachyarrhythmia—beta blockers such as propranolol 0.02–0.04 mg/kg IV or esmolol or metoprolol.
• Ventricular premature contractions—lidocaine: dogs at 2–4 mg/kg IV (to maximum of 8 mg/kg over a 10-minute period). Cats—start with 0.1–0.4 mg/kg and increase cautiously to 0.25–0.75 mg/kg IV slowly if no response. Cats are reportedly very sensitive to lidocaine, so monitor carefully if used.

Promote Elimination
Ascorbic acid or ammonium chloride—for urinary acidification to promote elimination; however, only use if can measure acid-base status.

CONTRAINDICATIONS
• While diazepam has been successfully used to treat amphetamine exposures, there is evidence that benzodiazepines may intensify neurologic signs.
• Urinary acidification if unable to monitor acid-base status or if myoglobinuria is present.
• Inducing emesis in a symptomatic patient.

PRECAUTIONS
N/A

POSSIBLE INTERACTIONS
• Amphetamines inhibit the metabolism of adrenergic blockers (doxazosin, phenoxybenzamine, prazosin, terazosin), phenobarbital, and phenytoin.
• Amphetamines potentiate the metabolism of coumarin anticoagulants, monoamine oxidase inhibitors, opioid analgesics, and tricyclic antidepressants.

ALTERNATIVE DRUG(S)
Phenobarbital, pentobarbital, and propofol for CNS stimulatory signs.

FOLLOW-UP

PATIENT MONITORING
• Monitor in hospital until resolution of clinical signs.
• If severely affected, monitor liver and kidney values every 24 hours for 72 hours or until resolution.

PREVENTION/AVOIDANCE
All medications and illicit drugs should be kept out of pets' reach at all times.

POSSIBLE COMPLICATIONS
Acute renal failure secondary to myoglobinuria or DIC (rare).

EXPECTED COURSE AND PROGNOSIS
• Expected course of clinical signs is 12–72 hours, depending on dose, product formulation, effectiveness of decontamination and treatment, and rate of elimination.
• Prognosis—most patients do well with prompt and appropriate veterinary care. Seizures or severe hyperthermia may be a poor prognostic indicator.

MISCELLANEOUS

ASSOCIATED CONDITIONS
N/A

AGE-RELATED FACTORS
N/A

ZOONOTIC POTENTIAL
Pets exposed to human waste products from those taking amphetamines or derivatives could become symptomatic.

PREGNANCY/FERTILITY/BREEDING
Amphetamines are a known teratogen in humans. They have been found to cross the placenta in animals and may also be found in milk.

SYNONYMS
• Common brand names of prescription amphetamine drugs and their active ingredient: Adderall (amphetamine and dextroamphetamine); Ritalin, Metadate, and Concerta (methylphenidate); Daytrana (methylphenidate transdermal patch); Focalin (dexmethylphenidate); Vyvanse (lisdexamfetamine), Cylert (pemoline), Adipex-P (phentermine), Dexedrine (Dextroamphetamine).
• Illicit drug street names: ice, glass, crank, speed, uppers, ecstasy, meth, and many others.

SEE ALSO
• Antidepressant Toxicosis—SSRIs and SNRIs
• Antidepressant Toxicosis—Tricyclics
• Pseudoephredrine/Phenylephrine Toxicosis

ABBREVIATIONS
• ADD = attention deficit disorder
• ADHD = attention deficit hyperactivity disorder
• CNS = central nervous system
• DIC = disseminated intravascular coagulation
• ECG = electrocardiogram
• GI = gastrointestinal

INTERNET RESOURCES
• http://www.aspcapro.org/animal-poison-control-center-articles.php
• http://www.aspca.org/pet-care/animal-poison-control
• http://www.petpoisonhelpline.com/

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AMYLOIDOSIS

BASICS

DEFINITION
A group of conditions of diverse cause in which extracellular deposition of insoluble fibrillar proteins (amyloid) in various organs and tissues compromises their normal function.

PATHOPHYSIOLOGY
• Patients usually affected by systemic reactive amyloidosis; tissue deposits contain AA, which is a fragment of an acute-phase reactant protein called SAA. • Phases of amyloid deposition: ◦ Predeposition phase: SAA concentration is high but without amyloid deposits; colchicine administration during this phase may prevent development of the disease. ◦ Deposition phase (rapid portion): amyloid deposits increase rapidly; colchicine administration delays but does not prevent tissue deposition of amyloid; DMSO may promote resolution of amyloid deposits and a persistent decrease in SAA concentration. ◦ Deposition phase (plateau portion): net deposition of amyloid changes little; neither DMSO nor colchicine is beneficial.
• Clinical signs in dogs and cats usually are associated with amyloid deposition in the kidneys. • Dogs—amyloid deposits usually found in the glomeruli leading to proteinuria and nephrotic syndrome. • Cats—amyloid deposits usually found in the medullary interstitium but may occur in glomeruli.
• Some Chinese shar-pei dogs with familial amyloidosis have medullary amyloidosis without glomerular involvement. • Siamese and Oriental shorthair cats with familial amyloidosis have hepatic amyloidosis. • A different type amyloid, pancreatic islet amyloid polypeptide, or amylin, deposits in the pancreas of old cats. Amylin is a hormone secreted along with insulin by the pancreatic beta cells. Chronic increased stimulus for secretion of amylin by beta cells (e.g., states of insulin resistance) lead to pancreatic islet cell amyloidosis.

SYSTEMS AFFECTED
Renal/Urologic—predilection for renal AA deposition. Liver, spleen, adrenal glands, pancreas, tracheobronchial tree, and gastrointestinal tract also may be affected.

GENETIC
(See "Breed Predilections.") No genetic involvement is clearly established; familial amyloidosis occurs in Chinese shar-pei, English foxhound, and beagle dogs, and in Abyssinian, Oriental shorthair, and Siamese cats.

INCIDENCE/PREVALENCE
Uncommon, occurs mostly in dogs; rare in cats, except Abyssinians.

SIGNALMENT

Species
Dog and cat

Breed Predilections
• Dog—Chinese shar-pei, beagle, collie, pointer, English foxhound, and walker hound; German shepherd dog and mixed breeds are at lower risk. • Cat—Abyssinian, Oriental shorthair, and Siamese.

Mean Age and Range
• Cats—mean age at diagnosis 7 years; range 1–17 years. • Dogs—mean age at diagnosis is 9 years; range 1–15 years. Chinese shar-Pei dogs—median age at diagnosis is 5 years; range 3.6–17 years. • Prevalence increases with age. • Abyssinian cats—range < 1–17 years. • Chinese shar-pei dogs—usually < 6 years of age when signs of renal failure develop. • Siamese cats with familial amyloidosis of the liver and thyroid gland usually develop signs of liver disease when 1–4 years old.

Predominant Sex
Dogs and Abyssinian cats—females at a slightly higher risk (< 2:1). Female-to-male ratio is higher in Chinese shar-pei dogs (~ 2.5:1).

SIGNS

General Comments
• Depend on the organs affected, the amount of amyloid, and the reaction of the affected organs to amyloid deposits. • Usually caused by kidney involvement; occasionally, hepatic involvement may cause signs in Chinese shar-pei dogs and Oriental shorthair and Siamese cats.

Historical Findings
• No clear history of a predisposing disorder in most (~75%) cases. • Anorexia, lethargy, polyuria and polydipsia, weight loss, vomiting. • Ascites and peripheral edema in animals with nephrotic syndrome. • Chinese shar-pei dogs may have a history of previous episodic joint swelling and high fever that resolves spontaneously within a few days.
• Beagle dogs with juvenile polyarteritis may have a history of fever and neck pain that persist for 3–7 days. • Oriental shorthair and Siamese cats may present with spontaneous hepatic hemorrhage leading to acute collapse and hemoabdomen.

Physical Examination Findings
• Related to renal failure—oral ulceration, emaciation, vomiting, and dehydration; kidneys usually small, firm, and irregular in affected cats; they may be small, normal-sized, or slightly enlarged in affected dogs. • Signs of nephrotic syndrome (e.g., ascites, subcutaneous edema). • Related to the primary inflammatory or neoplastic disease process. • Thromboembolic phenomena—may occur in up to 40% of affected dogs; signs vary with the location of the thrombus; patients may develop pulmonary thromboembolism (e.g., dyspnea) or iliac or femoral artery thromboembolism (e.g., caudal paresis). • Chinese shar-pei dogs and Oriental shorthair and Siamese cats may have signs of hepatic disease (e.g., jaundice, cachexia, and spontaneous hepatic rupture with intraperitoneal bleeding).

CAUSES
• Neoplasia and chronic infectious and non-infectious inflammatory conditions can be found in 30–50% of dogs with reactive amyloidosis. • Chronic inflammation—systemic mycoses (e.g., blastomycosis, coccidioidomycosis), chronic bacterial infections (e.g., osteomyelitis, broncho-pneumonia, pleuritis, steatitis, pyometra, pyelonephritis, chronic suppurative dermatitis, chronic suppurative arthritis, chronic peritonitis, nocardiosis, chronic stomatitis), parasitic infections (e.g., dirofilariasis, leishmaniasis, hepatozoonosis), and immune-mediated diseases (e.g., systemic lupus erythematosus). Amyloid deposits can be found in up to 35% of FIV-positive cats.
• Neoplasia (e.g., lymphoma, plasmacytoma, multiple myeloma, mammary tumors, testicular tumors). • Familial (e.g., Chinese shar-pei, English foxhound, and beagle dogs; Abyssinian, Siamese, and Oriental shorthair cats). • Others—cyclic hematopoiesis in gray collies; juvenile polyarteritis in beagles.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Dogs—GN; proteinuria tends to be more severe in dogs with glomerular amyloidosis than those with GN but there is great overlap.
• Cats and Chinese shar-pei dogs with medullary amyloidosis—consider other causes of medullary renal disease (e.g., pyelonephritis, chronic interstitial disease).

CBC/BIOCHEMISTRY/URINALYSIS
• Nonregenerative anemia is found in some dogs and cats with amyloid-induced renal failure. • Dogs—may see hypercholesterolemia (> 85%), azotemia (> 70%), hypoalbuminemia (70%), hyperphosphatemia (> 60%), hypocalcemia (50%), and metabolic acidosis.
• Hypercholesterolemia—common finding in cats with renal disorders (> 70% of cats with renal disease in one study) but does not reliably predict glomerular disease.
• Hypoproteinemia—more common than hyperproteinemia (24 vs. 8.5%) in dogs with amyloidosis; hyperglobulinemia common in cats. • Proteinuria—with an inactive sediment common in dogs; mild or absent in animals with medullary amyloidosis without glomerular involvement (most mixed-breed cats, at least 25% of Abyssinian cats, and at least 33% of Chinese shar-pei dogs). In a retrospective study with 91 cases of renal

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AMYLOIDOSIS (CONTINUED)

amyloidosis in dogs, hypoalbuminemia was more common in non-Chinese shar-pei dogs (100%) versus shar-pei dogs (65%).
• Isosthenuria, and hyaline, granular, and waxy casts in some patients.

OTHER LABORATORY TESTS
Proteinuria—urinary protein:creatinine ratio to estimate severity.

IMAGING
Abdominal Radiographic Findings
• Kidneys usually small in affected cats.
• Kidneys small, normal-sized, or large in affected dogs.

Abdominal Ultrasonographic Findings
Kidneys usually hyperechoic and small in affected cats; may be small, normal-sized, or large in affected dogs.

DIAGNOSTIC PROCEDURES
Renal biopsy needed to differentiate amyloidosis from GN. In dogs other than Chinese shar-pei, amyloidosis is primarily a glomerular disease; diagnose by renal cortical biopsy. In most domestic cats, some Abyssinian cats, and some Chinese shar-pei dogs, medullary amyloidosis can occur without glomerular involvement; diagnose by renal medullary biopsy.

PATHOLOGIC FINDINGS
• Small kidneys in cats; small, normal, or large kidneys in dogs. • Amyloid deposits appear homogeneous and eosinophilic when stained by hematoxylin and eosin and viewed by conventional light microscopy. They demonstrate green birefringence after Congo red staining when viewed under polarized light. Evaluation of Congo red—stained sections before and after permanganate oxidation permits presumptive diagnosis of AA amyloidosis (vs. other types) because AA amyloidosis loses its Congo red affinity after permanganate oxidation. • The liver is very friable and usually contains extensive amyloid deposits in cats presented with acute hepatic hemorrhage.

TREATMENT
APPROPRIATE HEALTH CARE
• Hospitalize patients with chronic renal failure and dehydration for initial medical management. • Can manage stable patients and those with asymptomatic proteinuria as outpatients.

DIET
• Patients with chronic renal failure—restrict phosphorus and moderately restrict protein.
• Patients with hypertension—restrict sodium.

CLIENT EDUCATION
• Discuss progression of the disease. • Discuss familial predisposition in susceptible breeds.

MEDICATIONS
DRUG(S) OF CHOICE
• Identify underlying inflammatory and neoplastic processes and treat if possible.
• Manage renal failure according to the principles of conservative medical treatment (see Renal Failure, Acute, and Renal Failure, Chronic).
• Normalize blood pressure in patients with hypertension (see Hypertension, Systemic).
• Patients with thromboembolic syndrome and nephrotic syndrome caused by glomerular amyloidosis usually have a low plasma concentration of antithrombin; thus heparin is relatively ineffective. Aspirin (0.5 mg/kg PO q12h) has been suggested for dogs with glomerular disease; this low dosage is as effective in preventing platelet aggregation as is 10 mg/kg PO q24h.
• DMSO—may help patients by solubilizing amyloid fibrils, reducing serum concentration of SAA, and reducing interstitial inflammation and fibrosis in the affected kidneys; may cause lens opacification in dogs. Perivascular inflammation and local thrombosis may occur if undiluted DMSO is administered intravenously. Subcutaneous administration of undiluted DMSO may be painful. The authors have used 90% DMSO diluted 1:4 with sterile water subcutaneously at a dosage of 90 mg/kg 3 times per week in dogs. Whether or not DMSO treatment benefits renal amyloidosis in dogs remains controversial.
• Methylsulfonylmethane is an active metabolite of DMSO that can be given orally and lacks the smell of DMSO. It has been used empirically in dogs with amyloidosis, but there is no evidence that it benefits dogs with renal amyloidosis.
• Colchicine—impairs release of SAA from hepatocytes; prevents development of amyloidosis in humans with familial Mediterranean fever (a familial amyloidosis) and stabilizes renal function in patients with nephrotic syndrome but without overt renal failure; no evidence of benefit once the patient develops renal failure; may cause vomiting, diarrhea, and idiosyncratic neutropenia in dogs. Colchicine (0.01–0.04 mg/kg PO q24h) is used particularly in shar-pei dogs with episodic fever or polyarthritis before development of renal failure.

PRECAUTIONS
• Dosage of drugs excreted by the kidneys may need adjustment in patients with renal failure. • Use nonsteroidal anti-inflammatory drugs cautiously in patients with medullary amyloidosis; they can decrease renal blood flow in dehydrated patients.

FOLLOW-UP
PATIENT MONITORING
• Appetite and activity level daily by the owner; body weight weekly. • Serum albumin, creatinine, and BUN concentrations every 2–6 months in stable patients. • Can assess degree of proteinuria serially by urine protein:creatinine ratios.

PREVENTION/AVOIDANCE
Do not breed affected animals.

POSSIBLE COMPLICATIONS
• Renal failure • Nephrotic syndrome
• Systemic hypertension • Hepatic rupture causing intraperitoneal hemorrhage
• Thromboembolic disease

EXPECTED COURSE AND PROGNOSIS
Disease is progressive and usually advanced at the time of diagnosis. Prognosis improves if an underlying immune, inflammatory, or neoplastic disease is detected and successfully treated. Survival for dogs with glomerular amyloidosis varied from 3 to 20 months in 1 study; some dogs may occasionally live longer. Cats with renal failure because of amyloidosis usually survive < 1 year. Mildly affected cats may not develop renal failure and have an almost normal life expectancy.

MISCELLANEOUS
ASSOCIATED CONDITIONS
• Urinary tract infection • Polyarthritis in Chinese shar-pei • Polyarteritis in beagle

SEE ALSO
• Glomerulonephritis • Nephrotic Syndrome Proteinuria • Renal Failure, Acute • Renal Failure, Chronic

ABBREVIATIONS
• AA = amyloid A protein • DMSO = dimethylsulfoxide • GN = glomerula nephritis • SAA = serum amyloid A protein

Suggested Reading
Bartges J, Wall J. Amyloidosis. In Bartges J, Polzin DJ. Nephrology and Urology of Small Animals, Oxford: Wiley-Blackwell, 2011, pp. 547–554.
Segev G, Cowgill, LD, Jessen, S et al. Renal amyloidosis in dogs: a retrospective study of 91 cases with comparison of the between Shar-pei and non-Shar-pei dogs. J Vet Intern Med 2012, 26:259–268.
Authors Helio S. Autran de Morais and Stephen P. DiBartola
Consulting Editor Carl A. Osborne

Client Education Handout available online

ANAEROBIC INFECTIONS

BASICS

OVERVIEW

• Anaerobic bacteria (i.e., bacteria requiring low oxygen tension) comprise a large portion of the normal flora, especially on mucosal surfaces. • May be Gram-positive or Gram-negative cocci or rods. • Most common genera—*Bacteroides, Fusobacterium, Actinomyces, Propionibacterium, Peptostreptococcus* (enteric *Streptococcus*), *Porphyromonas,* and *Clostridium*. • Most anaerobic infections are polymicrobial and contain at least two different anaerobe species admixed with facultative anaerobes or aerobic bacteria (especially *E. coli).* • Individual organisms vary in potential to withstand oxygen exposure. • Injurious toxins and enzymes may be elaborated by the organisms, leading to extension of the infection into adjacent, healthy tissue. • All body systems are at potential risk for anaerobic infection.

SIGNALMENT

Dog and cat

SIGNS

General Comments

• Determined by the body system involved. • Certain areas more commonly associated with anaerobic infection (mucous membrane proximity). • It is possible to overlook anaerobes in an infectious process, leading to confusion in interpreting culture results and selection of antimicrobials.

Physical Examination Findings

• A foul odor associated with a wound or exudative discharge. • Gas in the tissue or associated exudates. • Discolored tissue, especially when black. • Peritonitis, pyothorax, or pyometra. • Severe dental disease. • Wounds or deep abscesses that do not heal as anticipated.

CAUSES & RISK FACTORS

• Usually caused by normal flora of the body; a break in protective barriers allows bacterial invasion. • Infection in the proximity of a mucous membrane should raise one's index of suspicion for anaerobe involvement. • Predisposing factors—immunosuppression, bite wounds, dental disease, open fractures, abdominal surgery, and foreign bodies.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Wounds that fail to respond to appropriate medical therapy—if aerobic cultures are negative, suspect anaerobic organisms. • Cats with non-healing wounds—test for FeLV and FIV. • Middle-aged and old animals—tumor invasion (e.g., in the gastrointestinal tract).

CBC/BIOCHEMISTRY/URINALYSIS

• Neutrophilic leukocytosis and monocytosis common. • Biochemical abnormalities depend on specific organ involvement. • Systemic spread of infection suggested by leukocytosis, hypoglycemia, increased ALP, and hypoalbuminemia.

OTHER LABORATORY TESTS

• Culture of anaerobic bacteria is often unrewarding because of their fastidious nature and errors in sample handling and submission. • Appropriate media and containers should be on-hand prior to sample collection; diagnostic laboratories can provide guidance. • Samples should not be refrigerated prior to submission. • Suitable samples for culture may include fluid (e.g., pleural, peritoneal, etc.) or tissue.

IMAGING

As required for the circumstances of the individual patient (e.g., suspected bone infection, peritonitis, etc.).

DIAGNOSTIC PROCEDURES

• Cytologic inspection reveals abundant degenerate neutrophils with morphologically diverse forms of intracellular and extracellular bacteria; presence of large filamentous bacteria is suggestive. • If not performed in-house, Gram staining should be requested when the sample is submitted.

MEDICATIONS

• Thoracic drainage—important with pyothorax (see specific chapter). • Hyperbaric oxygen—some potential use; limited in availability.

SURGERY

• Should not be delayed when anaerobes are suspected. • Combined with systemic antimicrobial therapy—the best chance of a positive outcome. • Usually indicated when anaerobic organisms complicate pyometra, osteomyelitis, and peritonitis. • Cleanse the wound of toxins and devitalized tissue. • Enhance drainage of pus. • Improve local blood flow. • Increase oxygen tension.

DRUG(S)

• Antimicrobial therapy alone—unlikely to be successful; poor drug penetration into exudates.
• Antibiotic selection—largely empiric, owing to the difficulty of isolating anaerobes and the delay in return of culture results.
• Because most anaerobic infections are polymicrobial, therapy targeted against both anaerobes *and* any aerobic components offers the greatest chance of success.
• Amoxicillin with clavulanate—in many cases, considered the antibiotic of choice; convenient and accessible; clavulanate improves activity against *Bacteroides.*
• Imipenem—beta lactam with significant activity against serious, resistant infections.
• Cefoxitin—a cephalosporin with reliable activity against anaerobes.
• Clindamycin—may be especially useful for respiratory tract infections; concentrated within leukocytes.
• Chloramphenicol—good tissue penetration but bacteriostatic and associated with adverse effects, especially in cats; concern for human exposure also limits use.
• Metronidazole—useful against all clinically significant anaerobes (except *Actinomyces*).
• Aminoglycosides—uniformly ineffective.
• Trimethoprim-sulfa combinations—ineffective; poor penetration into exudates.
• Quinolones—routinely ineffective, although newer expanded-spectrum quinolones do have activity against anaerobes (e.g., pradofloxacin).

FOLLOW-UP

PATIENT MONITORING

Monitoring parameters will vary with the circumstances of each patient.

POSSIBLE COMPLICATIONS

Localized infection may progress to systemic infection if not appropriately identified and treated.

EXPECTED COURSE AND PROGNOSIS

Dependent upon identification and resolution of the underlying cause; long-term antibiotic therapy may be required.

MISCELLANEOUS

ASSOCIATED CONDITIONS

See "Causes & Risk Factors"

ABBREVIATIONS

• ALP = alkaline phosphtase • FeLV = feline leukemia virus • FIV = feline immunodeficiency virus

Suggested Reading

Hirsh DC, Jang SS. Anaerobic infections. In: Greene CE, ed., Infectious Diseases of the Dog and Cat, 3rd ed. St. Louis, MO: Saunders Elsevier, 2006, pp. 381–388.

Author Sharon Fooshee Grace
Consulting Editor Stephen C. Barr

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ANAL SAC DISORDERS

BASICS

OVERVIEW
• Anal sacs are reservoirs for secretions normally evacuated by compression during defecation.
• Normal gland secretions vary in consistency and color.
• Disorders include impaction, infection (sacculitis), abscess, and neoplasia.
• Treatment options include manual expression, flushing, antibiotics, and surgical excision.

SIGNALMENT
• Dogs and cats (rarely): no age or sex predisposition.
• Breeds predisposed:
  ◦ Impaction—miniature and toy poodle, American cocker and English springer spaniel, Chihuahua.
  ◦ Neoplasia (adenocarcinoma)—German shepherd dog, golden retriever, American cocker and English springer spaniel.

SIGNS
Impaction/Infection
• Anal pruritus—often manifested by "scooting"
• Perianal pruritus
• Hesitancy to defecate
• Tenesmus
• Tail chasing
• Foul-smelling, non-feces anal discharge
• Refusal to sit and/or lift tail
• Cats—excessive licking of the ventral abdomen and tail head
• Abscess—often unilateral; localized pain and discharge

CAUSES & RISK FACTORS
• Predisposing factors—soft feces or diarrhea leading to retention of secretions within anal sacs due to lack of expression; excessive glandular secretions; dermatologic disorders that alter the characteristics (cellularity and organism colonization) of anal sac secretions.
• Retained secretions may lead to infection and abscess formation.
• Other predisposing factors:
  ◦ Obesity
  ◦ Infection – hypersensitivity and/or endocrinopathy.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Adverse food reaction or food hypersensitivity
• Flea bite hypersensitivity
• Atopic dermatitis
• Tapeworm infestation
• Tail fold bacterial folliculitis
• Malassezia dermatitis
• Compulsive disorder (anal licking)
• Colitis or other intestinal disorder
• Keratinization disorder
• Anal sac neoplasia (including adenocarcinoma, squamous cell carcinoma)
• Perianal adenoma
• Perianal adenocarcinoma
• Perianal fistulae

CBC/BIOCHEMISTRY/URINALYSIS
• Usually normal
• Hypercalcemia—anal sac adenocarcinoma

OTHER LABORATORY TESTS
None unless indicated by an underlying cause

IMAGING
None unless indicated by an underlying cause

DIAGNOSTIC PROCEDURES
• Digital palpation of the anal sacs—normal anal sacs should not be palpable externally.
• Normal anal sac contents vary widely in gross appearance and microscopic characteristics; usually thin or watery, with minimal cellularity and primarily extracellular organisms, but may vary widely in numbers of inflammatory cells and bacteria.
• Impaction—generally more thick, pasty brown secretion; higher numbers of *Malassezia* and intracellular bacteria.
• Anal sacculitis and abscessation—purulent, often blood-tinged, foul-smelling discharge.
• Cytology of anal sac secretions—increased number of neutrophils, erythrocytes, *Malassezia,* and intracellular bacteria indicate infection; reports vary but Gram-positive cocci more common in normal secretions.
• Bacterial culture and sensitivity—normal secretions may contain *Proteus mirabilis, Streptococcus spp., Escherichia coli, Bacillus spp., Clostridium perfringens*, and *Pseudomonas aeruginosa.*

TREATMENT
• Gentle manual expression of contents for impaction and sacculitis.
• Sedation may be necessary to flush severely impacted or painful anal sacs.
• Infusion of antibiotic and/or corticosteroid medications directly into the anal sacs.
• Drainage of abscesses.
• Use of appropriate oral antibiotics and/or antiyeast medication.
• Anal sac excision with chronic disease.
• Surgical excision and staging of anal sac neoplasia; combine with chemotherapy.
• Identification of underlying causes of predisposing disease.
• Feeding high-fiber diets may help natural expression of anal sacs.

MEDICATIONS

DRUG(S)
• Infection—use of appropriate antibiotics: cephalexin (22 mg/kg q12h), amoxicillin trihydrate-clavulanate potassium (10–15 mg/kg q12h), clindamycin (11 mg/kg q24h), trimethoprim-sulfamethoxasole (15 mg/kg q12h); metronidazole (10–15 mg/kg q12h); enrofloxacin (dogs, 10–20 mg/kg q24h; cats, 5 mg/kg/day), and orbifloxacin (5 mg/kg q24h).
• Chronic disease associated with perianal fistulae; cyclosporine, modified (name brand preferred: Atopica 5 mg/kg q24h) and/or topical tacrolimus.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
N/A

FOLLOW-UP
• Reassess patients weekly initially; then as necessary to monitor healing.
• Manually express anal sac contents and/or flush contents until sacs empty without intervention.
• CBC, serum chemistry profile, and urinalysis with culture—recommended every 3–12 months for patients on chronic corticosteroid or cyclosporine therapy.

MISCELLANEOUS

SEE ALSO
• Adenocarcinoma, Anal Sac
• Perianal Fistula

Suggested Reading
Muse R. Diseases of the anal sac. In: Bonagura JD, Twedt DC, eds., Kirk's Current Veterinary Therapy, 14th ed. St. Louis, MO: Saunders, 2009, pp. 465–468.
Zoran DL. Rectoanal disease. In: Ettinger SJ, ed., Textbook of Veterinary Internal Medicine, 6th ed. Philadelphia: Saunders, 2005, pp. 1408–1420.

Author Alexander H. Werner
Consulting Editor Alexander H. Werner

ANAPHYLAXIS

BASICS

DEFINITION
• Acute manifestation of a Type I hypersensitivity reaction mediated through the rapid introduction of an antigen into a host having antigen-specific antibodies of the IgE subclass.
• The binding of antigen to mast cells sensitized with IgE results in the release of preformed and newly synthesized chemical mediators.
• Anaphylactic reactions may be localized (atopy) or systemic (anaphylactic shock).
• Anaphylaxis not mediated by IgE is designated an anaphylactoid reaction and will not be discussed.

PATHOPHYSIOLOGY
• First exposure of the patient to a particular antigen (allergen) causes a humoral response and results in production of IgE, which binds to the surface of mast cells; the patient is then considered to be sensitized to that antigen.
• Second exposure to the antigen results in cross-linking of two or more IgE molecules on the cell surface, resulting in mast cell degranulation and activation; release of mast cell granules initiates an anaphylactic reaction.
• Major mast cell-derived mediators include histamine, eosinophilic chemotactic factor, arachidonic acid, metabolites (e.g., prostaglandins, leukotrienes, and thromboxanes), platelet-activating factor, and proteases, which cause an inflammatory response of increased vascular permeability, smooth muscle contraction, inflammatory cell influx, and tissue damage.
• Clinical manifestations depend on the route of antigen exposure, the dose of antigen, and the level of the IgE response.

SYSTEMS AFFECTED
• Gastrointestinal—salivation, vomiting, and diarrhea
• Hepatobiliary (dogs)—because of portal hypertension and vasoconstriction
• Respiratory (cats)—dyspnea and cyanosis
• Skin/Exocrine—pruritus, urticaria, and edema

GENETICS
Familial basis reported for Type I hypersensitivity reaction in dogs.

INCIDENCE/PREVALENCE
• Localized Type I hypersensitivity reactions not uncommon.
• Systemic Type I hypersensitivity reactions rare.

GEOGRAPHIC DISTRIBUTION
None

SIGNALMENT
Species
Dog and cat

Breed Predilections
• Dogs—numerous breeds documented as having a predilection for developing atopy.
• Cats—no breeds documented as having predilection for atopy.

Mean Age and Range
• Dogs—age of clinical onset ranges from 3 months to several years of age; most affected animals 1–3 years old.
• Cats—age of clinical onset ranges from 6 months to 2 years.

Predominant Sex
• Dogs—atopy more common in females.
• Cats—no reported sex predilection.

SIGNS
General Comments
• Initial clinical signs vary depending on the route of exposure to the inciting antigen (allergen).
• Shock—end result of a severe anaphylactic reaction.
• Shock organ—dogs, liver; cats, respiratory and gastrointestinal systems.
• May be localized to the site of exposure but may progress to a systemic reaction.

Historical Findings
• Onset of signs immediate (usually within minutes).
• Dogs—pruritus, urticaria, vomiting, defecation, and urination.
• Cats—intense pruritus about the head, dyspnea, salivation, and vomiting.

Physical Examination Findings
• Localized cutaneous edema at the site of exposure.
• Hepatomegaly in some dogs.
• Hyperexcitability possible in early stages.
• Depression and collapse terminally.

CAUSES
Virtually any agent; those commonly reported include venoms, blood-based products, vaccines, foods, and drugs.

RISK FACTORS
Previous exposure (sensitization) increases the chance of the animal developing a reaction.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Other types of shock.
• Trauma.
• Depends on the major organ system involved or if reaction is localized; diagnosis can be made largely on the basis of history and clinical signs.

CBC/BIOCHEMISTRY/URINALYSIS
Because of the acute onset of disease, no tests available that reliably predict individual susceptibility.

OTHER LABORATORY TESTS
• Intradermal skin testing to identify allergens.
• Radioallergosorbent test to quantify the concentration of serum IgE specific for a particular antigen.

IMAGING
N/A

DIAGNOSTIC PROCEDURES
Limited because a severely allergic animal can develop an anaphylactic reaction when exposed to even small quantities of antigen.

PATHOLOGIC FINDINGS
• Lesions vary, depending on severity of reaction, from localized cutaneous edema to severe pulmonary edema (in cats) and visceral pooling of blood (in dogs).
• Other non-specific findings vary and are characteristic of shock.
• Non-specific characteristics of localized reactions include edema, vasculitis, and thromboembolism.

TREATMENT

APPROPRIATE HEALTH CARE
In an acutely affected animal, the reaction is considered a medical emergency requiring hospitalization.

NURSING CARE
Elimination of inciting antigen, if possible.

Systemic Anaphylaxis
• Goal—emergency life support through the maintenance of an open airway, preventing circulatory collapse, and reestablishing physiologic parameters.
• Administer fluids intravenously at shock dosages to counteract hypotension.

Localized Anaphylaxis
Goal—limit the reaction and prevent progression to a systemic reaction.

ACTIVITY
N/A

DIET
If a food-based allergen is suspected (uncommon), avoid foods associated with hypersensitivity reaction.

CLIENT EDUCATION
• Discuss the unpredictable nature of the disease.
• Discuss the need to recognize that the animal has an allergic condition that may require immediate medical care.

SURGICAL CONSIDERATIONS
None

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ANAPHYLAXIS (CONTINUED)

MEDICATIONS

DRUG(S) OF CHOICE

Systemic Anaphylaxis

• Epinephrine hydrochloride parenterally (1:1,000; 0.01 mL/kg) for shock.
• Corticosteroids for shock—prednisolone sodium succinate (2 mg/kg IV q8h) or dexamethasone sodium phosphate (0.25 mg/kg IV q12h).
• Atropine sulfate (0.04 mg/kg IM) to counteract bradycardia and hypotension.
• Aminophylline (10 mg/kg IM or slowly IV) in severely dyspneic patients.

Localized Anaphylaxis

• Diphenhydramine hydrochloride (1–2 mg/kg IV or IM).
• Prednisolone (2 mg/kg PO).
• Epinephrine hydrochloride (0.15 mL SC at site of initiation).
• If shock develops, initiate treatment for a systemic anaphylaxis.

CONTRAINDICATIONS

None

PRECAUTIONS

Localized reaction can develop into systemic reaction.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

FOLLOW-UP

PATIENT MONITORING

Closely monitor hospitalized patients for 24–48 hours.

PREVENTION/AVOIDANCE

If inciting antigen (allergen) can be identified, eliminate or reduce exposure.

POSSIBLE COMPLICATIONS

None

EXPECTED COURSE AND PROGNOSIS

• If localized reaction is treated early, prognosis is good.
• If the animal is in shock on examination, prognosis is guarded to poor.

MISCELLANEOUS

ASSOCIATED CONDITIONS

None

AGE-RELATED FACTORS

None

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

Shock, Cardiogenic

INTERNET RESOURCES

Merck Veterinary Manual: www.merckvetmanual.com.

Suggested Reading

Shmuel DL, Cortes Y. Anaphylaxis in dogs and cats. J Vet Emerg Crit Care (San Antonio) 2013, 23(4):377–394.

Author Paul W. Snyder
Consulting Editor Alan H. Rebar

Client Education Handout available online

ANEMIA OF CHRONIC KIDNEY DISEASE

BASICS

DEFINITION
Progressive decreases in PCV, RBC count, and hemoglobin and hypoplasia of erythroid elements of the bone marrow are predictable features of progressive CKD. Anemia is normocytic, normochromic, nonregenerative, and proportional to the stage of CKD. The underlying cause of the anemia of CKD is multifactorial. Although factors such as gastrointestinal blood loss, reduced red blood cell survival, deficiencies in iron and/or folate, cytokines and inflammatory mediators may be involved, the primary contributing factor to anemia of CKD is an inadequate production of erythropoietin (EPO) by the kidneys. Erythropoietin is a glycoprotein hormone that regulates red blood cell generation at the level of the bone marrow. Erythropoietin is produced in the peritubular interstitial cells of the kidney in response to decrease in tissue oxygen.

SIGNALMENT
Middle-aged to old dogs and cats mostly affected; seen in young animals with heritable, congenital, or acquired CKD.

SIGNS
- Anemia contributes to development of anorexia, weight loss, fatigue, lethargy, depression, weakness, apathy, cold intolerance, and behavior and personality changes characterizing CKD.
- Pallor of the mucous membranes.
- Tachypnea.
- Tachycardia.
- Systolic murmur.
- Syncope and seizures (rare).

CAUSES & RISK FACTORS
- All inherited, congenital, and acquired forms of CKD (e.g., pyelonephritis, glomerulonephritis, amyloidosis, polycystic kidney disease, and lymphoma).
- Exacerbated by iron deficiency, inflammatory or neoplastic disease, gastrointestinal blood loss, hemolysis, and myeloproliferative disorders.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
- Anemia of chronic infectious, inflammatory, or neoplastic disease; myeloproliferative disease; chronic blood loss; aplastic anemia; endocrine disease; drug reaction; and chronic immune-mediated, toxic, viral, rickettsial, or parasitic anemia; hemodilution.
- Regenerative anemia excludes diagnosis of anemia of CKD.
- Generally masked until advanced CKD.

CBC/BIOCHEMISTRY/URINALYSIS
- Normocytic, normochromic, hypoproliferative anemia (progressive; anemia may be masked by dehydration).
- Reticulocytes—low corrected indices and absolute counts ($\leq 10{,}000/\mu L$).
- Moderate to advanced CKD—elevated BUN, creatinine, and phosphorus; variably high calcium; variably low bicarbonate and potassium.
- High BUN:creatinine ratio may predict concurrent" gastrointestinal blood loss.
- Impaired urine-concentrating ability, possible proteinuria, and variably active sediment.

OTHER LABORATORY TESTS
- Serum iron—normal or variably low.
- Transferrin saturation—normal or variably low ($< 20\%$).
- FeLV and FIV and/or haemobartonella testing (cats) or rickettsial titers or PCR (dogs) to exclude agent-induced myelodyscrasia.
- Serum erythropoietin—normal (inappropriately) or low.

IMAGING
- Small, irregular kidneys with loss or disruption of renal architecture detected by radiography or ultrasonography.
- Enlarged, polycystic, hydronephrotic, infiltrative.

DIAGNOSTIC PROCEDURES
Cytologic examination of bone marrow—erythroid hypoplasia; myeloid:erythroid ratio normal or high; stainable iron normal or variably low.

TREATMENT

- Stabilize azotemia in patients in with uremic crisis.
- Ensure adequate and appropriate nutrition.
- Stabilize any metabolic derangement (e.g., acidosis) that could contribute to shortened RBC lifespan and or anorexia.
- Minimize micronutrient deficiencies that could negatively impact rbc production.
- Identify and manage GI blood loss (gastric acid suppression with H2 blockers or proton pump inhibitors) (GI protectants such as sucralfate).
- Ensure that patient is iron replete (serum iron panel).
- Correct systemic hypertension.

MEDICATIONS

DRUG(S) AND FLUIDS

Blood Transfusion
- Short-term, rapid correction if hypoxic distress (typically PCV $\leq$ 15%)—give compatible whole blood or packed RBCs.
- Target PCV is 25–30%.
- May be given intermittently for prolonged management, although compatibility issues are likely to occur long term.
- EPO support for progressive or symptomatic anemia (dogs, PCV $\leq$ 25%; cats, PCV $\leq$ 23%).

Erythropoietin Replacement
- Epoetin alfa (r-HuEPO)—original synthetic erythropoiesis stimulating protein, replica of human erythropoietin (Epogen and Procrit); provides consistent, rapid, and long-term correction of anemia in dogs and cats with CKD; potential for anti-r-HuEPO antibody production and pure red cell aplasia.
- Darbepoetin alfa (Aranesp), a new hyperglycolylated analogue of r-HuEPO with prolonged half-life and sustained effects; very effective with significantly less tendency for antibody induction; should be used preferentially to epoetin alfa.
- Target PCV—dogs, 30–35%; cats, 30%.
- Initial dosage: darbepoetin alfa—0.5–2.0 μg/kg SC/IV once weekly until PCV reaches low end of target, then decrease to q2–4 weeks as needed to maintain target. Recommend PCV prior to EVERY injection to avoid overtreatment.
- Epoetin alfa—50–100 U/kg SC thrice weekly until low end of target, then decrease to once to twice weekly.
- If converting from epoetin alfa to darbepoetin—divide weekly units by 400 to establish μg to give once weekly.
- Individualize to each patient; life-long treatment required.
- If PCV exceeds target, discontinue until upper target range is achieved, then increase dosage interval.
- Serum iron and transferrin saturation should be normalized before initiating and during treatment. Injectable iron (10 mg/kg IM) should be administered when indicated on iron panel. Injectable iron is preferable and better tolerated than oral preparations.
- Species-specific erythropoietins for dogs and cats are not currently commercially available.
- Alternative erythropoietin-stimulating treatments are under development.

Anabolic Steroids
Little or no efficacy or indication for use.

FOLLOW-UP

PATIENT MONITORING
- PCV—weekly to semi-monthly for 3 months, then monthly to bimonthly.
- Blood pressure—semi-monthly to monthly.
- Iron and transferrin saturation—at 1, 3, and 6 months, then semiannually.
- Discontinue erythropoietin if patient develops evidence of erythrocythemia, local or systemic sensitivity, anti-r-HuEPO antibody

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ANEMIA OF CHRONIC KIDNEY DISEASE (CONTINUED)

formation, pure red cell aplasia, or refractory hypertension.

POSSIBLE COMPLICATIONS

Erythropoietin-Related

- Development of erythrocythemia, seizures, hypertension, iron depletion, injection pain, and mucocutaneous reactions.
- Development of a pure red cell aplasia during the course of epoetin alfa treatment suggests formation of anti-r-HuEPO antibodies, which neutralize r-HuEPO and native erythropoietin, causing severe anemia in 20–30% of animals; often reversible with cessation of treatment.
- Development of anti-r-HuEPO antibodies occurs in less than 5% of patients with darbepoetin alfa therapy.
- Signs associated with production of anti-r-HuEPO antibodies while the patient is receiving epoetin alfa include decreasing PCV, erythroid hypoplasia, absolute reticulocyte counts approaching zero, and myeloid:erythroid ratio ≥ 8.
- Erythropoietin replacements should be used cautiously or withheld if hypertension or iron deficiency develop; treatment can be reinstituted once hypertension and iron deficiency are corrected.

Transfusion-Related

- Incompatibility reaction
- Circulatory or iron overload
- Systemic hypertension
- Transmissible infection

EXPECTED COURSE AND PROGNOSIS

- Correction of anemia increases appetite, activity, grooming, affection and playfulness, weight gain, and cold tolerance, and decreases sleeping.
- Use of erythropoietin replacement agents in dogs and cats requires careful assessment of the risks and benefits for individual patients.
- Short-term prognosis depends on the severity of the renal failure.
- Long-term prognosis is guarded to poor because of the underlying chronic renal failure.

MISCELLANEOUS

ABBREVIATIONS

- CKD = chronic kidney disease
- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus
- PCR = polymerase chain reaction
- PCV = packed cell volume
- RBC = red blood cell
- r-HuEPO = recombinant human erythropoietin

Suggested Reading

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ANEMIA, APLASTIC

BASICS

OVERVIEW
• A disorder of hematopoietic precursor cells characterized by replacement of normal bone marrow with adipose tissue. There is decreased production of granulocytes, erythrocytes, and platelets, resulting in pancytopenia in the peripheral blood. The disease is sometimes also referred to as aplastic pancytopenia.
• In the acute form, neutropenia and thrombocytopenia predominate because of the shorter life spans of these cells; in the chronic form, nonregenerative anemia also occurs. In both forms, the bone marrow exhibits variable degrees of panhypoplasia.
• There are many precipitating causes of deficient hematopoiesis, including infectious diseases, drug administration, starvation and toxin exposure; immune-mediated mechanisms are often suspected.
• Hemic/lymphatic/immune systems affected.

SIGNALMENT
Dogs and cats, no apparent breed or sex predilection. In one study, the mean age of nine affected dogs was 3 years.

SIGNS
• Acute form: fever, petechial hemorrhages, epistaxis, hematuria, melena; i.e., signs due to neutropenia and thrombocytopenia.
• Chronic form: pale mucous membranes, weakness, lethargy; i.e., signs due to anemia, in addition to signs observed in acute forms.

CAUSES & RISK FACTORS
Often not identified

Infectious Agents
• FeLV, FIV
• Canine and feline parvovirus
• Rickettsial organisms (e.g., *Ehrlichia* spp.)

Drugs and Chemicals
• Estrogen (exogenous administration, Sertoli and interstitial cell tumors)
• Methimazole (cats)
• Chemotherapeutic drugs, including azathioprine, cyclophosphamide, cytosine arabinoside, doxorubicin, vinblastine, and hydroxyurea
• Antibiotics, including trimethoprim-sulfadiazine, cephalosporins, and chloramphenicol
• Griseofulvin
• NSAIDs, including phenylbutazone and meclofenamic acid
• Fenbendazole, albendazole
• Captopril
• Quinidine
• Thiacetarsamide
• Ionizing radiation
• Mycotoxins (cats)

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Causes of pancytopenia with normal to increased bone marrow cellularity (e.g., myelodysplastic disorders, leukemia, myelofibrosis).

CBC/BIOCHEMISTRY/URINALYSIS
• Leukopenia characterized by neutropenia with or without lymphopenia.
• Normocytic, normochromic, nonregenerative anemia.
• Thrombocytopenia.

OTHER LABORATORY TESTS
• Immunologic tests for infectious diseases (e.g., serologic titers, ELISA, IFA).
• PCR for infectious agents.
• Serologic test for antierythrocyte antibodies (Coombs' test).

IMAGING
N/A

DIAGNOSTIC PROCEDURES
• Bone marrow aspiration—frequently an inadequate or fatty sample is obtained because of decreased hematopoietic tissue and replacement by adipocytes.
• Bone marrow core biopsy—permits an evaluation of architecture and reveals hypoplasia of cell lines and replacement by adipose tissue.

TREATMENT
Supportive treatment, antibiotics, blood component therapy, as dictated by clinical condition.

MEDICATIONS

DRUG(S) OF CHOICE
• Cyclosporine A—10–25 mg/kg PO q12h (dogs), 4–5 mg/kg PO q12h (cats).
• Recombinant hematopoietic growth factors (e.g., rhG-CSF: 5 μg/kg/day SC).
• Androgen and corticosteroid administration have been largely unsuccessful.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
N/A

OTHER DRUGS
• Antibiotics to treat secondary infections if fever and neutropenia present.
• Whole or component blood transfusion if indicated.

FOLLOW-UP

PATIENT MONITORING
• Daily physical examination.
• CBC every 3–5 days to weekly.
• Repeat bone marrow evaluation if necessary.

PREVENTION/AVOIDANCE
• Castration of cryptorchid males.
• Vaccination for infectious diseases.
• Frequent monitoring of CBC in cancer patients receiving chemotherapy or radiation.

POSSIBLE COMPLICATIONS
• Sepsis
• Hemorrhage

EXPECTED COURSE AND PROGNOSIS
• Guarded to poor.
• Recovery of hematopoiesis may take weeks to months, if it occurs at all.
• Spontaneous recovery occasionally occurs, especially in younger animals.

MISCELLANEOUS

SEE ALSO
Pancytopenia

ABBREVIATIONS
• ELISA = enzyme-linked immunosorbent assay
• FeLV = feline leukemia virus
• FIV = feline immunodeficiency virus
• IFA = immunofluorescent antibody (test)
• NSAID = nonsteroidal anti-inflammatory drug
• PCR = polymerase chain reaction
• rhG-CSF = recombinant human granulocyte colony-stimulating factor

Suggested Reading

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ANEMIA, HEINZ BODY

BASICS

OVERVIEW

• Heinz bodies cause hemolytic anemia and indicate oxidative damage to RBCs. • Heinz bodies form when oxidants overwhelm protective reductive pathways in RBCs; irreversible denaturation of the globin chains in hemoglobin causes precipitation and attachment of altered hemoglobin to the cell membrane. • RBCs with Heinz bodies are targeted for removal by macrophages in the spleen, and occasionally undergo intravascular lysis. • The pitting function of the spleen may remove Heinz bodies, resulting in spherocytes. • Heinz bodies are usually caused by exposure to chemical or dietary oxidants. • Cats are particularly susceptible to Heinz body formation because their hemoglobin contains more sulfhydryl groups than that of dogs. • Healthy cats may have Heinz bodies with no anemia, possibly because cats have a nonsinusoidal spleen with limited pitting function. • Heinz bodies are reported in hyperthyroidism (cats), lymphoma (cats, dogs), and diabetes mellitus (cats, dogs), possibly due to increased endogenous oxidants (e.g., β-hydroxybutyrate in ketoacidosis). Anemia may or may not be present. • Heinz bodies may be accompanied by methemoglobinemia (hemoglobin containing Fe^{3+}) and/or eccentrocytes (oxidative damage to RBC membranes causing adhesion of opposing membranes and displacement of hemoglobin to one side of the cell).

SIGNALMENT

• Dogs and cats • No sex, breed, or age disposition

SIGNS

Historical Findings

• Exposure to oxidant. • Sudden onset of weakness, lethargy, or anorexia. • Reddish-brown urine (hemoglobinuria) if severe intravascular hemolysis. • Signs related to underlying disease in animals with systemic disease and Heinz bodies.

Physical Examination Findings

• Pale and occasionally icteric mucous membranes • Dark or chocolate-colored blood with methemoglobinemia • Tachypnea, tachycardia

CAUSES & RISK FACTORS

• Dietary: onions (raw, cooked, dehydrated, and powdered), garlic (dogs), propylene glycol (cats), Chinese chives (dog). • Drugs: acetaminophen, phenacetin (cats), phenazopyridine (cats), methylene blue, vitamin K1 or K3 (dogs), DL-methionine (cats), benzocaine (topical), phenylhydrazine (dog), propofol (cats). • Miscellaneous: zinc (nuts, bolts, pennies, dermatologic creams), naphthalene (moth ball ingestion in dogs), skunk musk exposure (dogs).

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Other causes of regenerative, hemolytic anemia (e.g., immune mediated, hemoparasites). • Heinz bodies may be found in healthy or ill cats without anemia. Diagnosis of a Heinz body anemia requires documentation of a regenerative anemia, supporting evidence of a hemolytic process (e.g. hyperbilirubinemia), identification of Heinz bodies on a blood smear, and elimination of other causes of hemolysis or blood loss.

CBC/BIOCHEMISTRY/URINALYSIS

• Regenerative anemia (decreased HCT, polychromasia, nucleated RBCs) is expected if there has been sufficient time for a bone marrow response; the severity of anemia depends on dose of oxidant and duration of exposure. • Hemoglobin concentration and MCHC may be falsely increased due to Heinz body interference with hemoglobin measurement. • Heinz bodies are visible on a routinely stained blood smear as small, pale red, round inclusions that may protrude from RBC surface. They may be difficult to identify if there is marked poikilocytosis. • Single, small (< 0.5 μm) Heinz bodies may be found in RBCs of cats without anemia. • Large and/or multiple Heinz bodies in an anemic cat suggest a Heinz body hemolytic anemia. • Dogs may have concurrent eccentrocytosis on a blood smear. • Hyperbilirubinemia and bilirubinuria are possible. • Hemoglobinemia and hemoglobinuria are uncommon but occur with severe intravascular hemolysis. • Neutrophilia and monocytosis may occur.

OTHER LABORATORY TESTS

• New methylene blue stains Heinz bodies blue, making them easy to identify and quantify on a blood smear, even with marked poikilocytosis. • Measure methemoglobin if blood is dark or chocolate colored. • Serum zinc concentration if indicated.

IMAGING

Abdominal radiographs may reveal gastrointestinal metal objects in zinc toxicity.

TREATMENT

• Immediate identification and removal of oxidant may be sufficient, though it often take several days after exposure for the severity of anemia to reach nadir. • Consider administration of emetics with recent ingestion of an oxidant. • Supportive care depends on the severity of the hemolytic crisis and includes IV fluids, RBC transfusions, oxygen, and restricted activity. • Endoscopy or surgery to remove metallic items in gastrointestinal tract.

MEDICATIONS

DRUG(S) OF CHOICE

Acetaminophen toxicity in cats—N-acetylcysteine (140 mg/kg PO or IV, followed by seven additional treatments of 70 mg/kg q8h).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Administration of methylene blue to treat methemoglobinemia may exacerbate Heinz body formation.

ALTERNATIVE DRUG(S)

The use of dietary antioxidants (e.g., bioflavonoids) is controversial but may help prevent further formation of Heinz bodies.

FOLLOW-UP

PATIENT MONITORING

Serial CBCs and review of blood smears are recommended to assess RBC regeneration and disappearance of Heinz bodies.

PREVENTION/AVOIDANCE

Counsel clients about preventing exposure to oxidants.

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

Prognosis is good with removal of oxidant and supportive care once the hemolytic crisis is over.

MISCELLANEOUS

SEE ALSO

• Acetaminophen (APAP) Toxicosis
• Anemia, Regenerative
• Methemoglobinemia • Zinc Toxicosis

ABBREVIATIONS

• HCT = hematocrit • MCHC = mean corpuscular hemoglobin concentration
• RBC = red blood cell

Suggested Reading

Andrews D. Disorders of red blood cells. In: Handbook of Small Animal Practice, 5th ed. St. Louis: Saunders, 2008, pp. 632–635.
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ANEMIA, IMMUNE-MEDIATED

BASICS

DEFINITION
Accelerated destruction or removal of RBCs due to a Type II hypersensitivity reaction.

PATHOPHYSIOLOGY
• Antibodies form against endogenous unaltered RBC surface antigens (primary IMHA) or altered RBC membrane antigens (secondary IMHA). • Infectious organisms, drugs, exposure of previously unexposed antigens, or adsorption of preformed antigen-antibody complexes to the RBC membrane can alter RBC membrane antigens. • Immunoglobulin deposits on RBC membrane, causing either direct intravascular hemolysis or accelerated removal by the monocyte/macrophage system. • Intravascular hemolysis occurs when adsorbed antibodies (usually IgG) activate complement. • In vivo agglutination of RBCs occurs when IgM or high titers of IgG molecules cause bridging of RBCs. • Extravascular removal of RBCs occurs primarily in spleen, liver, bone marrow. • Nonregenerative IMHA is believed to be caused by immune-mediated destruction of RBC precursors in the bone marrow. • Rarely cold-acting antibodies cause in vivo hemolysis and erythrocyte agglutination in peripheral vasculature.

SYSTEMS AFFECTED
• Cardiovascular—tachycardia; low-grade heart murmur. • Hemic/Lymphatic/Immune—immune-mediated destruction of RBCs, elaboration of proinflammatory mediators, DIC. • Hepatobiliary—hyperbilirubinemia and icterus plus bilirubinuria when hepatic function is overwhelmed; centrilobular necrosis. • Respiratory—tachypnea. PTE may result from hypercoagulable state. • Skin—rarely cold-type IMHA may cause necrosis of extremities and ear tips.

GENETICS
Cocker spaniels are at increased risk (absence of dog erythrocyte antigen 7).

GEOGRAPHIC DISTRIBUTION
Secondary IMHA may have higher prevalence where associated infectious diseases are endemic.

SIGNALMENT
Species
Dog and cat

Breed Predilections
• Cocker spaniel at highest risk. Also, English springer spaniel, Old English sheepdog, Doberman pinscher, collie, bichon frise, miniature pinscher, and Finnish spitz. • Domestic shorthair cats.

Mean Age and Range
• Dogs, mean age 5–6 years (range 1–13 years) • Cats, mean age 2 years (range 0.5–9 years)

Predominant Sex
• Female dogs at higher risk • Male cats overrepresented

SIGNS
Historical Findings
• Lethargy/weakness/collapse • Anorexia • Exercise intolerance/dyspnea, tachypnea • Vomiting and/or diarrhea • Dark red urine • Pica (cats)

Physical Examination Findings
• Pale mucous membranes, tachycardia, tachypnea. • Splenomegaly/hepatomegaly. • Icterus and pigmenturia (hemoglobin or bilirubin). • Fever/lymphadenomegaly. • Systolic murmur. • Petechiae, ecchymoses, or melena (if concurrent thrombocytopenia or DIC). • Other findings possible (e.g., joint pain) when IMHA is component of SLE. • Necrosis of extremities and ear tips in cold-type IMHA (rare).

CAUSES AND RISK FACTORS
Primary IMHA
Poorly characterized immune dysregulation

Secondary IMHA
• Infectious causes: hemotrophic *Mycoplasma* spp., *Ehrlichia* spp., *Anaplasma phagocytophilum, Anaplasma platys, Babesia* spp., *Leishmaniasis, Dirofilaria immitis,* FeLV, FIP, chronic bacterial infection. • Neoplasia: lymphoma, lymphoid leukemia, hemangiosarcoma, hemophagic histiocytic sarcoma. • Drugs: beta lactam antibiotics, propylthiouracil, methimazole, sulfonamides. • SLE • Neonatal isoerythrolysis • Hemolysis due to DEA incompatible blood transfusion • Exposure to infectious agents, vaccination, chemicals/drugs, surgery, hormonal change, or other stressful event is hypothesized as potential trigger for IMHA.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Dogs
• Pyruvate kinase deficiency • Phosphofructokinase deficiency • Toxicity (zinc, onions, garlic, broccoli, copper, naphthalene, skunk musk) • Snake/spider evenomation (coral snakes, recluse spiders) • Severe hypophosphatemia • Anemia due to hemorrhage (immune-mediated thrombocytopenia, rodenticide toxicosis) • Microangiopathic anemia due to splenic neoplasia, DIC, splenic torsion

Cats
• Toxicity (acetaminophen zinc, onions, garlic) • Severe hypophosphatemia • Congenital feline porphyria • Increased osmotic fragility (Abyssinian, Somali)

CBC/BIOCHEMISTRY/URINALYSIS
• CBC—anemia, high MCV (3–5 days post-hemolytic episode), spherocytes, polychromasia, increased RBC distribution width, leukocytosis with neutrophilia and left shift, monocytosis, lymphocytosis (cats). Anemia is nonregenerative in 30% of dogs and 50% of cats. • Serum biochemistry—hyperbilirubinemia, hemoglobinemia, high ALT. • Urinalysis—hemoglobinuria, bilirubinuria.

OTHER LABORATORY TESTS
• Spontaneous saline agglutination test—before and after washing RBCs. • Positive direct antiglobulin test (Coombs' test)—positive in up to 75% of animals with IMHA. • Flow cytometric detection of membrane-bound immunoglobulin and complement. • Reticulocytosis—absolute count $>60{,}000/\mu$L (dogs) or $>50{,}000/\mu$L (cats) in regenerative IMHA. • Thrombocytopenia 60% of dogs. • Prolonged APTT and PT, increased fibrin degradation products and d-dimer, decreased antithrombin in animals with DIC. • Positive ANA titer and LE cell test (animals with SLE). • Positive serologic titers or PCR in secondary IMHA due to infectious causes. • Evidence of hematologic parasites in blood smears (secondary IMHA due to infectious causes).

IMAGING
• Radiographic findings—hepatomegaly/splenomegaly; thorax usually normal; may see evidence of PTE (patchy alveolar pattern, interstitial pattern, pleural fluid), but dogs with pulmonary embolism may have normal thoracic radiographs. • Ultrasonographic findings—hepatomegaly/splenomegaly; liver/spleen can be mottled and hyperechoic or hypoechoic.

DIAGNOSTIC PROCEDURES
• Bone marrow aspirate usually reveals erythroid hyperplasia. • With nonregenerative IMHA, maturation arrest or erythroid hypoplasia may be evident. • In chronic IMHA, myelofibrosis may be present.

PATHOLOGIC FINDINGS
• Hepatosplenomegaly, centrilobular hepatic necrosis • Splenic and hepatic extramedullary hematopoiesis • Reactive lymphadenomegaly • PTE and DIC

TREATMENT

APPROPRIATE HEALTH CARE
• Inpatient during acute hemolytic crisis; outpatient when PCV stabilized, ongoing hemolysis controlled, and clinical signs of anemia resolved. • Inpatient if complications such as DIC, PTE, thrombocytopenia, gastrointestinal bleeding, or a need for

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ANEMIA, IMMUNE-MEDIATED (CONTINUED)

multiple transfusions. • Chronic low-grade extravascular hemolysis can be treated on outpatient basis if the patient not exhibiting clinical signs secondary to anemia.

NURSING CARE

• Fluid therapy to maintain vascular volume and correct dehydration. • Packed RBCs typed or cross-matched for naive recipient. Blood should be cross-matched for recipients that have received prior transfusions. Whole blood acceptable if packed RBCs not available. • Transfusion volume = recipient weight (kg) × 85 (dog) or 50 (cat) × desired PCV-current PCV/donor PCV. • Transfusion rate 0.25 mL/kg/hr for first 30 minutes then 5–10 mL/kg/h. • Monitoring for complications such as PTE, bleeding (especially GI), DIC, infection. • Cage rest.

CLIENT EDUCATION

• IMHA and complications (e.g., DIC, PTE) can be fatal. • Life-long treatment may be needed; disease may recur. • Side effects of treatment may be severe.

SURGICAL CONSIDERATIONS

• Splenectomy can be considered if medical management fails to control disease.
• Consider blood product administration preoperatively.

MEDICATIONS

DRUG(S) OF CHOICE

• Corticosteroids—prednisone 1–2 mg/kg/day q12h for 2–4 weeks. Use prednisolone in cats due to higher bioavailability. • Once PCV above 30%, decrease dose to 1 mg/kg q12h. Then taper by a maximum rate of 25–50% per month over a 3- to 6-month period, depending upon PCV and severity of side effects. If after 3–6 months disease is in remission on a low q48h dose, try discontinuing the drug. • Add additional immunosuppressive drug such as azathioprine (dogs) cyclosporine (cats) if poor response to prednisone after 5–7 days or if poor prognostic indicators (e.g., intravascular hemolysis, serum bilirubin > 8–10 mg/dL, persistent autoagglutination, Evans syndrome). • Azathioprine dose 2 mg/kg/day, can decrease to 0.5–1.0 mg/kg q48h if bone marrow suppression. Monitor for immuno-suppression, hepatotoxicosis, pancreatitis.
• For prevention of thromboembolism (dogs) consider unfractionated heparin 300 U/kg SC q6–8h (dose adjusted based on APTT prolongation or measurement of anti-Xa activity) or ultra-low-dose aspirin 0.5–1.0 mg/kg/day or enoxaparin (low-molecular-weight heparin) 0.8 mg/kg SC q6h or 1.5 mg/kg q12h, or clopidogrel 2–3 mg/kg PO q24h (loading dose 10 mg/kg/day).
• Address underlying cause (e.g., infection and drugs) if secondary IMHA.

CONTRAINDICATIONS

• No heparin, enoxaparin, or aspirin in dogs with severe thrombocytopenia (< 80,000/μL).
• Do not use multiple cytotoxic drugs concurrently.

PRECAUTIONS

• No azathioprine in cats because of risk of bone marrow toxicity. • Prednisone/prednisolone can cause signs of Cushing's syndrome and may increase risk of PTE, pancreatitis, diabetes mellitus, secondary infection, gastric ulcers (consider gastric protectants). • Cytotoxic drugs can cause bone marrow suppression, secondary infection, pancreatitis (azathioprine), GI upset (cyclosporine, azathioprine, mycophenolate mofetil), gingival hyperplasia, papillomatosis (cyclosporine), infertility.

POSSIBLE INTERACTIONS

Azathioprine and prednisone have been associated with development of pancreatitis.

ALTERNATIVE DRUG(S)

• Dexamethasone (0.25–0.5 mg/kg/day IV)—can be used instead of prednisone/prednisolone in animals that do not tolerate oral drugs, until oral intake is possible.
• Chlorambucil—for cats, 0.1–0.2 mg/kg PO q24h initially, then q48h. • Cyclosporine—microemulsion, e.g., Atopica—dogs, 5–10 mg/kg/day PO divided twice daily; cats, 0.5–3 mg/kg q12h. • Mycophenolate mofetil 10–17 mg/kg q24h.

FOLLOW-UP

PATIENT MONITORING

• Monitor heart rate, respiratory rate, temperature frequently. • Monitor for adverse reactions to treatment (e.g., transfusion reactions/overhydration). • If PTE suspected, monitor thoracic radiographs and arterial blood gases frequently. • During first days of treatment, check PCV daily until stable, then every 1-2 weeks for 2 months; if still stable, recheck PCV monthly for 6 months, then 2–4 times per year; rechecks need to be more frequent if patient is on long-term medication especially cytotoxic drugs. • CBC and reticulocyte count should be rechecked at least monthly during treatment,; if the neutrophil count falls < 3,000 cells/μL, discontinue cytotoxic drugs until count recovers; reinstitute at lower dosage.
• Coombs' tests and reticulocyte counts to assist in drug tapering.

PREVENTION/AVOIDANCE

Consider need for vaccination on case-by-case basis in dogs that developed IMHA after vaccination.

POSSIBLE COMPLICATIONS

• Pulmonary/multiorgan thromboembolism (up to 80% of all cases at necropsy). • DIC. • Centrilobular hepatic necrosis and renal tubular necrosis secondary to hypoxia. • Infection secondary to immunosuppressive therapy. • GI ulceration due to high-dose glucocorticoids. • Iatrogenic hyperadrenocorticism.

EXPECTED COURSE AND PROGNOSIS

• Mortality: 30–80% (dog), 25% (cat).
• Causes of death include thromboembolism, infection due to immunosuppression, DIC, persistent anemia. • Hyperbilirubinemia > 5 mg/dL, autoagglutination, intravascular hemolysis, severe thrombocytopenia, hypoalbuminemia are associated with poorer prognosis. • Response to treatment may take weeks to months; nonregenerative IMHA may have more gradual onset than typical IMHA and may be slower to respond to treatment. • IMHA may recur despite previous/current therapy.

MISCELLANEOUS

SYNONYMS

• Autoimmune hemolytic anemia
• Immune-mediated anemia

SEE ALSO

• Anemia, Regenerative • Chapters on causes of secondary IMHA • Cold Agglutinin Disease • Disseminated Intravascular Coagulation

ABBREVIATIONS

• ALT = alanine aminotransferase • ANA = antinuclear antibody • APTT = activated partial thromboplastin time • DEA = dog erythrocyte antigen • DIC = disseminated intravascular coagulation • FeLV = feline leukemia virus • FIV = feline immunodeficiency virus IMHA = immune-mediated hemolytic anemia • LE = lupus erythematosus • MCV = mean cell volume • PCR = polymerase chain reaction • PCV = packed cell volume • PTE = pulmonary thromboembolism • PT = prothrombin time • RBC = red blood cell • SLE = systemic lupus erythematosus

Suggested Reading

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Client Education Handout available online

ANEMIA, IRON-DEFICIENCY

BASICS

OVERVIEW
• Adults—caused by chronic external hemorrhage.
• RBC produced by iron-limited erythropoiesis.
• Importance—prompts clinician to look for chronic external blood loss.

SIGNALMENT
• Fairly common in adult dogs.
• Rare in adult cats.
• Transient neonatal iron-deficiency anemia may occur at 5–10 weeks of age in kittens.

SIGNS
• Signs of anemia (e.g., lethargy, weakness, and tachypnea) and underlying disease.
• Intermittent melena with gastrointestinal blood loss.
• Possible heavy bloodsucking parasite load.

CAUSES & RISK FACTORS
• Chronic external blood loss.
• Common causes—GI lymphoma, hookworms, GI neoplasia.
• Less common—skin (e.g., severe flea infestation) and urinary tract.
• Blood donor overuse.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Any cause of anemia, especially hemorrhage.
• Microcytic anemia in portosystemic shunt disease may or may not be due to iron deficiency.
• Anemia of inflammatory disease iron-limited erythropoiesis.

CBC/BIOCHEMISTRY/URINALYSIS
• PCV usually but not always decreased, generally 10–40% in dogs.
• Anemia either regenerative or non-regenerative.
• Microcytosis—indicated by low normal or low MCV, accompanied by increased heterogeneity, detected by erythrocyte histogram widening or increased RDW.
• RBC changes include microcytosis, hypochromia due to thin cell geometry, and keratocyte and schistocyte formation.
• Newer erythrocyte indices MCVr and CHr, are sensitive for detecting iron-limited erythropoiesis; available on one hematology system.
• Lab tests indicate iron-limited erythropoiesis, but may not differentiate true from functional iron deficiency. Clinical findings of inflammatory disease versus blood loss are required to differentiate cause of iron limited erythropoiesis. It is also possible that inflammatory disease and true iron deficiency may occur concurrently.
• RBC morphologic changes—hypochromia (increased central pallor), oxidative lesions (e.g., keratocytes), fragmentation.
• Decreased MCHC not sensitive or specific.
• Thrombocytosis may occur.
• Hypoproteinemia—consistent with blood loss.

OTHER LABORATORY TESTS
• Hypoferremia (serum iron < 70 μg/dL) and transferrin saturation < 15% support the diagnosis.
• Serum iron values may be normal during iron repletion, if blood loss is intermittent.
• Fecal exam for hookworms.
• Fecal examination for occult blood or melena.

IMAGING
Imaging studies—GI disease that may account for blood loss.

DIAGNOSTIC PROCEDURES
As indicated by underlying disease.

TREATMENT

• Identify / correct cause of blood loss.
• Administer iron until hematologic features of iron deficiency resolve.
• If severe (i.e., PCV < 15%), transfusion may be required; whole blood (10–20 mL/kg IV) or packed RBC.

MEDICATIONS

DRUG(S)
Iron Supplementation

Parenteral Iron Supplementation
• Initiate iron therapy with injectable iron.
• Iron dextran—a slowly released form of injectable iron; one injection (10–20 mg/kg IM) followed by oral supplementation.

Oral Iron Supplementation
• Animals with severe iron deficiency may have impaired intestinal iron absorption, making oral therapy of little value until partial iron repletion has occurred.
• Follow injected iron with oral iron supplement for 1–2 months, or until resolved.
• Kittens undergo spontaneous iron repletion beginning at 5–6 weeks of age.

Oral Iron Supplements
• Ferrous sulfate powder—place in food or drinking water (100–300 mg PO q24h).
• Ferrous gluconate—one (325 mg) tablet PO q24h.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
Oral iron is associated with unexplained death in kittens and should be avoided.

FOLLOW-UP

• Monitor CBC every 1–4 weeks; if the anemia is severe, more frequently as needed.
• Effective treatment associated with an increase in MCV and reticulocyte volume.
• Erythrocyte histogram—effective treatment associated with microcytic subpopulation reduction over time; it may take a few months to normalize the histogram.

MISCELLANEOUS

ABBREVIATIONS
• CHr = reticulocyte hemoglobin content
• GI = gastrointestinal
• MCHC = mean cell hemoglobin concentration
• MCV = mean cell volume
• MCVr = mean reticulocyte volume
• PCV = packed cell volume
• RBC = red blood cell
• RDW = red cell distribution width

Suggested Reading

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ANEMIA, METABOLIC (ANEMIAS WITH SPICULATED RED CELLS)

BASICS

OVERVIEW
• Sometimes occurs concomitantly with diffuse diseases of the liver, kidney, and, rarely, spleen.
• In most animals with liver disease, spiculated cells have 2–10 elongated, blunt, finger-like projections from their surfaces and are classified as acanthocytes.
• Acanthocytic anemias can be associated with renal disease; anemias of renal disease more often have oval red cells with irregular or ruffled membranes (burr cells).
• Rarely, acanthocytic anemias can be seen in association with splenic disease alone.
• Pathogenesis not entirely clear; abnormal lipid metabolism with free cholesterol loading of RBC membranes is most frequently implicated as cause.
• Dogs with disseminated abdominal hemangiosarcoma with liver involvement often have acanthocytes.

SIGNALMENT
Dogs and cats (infrequently)

SIGNS
• None in most animals (usually mild to moderate condition).
• Detection of spiculated RBCs on peripheral blood film can be first marker for liver, kidney, or splenic disease.
• In large-breed dogs with vague signs or large spleen, suggests possibility of splenic or hepatic hemangiosarcoma.

CAUSES & RISK FACTORS
• Any disease of the liver, kidneys, or possibly spleen.
• The likelihood of RBC morphologic abnormalities parallels the severity of organ involvement.
• Hemangiosarcoma involving the liver is a frequent cause.
• Observed in cats with fatty liver syndrome.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Determination of renal or hepatic causes based on results of biochemistry profile and urinalysis.

CBC/BIOCHEMISTRY/URINALYSIS
• Mild to moderately low PCV, RBC count, and hemoglobin.
• Normal mean corpuscular volume and mean corpuscular hemoglobin concentration in most animals.
• Normocytic, normochromic, and nonregenerative.
• Polychromasia on blood films only with accompanying blood loss (as with hepatic hemangiosarcoma).
• WBC changes variable, based on underlying cause of hepatic or renal pathology.
• Inflammatory conditions likely to be accompanied by inflammatory leukogram.
• Variable findings in liver and kidney function tests (serum biochemistry and urinalysis).

Hepatic Diseases
• High ALT, ALP, and γ-glutamyl transferase.
• High bile acids, serum ammonia.
• Possibly low albumin and serum urea nitrogen.
• Bilirubinuria, bilirubin crystals in urine.

Renal Diseases
• High serum urea nitrogen, creatinine, and phosphorus.
• Highly variable urinalysis findings, including isosthenuria (urine specific gravity 1.008–1.025 in dogs; 1.008–1.035 in cats).
• Tubular and/or protein casts.
• Pyuria.
• Proteinuria.
• Hematuria.

OTHER LABORATORY TESTS
None

IMAGING
Abdominal radiographs and ultrasound—evaluate hepatic, renal, and splenic structure.

DIAGNOSTIC PROCEDURES
Liver or kidney biopsy if indicated.

TREATMENT
Focus treatment on diagnosis and treatment of underlying hepatic, renal, or splenic disease.

MEDICATIONS

DRUG(S)
Variable according to underlying cause.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
Variable according to underlying cause.

FOLLOW-UP
Monitor CBC periodically while treating the underlying condition.

MISCELLANEOUS

SEE ALSO
• Anemia of Chronic Kidney Disease
• Hemangiosarcoma, Spleen and Liver

ABBREVIATIONS
• ALP = alkaline phosphatase
• ALT = alanine aminotransferase
• PCV = packed cell volume
• RBC = red blood cell
• WBC = white blood cell

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ANEMIA, NONREGENERATIVE

BASICS

DEFINITION
Low RBC mass without evidence of increased polychromasia or reticulocytosis in the peripheral blood.

PATHOPHYSIOLOGY
• Low erythroid production or release. • Onset of anemia and its related signs insidious unless RBC survival is concurrently shortened by hemorrhage or hemolysis. • May be caused by selective alteration in erythropoiesis or generalized bone marrow injury affecting leukocytes and platelets as well. • Mechanisms for selectively altered erythropoiesis include deficient hormonal stimulation, nutritional deficiency, cytokine-mediated iron sequestration, and disturbed metabolism in or destruction of precursors; generalized bone marrow injury usually caused by toxin, infection, or infiltrative process.

SYSTEMS AFFECTED
• Cardiovascular—heart murmur from low blood viscosity • Hemic/Lymph/Immune • Hepatobiliary—centrilobular degeneration from hypoxic injury

SIGNALMENT
• Varies with primary cause. • Giant schnauzer, Australian shepherd dog, border collie, beagle—congenital cobalamin malabsorption.

SIGNS
General Comments
• Usually secondary. • Signs associated with primary disease often precede signs of anemia.

Historical Findings
• Lack of energy, exercise intolerance, inappetence, and cold intolerance. • Other findings reflect primary condition: polyuria and polydipsia (e.g., CRF), paint exposure from remodeling old houses (e.g., lead poisoning), treating female dogs for mismating or urinary incontinence or feminization in male dogs (e.g., hyperestrogenism), failure to thrive observed at 8–12 weeks of age (hereditary cobalamin malabsorption).

Physical Examination Findings
• Pallor, heart murmur (severe anemia), and possibly tachycardia or polypnea. • Signs reflecting primary condition: oral ulcerations (e.g., CRF), cachexia (e.g., cancer), organomegaly (e.g., lymphoma), gastrointestinal or CNS signs (e.g., lead poisoning), symmetrical alopecia (e.g., hypothyroidism and hyperestrogenism).

CAUSES
Nonregenerative Anemia without Other Cytopenias
• Anemia of inflammatory disease (AID)—most common cause of mild nonregenerative anemia; can be seen within 3–10 days of infection, inflammation, tissue injury, immune-mediated processes, and neoplasia; increased liver production of hepcidin and release of cytokines from T-lymphocytes and macrophages lead to iron sequestration in macrophages, decreased iron absorption; low serum iron and transferrin, increased ferritin, decreased EPO production and function, and shortened RBC lifespan. • Chronic renal failure—kidneys fail to produce adequate EPO; uremic toxins shorten RBC lifespan and impair response to EPO. • Chronic liver disease—shortened RBC survival caused by changes in RBC membrane lipids; functional iron deficiency due to decreased transferrin synthesis and impaired mobilization of hepatic iron. • Endocrine disease—thyroid hormones and cortisol stimulate erythropoiesis and facilitate the effect of erythropoietin. • Immune-mediated destruction of precursors—pure red cell aplasia. • Infectious destruction of precursors (although usually > one cell line is involved), e.g., FeLV and ehrlichiosis, *Cytauxzoon felis*.

Nutritional or Mineral Deficiency/Toxicity
• Iron deficiency—usually due to chronic external blood loss; initially regenerative, but as severity increases, anemia becomes nonregenerative. • Cobalamin (vitamin B_{12}) and/or folate deficiency—rare in dogs and cats; can be caused by dietary insufficiency, malabsorption, or chronic drug administration (e.g., sulfas, methotrexate, anticonvulsants) that inhibits folate; congenital defect in cobalamin absorption in giant schnauzers, border collies, Australian shepherd dogs, and beagles; can occasionally cause normocytic anemia and hypersegmented neutrophils; megaloblastic changes possible in the marrow. • Disruption of precursor metabolism—chronic lead toxicity and possibly high concentrations of aluminum, arsenic, and cadmium inhibit heme synthesis; cadmium and lead cause renal toxicity and impaired EPO production.

Nonregenerative Anemia with Other Cytopenias
• Toxicities—drugs or chemicals (e.g., cancer chemotherapeutics, chloramphenicol, phenylbutazone, trimethoprim-sulfadiazine, zonisamide, phenobarbital, griseofulvin, methimazole, fenbendazole, albendazole, and benzene), hormones (e.g., estrogen toxicity secondary to abortifacient therapy and Sertoli cell tumor). • Infections—FeLV, FIV, ehrlichiosis, babesiosis, and parvoviral infection (recovery usually precedes development of anemia). • Infiltrative processes—myelodysplasia, myeloproliferative and lymphoproliferative diseases, metastatic neoplasia, myelofibrosis, and osteosclerosis.

RISK FACTORS
• Renal failure • Inflammatory or chronic disease • Liver failure • Sertoli cell tumor • Cancer • Chronic blood loss • Cats from multicat households (FeLV) • Lead or arsenic exposure—chronic

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Regenerative anemia initially nonregenerative; sudden onset of signs more consistent with regenerative than nonregenerative anemia; exacerbation of a chronic condition may produce the appearance of an acute onset.

LABORATORY FINDINGS
Disorders That May Alter Laboratory Results
• Lipemia can falsely elevate hemoglobin and MCHC values. • Lead toxicity-increased NRBC may falsely elevate the WBC count.

Valid If Run in Human Laboratory?
• Dogs—yes. • Cats—yes, if hematology instrument uses species-specific parameters; instruments designed strictly for human specimens may under-count small feline RBCs.

CBC/BIOCHEMISTRY/URINALYSIS
CBC and Blood Smear
• PCV, RBC count, and hemoglobin low. • Anemia usually normocytic, normochromic, with normal MCV and MCHC. • Macrocytosis (high MCV)—without polychromasia suggests nuclear maturation defect (cells skip a division); seen in cats with FeLV; rarely caused by vitamin B_{12} or folate deficiency. • Microcytosis (low MCV)—suggests cytoplasmic maturation defect (cells undergo extra division); iron deficiency most common cause; in late stages, concurrent hypochromasia (low MCHC) common in dogs but not in cats; seen in approximately one-third of patients with hepatic insufficiency or vascular shunting. • Specific RBC morphologies—schistocytes common with iron deficiency ± visibly hypochromic RBCs (dogs); acanthocytes with liver disease; target cells with iron deficiency, liver disease, and hypothyroidism. • Inflammatory leukogram supports AID. • Thrombocytosis common in iron deficiency. • High number of NRBCs without polychromasia or disproportionate to the degree of anemia and polychromasia seen with lead toxicity, EMH, heat stroke, and injury to bone marrow stroma by endotoxemia or hypoxia. • RBC or WBC precursors in peripheral blood without orderly progression to more mature forms suggest myelodysplasia or myeloproliferative disease. • Concurrent

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ANEMIA, NONREGENERATIVE (CONTINUED)

cytopenia in other cell lines without evidence of marrow responsiveness (e.g., band neutrophils and macroplatelets) suggests generalized bone marrow injury.

Serum Biochemistry and Urinalysis

• CRF: high BUN and creatinine with inadequate urine concentration (dogs, < 1.030; cats, < 1.035). • Liver disease: high ALT, total bilirubin, or elevated bile acids suggests liver disease. • Hypothyroidism: high serum cholesterol (> 500 mg/dL).
• Hypoadrenocorticism: Na/K < 23, lymphocytosis, and eosinophilia.

OTHER LABORATORY TESTS

• Reticulocyte count—value of < 95,000/μL (dogs) or < 60,000/μL (cats) (automated counts) accompanied by a low PCV confirms nonregenerative anemia. • Direct antiglobulin test (Coombs')—spherocytosis, autoagglutination, or positive Coombs' test provides support for immune-mediated destruction of erythroid precursors. • Serum iron profile—may be indicated for patients with microcytic anemia; with iron deficiency both serum iron and ferritin are low, while total iron-binding capacity varies; with AID, serum iron is low but serum ferritin is high (MCV and MCHC usually normal). • Bile acids measurement—may be indicated for evaluation of microcytic anemia; high values suggest hepatic insufficiency or vascular shunting. • Serum lead—indicated when NRBCs are present, especially with concurrent gastrointestinal or CNS signs; value > 30 μL/dL (0.3 ppm) strongly supports lead intoxication. • Serologic testing—FeLV test in any cat with nonregenerative anemia; *Ehrlichia canis, Anaplasma phagocytophilia,* and *Babesia* PCR assays indicated in dogs with unexplained anemia, especially when concurrent with thrombocytopenia. • Endocrine testing—when clinical signs and laboratory tests suggest hypothyroidism (T_4, free T_4, and TSH concentrations) or hypoadrenocorticism (ACTH stimulation test). • Serum cobalamin ± urine methylmalonic acid concentrations—puppies at risk for hereditary cobalamin malabsorption.

DIAGNOSTIC PROCEDURES

Cytologic Examination of Bone Marrow and Core Biopsy

• Cytologic examination of aspirate indicated in all patients unless primary cause is apparent (e.g., AID and CRF). • Bone marrow core biopsy—useful in evaluation of bone marrow architecture and overall cellularity; important for diagnosis of aplastic marrow or myelofibrosis. • Erythroid hypoplasia or aplasia confirms the problem, although history and other tests may be needed to determine the underlying etiology. • Myeloid hyperplasia and high iron stores support AID. • Classically, iron deficiency has expanded erythron and high numbers of metarubricytes; absence of iron stores supportive in dogs, but not cats. • Increased erythrophagocytosis suggests injury to cells (e.g., immune-mediated and toxic causes). • Incomplete maturation sequence suggests injury to specific maturation stage (e.g., immune-mediated and toxic causes) or possibly incomplete recovery from a previous injury (recheck in 3–5 days). • Disorderly maturation and atypical cellular morphology suggest myelodysplastic syndrome. • Hypercellular marrow with increased blast cells (> 20% of nucleated cells) indicates hematopoietic neoplasia; immunophenotyping can identify affected cell line(s); circulating neoplastic cells may or may not be seen. • Non-marrow cells indicate metastatic neoplasia.

Abdominal Ultrasound

Evaluation of microcytic anemia; look for intestinal neoplasia or other source of external blood loss.

TREATMENT

• Anemia usually resolves with resolution of underlying disease. • Conditions associated with severe anemia or pancytopenia often carry guarded-to-poor prognosis and may involve long-term treatment without complete resolution. • Metabolic compensation occurs with slowly developing nonregenerative anemia; thus mild to moderately severe anemia (PCV > 15%) generally requires no supportive intervention. • For patients with severe anemia (PCV < 10–15%), the degree of hypoxia may require transfusion (e.g., 6–10 mL/kg for packed RBCs; 10–20 mL/kg for whole blood). Less blood may be needed in animals with chronic anemia. • Determine blood type prior to transfusion to ensure compatibility. Cross match against donor blood if blood typing reagents are not available, or if patient requires a second transfusion more than 4 days after the first transfusion. • If blood volume and tissue perfusion are compromised by concurrent blood loss or shock, administer lactated Ringer's solution or colloids. • With chronic anemia, volume overload is a concern—blood products and fluids should be given slowly.

MEDICATIONS

DRUG(S)

• Erythropoietin in patients with anemia of CRF (see Anemia of Chronic Kidney Disease).
• Iron supplementation in patients with iron deficiency anemia (see Anemia, Iron-Deficiency).
• May supplement with folic acid at rate of 4–10 mg/kg/day.
• May supplement with cobalamin (vitamin B_{12}) at rate of 100–200 mg/day PO (dogs) or 50–100 mg/day PO (cats); parenteral cyanocobalamin administration (50 μg/kg or 0.5–1 mg/dog SC weekly to monthly) needed in dogs with inherited cobalamin malabsorption.

PRECAUTIONS

Monitor for transfusion reactions (see Blood Transfusion Reactions).

FOLLOW-UP

PATIENT MONITORING

• With severe anemia: PCV and blood smear examination every 1–2 days. • Stable animals with chronic or slowly improving disease course: reevaluate every 1–2 weeks.

MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

Some pregnant animals have mildly low PCV, caused by expanded blood volume.

SYNONYMS

Non-responsive anemia

ABBREVIATIONS

• ACTH = adrenocorticotropic hormone
• AID = anemia of inflammatory disease
• ALT = alanine aminotransferase • CNS = central nervous system • CRF = chronic renal failure • EMH = extramedullary hematopoiesis • EPO = erythropoietin
• FeLV = feline leukemia virus • FIV = feline immunodeficiency virus • IL-1 = interleukin-1 • MCHC = mean corpuscular hemoglobin concentration • MCV = mean cell volume • NRBC = nucleated red blood cells • PCR = polymerase chain reaction
• TSH = thyroid stimulating hormone

INTERNET RESOURCES

Erythrocytes: Overview, Morphology, Quantity; A.H. Rebar, P.S. MacWilliams, B.F. Feldman, et al.: http://www.ivis.org/advances/Rebar/Chap4/chapter.asp?LA=1

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ANEMIA, NUCLEAR MATURATION DEFECTS (ANEMIA, MEGALOBLASTIC)

BASICS

OVERVIEW

• Nonregenerative anemia characterized by arrested development of the nuclei of RBC precursors (as a result of interference with DNA synthesis) while the cytoplasm develops normally (nuclear-cytoplasmic asynchrony). • Affected RBC precursors fail to divide normally and thus are larger than corresponding normal precursors with the same degree of cytoplasmic maturity (hemoglobinization); because their nuclei are deficient in chromatin (DNA), they have a distinctive open and stippled appearance; these giant precursors with atypical, immature nuclei are known as megaloblasts. • Although these asynchronous changes are most prominent in RBC precursors, WBC and platelet precursors are similarly affected.

SIGNALMENT

• Dogs and cats. • Spontaneous, clinically unimportant occurrence in toy poodles (occasional). • Breed predilection: giant schnauzers, also border collies, Australian shepherds, and beagles with inherited cobalamin malabsorption. • Defect usually acquired.

SIGNS

• In dogs, generally mild, usually not clinically important. • In cats with FeLV-associated nuclear maturation anemia, FeLV-related signs can be anticipated. Anemia may be mild to severe.

CAUSES & RISK FACTORS

• Infectious—FeLV; retroviral infection the most common cause of megaloblastic anemia in cats. FIV has been reported as a cause much less frequently. • Nutritional—folic acid and vitamin B_{12} deficiencies (Giant Schnauzers and other with inherited cobalamin malabsorption). • Toxic—phenytoin, methotrexate (folate antagonist), alkylating agents (cyclophosphamide), plant alkaloids (vincristine), antimetabolites (azathioprine). • Congenital—toy and miniature poodles.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• In dogs, all other mild to moderate nonregenerative anemias, including anemia of inflammatory disease, renal disease, and lead poisoning. • Differentiation based on the distinctive CBC and bone marrow findings listed. • In cats, FeLV infection is the primary differential.

CBC/BIOCHEMISTRY/URINALYSIS

• In dogs, mild to moderate anemia (PCV: 30–40%). • In cats, anemia can be mild to severe. • Anemia classically macrocytic (high mean corpuscular volume) and normochromic (normal mean corpuscular hemoglobin concentration). However, mean corpuscular volume and mean corpuscular haemoglobin concentration can be normal. • Large, fully hemoglobinized RBC; occasional to numerous megaloblasts, particularly at the feather edge; minimal to no polychromasia. • In cats with FeLV, anemia may occur in association with a myelodysplastic syndrome or in conjunction with leukemia of a different cell line.

OTHER LABORATORY TESTS

FeLV

IMAGING

N/A

OTHER DIAGNOSTIC PROCEDURES

Bone Marrow Biopsy

• In dogs, usually hyperplastic, often in all cell lines. • In cats, marrow findings are highly variable and may be hyper- to hypocellular. • Maturation arrest with nuclear and cytoplasmic asynchrony may be seen in all cell lines. • Many megaloblastic RBC precursors may be observed. • Macrophagic hyperplasia with active phagocytosis of nucleated RBCs and megaloblasts (common).

TREATMENT

• Treat by targeting the underlying cause if possible. • Except for that occurring with FeLV in cats, megaloblastic anemia is a relatively mild condition. • Treat most patients on an outpatient basis.

MEDICATIONS

DRUG(S)

• In animals with drug toxicity, discontinue the offending drug.
• In all animals, consider supplementation with folic acid (4–10 mg/kg/day) or vitamin B_{12} (dogs, 100–200 mg/day PO; cats, 50–100 mg/day PO).
• Giant schnauzers with inherited cobalamin malabsorption require parenteral treatment with vitamin B_{12} (0.5–1 mg IM weekly to every few months).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Drugs known to cause megaloblastic anemia (e.g., methotrexate and phenytoin) should be avoided in patients whose condition results from other causes.

FOLLOW-UP

• Monitor response to treatment by CBC (weekly) and occasional bone marrow collection and evaluation. • Closely monitor FeLV-positive cats for evidence of onset of other signs of hematopoietic dyscrasia in the peripheral blood and bone marrow.
• Prognosis—depends on underlying cause; in FeLV-positive cats, prognosis guarded; in animals with drug-associated anemia, prognosis good when use of offending drug is interrupted.

MISCELLANEOUS

SEE ALSO

• Anemia, Nonregenerative • Feline Leukemia Virus Infection (FeLV)

ABBREVIATIONS

• FeLV = feline leukemia virus • PCV = packed cell volume • RBC = red blood cell • WBC = white blood cell • FIV = feline immunodeficiency virus

Suggested Reading

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ANEMIA, REGENERATIVE

BASICS

DEFINITION
Decreased circulating RBC mass (indicated by low PCV, hemoglobin, and total RBC count) accompanied by appropriate, compensatory increase in RBC production by the bone marrow (e.g., reticulocytosis in the peripheral blood and RBC hyperplasia in the bone marrow).

PATHOPHYSIOLOGY
• Caused by blood loss or hemolysis. • Hemolysis—caused by intrinsic RBC defects (e.g., congenital RBC membrane defects or enzyme deficiencies) or extrinsic factors (e.g., RBC parasites, oxidative injury, hemolysins, osmotic changes, immune-mediated RBC destruction, heat stroke, and severe hypophosphatemia. • Intravascular hemolysis may lead to DIC.

SYSTEMS AFFECTED
• Cardiovascular—murmurs with marked anemia; tachycardia. • Hemic/Lymph/Immune—erythroid hyperplasia in bone marrow; splenic EMH; splenomegaly due to EMH and histiocytic hyperplasia can be feature of extravascular hemolytic anemia. • Hepatic—anoxia causes centrilobular degeneration of the liver; hemosiderosis ± hemochromatosis possible with chronic hemolytic anemia (e.g., PK-deficient dogs) especially following repeated transfusions. • Renal—severe intravascular hemolysis rarely leads to renal tubular necrosis and acute renal failure. • Musculoskeletal—progressive osteoclerosis seen in PK-deficient dogs.

SIGNALMENT
• PK deficiency—basenji, beagle, cairn terrier, Chihuahua, dachshund, Labrador retriever, miniature poodle, pug, West Highland white terrier, and American Eskimo; and Somali, Abyssinian, and domestic shorthair cats. • PFK deficiency—English springer spaniel, American cocker spaniel, whippet, wachtelhund, and mixed breed dogs with spaniel parentage. • Marked RBC osmotic fragility—English springer spaniel and Abyssinian, Somali, Siamese, and domestic shorthair cats. • Feline congenital porphyria—Siamese and domestic shorthair cats. • Some dog breeds have a genetic predisposition for heritable coagulopathies such as factor VIII deficiency and von Willebrand disease. • Middle-aged female dogs, especially American cocker spaniel, English springer spaniel, Irish setter, Old English sheepdog, poodle, and Shetland sheepdog, are predisposed to immune-mediated syndromes, such as SLE and immune-mediated hemolytic anemia.

SIGNS
• Pallor. • Weakness, exercise intolerance. • Anorexia. • Possible heart murmur, tachycardia, bounding pulses. • Possible jaundice and hemoglobinuria. • Petechiae, epistaxis, melena suggest blood loss due to vasculitis or a platelet problem. • Hematomas or cavity bleeds suggest a coagulation factor deficiency. • Clinical signs depend on degree of anemia and rapidity of onset. • Rapid loss of 15–25% blood volume or acute hemolysis results in shock and possible death. • With chronic anemia, compensatory increases in heart rate, and eventually heart size, lessens RBC circulation time; hemoglobin can drop to as low as 50% of minimum normal value without overt signs of hypoxia.

CAUSES
Immune Mediated
• Antibodies ± complement on membrane shorten RBC lifespan. Antibodies may target RBC membrane components or may be directed against tumor antigens, infectious agents, vaccines, or drugs (e.g., sulfonamides, penicillins, cephalosporins, methimazole, amiodarone) that are either directly adherent to RBC surface or part of immune complexes adherent to RBCs. • Anemia is usually regenerative, but up to 30% of cases will be nonregenerative due to immune-mediated destruction of erythroid precursors in bone marrow. • Hemolysis may be either intravascular, through IgM-mediated activation of complement, or extravascular, through IgG-mediated phagocytosis. • Hemolytic antibodies are generally reactive at body temperature; rarely cold-acting antibodies cause in vivo hemolysis and/or RBC agglutination in cooler, peripheral vasculature. • Transfusion of a blood type B cat with type A blood can result in rapid, severe, intravascular hemolysis; neonatal isoerythrolysis seen in kittens born to a blood type B queen mated to a blood type A tom. • Canine blood type DEA 1.1 can cause hemolysis in a DEA 1.1-negative dog, although a single incompatible transfusion can be tolerated. • The newly identified blood types *Mik* (cats) and *Dal* (dogs) can cause significant hemolytic transfusion reactions in animals lacking these common RBC antigens.

Oxidant Injury
• Oxidants can cause Heinz body formation (aggregates of oxidized hemoglobin), eccentrocytes (oxidation of RBC membranes), and methemoglobinemia. • Heinz bodies are removed through extravascular hemolysis, while oxidized membrane components cause intravascular hemolysis. • Oxidants include onions, garlic, acetaminophen (especially in cats), zinc (from pennies minted after 1982, zinc oxide ointment, and zinc bolts), acute copper toxicosis, benzocaine, vitamin K_3 (dogs), propofol, phenolic compounds (moth balls), skunk musk, and phenazopyridine (cats). • In cats, some systemic diseases (e.g., diabetes mellitus, hyperthyroidism, lymphoma) enhance Heinz body formation but do not necessarily cause anemia.

Erythrocyte Parasites
• Cats: *Mycoplasma haemofelis, M. haemominutum, M. turicensis,* and *M. haematoparvum, Cytauxzoon felis.* • Dogs: *Mycoplasma haemocanis, Babesia canis,* and *B. gibsoni.*

Mechanical RBC Fragmentation
• Caused by vasculitis, thromboembolic disease or disease of any vascular organ (e.g., liver, kidney, spleen, heart). • Rare cause of anemia unless accompanied by hemorrhage.

Inherited RBC Abnormalities
• PK deficiency—impaired ATP formation, leading to premature RBC destruction; autosomal recessive trait. • PFK deficiency—marked alkaline fragility caused by impaired synthesis of 2,3-diphosphoglycerate; hemolytic episodes triggered by hyperventilation-induced alkalemia, especially after vigorous exercise; autosomal recessive trait. • Increased RBC osmotic fragility, (unknown RBC defect) leads to recurrent severe anemia and splenomegaly. • Feline congenital porphyria—enzyme deficiency in heme synthetic pathway leads to accumulation of heme precursors, hemolytic anemia and brown-red discoloration of teeth and bones. Siamese tend to have severe hemolytic anemia, while domestic shorthair cats have a less severe autosomal dominant trait that causes mild anemia.

Hypophosphatemia
Severe hypophosphatemia, secondary to treatment with insulin or phosphate binders, impairs ATP production, leading to increased erythrocyte fragility and hemolysis.

Blood Loss
• Trauma • Bleeding neoplasms (e.g., hemangiosarcoma, intestinal adenocarcinoma) • Coagulopathies (e.g., warfarin poisoning, hemophilia, thrombocytopenia) • Bloodsucking parasites (e.g., fleas, ticks, and *Ancylostoma*)
• Gastrointestinal ulcers

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Differentiated from nonregenerative anemia by high reticulocyte count.

LABORATORY FINDINGS
Disorders That May Alter Laboratory Results
• Lipemia can cause mild in vitro hemolysis, without appreciable anemia, and may falsely elevate MCHC. • Autoagglutination may falsely decrease the RBC count.
• Intraerythrocytic inclusions (e.g. basophilic

stippling or intraerythrocyte parasites may falsely increase automated reticulocyte count. • Exercise and excitement can increase RBC count, PCV, and reticulocyte count through splenic contraction.

Valid If Run in Human Laboratory?

• Dogs—yes. • Cats—yes, if hematology instrument uses species-specific parameters; instruments designed for analysis of human specimens may under-count small feline RBCs.

CBC/BIOCHEMISTRY/URINALYSIS

• PCV, RBC count, and hemoglobin low. • Total protein often low with blood loss anemia and may be the only sign with acute blood loss; normal PCV may be maintained through transient splenic contraction. • Severity of acute blood loss may be underestimated until the plasma volume has been restored by fluid administration and/or internal fluid shifts. • RBC indices vary depending on the cause of anemia and degree of regenerative response—MCV, normal to high; MCHC, normal to low in most patients; MCHC, artificially high with intravascular hemolysis and hemoglobinemia. • With iron deficiency, dogs may have a low MCV, MCH, and MCHC; cats have a low MCV but normal MCH and MCHC. • Specific RBC morphologies may suggest cause of hemolysis: marked spherocytosis suggests immune-mediated disease (not as easily detected in cats whose RBCs generally lack central pallor); Heinz bodies or eccentrocytes suggest oxidant injury; numerous schistocytes suggest microangiopathy. • Agglutinated RBCs indicate anemia is immune mediated; distinguish autoagglutination from rouleaux by generous sample dilution with saline. • Hemolysis may cause inflammatory leukogram (neutrophilia with a left shift and monocytosis). Acute blood loss may be associated with stress leukogram (mild neutrophilia and lymphopenia). • Blood loss may be accompanied by either thrombocytopenia or rebound thrombocytosis; iron deficiency is often accompanied by thrombocytosis. • Hyperbilirubinemia and bilirubinuria accompany marked hemolysis; hemoglobinemia and hemoglobinuria seen with intravascular hemolysis.

OTHER LABORATORY TESTS

• In anemia automated absolute reticulocyte count (RBC count × reticulocyte %) > 60,000/μL (cats) or > 95,000/μL (dogs) suggests regenerative anemia. • It takes 3–5 days for bone marrow to mount a peak regenerative response, so reticulocytosis may initially be absent with blood loss or hemolysis. • Direct antiglobulin test (Coombs' test) indicated when immune-mediated hemolytic anemia suspected; a positive test and evidence of spherocytosis (canine) in the peripheral blood is confirmatory; false negatives and false positives are possible. • PCR test for PK deficiency: young Basenji, beagle, dachshund, Toy Eskimo, West Highland white terrier, and cairn breeds with persistent anemia, massive reticulocytosis and a negative Coombs' test. • PCR test for PFK deficiency: spaniels and whippets with recurrent hemolytic crises.

DIAGNOSTIC PROCEDURES

• Bone marrow aspirate—needed only when reticulocytosis is lacking; RBC hyperplasia confirms regenerative response. • Bone marrow biopsy—useful in evaluation of bone marrow architecture and overall cellularity; important for confirmation of nonregenerative process.

TREATMENT

• Emergency if anemia is severe and develops rapidly. • Massive hemorrhage leads to hypovolemic shock and anoxia; acute hemolysis leads to anoxia. • Cage rest and careful observation indicated, depending on severity of signs.

Blood Loss Anemias

• Traumatic blood loss leading to shock-crystalloid fluids can rapidly correct hypovolemia and restore circulation. • RBC replacement (packed RBCs or whole blood) indicated if PCV < 15–20% and signs of severe hypoxia (i.e., extremely pale mucous membranes, weakness, tachycardia, pounding pulses, tachypnea). Initial dosage depends on product selected; 6–10 mL/kg for packed RBCs; 10–20 mL/kg for whole blood. Less blood may be needed in animals with chronic anemia. Determine blood type prior to transfusion, to ensure compatibility. Cross match against donor blood if blood typing reagents not available, or if patient requires second transfusion more than 4 days after first transfusion. • Animals with chronic blood loss are normovolemic with increased cardiac output, therefore transfusion volumes and rates should be conservative to avoid cardiac failure.

Hemolytic Anemias

Blood transfusion may be indicated; in patients with immune-mediated process, RBCs probably survive similarly to patient's own RBCs, so transfusion should not be withheld if marked signs of anemia present.

MEDICATIONS

DRUG(S)

• Iron may benefit animals with chronic blood-loss anemia (see Anemia, Iron-Deficiency).

• Hemolytic anemias—varies with cause of hemolysis.

FOLLOW-UP

PATIENT MONITORING

• Initially, monitor of RBC mass (e.g., PCV, RBC count, and hemoglobin) and morphologic features on a blood film (i.e., polychromasia) every 24 hours to evaluate effectiveness of treatment and bone marrow responsiveness. • As regeneration becomes apparent (rising RBC values and polychromasia), recheck patients every 3–5 days; return to normal values occurs about 14 days after acute hemorrhage but may take longer with immune-mediated process. • Following transfusion, monitor for complications (see Blood Transfusion Reactions).

MISCELLANEOUS

SEE ALSO

• Anemia, Heinz Body • Anemia, Immune-Mediated • Anemia, Iron-Deficiency • Babesiosis • Bartonellosis • Cytauxzoonosis • Lupus Erythematosus, Systemic • Zinc Toxicosis

ABBREVIATIONS

• ATP = adenosine triphosphate • DIC = disseminated intravascular coagulation • EMH = extramedullary hematopoiesis • MCH = mean corpuscular hemoglobin • MCHC = mean corpuscular hemoglobin concentration • MCV = mean cell volume • PCV = packed cell volume • PFK = phosphofructokinase • PK = pyruvate kinase • RBC = red blood cell • SLE = systemic lupus erythematosus

INTERNET RESOURCES

Erythrocytes: Overview, Morphology, Quantity; A.H. Rebar, P.S. MacWilliams, B.F. Feldman, et al.: http://www.ivis.org/advances/Rebar/Chap4/chapter.asp?LA=1.

Suggested Reading

Mitchell K, Krush S. Immune-mediated haemolytic anemia and other regenerative anemias. In: Ettinger SJ, Feldman EC, eds., Textbook of Veterinary Internal Medicine: Diseases of the Dog and Cat, 7th ed. St Louis, MO: Elsevier Saunders, 2010, pp. 761–772.

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A

ANISOCORIA

BASICS

DEFINITION
Asymmetric pupils

PATHOPHYSIOLOGY
• Disruption of sympathetic (causing miosis) or parasympathetic (causing mydriasis) innervation to the eye.
• Ocular disease – numerous causes.

SYSTEMS AFFECTED
• Nervous
• Ophthalmic

GENETICS
None

INCIDENCE/PREVALENCE
Common

GEOGRAPHIC DISTRIBUTION
None

SIGNALMENT
• Dog and cat
• All ages affected
• No gender predisposition

SIGNS
Unequal pupil size

CAUSES
Neurologic
See Table 1

Ocular
See Table 2

RISK FACTORS
N/A

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Must determine which pupil is abnormal—see Figure 1 and Tables 1 and 2.
• Distinguish between neurologic and ocular causes.

CBC/BIOCHEMISTRY/URINALYSIS
N/A

OTHER LABORATORY TESTS
N/A

IMAGING
• See Table 1.
• Ultrasound—use to identify ocular, retrobulbar or jugular groove lesions.
• MRI—use to identify CNS lesions.
• CT—use to identify tympanic bulla lesions.

DIAGNOSTIC PROCEDURES
• See Table 1.
• CSF tap—evaluate CNS inflammation/infection.
• ERG—evaluate retinal function.
• Pharmacologic testing—see Figure 1; postganglionic lesions cause denervation supersensitivity resulting in more rapid constriction or dilation with application of pharmacologic agents. Differentiation of pre- or postganglionic lesions can be difficult if based solely on pharmacologic testing.

PATHOLOGIC FINDINGS
Dependent on the underlying diagnosis

TREATMENT
Dependent on underlying disease

Table 1

Neurologic lesions causing anisocoria.

Sign	*PLR*	*Lesion Localization*	*Differential List*	*Diagnostic Test*
Mydriasis—Inability to constrict the pupil	No direct, present indirect	Ipsilateral optic nerve/chiasm Ipilateral oculomotor nerve/nucleus	Neuritis, neoplasia Encephalitis, neoplasia, trauma, retrobulbar mass	MRI/CSF tap/ERG MRI/CSF tap Ultrasound orbit
Miosis—Inability to dilate the pupil	Present	Brainstem C1-T2 myelopathy or C6-T2 brachial plexus Vagosympathetic trunk Tympanic bulla Trigeminal nerve	Encephalitis, neoplasia, trauma Trauma, myelitis, neoplasia, IVDH (rare) Jugular venipuncture, trauma Otitis media, neoplasia, trauma Neuritis, neoplasia	MRI/CSF tap MRI/myelogram/CT MRI/ultrasound MRI/CT MRI

Table 2

Ocular diseases causing anisocoria.

Lesion	*Associated Signs*	*Causes*
Anterior uveitis	Miosis, aqueous flare, corneal edema, conjunctival hyperemia	Infectious/inflammatory disease, trauma, neoplasia
Glaucoma	Mydriasis Sluggish/absent PLR, increased intraocular pressure, corneal edema	Primary glaucoma, secondary glaucoma
Neoplasm	Miosis/mydriasis, iris color change	Lymphoma, melanoma
Posterior synechia	Variable pupil shape, sluggish/absent PLR, anterior uveitis	Secondary to anterior uveitis
Iris atrophy	Variable pupil shape, iridal thinning, sluggish PLR	Old age change
Iris hypoplasia	Sluggish/absent PLR, irregular pupil margin, other ocular abnormalities	Congenital
Pharmacologic blockade	Mydriasis Absent direct/consensual PLR Normal vision	Atropine
Spastic pupil syndrome	Miosis, normal vision	FeLV

(CONTINUED) ANISOCORIA A

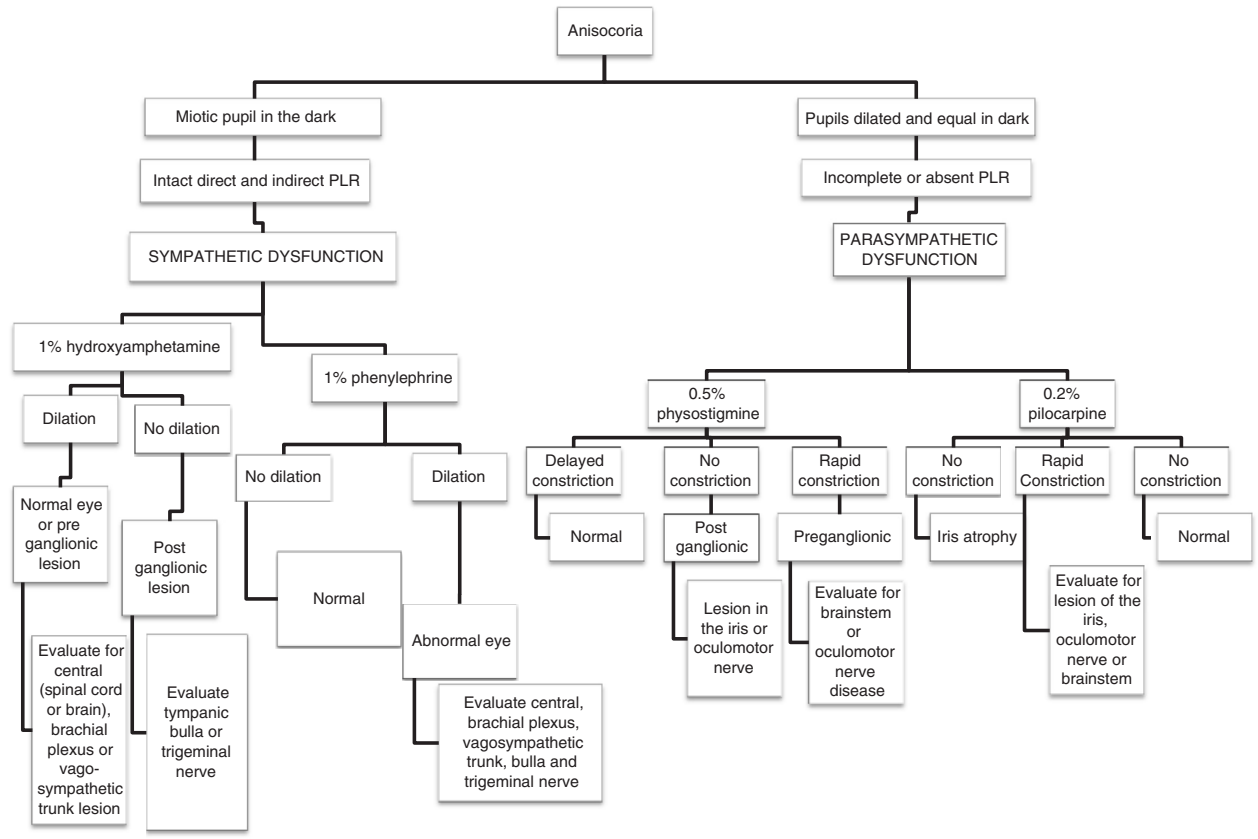

Figure 1.

MEDICATIONS

DRUG(S) OF CHOICE
Dependent on underlying disease

CONTRAINDICATIONS
N/A

PRECAUTIONS
N/A

POSSIBLE INTERACTIONS
N/A

ALTERNATIVE DRUG(S)
N/A

FOLLOW-UP

PATIENT MONITORING
N/A

PREVENTION/AVOIDANCE
N/A

POSSIBLE COMPLICATIONS
N/A

EXPECTED COURSE AND PROGNOSIS
Dependent on the underlying disease

MISCELLANEOUS

ASSOCIATED CONDITIONS
N/A

AGE-RELATED FACTORS
N/A

ZOONOTIC POTENTIAL
N/A

PREGNANCY/FERTILITY/BREEDING
N/A

SYNONYMS
None

SEE ALSO
- Anterior Uveitis—Cats
- Anterior Uveitis—Dogs
- Glaucoma
- Horner's Syndrome
- Iris Atrophy
- Optic Neuritis and Papilledema

ABBREVIATIONS
- CNS = central nervous system
- CSF = cerebrospinal fluid
- CT = computed tomography
- ERG = electroretinogram
- FeLV = feline leukemia virus
- MRI = magnetic resonance imaging
- PLR = pupillary light reflex

INTERNET RESOURCES
None

Suggested Reading

Cottrill NB, Differential diagnosis of anisocoria. In: Kirk's Current Veterinary Therapy, 14th ed. St Louis, MO: Saunders, 2009, pp. 1168–1174.

Lorenz MD, Kornegay JN. Blindness, anisocoria and abnormal eye movements. In: Handbook of Veterinary Neurology, 4th ed. St. Louis, MO: Saunders, 2004, pp. 283–295.

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Client Education Handout available online

A

ANOREXIA

BASICS

DEFINITION
The lack or loss of appetite for food; appetite is psychological and its existence in animals is assumed. Hunger is physiologically aroused by the body's need for food. Anorexia may be partial (hyporexia) or complete. Anorexia results in decreased food intake, which then leads to weight loss. Pseudoanorexia is associated with the inability to prehend or swallow food rather than actual loss of appetite.

PATHOPHYSIOLOGY
• The control of appetite is a complex interaction between the central nervous system and the periphery. • The hypothalamus and brainstem contain peptidergic feeding-regulatory neurons that act as input stations for sensory and metabolic signals. These cell populations project to several brain regions and interconnect extensively. • Sensory signals that affect appetite include the odor, taste, texture, and temperature of food as well as gastric and duodenal distention. • Metabolic signals for hunger and satiety include a variety of peptides and hormones released during the fasting and fed states as well as plasma concentrations of glucose and fatty acids interacting with nutrient-specific receptors in the liver and gastrointestinal tract. • Leptin is primarily produced by adipocytes and acts on specific hypothalamic receptors to decrease metabolism and decrease appetite.
• Neuropeptide Y release from the gastrointestinal tract induces hunger and hyperphagia, and decreases energy expenditure after food restriction. • Ghrelin produced by the stomach is a prokinetic and decreases leptin and increases neuropeptide Y production. • Cholecystokinin and bombesin released from the gastrointestinal tract decrease appetite. • Serotonin is an important and perhaps final mediator centrally via a serotonergic tract that passes near the ventromedial hypothalamus. • Dopaminergic tracts in the hypothalamus help regulate food intake and are closely associated with the lateral hypothalamus (classical feeding center). • Environmental factors including the location and timing of meals as well as learned behaviors and circadian rhythms modulate appetite and may override other signals for satiety and hunger. • Appetite is stimulated by aldosterone and corticosterone and suppressed by glucagon and somatostatin.
• Inflammatory and neoplastic disease can cause hyporexia by releasing proinflammatory cytokines such as interleukin-1, tumor necrosis factor, and interferon. • The expected upregulation of dietary intake in response to elevated energy expenditure is frequently absent in cancer patients. • Exogenous and endogenous toxins (e.g., renal and liver failure) cause hyporexia. • Any disorder that decreases cerebral arousal will potentially decrease food intake. • Gastroparesis associated with neoplasia, metabolic disorders, and primary gastrointestinal disease is associated with decreased appetite. • Fear, pain, and stress may decrease appetite.

SYSTEMS AFFECTED
All body systems

SIGNALMENT
Species
Dog and cat

Breed Predilections
N/A

Mean Age and Range
N/A

Predominant Sex
N/A

SIGNS
Historical Findings
• Refusal to eat is a common presenting complaint because pet owners strongly associate poor appetite with illness. • Patients with disorders causing dysfunction or pain of the face, neck, oropharynx, and esophagus may display an interest in food but cannot eat. These patients are referred to as being pseudoanorectic. • Animals lacking a sense of smell (anosmia) often show no sniffing behavior. • Weight loss may be noted.

Physical Examination Findings
• Clinical signs in animals with anorexia/hyporexia vary depending on the underlying cause but may include fever, pallor, icterus, pain, changes in organ size, ocular changes, abdominal distention, dyspnea, muffled heart and lung sounds, adventitious lung sounds, cardiac murmurs, and masses. Weight loss and muscle wasting may be evident depending upon the extent and duration of decreased food intake. • Pseudoanorectic patients commonly display weight loss, halitosis, excessive drooling, difficulty in prehending and masticating food, and odynophagia (painful swallowing).

CAUSES
Anorexia/Hyporexia
• Almost any systemic disease process can cause anorexia/hyporexia. • Psychological—unpalatable diet, food aversion, stress, alterations in routine and environment. • Pain. • Toxicities and drug side-effects. • Gastrointestinal disease. • Acid-base disorders. • Cardiac failure. • Endocrine and metabolic disease. • Neoplasia. • Infectious disease. • Immune mediated disease. • Respiratory disease. • Musculoskeletal disease. • Neurologic disease. • Miscellaneous (e.g., motion sickness, high environmental temperature).

Pseudoanorexia
• Any disease causing painful or dysfunctional prehension, mastication, and swallowing. • Stomatitis, glossitis, gingivitis, pharyngitis, and esophagitis (e.g., physical agents, caustics, bacterial or viral infections, foreign bodies, immune-mediated diseases, uremia). • Retropharyngeal disorders (e.g., lymphadenopathy, abscess, hematoma, sialocele). • Dental disease or periodontal disease. • Retrobulbar abscess. • Oral, glossal, pharyngeal, or esophageal neoplasia. • Neurologic disorders (e.g., rabies; neuropathies of cranial nerves V, VII, IX, X, XII; and central nervous system lesions). • Musculoskeletal lesions (e.g., masticatory myositis, temporomandibular joint disease, fractures, craniomandibular osteopathy, myasthenia gravis, botulism, and cricopharyngeal achalasia). • Salivary gland neoplasia or inflammation.

RISK FACTORS
N/A

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Perform a nutritional assessment. Gather information about the patient's diet (including all foods fed to the patient), food intake (current and normal) and obtain body and muscle condition scores. • Elicit a thorough history regarding the patient's environment, changes in routine, people, or other pets to help identify potential psychological etiologies. • Question owners about the patient's interest in food and ability to prehend, masticate, and swallow food. • A complete physical examination is required to determine the presence of systemic disease.
• Perform a thorough ophthalmic, dental, oropharyngeal, facial, and cervical examination (sedation or anesthesia may be required) in addition to observing the patient eating to rule out pseudoanorexia. • A database including a complete blood count, serum biochemistry panel, urinalysis, heartworm serology, retrovirus serology, abdominal, thoracic and cervical imaging studies, endoscopy, and histologic/cytologic examination of tissue/cell samples are often required to make a definitive diagnosis.
• Only if the history, physical examination, and database strongly suggest psychologic anorexia should further diagnostic work-up be forgone; in such cases, daily contact with the pet owner is essential until the anorexia has resolved.

CBC/BIOCHEMISTRY/URINALYSIS
• Abnormalities vary with different underlying diseases and causes of pseudoanorexia and anorexia. • Can be

(CONTINUED) ANOREXIA A

normal in patients with medical as well as psychologic causes of anorexia.

OTHER LABORATORY TESTS
Special diagnostic tests may be necessary to rule out specific diseases suggested by history, physical examination, and preliminary tests.

IMAGING
• Thoracic and abdominal imaging (radiographic and ultrasound) studies are often included in the minimum database to detect anatomic or functional abnormalities. • Videofluoroscopy may be indicated to specifically evaluate pharyngeal and esophageal function.

DIAGNOSTIC PROCEDURES
• Vary with underlying condition suspected. • Endoscopy may be useful for visualization of the pharyngeal and esophageal structures.

TREATMENT
• The mainstay of treatment is aimed at identifying and correcting the underlying disease. • Symptomatic therapy includes attention to fluid and electrolyte derangements, control of pain and/or nausea, reduction in environmental stressors, and modification of the diet to improve palatability. • Palatability can be improved by adding flavored toppings such as chicken and beef broth, seasoning with condiments such as garlic powder, increasing the moisture, fat or protein content of the food, and warming the food to body temperature. • When learned food aversion is suspected, food should be offered cautiously and removed immediately at the first signs of aversion. A patient showing signs of aversion to its normal diet may accept novel foods. • Medications the patient is receiving should be reviewed for possible side-effects leading to reduced food intake. • Significantly malnourished dogs and cats are immediate candidates for assisted feeding (enteral or parenteral feeding). Well-nourished patients with debilitating disease should not go without food for longer than 3–5 days before assisted feeding is started. • The decision to institute enteral or parenteral feeding can be influenced by several factors. In animals with inadequate food intake that have ≥ 10% body weight loss, hypoalbuminemia, poor body condition score, evidence of muscle wasting, and/or chronic disease processes, supplemental nutrition should be considered. • Techniques for providing enteral nutrition include coax feeding and placement of a nasoesophageal, esophagostomy, gastrostomy, or jejunostomy tube. Force feeding should be avoided, particularly in cats in light of the association with conditioned food aversions.

MEDICATIONS
DRUG(S) OF CHOICE
• Diazepam is a short-acting appetite stimulant with sedative properties dosed at 0.1 mg/kg IV q24h or 1 mg PO q24h in cats. • Oxazepam (2 mg/cat PO q12h) is a short-acting appetite stimulant and sedative. • Cyproheptadine, an antihistamine with antiserotonergic properties, has been used as an appetite stimulant with mixed success at a dose range of 0.2–0.4 mg/kg PO 10–20 minutes prior to feeding. • Mirtazapine is a serotonin antagonist that is dosed at 3.75–7.5 mg/dog PO q24h or 1.9 mg/cat PO q24–72h. • Analgesics may promote appetite in painful conditions but their use must be balanced with the potential to cause gastrointestinal side-effects. • Metoclopramide (0.2–0.4 mg/kg SC or PO q8–12h), ranitidine (2 mg/kg SC, IV, or PO q12h), or erythromycin (0.5–1 mg/kg PO q12h) are useful if anorexia is associated with gastroparesis or ileus. • Antiemetics such as prochlorperazine (0.1–0.5 mg/kg PO q12h), maropitant (dogs: 1 mg/kg SC or 2 mg/kg PO q24h; cats: 1 mg/kg SC or PO q24h) or metoclopramide are useful to decrease nausea-associated anorexia.

CONTRAINDICATIONS
• Avoid antiemetics and prokinetics if gastrointestinal obstruction is present or suspected. • Drugs with sedative properties should be used with caution in severely debilitated animals.

PRECAUTIONS
N/A

POSSIBLE INTERACTIONS
N/A

ALTERNATIVE DRUG(S)
N/A

FOLLOW-UP
PATIENT MONITORING
• Body weight, body and muscle condition score assessment, and hydration determination. • Monitor caloric intake to ensure return of appetite is sufficient to meet nutritional needs.

PREVENTION/AVOIDANCE
• Maximize patient comfort and wellbeing. • Enhance the palatability of the diet.

POSSIBLE COMPLICATIONS
• Dehydration, malnutrition, and cachexia are most likely; these exacerbate the underlying disease. • A loss of more than 25–30% of body protein compromises the immune system and muscle strength, and death results from infection and/or pulmonary failure. • Feline hepatic lipidosis is a possible complication of anorexia in obese cats. • Breakdown of the intestinal mucosal barrier is a concern in debilitated patients.

EXPECTED COURSE AND PROGNOSIS
Varies with underlying cause

MISCELLANEOUS
ASSOCIATED CONDITIONS
N/A

AGE-RELATED FACTORS
Nutritional support and glucose-containing fluids may be necessary to treat or prevent hypoglycemia in anorectic puppies and kittens.

ZOONOTIC POTENTIAL
N/A

PREGNANCY/FERTILITY/BREEDING
N/A

SYNONYMS
N/A

SEE ALSO
See "Causes"

ABBREVIATION
• CCK = cholecystokinin

Suggested Reading

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Remillard RL, Armstrong PJ, et al. Assisted feeding in hospitalized patients: Enteral and parenteral nutrition. In: Hand MS, Thatcher CD, Remillard RL, et al., eds., Small Animal Clinical Nutrition, 4th ed. Topeka, KS: Mark Morris Institute, 2000, pp. 351–399.

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Consulting Editor Stanley L. Marks
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Client Education Handout available online

A

ANTEBRACHIAL GROWTH DEFORMITIES

BASICS

DEFINITION
Abnormally shaped forelimbs and/or malalignments of the elbow or antebrachial carpal joints that result from maldevelopment of the radius or ulna in the growing animal.

PATHOPHYSIOLOGY
• Antebrachium—predisposed to deformities resulting from growth of one bone after premature growth cessation or decreased growth rate of the paired bone. • Decreased rate of elongation in one bone behaves as a retarding strap; the growing paired bone must twist and curve around the short bone or overgrow at the elbow or carpus; causes joint malalignment. • Normal growth—bones elongate through the process of endochondral ossification, which occurs in the physis; physis closure occurs when the germinal cell layer stops producing new cartilage and the existing cartilage hypertrophies, ossifies, and is remodeled into bone. • Hereditary—may be a component of common elbow joint malalignment in many chondrodysplastic breeds (e.g., basset hound and Lhasa apso). • Osteochondrosis or dietary oversupplementation—possibly associated with retardation of endochondral ossification (retained cartilaginous cores) in giant-breed dogs. • Hypertrophic osteodystrophy—juvenile growth syndrome with physeal and periosteal inflammation that may impede growth. • Trauma—most common cause; if germinal cell layer of the physis is damaged, new cartilage production and bone elongation are stopped. Commonly occurs with fractures involving the distal ulnar or radial growth plates. A crushing-type fracture (Salter-Harris type V) may not be detected on radiographs of the injured antebrachium, and angular deformity only becomes evident over time due to lack of growth of the affected bone.

SYSTEMS AFFECTED
Musculoskeletal

GENETICS
• Skye terriers—reported as a recessive inheritable trait. • Chondrodysplastic breeds (dogs)—disturbed endochondral ossification results in asynchronous growth of the paired bone system, resulting in altered growth and angular deformity. Affected dogs are predisposed to elbow malalignment.

INCIDENCE/PREVALENCE
• Traumatic—may occur in up to 10% of actively growing dogs that sustain injuries of the antebrachium; uncommon in cats.
• Elbow malalignment syndrome ± angular deformity (chondrodysplastic dog breeds)—fairly common and can be bilateral. Clinical abnormality in affected individuals is variable.
• Nutritionally induced—incidence decreasing as nutritional standards are improved. • Congenital agenesis of the radius (cats and rarely dogs)—occurs infrequently; results in severely bowed antebrachium and carpal subluxation.

GEOGRAPHIC DISTRIBUTION
N/A

SIGNALMENT
Species
Dog and cat

Breed Predilections
• Skye terrier—recessive inheritable form.
• Chondrodysplastic and toy breeds (especially basset hound, dachshund, Lhasa apso, Pekingese, Jack Russell terrier)—may be predisposed to elbow malalignment and incongruity. • Giant breeds (e.g., Great Dane, wolfhound)—may be induced by rapid growth owing to excessive or unbalanced nutrition, osteochondrosis, or hypertrophic osteodystrophy.

Mean Age and Range
• Traumatic—any time during the active growth phase. • Elbow malarticulations—during growth; may not be recognized until secondary arthritic changes become severe, occasionally at several years of age.

Predominant Sex
N/A

SIGNS
General Comments
• Longer-limbed dogs—angular deformities generally more common. • Shorter-limbed dogs—tend to develop more severe joint malalignments. • Age at the time of premature closure—affects relative degree of deformity and joint malarticulation; dogs with more growth potential remaining tend to develop more severe deformity.

Historical Findings
• Traumatic—progressive limb angulation or lameness 3–4 weeks after injury; owner may not be aware of causative event.
• Developmental elbow malalignments—insidious onset of lameness in one or both forelimbs; most apparent after exercise.

Physical Examination Findings
Premature Distal Ulnar Closure
• Results in three deformities of the distal radius—lateral deviation (valgus), cranial bowing (procurvatum), and external torsion resulting in supination of the manus.
• Relative shortening of limb length compared to the contralateral normally growing limb. • Caudolateral subluxation of the radiocarpal joint and malarticulation of the elbow joint—may occur; causes lameness and painful joint restriction.
Premature Radial Physeal Closure
• Affected limb—significantly shorter than the normal contralateral. • Severity of lameness—depends on degree of joint malarticulation. • Complete symmetrical closure of distal physis—may note straight limb with a widened radiocarpal or radiohumeral joint space; may note caudal bow (recurvatum) to radius and ulna.
• Asymmetrical closure of medial aspect of distal radial physis—varus angular deformity; occasionally internal torsion and pronation.
• Closure of lateral aspect of distal radial physis—valgus angular deformity; external torsion. • Closure of proximal radial physis with continued ulnar growth—malarticulation of the elbow joint; widened radiohumeral space, and proximal subluxation of the humeroulnar joint (increased humerus to anconeal process space).

CAUSES
• Trauma • Developmental basis
• Nutritional basis

RISK FACTORS
• Forelimb trauma • Excessive dietary supplementation

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Elbow dysplasia • Fragmented medial coronoid process • Ununited anconeal process • Panosteitis • Flexor tendon contracture • Hypertrophic osteodystrophy

CBC/BIOCHEMISTRY/URINALYSIS
N/A

OTHER LABORATORY TESTS
N/A

IMAGING
• Damage to growth potential of the physis—commonly cannot be seen at the time of trauma; usually 2–4 weeks before radiographically apparent. • Standard craniocaudal and mediolateral radiographic views—include entire elbow joint; from mid-humerus proximally extend to digits distally; take same series for comparison to normal contralateral limb. • Degree of angular deformities and relative shortening—determined by comparing relative lengths of radius and ulna within the deformed pair to the normal contralateral pair. • Degree of torsional deformity—determined by comparing position of the elbow and carpus on same view, i.e., lateral projection of elbow and 45° oblique of carpus on same view indicates torsional deformity. Cross-sectional imaging and creation of models using stereolithography is useful for full appreciation of the deformity. • Elbow and carpal joints—evaluate for malalignment anddegenerative change.. Presence of degenerative change is associated with less optimal outcome following surgical treatment. • Elbow joint—evaluate for associated ununited anconeal process and fragmented medial coronoid process.

(CONTINUED)

ANTEBRACHIAL GROWTH DEFORMITIES

DIAGNOSTIC PROCEDURES
N/A

PATHOLOGIC FINDINGS
Cartilage of abnormal growth plate often replaced with bone. Angular deformity can occur due to retained cartilage core (osteochondrosis) of the ulna.

TREATMENT

APPROPRIATE HEALTH CARE
• Genetic predisposition—do not breed. • Traumatic physeal damage—not seen at time of injury; revealed 2–4 weeks later. • In young (< 6 months) animals, surgical treatment is generally recommended as soon as possible following diagnosis. Treatment may require multiple surgical procedures.

NURSING CARE
N/A

ACTIVITY
Exercise restriction—reduces joint malalignment damage; slows arthritic progression.

DIET
• Decrease nutritional supplementation in giant-breed dogs—slows rapid growth; may reduce incidence. • Avoid excess weight—helps control arthritic pain resulting from joint malalignment and overuse.

CLIENT EDUCATION
• Discuss heritability in chondrodysplastic breeds. • Explain that damage to physeal growth potential is not apparent at time of forelimb trauma and that the diagnosis is often made 2–4 weeks following an injury. • Discuss the importance of joint malalignment and resultant osteoarthritis as primary causes of lameness. • Emphasize that early surgical treatment leads to a better prognosis. • Depending on the patient's age, treatment may involve multiple procedures.

SURGICAL CONSIDERATIONS
• Premature distal ulnar physeal closure in a patient < 5–6 months of age (significant amount of radial growth potential remaining)—treated with partial ulnar ostectomy, valgus deformities ≤ 25°: may improve and may not require additional surgery; young patients and those with more severe deformities: often require a second definitive correction after maturity. • Radial or ulnar physeal closure in a mature patient (limited or no growth potential) requires definitive deformity correction, joint realignment, or both. • Deformity correction—may be accomplished with a variety of osteotomy techniques; may be stabilized with several different internal or external fixation devices; must correct both torsional and angular deformities; performed at the point of greatest curvature. • Joint malalignment (particularly elbow)—must correct to minimize arthritis development (primary cause of lameness); obtain optimal joint alignment via dynamic proximal ulnar osteotomy (use triceps brachii muscle traction and joint pressure) or shortening longer bone (radial or ulnar ostectomy as indicated). • Significant limb length discrepancies—distraction osteogenesis; osteotomy of the shortened bone is progressively distracted at the rate of 1 mm/day with an external fixator system to create new bone length.

MEDICATIONS

DRUG(S) OF CHOICE
Anti-inflammatory drugs—symptomatic treatment of osteoarthritis

CONTRAINDICATIONS
Corticosteroids—do not use owing to potential systemic side effects and cartilage damage seen with long-term use.

PRECAUTIONS
Warn client of possible gastrointestinal upset associated with chronic anti-inflammatory therapy.

POSSIBLE INTERACTIONS
N/A

ALTERNATIVE DRUG(S)
Neutraceuticals (e.g., chondroitin sulfate and glucosamine)—may help minimize cartilage damage and osteoarthritis development, but not proven.

FOLLOW-UP

PATIENT MONITORING
• Postoperative—depends on surgical treatment. • Periodic checkups—evaluate arthritic status and anti-inflammatory therapy.

PREVENTION/AVOIDANCE
• Selective breeding of susceptible breeds. • Avoid dietary oversupplementation in rapidly growing giant-breed dogs.

POSSIBLE COMPLICATIONS
Routinely seen with various osteotomy fixation techniques (e.g., infection, non-union of osteotomy, fixator pin tract inflammation, undercorrection).

EXPECTED COURSE AND PROGNOSIS
• Generally, best results seen with early diagnosis and surgical treatment—minimizes osteoarthritis. • Premature ulnar closure—tends to be easier to manage than premature closure of the radial growth plates. Prognosis is dependent on severity of the deformity, joint congruity, and presence of degenerative joint disease. The prognosis worsens with increasing severity. • Limb lengthening by distraction osteogenesis— requires extensive postoperative management by the veterinarian and owner; high rate of complications.

MISCELLANEOUS

ASSOCIATED CONDITIONS
• Osteochondrosis • Hypertrophic osteodystrophy • Un-united anconeal process

AGE-RELATED FACTORS
The younger the patient at the time of traumatically induced physeal closure, the more severe the deformity and malarticulation.

ZOONOTIC POTENTIAL
N/A

PREGNANCY/FERTILITY/BREEDING
N/A

SYNONYMS
Radius curvus

ABBREVIATIONS
• HOD = hypertrophic osteodystrophy • OCD = osteochondrodysplasia • UAP = ununited anconeal process

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Client Education Handout available online

A

ANTERIOR UVEITIS—CATS

BASICS

DEFINITION

• Inflammation of the anterior uveal tissues, including iris (iritis), ciliary body (cyclitis), or both (iridocyclitis). • May be associated with concurrent posterior uveal and retinal inflammation (choroiditis; chorioretinitis). • May be unilateral or bilateral.

PATHOPHYSIOLOGY

• Increased permeability of the blood-aqueous barrier related to infectious, immune-mediated, neoplastic, traumatic, or other causes; allows entrance of plasma proteins and blood cellular components into aqueous humor. • Disruption of blood-aqueous barrier is initiated and maintained by numerous chemical mediators, including histamine, prostaglandins, leukotrienes, serotonin, kinins, and complement.

SYSTEMS AFFECTED

• Ophthalmic. • Other systems may also be affected by underlying disease process.

INCIDENCE/PREVALENCE

• Relatively common condition. • True incidence/prevalence unknown.

GEOGRAPHIC DISTRIBUTION

Geographic location may affect incidence of certain infectious causes of uveitis.

SIGNALMENT

Species

Cat

Mean Age and Range

• Mean age 7–9 years. • Any age may be affected.

Predominant Sex

Males/neutered males more commonly affected than females.

SIGNS

Historical Findings

• Cloudy eye—due to corneal edema, aqueous flare, hypopyon, etc. • Painful eye—manifest by blepharospasm, photophobia, or rubbing eye; usually less pronounced than in dogs. • Red eye—due to conjunctival hyperemia and ciliary flush; less pronounced than in dogs in most cases. • Vision loss—variable.

Physical Examination Findings

Importance of a thorough physical examination in cats presenting with uveitis cannot be overstated.

Ophthalmic Findings

• Ocular discomfort—manifest by blepharospasm and photophobia • Ocular discharge—usually serous; sometimes mucoid to mucopurulent. • Conjunctival hyperemia—bulbar and palpebral conjunctiva both usually affected. • Corneal edema—diffuse; mild to severe. • Keratic precipitates—multifocal aggregates of inflammatory cells adherent to corneal endothelium; most notable ventrally. • Aqueous flare and cells—cloudiness of aqueous humor due to increased protein content and suspended cellular debris; best visualized with a bright, narrow beam of light shined through anterior chamber. • Ciliary flush—injection of deep perilimbal anterior ciliary vessels. • Deep corneal vascularization—circumcorneal distribution (brush border). • Miosis and/or resistance to pharmacologic dilation. • Iridal swelling—may be generalized or nodular. • Reduced IOP is consistent with anterior uveitis but is not a uniform finding. • Posterior synechia—adhesions between posterior iris and anterior lens surface. • Fibrin in anterior chamber. • Hypopyon or hyphema—accumulations of white blood cells or red blood cells, respectively, in the anterior chamber; usually settles horizontally in ventral aspect of chamber but may be diffuse. • Chronic changes may include rubeosis iridis, iridal hyperpigmentation, secondary cataract, lens luxation, pupillary seclusion, iris bombé, secondary glaucoma, and phthisis bulbi.

CAUSES

• Infectious—mycotic (*Blastomyces* spp., *Cryptococcus neoformans; Coccidiodes immitis; Histoplasma capsulatum*); protozoal (*Toxoplasma gondii; Leishmania infantum*); bacterial (*Bartonella* spp., *Mycobacterium* spp. or any bacterial septicemia); viral (FIV, FeLV, feline coronavirus; FHV-1); parasitic (ophthalmomyiasis; ocular larval migrans). • Idiopathic—lymphocytic-plasmacytic uveitis. • Immune-mediated—reaction to lens proteins (due to cataract or lens trauma). • Neoplastic—primary ocular tumors (esp. diffuse iris melanoma, ocular sarcoma); metastasis to uveal tract (esp. lymphoma). • Metabolic—hyperlipidemia; hyperviscosity; systemic hypertension. • Miscellaneous—trauma (blunt or penetrating); ulcerative keratitis; corneal stromal abscess; toxemia of any cause.

RISK FACTORS

None specific; immune suppression and geographic location may increase incidence of certain infectious causes of uveitis.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Conjunctivitis—redness limited to conjunctival hyperemia (i.e., no ciliary flush); ocular discharge usually thicker and more copious than in uveitis; discomfort may be alleviated by topical anesthetic. • Glaucoma—elevated IOP is most consistent distinguishing feature of this disease; others may include dilated pupil, Haab's striae, and buphthalmos. • Ulcerative keratitis—corneal fluorescein staining will detect ulcers; corneal edema associated with ulcers is either localized to, or most severe at, site of ulcer; ocular discharge often thicker and more copious than with uveitis; discomfort may be alleviated by topical anesthetic. • Horner's syndrome—miosis, enophthalmos, and nictitans protrusion are similar in both conditions, but Horner's is non-painful with no ocular discharge; ptosis with Horner's is distinguished from blepharospasm, as the latter is an active process; minor conjunctival hyperemia may be noted with Horner's, but cornea and anterior chamber are clear; clinical signs of Horner's syndrome resolve following topical application of ophthalmic 1–10% phenylephrine.

CBC/BIOCHEMISTRY/URINALYSIS

• CBC—often normal; changes may be present related to underlying disease. • Biochemistry—often normal; most common abnormality in cats with uveitis is elevated serum proteins (usually due to polyclonal gammopathy). • Urinalysis—often normal; changes may be present related to underlying disease.

OTHER LABORATORY TESTS

• FeLV serum titers. • FIV serum titers. • Coronavirus titers—not specific for FIP but may influence the index of suspicion for this disease. • *Toxoplasma gondii* IgM and IgG titers performed on serum and/or aqueous humor. • *Bartonella* spp. serology, PCR (serum or aqueous humor) and/or blood culture.

IMAGING

• Thoracic radiography—may show evidence of causative disease process (e.g., infiltrates related to infectious disease; evidence of metastatic neoplastic disease). • Ocular ultrasound—indicated if opacity of ocular media precludes direct examination; may reveal intraocular neoplasm or retinal detachment.

DIAGNOSTIC PROCEDURES

• Tonometry—low IOP consistent with uveitis; elevated IOP indicates glaucoma (primary disease or secondary to uveitis). • Ocular centesis—if retinal detachment is present, cytology of subretinal aspirate may reveal causative agents; anterior chamber centesis may be performed for *Toxoplasma gondii* or *Bartonella* IgM and IgG titers on aqueous humor.

PATHOLOGIC FINDINGS

• Gross—see physical examination findings. • Histopathologic—corneal edema; peripheral corneal deep stromal vascularization; keratic precipitates; preiridal fibrovascular membrane; peripheral anterior synechia; posterior synechia; entropion or ectropion uveae; leukocyte accumulation in iris, ciliary body, sclera, choroid (lymphocytic-plasmacytic, suppurative, or granulomatous infiltrates, depending on etiology); secondary cataract; with posterior segment involvement

(CONTINUED) ANTERIOR UVEITIS—CATS A

in inflammatory process, cyclitic membrane; vitreal traction bands and retinal detachment may be present. • Lymphoplasmacytic infiltrate of iris and ciliary body (either diffuse or nodular) is most common histopathologic finding.

TREATMENT

APPROPRIATE HEALTH CARE
• Outpatient medical management generally sufficient.

ACTIVITY
No changes indicated in most cases.

DIET
No changes indicated.

CLIENT EDUCATION
• Inform of potential systemic diseases causing ophthalmic signs and emphasize importance of appropriate diagnostic testing. • In addition to symptomatic uveitis treatment, treatment of underlying disease (when possible) is paramount to a positive outcome. • Inform of potential complications and emphasize compliance with treatment and follow-up recommendations that will reduce the likelihood of complications.

SURGICAL CONSIDERATIONS
• None in most cases. • Specific instances requiring surgical intervention include removal of ruptured lenses and surgical management of secondary glaucoma. • Chronic uveitis leading to secondary glaucoma commonly necessitates enucleation of affected globes. • Enucleation is recommended in cats with uveitis related to diffuse iris melanoma or other primary intraocular tumors.

MEDICATIONS

DRUG(S)
Corticosteroids
Topical
• Prednisolone acetate 1%—apply 2–8 times daily, depending on severity of disease; taper medication as condition resolves. • Dexamethasone 0.1%—apply 2–8 times daily, depending on severity of disease; taper medication as condition resolves. • Other topical corticosteroids (e.g., betamethasone, hydrocortisone) are considerably less effective in the treatment of intraocular inflammation. • Taper treatment frequency as condition improves; stopping topical corticosteroids abruptly may result in rebound of ocular inflammation.
Subconjunctival
• Triamcinolone acetonide 4 mg by subconjunctival injection. • Methylprednisolone 4 mg by subconjunctival injection. • Often not required. • Indicated only in severe cases as one-time injection, followed by topical and/or systemic anti-inflammatories.
Systemic
• Prednisone 1–3 mg/kg/day initially; taper dose after 7–10 days. • Use only if systemic infectious causes of uveitis have been ruled out.

Nonsteroidal Anti-inflammatory Drugs
Topical
• Flurbiprofen—apply 2–4 times daily, depending on severity of disease. • Diclofenac—apply 2–4 times daily, depending on severity of disease.
Systemic
• Meloxicam 0.2 mg/kg IV, SC, PO once, then 0.05 mg/kg IV, SC, PO q24h for 2 days, then 0.025 mg/kg q24–48h. Due to potential renal effects, limit duration of use to 4 days. • Robenacoxib 1 mg/kg PO once daily; limit duration of use to 3 days. • Ketoprofen 1 mg/kg PO q24h; limit duration of use to 5 days.

Topical Mydriatic/Cycloplegic
• Atropine sulfate 1%—apply 1–4 times daily, depending on severity of disease. Use lowest frequency adequate to maintain dilated pupil and ocular comfort; taper medication as condition resolves. Ointment is preferred over solution in cats as it causes less salivation.

CONTRAINDICATIONS
• Avoid the use of miotic medications (e.g., pilocarpine), including topical prostaglandins (e.g., latanoprost), in the presence of uveitis. • Topical and subconjunctival corticosteroids are absolutely contraindicated in the presence of ulcerative keratitis. • Corticosteroids (especially systemic) should be avoided in cats with systemic hypertension. Avoid systemic NSAIDs in cats with renal disease.

PRECAUTIONS
Owing to concern for secondary glaucoma, topical atropine should be used judiciously and IOP should be monitored periodically.

POSSIBLE INTERACTIONS
Systemic corticosteroids and nonsteroidal anti-inflammatory drugs should not be used concurrently.

FOLLOW-UP

PATIENT MONITORING
Recheck in 3–7 days, depending on severity of disease. IOP should be monitored at recheck to detect secondary glaucoma. Frequency of subsequent rechecks dictated by severity of disease and response to treatment.

POSSIBLE COMPLICATIONS
Systemic Complications
Occur as a result of the systemic etiology of the uveitis.

Ophthalmic Complications
• Secondary glaucoma—common complication of chronic uveitis in cats. • Secondary cataract. • Lens luxation. • Retinal detachment. • Phthisis bulbi.

EXPECTED COURSE AND PROGNOSIS
• Guarded prognosis for affected eyes. Depends on underlying disease and response to treatment. • Cats with treatable underlying disease (e.g., toxoplasmosis) are more likely to have a favorable ophthalmic outcome than those with idiopathic lymphocytic-plasmacytic uveitis or untreatable underlying condition (e.g., FIP, FIV).

MISCELLANEOUS

AGE-RELATED FACTORS
• Younger cats more likely to be diagnosed with infectious etiology. • Older cats at higher risk of idiopathic lymphocytic-plasmacytic uveitis and intraocular neoplastic causes.

ZOONOTIC POTENTIAL
• None in most cases. • Some forms of systemic infection causing uveitis may pose a slight risk to immunocompromised owners.

PREGNANCY/FERTILITY/BREEDING
Avoid systemic corticosteroids. Because of systemic absorption, topical corticosteroids may also pose a risk, especially with frequent application.

SYNONYM
Iridocyclitis

SEE ALSO
• Horner's Syndrome • Red Eye

ABBREVIATIONS
• FeLV = feline leukemia virus • FHV-1 = feline herpesvirus type 1 • FIP = feline infectious peritonitis • FIV = feline immunodeficiency virus • IOP = intraocular pressure

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Client Education Handout available online

A

ANTERIOR UVEITIS—DOGS

BASICS

DEFINITION
• Inflammation of the anterior uveal tissues, including iris (iritis), ciliary body (cyclitis), or both (iridocyclitis). • May be associated with concurrent posterior uveal and retinal inflammation (choroiditis; chorioretinitis).
• May be unilateral or bilateral.

PATHOPHYSIOLOGY
• Increased permeability of the blood-aqueous barrier related to infectious, immune-mediated, traumatic, or other causes allows entrance of plasma proteins and blood cellular components into aqueous humor.
• Disruption of blood-aqueous barrier is initiated and maintained by numerous chemical mediators, including histamine, prostaglandins, leukotrienes, serotonin, kinins, and complement.

SYSTEMS AFFECTED
• Ophthalmic. • Other systems may also be affected by underlying disease process.

INCIDENCE/PREVALENCE
• Relatively common condition. • True incidence/prevalence unknown.

GEOGRAPHIC DISTRIBUTION
Geographic location may affect incidence of certain infectious causes of uveitis.

SIGNALMENT
Species
Dog

Breed Predilections
• None for most causes. • Uveitis associated with iridociliary cysts in golden retriever (a.k.a. golden retriever uveitis, pigmentary uveitis). • Increased incidence of uveodermatologic syndrome in Siberian husky, Akita, Samoyed, and Shetland sheepdog.

Mean Age and Range
• Any age may be affected. • Mean age in uveodermatologic syndrome—2.8 years.
• Mean age in golden retriever uveitis—8.6 years.

SIGNS
Historical Findings
• Red eye—due to conjunctival hyperemia and ciliary flush. • Cloudy eye—due to corneal edema, aqueous flare, hypopyon, etc.
• Painful eye—manifest by blepharospasm, photophobia, or rubbing eye. • Vision loss—variable.

Physical Examination Findings
The importance of a thorough physical examination in dogs presenting with uveitis cannot be overstated.

Ophthalmic Findings
• Ocular discomfort—manifest by blepharospasm, photophobia, and rubbing eye. • Ocular discharge—usually serous; sometimes mucoid to mucopurulent.
• Conjunctival hyperemia—bulbar and palpebral conjunctiva both usually affected.
• Corneal edema—diffuse; mild to severe.
• Keratic precipitates—multifocal aggregates of inflammatory cells adherent to corneal endothelium; most notable ventrally.
• Aqueous flare and cells—cloudiness of aqueous humor due to increased protein content and suspended cellular debris; best visualized with a bright, narrow beam of light shined through anterior chamber.
• Ciliary flush—injection of deep perilimbal anterior ciliary vessels. • Deep corneal vascularization—circumcorneal distribution (brush border). • Miosis and/or resistance to pharmacologic dilation. • Iridal swelling.
• Reduced IOP is consistent with uveitis but is not a uniform finding. • Posterior synechia—adhesions between posterior iris and anterior lens surface. • Fibrin in anterior chamber. • Hypopyon or hyphema—accumulations of white blood cells or red blood cells, respectively, in the anterior chamber; usually settles horizontally in ventral aspect of chamber but may be diffuse.
• Chronic changes may include rubeosis iridis, iridal hyperpigmentation, secondary cataract, lens luxation, pupillary seclusion, iris bombé, secondary glaucoma, and phthisis bulbi.

CAUSES
• Infectious—mycotic (*Blastomyces dermatitidis, Cryptococcus neoformans, Coccidiodes immitis, Histoplasma capsulatum*); protozoal (*Toxoplasma gondii, Neospora caninum, Leishmania donovani*); rickettsial (*Ehrlichia canis, Rickettsia rickettsii*); bacterial (*Leptospira* spp., *Bartonella* spp., *Brucella canis, Borrelia burgdorferi,* any bacterial septicemia); algal *(Prototheca* spp.); viral (adenovirus, distemper, rabies, herpes); parasitic (ocular filariasis, ocular larval migrans). • Immune-mediated—reaction to lens proteins (due to cataract or lens trauma); uveodermatologic syndrome; post-vaccinal reaction to canine adenovirus vaccine; vasculitis. • Neoplastic—primary ocular tumors (especially uveal melanoma, iridociliary adenoma/adenocarcinoma); metastasis to uveal tract (lymphosarcoma most common). • Metabolic—hyperlipidemia; hyperviscosity; systemic hypertension. • Miscellaneous—idiopathic; trauma; pigmentary uveitis of golden retrievers; ulcerative keratitis; corneal stromal abscess; scleritis; lens instability/luxation; dental/periodontal disease; toxemia.

RISK FACTORS
None specific; immune suppression and geographic location may increase incidence of certain infectious causes of uveitis; breed predispositions should be considered.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Conjunctivitis—redness limited to conjunctival hyperemia (i.e., no ciliary flush); ocular discharge usually thicker and more copious than in uveitis; discomfort may be alleviated with application of topical anesthetic. • Glaucoma—elevated IOP is most consistent feature of this disease; others may include dilated pupil, Haab's striae, and buphthalmos. • Lens luxation—corneal edema may be localized to site of lens contact with endothelium or may be diffuse as a result of associated uveitis and/or glaucoma; lens luxation is highly breed associated.
• Ulcerative keratitis—corneal fluorescein staining will detect ulcers; corneal edema associated with ulcers is either localized to, or most severe at, site of ulcer; ocular discharge often thicker and more copious than with uveitis; discomfort may be partially alleviated by topical anesthetic. • Corneal endothelial dystrophy or degeneration—diffuse corneal edema is present, but IOP is normal; conjunctival hyperemia and signs of ocular discomfort are generally absent. • Horner's syndrome—miosis, enophthalmos, and nictitans protrusion are similar in both conditions, but Horner's is non-painful with no ocular discharge; ptosis with Horner's is distinguished from blepharospasm as the latter is an active process; minor conjunctival hyperemia may be noted with Horner's, but cornea and anterior chamber are clear; clinical signs of Horner's syndrome resolve following topical application of 1–10% phenylephrine.

CBC/BIOCHEMISTRY/URINALYSIS
Often normal; changes related to underlying disease may be present.

OTHER LABORATORY TESTS
• Serology for infectious diseases listed under "Causes" may be appropriate, depending on index of suspicion for infectious etiology.
• Clinical signs raising the suspicion of systemic disease including lethargy, pyrexia, weight loss, coughing, lymphadenopathy, etc., warrant serology for infectious diseases.

IMAGING
• Thoracic radiography may show evidence of causative disease process (e.g., systemic mycoses; metastatic neoplasia). • Abdominal ultrasound may be warranted if suspicion for metastatic neoplastic disease is high. • Ocular ultrasound is indicated if opacity of ocular media precludes direct examination; may reveal intraocular neoplasm or retinal detachment.

DIAGNOSTIC PROCEDURES
• Tonometry—low IOP consistent with uveitis; elevated IOP indicates glaucoma (primary disease or secondary to uveitis).
• Lymph node aspirates—if enlarged nodes

are palpable, aspiration for cytology is indicated. • Ocular centesis—if retinal detachment is present, cytology of subretinal aspirate may reveal causative agents; anterior chamber centesis is generally unrewarding.

PATHOLOGIC FINDINGS

• Gross—see "Physical Examination Findings." • Histopathologic—corneal edema; peripheral corneal deep stromal vascularization; keratic precipitates; preiridal fibrovascular membrane; peripheral anterior synechia; posterior synechia; entropion or ectropion uveae; leukocyte accumulation in iris, ciliary body, sclera, choroid (lymphocytic, plasmacytic, suppurative, or granulomatous infiltrates, depending on etiology); secondary cataract; with posterior segment involvement in inflammatory process, cyclitic membrane; vitreal traction bands and retinal detachment may be present.

TREATMENT

APPROPRIATE HEALTH CARE

Outpatient medical management is generally sufficient.

NURSING CARE

None

ACTIVITY

• No changes indicated in most cases.
• Reduced exposure to bright light may alleviate discomfort.

DIET

No changes indicated.

CLIENT EDUCATION

• Inform of potential systemic diseases causing ophthalmic signs and emphasize importance of appropriate diagnostic testing. • In addition to symptomatic uveitis treatment, treatment of underlying disease (when possible) is paramount to a positive outcome. • Inform of potential complications and emphasize compliance with treatment and follow-up recommendations that will reduce the likelihood of complications.

SURGICAL CONSIDERATIONS

None in most cases. Specific instances requiring surgical intervention include removal of ruptured lenses, removal of cataracts causing uveitis (if prognosis for successful surgery is otherwise favorable), and surgical management of secondary glaucoma.

MEDICATIONS

DRUG(S) OF CHOICE

Corticosteroids

Topical

• Prednisolone acetate 1% apply 2–8 times daily, depending on severity of disease; taper medication as condition resolves.
• Dexamethasone 0.1%—apply 2–8 times daily, depending on severity of disease; taper medication as condition resolves.
• Other topical corticosteroids (e.g., betamethasone, hydrocortisone) are considerably less effective in the treatment of intraocular inflammation.
• Taper treatment frequency over several weeks as condition improves; stopping topical corticosteroids abruptly may result in rebound of ocular inflammation.

Subconjunctival

• Triamcinolone acetonide 4–6 mg by subconjunctival injection.
• Methylprednisolone 3–10 mg by subconjunctival injection.
• Often not required.
• Indicated only in severe cases as one-time injection followed by topical and/or systemic anti-inflammatories.

Systemic

• Prednisone 0.5–2.2 mg/kg/day initially; taper dose after 7–10 days.
• Use only if systemic infectious causes of uveitis have been ruled out.

Nonsteroidal Anti-inflammatory Drugs

Topical

• Less effective than topical corticosteroids.
• Flurbiprofen—apply 2–4 times daily, depending on severity of disease.
• Diclofenac—apply 2–4 times daily, depending on severity of disease.

Systemic

• Do not use concurrently with systemic corticosteroids; avoid in the presence of hyphema.
• Carprofen 2.2 mg/kg PO q12h or 4.4 mg/kg PO q24h.
• Tepoxalin 10 mg/kg PO q24h.
• Meloxicam 0.2 mg/kg PO q24h.
• Firocoxib 5 mg/kg PO q24h.

Topical Mydriatic/Cycloplegic

• Atropine sulfate 1%—apply 1–4 times daily, depending on severity of disease. Use lowest frequency adequate to maintain dilated pupil and ocular comfort; taper medication as condition resolves.

CONTRAINDICATIONS

• Avoid the use of miotic medications (e.g., pilocarpine, demecarium bromide), including topical prostaglandins (e.g., latanoprost), in the presence of uveitis. • Topical and subconjunctival corticosteroids are contraindicated in ulcerative keratitis. • Avoid systemic corticosteroids in dogs with systemic hypertension or systemic infections.

PRECAUTIONS

Out of concern for secondary glaucoma, topical atropine should be used judiciously and IOP should be monitored periodically.

POSSIBLE INTERACTIONS

Systemic corticosteroids and NSAIDS should not be used concurrently.

ALTERNATIVE DRUG(S)

N/A

FOLLOW-UP

PATIENT MONITORING

Recheck in 3–7 days, depending on severity of disease. IOP should be monitored at recheck to detect secondary glaucoma. Frequency of subsequent rechecks dictated by severity of disease and response to treatment.

POSSIBLE COMPLICATIONS

• Many systemic complications, including death, may occur due to systemic etiology of uveitis. • Ophthalmic complications include secondary cataract, secondary glaucoma, lens luxation, retinal detachment, phthisis bulbi.

EXPECTED COURSE AND PROGNOSIS

Extremely variable; depends on underlying disease and response to treatment.

MISCELLANEOUS

ZOONOTIC POTENTIAL

None in most cases. Some forms of systemic infection causing uveitis may pose a slight risk to immune-compromised owners.

PREGNANCY/FERTILITY/BREEDING

Avoid systemic corticosteroids. Because of possibility of systemic absorption, topical corticosteroids may also pose risk, especially with frequent application in small dogs.

SYNONYMS

Iridocyclitis

SEE ALSO

Red Eye

ABBREVIATIONS

• IOP = intraocular pressure • NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

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Client Education Handout available online

A

ANTIDEPRESSANT TOXICOSIS—SSRIS AND SNRIS

BASICS

DEFINITION
• Toxicity secondary to the overdose of a selective serotonin reuptake inhibitor (SSRI), serotonin and norepinephrine reuptake inhibitor (SNRI) or co-ingestion of two types of serotonergic drugs.
• SSRIs include citalopram (Celexa), escitalopram (Lexapro), fluoxetine (Prozac), fluvoxamine (Luvox), paroxetine (Paxil), sertraline (Zoloft), vilazodone (Viibryd), vortioxetine (Brintellix). SNRIs include desvenlafaxine (Pristiq), duloxetine (Cymbalta), levomilnacipran (Fetzima), milnacipran (Ixel, Savella), tofenacin (Elamol, Tofacine), and venlafaxine (Effexor).

PATHOPHYSIOLOGY
• SSRIs and SNRIs are antidepressants that inhibit reuptake of serotonin, a neurotransmitter involved in aggression, anxiety, appetite, depression, migraine, pain, and sleep. The SNRIs also inhibit the reuptake of norepinephrine.
• Excessive stimulation of serotonin receptors can occur by enhanced serotonin synthesis, increased presynaptic serotonin release, inhibition of serotonin uptake into the presynaptic neuron, inhibition of serotonin metabolism, or serotonin agonism. Serotonin syndrome is characterized in humans as a combination of symptoms that include at least three of the following: myoclonus, mental aberration, agitation, hyperreflexia, tremors, diarrhea, ataxia, or hyperthermia.
• Toxic dosage varies widely among commonly available SSRIs and SNRIs and are not well defined in veterinary medicine.

SYSTEMS AFFECTED
• Cardiovascular—decreased vascular tone (hypotension), increased heart rate and stroke volume (tachycardia).
• Gastrointestinal—increased smooth muscle contractility (vomiting, diarrhea).
• Nervous—stimulation (agitation, restlessness, seizures) and altered mental status (vocalization, disorientation).
• Neuromuscular—autonomic dysfunction (hyperactivity) and neuromuscular hyperactivity (hyperreflexia, myoclonus, tremors).
• Ophthalmic—increased autonomic function (mydriasis).
• Respiratory—increased bronchial smooth muscle contraction (dyspnea).

INCIDENCE/PREVALENCE
Second most common human prescription medication toxicosis (after cardiac medications).

SIGNALMENT
Species
Dogs and cats

Mean Age and Range
Any age can be affected.

SIGNS
Historical Findings
• Agitation or lethargy
• Dilated pupils
• Vomiting
• Tremors
• Hypersalivation
• Diarrhea
• Seizures
• Nystagmus

Physical Examination Findings
• Agitation
• Ataxia
• Mydriasis
• Tremors
• Vomiting
• Disorientation
• Hyperthermia
• Vocalization
• Depression
• Tachycardia
• Hypotension
• Diarrhea
• Blindness
• Seizures
• Hypersalivation
• Death

CAUSES
• SSRI/SNRI overdose—accidental exposure, inappropriate administration, or therapeutic use.
• Ingestion of an SSRI/SNRI along with another class of medications that increases serotonin (TCAs, MAOIs, novel antidepressants, tramadol, fentanyl, meperidine, amphetamines, cocaine, dextromethorphan, 5-HTP, buspirone, bupropion, triptans, LSD).

RISK FACTORS
• Animals on a serotonergic drug.
• Underlying liver or kidney disease. Cats are attracted to venlafaxine and will eat multiple capsules.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Toxicologic: TCAs, MAOIs, metaldehyde, lead, ethylene glycol, hops, anticholinergics, antihistamines.
• Non-toxicologic: meningitis e.g., (rabies, canine distemper), neoplasia, heat stroke, malignant hyperthermia.

CBC/BIOCHEMISTRY/URINALYSIS
• CBC/biochemistry: no changes are expected.
• Urinalysis: myoglobinuria secondary to rhabdomyolysis may be seen.

OTHER LABORATORY TESTS
• Blood gas: metabolic acidosis may be seen.
• Testing for SSRIs/SNRIs can be performed, but the tests are not clinically useful.
• Note: venlafaxine will give a false positive for PCP on many urine drug screens.

DIAGNOSTIC PROCEDURES
There are no diagnostic tests to confirm serotonin syndrome.

TREATMENT

APPROPRIATE HEALTH CARE
• Emesis (if asymptomatic and recent ingestion) or gastric lavage (if large number of pills ingested).
• Activated charcoal with cathartic (if severe signs are expected, may need to repeat due to long half-life).

NURSING CARE
IV fluids to help maintain blood pressure and body temperature, and to protect kidneys from myoglobinuria.

CLIENT EDUCATION
If animal appears blind, sight should return.

MEDICATIONS

DRUG(S) OF CHOICE
• Agitation:
  ◦ Phenothiazines (acepromazine 0.025–0.05 mg/kg IV, titrate up as needed).
  ◦ Cyproheptadine (dog, 1.1 mg/kg; cat, 2–4 mg PO q4–6h or can be given rectally if vomiting).
  ◦ Benzodiazepines (diazepam 0.5–2 mg/kg IV) (see "Precautions").
• Tremors: methocarbamol (50–150 mg/kg IV, titrate up but do not exceed 330 mg/kg/day).

CONTRAINDICATIONS
• High risk of serotonin syndrome: other SSRIs, SNRIs, MAOIs, TCAs, amphetamines, 5-HTP, clarithromycin, dextromethorphan, lithium, St. John's wort.
• Low risk of serotonin syndrome: tramadol, fentanyl, amantadine, bupropion, carbamazepine, codeine.

PRECAUTIONS
• Benzodiazepines (e.g., diazepam) are reported by some sources to exacerbate serotonin syndrome and their use for SSRI/SNRI toxicosis is not universally recommended.

POSSIBLE INTERACTIONS
• Decreased metabolism of SSRIs/SNRIs: cimetidine, diuretics, quinidine, lithium.
• Increased levels of medications (decreased metabolism): theophylline, coumadin, digoxin.

(CONTINUED) ANTIDEPRESSANT TOXICOSIS—SSRIS AND SNRIS

FOLLOW-UP

PATIENT MONITORING

Blood pressure, heart rate, urine color: monitor hourly, then less frequently as the animal remains stable.

PREVENTION/AVOIDANCE

- Keep medications out of the reach of animals.
- Follow label directions when giving serotonergic drugs to animals.

POSSIBLE COMPLICATIONS

Renal failure secondary to myoglobinuria from rhabdomyolysis. DIC secondary to hyperthermia.

EXPECTED COURSE AND PROGNOSIS

- Prognosis is good in most cases, with recovery in 12–24 hours.
- Patients that present in status epilepticus or with severe hyperthermia have a guarded prognosis.

MISCELLANEOUS

AGE-RELATED FACTORS

Young and elderly animals are more at risk for developing serious toxicosis.

PREGNANCY/FERTILITY/BREEDING

SSRIs and SNRIs can cause increased litter mortality and possible birth defects.

ABBREVIATIONS

- 5-HTP = 5-hydroxytryptophan
- MAOI = monoamine oxidase inhibitor
- PCP = phencyclidine (angel dust)
- SNRI = serotonin and norepinephrine reuptake inhibitor
- SSRI = selective serotonin reuptake inhibitor
- TCA = tricyclic antidepressant

Suggested Reading

Pugh CM, Sweeney JT, Bloch CP, et al. Selective serotonin reuptake inhibitor (SSRI) toxicosis in cats: 33 cases (2004–2010). J Vet Emerg Crit Care 2013, 23(5):565–570.

Thomas DE, Lee JA, Hovda LR. Retrospective evaluation of toxicosis from selective serotonin reuptake inhibitor antidepressants: 313 dogs (2005–2010). J Vet Emerg Crit Care 2012, 22(6):674–681.

Wismer TA. Antidepressant drug overdoses in dogs. Vet Med 2000, 95(7):520–525.

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A

ANTIDEPRESSANT TOXICOSIS—TRICYCLIC

BASICS

DEFINITION
• Toxicity secondary to the acute or chronic ingestion of a tricyclic antidepressant (TCA).
• TCA medications include amitriptyline, amoxapine, clomipramine, desipramine, doxepin, imipramine, maprotiline (tetracyclic antidepressant), nortriptyline, protriptyline, trimipramine, and many others.

PATHOPHYSIOLOGY
• TCAs block the reuptake of norepinephrine, dopamine, and serotonin at the neuronal membrane. They also have anticholinergic activity and are thought to have membrane stabilizing effects on the myocardium (particularly inhibiting fast sodium channels in the ventricular myocardium). They can also have slight alpha-adrenergic blocking activity and antihistaminic effects.
• TCAs are rapidly and well absorbed across the digestive tract. They can decrease GI motility and delay gastric emptying, resulting in delayed drug absorption.
• Lipophilic, protein bound, and well distributed across all tissues.
• They are metabolized by the liver and undergo enterohepatic recirculation. The inactive metabolites are eliminated in the urine.

SYSTEMS AFFECTED
• Nervous—increased dopamine, serotonin, and norepinephrine levels in the CNS contribute to CNS signs.
• Cardiovascular—anticholinergic effects and inhibition of norepinephrine reuptake contribute to tachycardia; alpha adrenergic blockade, cardiac membrane stabilization, and decreased cardiac contractility contribute to hypotension and arrhythmias.
• Gastrointestinal—anticholinergic effects may cause ileus and delayed gastric emptying.
• Ophthalmic—anticholinergic effects can cause pupillary dilation.
• Renal/Urologic—anticholinergic effects may cause urinary retention.

GENETICS
Species and individual differences in absorption, metabolism, and elimination can be significant.

INCIDENCE/PREVALENCE
Incidence is unknown.

SIGNALMENT
Species
Dogs and cats
Breed Predilections
None
Mean Age and Range
None
Predominant Sex
None

SIGNS
General Comments
• Signs can occur at therapeutic doses.
• Signs of toxicosis can occur within 30–60 minutes or be delayed by several hours.
Historical Findings
• Evidence of accidental consumption of the owner's or another pet's medication
• CNS depression (lethargy, ataxia)
• Vocalization
• Vomiting or hypersalivation
• Panting
• Agitation or restlessness
• Tachypnea or dyspnea
• Tremors
• Seizures
Physical Examination Findings
• CNS depression or stimulation
• Tachycardia
• Mydriasis
• Hypothermia
• Hypertension
• Pallor
• Cyanosis
• Hyperthermia
• Arrhythmias
• Hypotension
• Urinary retention
• Constipation

CAUSE
Accidental exposure, inappropriate administration, or therapeutic use.

RISK FACTORS
• Concurrent use of other antipsychotic medication
• Pre-existing cardiac disease

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Toxicity caused by other antipsychotic medication, stimulant substances (e.g., amphetamines, cocaine, methylxanthines, or pseudoephedrine) or substances capable of causing cardiac arrhythmias (e.g., quinidine, propranolol, albuterol, digoxin).
• Non-toxicologic differentials include hyperkalemia, cardiac ischemia, cardiomyopathy, and other diseases of cardiac conduction.

CBC/BIOCHEMISTRY/URINALYSIS
Expected to be normal

OTHER LABORATORY TESTS
• Blood gases—metabolic acidosis may be noted.
• OTC urine drug screen for TCAs—can be used to determine if exposure has occurred; not useful in determining degree of toxicity.
• Serum TCA levels—can be used to determine if exposure has occurred.

IMAGING
N/A

DIAGNOSTIC PROCEDURES
• ECG to monitor for arrhythmias
• Blood pressure monitoring

PATHOLOGIC FINDINGS
No specific lesions expected

TREATMENT

APPROPRIATE HEALTH CARE
• Outpatient—not recommended for symptomatic patients, patients with cardiac disease, or patients ingesting greater than a therapeutic dose of TCAs.
• Inpatient—asymptomatic:
  ◦ Decontamination with emesis (less than 15 minutes of exposure time), gastric lavage in large exposures, and activated charcoal.
  ◦ Monitor at a clinic for a minimum of 6 hours after exposure.
• Inpatient—symptomatic: stabilize the CV and CNS systems and provide supportive care.

NURSING CARE
• Fluid therapy—restore hydration due to vomiting, regulate blood pressure when hypotension is noted.
• Thermoregulation as needed.
• Enema with warm water if not defecating within 6–12 hours.

DIET
NPO if vomiting

CLIENT EDUCATION
• With a prescribed TCA, instruct client to monitor for adverse or idiosyncratic effects, and to stop the medication and contact the clinic if they occur.
• Prevent exposure to non-prescribed medication.

SURGICAL CONSIDERATIONS
N/A

MEDICATIONS

DRUG(S) OF CHOICE
Decontamination
• Emesis within 15 minutes of ingestion *only if asymptomatic;* induce emesis with either hydrogen peroxide (dog, 1–2 mL/kg PO) or apomorphine (dog/cat, 0.03–0.05 mg/kg IV, IM, or 0.1 mg/kg SC, or 0.25 mg instilled in conjunctiva of eye).
• Gastric lavage under anesthesia may be considered with large exposures.

(CONTINUED) ANTIDEPRESSANT TOXICOSIS—TRICYCLIC

A

• After emesis (or if > 15 minutes of exposure), administer activated charcoal (1–2 g/kg PO) with a cathartic such as sorbitol (70% sorbitol at 3 mL/kg) or sodium sulfate (0.25 tsp/5 kg) if no diarrhea.
• Repeat one-half dose of activated charcoal in 4–6 hours if patient is still symptomatic.

Other

• Cyproheptadine: dogs, 1.1 mg/kg q8h PO or rectally; cats, 2–4 mg/cat q12–24h PO or rectally; used for treatment of serotonin syndrome.
• 20% intravenous lipid emulsion-prevents lipophilic TCAs from reaching the site of action by acting as a sequestrant in an expanded plasma lipid phase; 1.5 mL/kg IV bolus followed by 0.25 mL/kg/min IV CRI for 1 hour. Can repeat bolus every 3–5 minutes as needed up to 3 mL/kg, not to exceed a total dose of 8 mL/kg.
• Sodium bicarbonate—used to maintain blood pH at 7.55; if not monitoring acid-base status, start with 2–3 mEq/kg IV over 15–30 minutes in a symptomatic patient.
• Diazepam 0.5–1 mg/kg IV, repeat if necessary; for agitation or seizures.
• Acepromazine 0.02 mg/kg IV, repeat if necessary; for agitation or mild hypertension.
• Phenobarbital—as needed for seizure control.

CONTRAINDICATIONS

• Atropine should not be used because TCAs have anticholinergic effects that are exacerbated by atropine.
• Magnesium sulfate should not be used as a cathartic. Ileus or reduced GI motility will enhance absorption of magnesium and may result in magnesium toxicity.
• Beta-blockers (e.g., propranolol, atenolol) should not be used for tachycardia because of their potential to exacerbate hypotension.
• Do not induce emesis in a patient already showing clinical signs.

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

• TCAs increase risk of hyperthermia, seizures, and death with use of MAOIs.
• Sympathomimetic and anticholinergic medications increase the risk for arrhythmias or cardiac effects from TCAs.
• Levothyroxine increases the risk for arrhythmias when used with TCAs.

ALTERNATIVE DRUG(S)

N/A

FOLLOW-UP

PATIENT MONITORING

• Acid-base status—monitor for acidosis and if implementing sodium bicarbonate therapy.
• Blood pressure—monitor until asymptomatic.
• ECG—monitor until asymptomatic.

PREVENTION/AVOIDANCE

Keep medications out of reach of pets.

POSSIBLE COMPLICATIONS

Pulmonary edema can occur secondary to aggressive fluid therapy.

EXPECTED COURSE AND PROGNOSIS

• Due to the variable half-lives of the different TCAs, signs can last 24 hours or longer.
• The prognosis is generally good in patients exhibiting mild to moderate signs.
• The prognosis is guarded in patients exhibiting severe signs such as seizures, arrhythmias, or hypotension that are poorly responsive to therapy.

MISCELLANEOUS

ASSOCIATED CONDITIONS

Serotonin syndrome may occur as a result of TCA ingestion.

AGE-RELATED FACTORS

None

PREGNANCY/FERTILITY/BREEDING

TCAs cross the placenta and be found in breast milk; the significance of this is not known at this time.

SEE ALSO

• Antidepressant Toxicosis—SSRIs and SNRIs
• Poisoning (Intoxication) Therapy

ABBREVIATIONS

• CNS = central nervous system
• CV = cardiovascular
• ECG = electrocardiogram
• GI = gastrointestinal
• MAOI = monoamine oxidase inhibitor
• OTC = over-the-counter
• TCA = tricyclic antidepressant

INTERNET RESOURCES

• http://www.aspcapro.org/poison
• http://www.petpoisonhelpline.com/

Suggested Reading

Gwaltney-Brant S. Antidepressants: Tricyclic antidepressants. In: Plumlee KH, ed., Clinical Veterinary Toxicology. St. Louis, MO: Mosby, 2004, pp. 286–288.
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Wismer TA. Antidepressant drug overdoses in dogs. Vet Med 2000, 95:520–525.

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A

AORTIC STENOSIS

BASICS

DEFINITION
A narrowing of the left ventricular outflow tract (LVOT) that restricts blood flow leaving the ventricle. It is most commonly congenital, often heritable. The lesion is most commonly subvalvular in dogs, but may be valvular or supravalvular (more often in cats). Subvalvular aortic stenosis (SAS) in dogs is caused by fibrous tissue manifested as nodules, a ridge, ring or tunnel-like lesion. SAS may be associated with other defects including mitral valve dysplasia.

PATHOPHYSIOLOGY
Restriction to outflow generates pressure overload of the LV. Degree of obstruction is related to severity of secondary changes. Left ventricular pressure overload causes thickened LV walls, resulting in diminished blood supply relative to muscle demand and myocardial ischemia. This may result in arrhythmogenesis and if severe or infarcted, mechanical dysfunction. The restriction to blood flow causes high velocity, turbulent flow across the valve, which may cause endothelial damage, lead to aortic insufficiency (AI) and predisposing to endocarditis. SAS may lead to chamber enlargement, distortion of the mitral valve annulus and mitral regurgitation with a possible sequela of left-sided congestive heart failure. Sudden death is common with severe SAS and may be secondary to arrhythmias or infarction.

SYSTEMS AFFECTED
• Cardiovascular—LV pressure overload leading to arrhythmias, syncope, sudden death, heart failure, endocarditis
• Respiratory—possible pulmonary edema with CHF • Multisystemic—possible due to low cardiac output or endocarditis

GENETICS
SAS is inherited in the Newfoundland, golden retriever, rottweiler and Dogue de Bordeaux. A mutation in the phosphatidylinositol-binding clathrin assembly protein gene (PICALM) is reported in Newfoundlands; a screening test is available. Dominant inheritance patterns are proposed with incomplete penetrance responsible for the disease appearing to skip generations. More than one gene or modifying genes may be involved.

INCIDENCE/PREVALENCE
SAS is one of the most common congenital heart defects of dogs. It is reported as second most common, but difficulty in diagnosing mild disease may underestimate true caseload. Aortic stenosis has been reported as a small contributor of feline congenital heart disease, about 6%. Approximately 2 out of 1,000 dogs and 0.2 per 1,000 cats evaluated at veterinary teaching hospitals are diagnosed with SAS (dogs), supravalvular aortic stenosis (cats), and dynamic LVOT obstruction (cats).

GEOGRAPHIC DISTRIBUTION
N/A

SIGNALMENT
Species
Dog and Cat

Breed Predilections
The Newfoundland, golden retriever, rottweiler, Bouvier des Flanders, Dogue de Bordeaux, German shepherd, and boxer have the highest incidence of SAS and a familial component or heritability is reported. Increased risk is also described for English bulldog, American Staffordshire terrier, bull Terrier, English bulldog, Great Dane, and Samoyed. No breed predilection is reported for cats.

Mean Age and Range
Clinical signs may be seen at any age. Although often inherited, SAS becomes identifiable during the first few weeks to months of life as the subvalvular lesion progresses. Full phenotype is appreciated by 1 year of age.

Predominant Sex
N/A

SIGNS
Historical Findings
Many dogs with SAS show no clinical signs and have no relevant historical findings. Historical findings are related to disease severity and may include syncope, exercise intolerance, sudden death, and signs due to CHF such as respiratory distress and/or coughing when severe.

Physical Examination Findings
• Systolic left basilar ejection murmur; may radiate to the apex, right side of the thorax, include the carotid arteries and if very loud the cranium. A precordial thrill may be palpable. Murmur intensity is loosely correlated to severity of stenosis. As the disease worsens during early life, some may have absence of or a quiet murmur that develops to a more characteristic finding by 1 year. • Diastolic murmur may be present with significant AI. The combination of this diastolic murmur with the systolic ejection murmur is a to-and-fro murmur.
• Arrhythmias may be ausculted. • Pulse deficits may be appreciated, often associated with ventricular arrhythmias. • Weak pulses may be appreciated that are late or slow to rise with severe SAS (pulsus parvus et tardus).
• Tachypnea, respiratory distress and crackles may occur with CHF.

General Comments
• Boxers have a relatively small aorta compared to other breeds, which can be difficult to distinguish from mild SAS. • Bull terriers are overrepresented for combined mitral valve dysplasia and SAS.
• Newfoundland dogs are overrepresented for combined patent ductus arteriosus and SAS.
• Volume overload of PDA can cause a relative aortic stenosis and be difficult to distinguish from PDA with mild SAS.

CAUSES
• Congenital heart disease. • Secondary to valvular change as with aortic valve endocarditis or calcification. • Dynamic or fixed LVOT obstruction in some cats with hypertrophic (obstructive) cardiomyopathy.
• A component of complex congenital heart disease as with some cases of mitral valve dysplasia.

RISK FACTORS
• Familial history of SAS. • SAS predisposes to aortic valve endocarditis. • Aortic valve endocarditis predisposes to valvar aortic stenosis. • HCM predisposes cats to fixed or dynamic LVOT obstruction.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
The systolic murmur must be differentiated from other causes of similar murmurs. Innocent or physiologic murmurs are commonly ausculted in athletic dogs, or with anemia, fever, stress or excitement. Pulmonic stenosis, tetralogy of Fallot, and atrial septal defects cause a similar murmur. Weak pulses may also occur with conditions that reduce cardiac output such as heart failure, cardiomyopathy, and severe pulmonic stenosis. Other obstruction to flow may cause reduced pulse quality, such as aortic thromboembolism or rarely aortic coarctation/tubular hypoplasia.

CBC/BIOCHEMISTRY/URINALYSIS
Typically within normal limits

OTHER LABORATORY TESTS
Genetic testing for the mutation associated with Newfoundland SAS is a breeding tool to reduce frequency in this breed.

IMAGING
Thoracic Radiography
• Mild disease may be radiographically silent.
• LV hypertrophy may be subtle as pressure overload causes concentric hypertrophy.
• Left heart enlargement. • Prominent aortic root and/or widened mediastinum. • Lung fields typically normal unless CHF with pulmonary venous distention and interstitial to alveolar infiltrates.

Echocardiography
• Findings are variably present and associated with disease severity. • Ridge, ring, nodule, or tunnel-like narrowing below the aortic valve with SAS. • Thickened LV free wall or interventricular septum. • Aortic valve thickening and increased echogenicity with valvar stenosis. • Mitral regurgitation and

(CONTINUED)

AORTIC STENOSIS

A

thickening of valve leaflet possible.
• Post-stenotic dilatation of the aorta.
• Hyperechoic myocardium associated with ischemia. • AI with secondary LV chamber enlargement and volume overload if significant. • Left atrial enlargement may be seen with significant valve regurgitation.
• Elevated LVOT flow velocity (> 2.4 m/s), with acceleration proximal to the stenosis and turbulent flow distal to the obstruction and valve. • Transvalvular pressure gradient estimated by the LVOT flow velocity (4 × flow velocity squared). Estimated gradients of 25–49 mmHg are considered mild; 50–79 mmHg moderate, and ≥ 80mmHg severe. • With myocardial failure the estimated pressure gradient may be falsely low.
• Effective valve orifice, if calculated, is reduced.

DIAGNOSTIC PROCEDURES
• ECG may show changes consistent with LV hypertrophy (tall R waves, widened QRS complexes, left axis deviation); signs of myocardial ischemia (ST segment deviation or slurring). Ventricular arrhythmias may occur and contribute to syncope or sudden death.
• Holter monitoring may be used to quantify arrhythmia severity and therapeutic response.

PATHOLOGIC FINDINGS
Findings vary with severity but typically include LV concentric or mixed (if significant AI) hypertrophy. A subvalvular lesion of dense fibrous tissue is seen with variable. Myocardial ischemia, necrosis and replacement fibrosis may be evident. Post–stenotic dilatation of the aorta and associated valvular endothelial damage and sometimes left atrial enlargement is reported.

TREATMENT

APPROPRIATE HEALTH CARE
Therapy is limited prior to the onset of complications and aimed at preventing clinical signs and avoiding sudden death.

NURSING CARE
Aimed at relieving symptoms and complications such as arrhythmias, syncope and CHF.

ACTIVITY
Restriction is warranted with severe disease; exertion may increase incidence of arrhythmias, syncope and sudden death.

DIET
Modest salt restriction with CHF.

CLIENT EDUCATION
SAS is considered an inherited disease; affected animals should not be bred. Owners should be counseled on the risk of endocarditis and appropriate antibiotics for any wounds, infections or surgical procedures. Alert owners to the risks of sudden death, CHF and increased anesthetic risk.

SURGICAL CONSIDERATIONS
No surgical or interventional technique has been shown to extend life beyond medical therapy. Balloon valvuloplasty or combined cutting and traditional balloon valvuloplasty may acutely reduce the pressure gradient and temporarily alleviate some clinical signs. However, the effects are not shown to be beneficial beyond those achieved with beta-blockers. Currently, data does not support surgery or intervention.

MEDICATIONS

DRUG(S) OF CHOICE
• Beta adrenergic blockers are advocated with moderate to severe SAS, particularly with ventricular arrhythmias, syncope or ECG evidence of ischemia. They may reduce myocardial oxygen demand, eliminate or protect against ventricular arrhythmias, and reduce heart rate. Atenolol is most common (dogs, 0.5–1.5 mg/kg PO q12h; cats 6.25 mg/cat PO q12–24h). • Therapy for ventricular arrhythmias, CHF, atrial fibrillation or endocarditis may be required.

CONTRAINDICATIONS
Beta blockers are contraindicated in animals with bronchoconstriction such as asthmatic cats. Starting beta-blockers with CHF is contraindicated and continued use in patients that develop CHF is controversial.

PRECAUTIONS
• Beta-blockers are negatively impact cardiac output and starting low doses with gradual uptitration is warranted. • Positive inotropes may worsen a fixed obstruction and are used with caution when treating CHF.
• Anesthetic drugs that cause hypotension, arrhythmias or cardiac depression should be avoided with severe SAS.

POSSIBLE INTERACTIONS
N/A

ALTERNATIVE DRUGS
• Carvedilol (dogs, 0.5–1.5mg/kg PO q12h)
• Metoprolol tartrate (dogs, 0.5–1.5mg/kg PO q12h)

FOLLOW-UP

PATIENT MONITORING
Monitor by ECG, Holter monitor, thoracic radiography, and echocardiography. Treatment of complications such as CHF and arrhythmias may necessitate additional monitoring for renal/electrolyte, blood pressure, and rhythm disturbances.

PREVENTION /AVOIDANCE
N/A

POSSIBLE COMPLICATIONS
Ventricular arrhythmias, syncope, myocardial infarction, sudden death, AI, mitral regurgitation, endocarditis.

EXPECTED COURSE AND PROGNOSIS
Mildly affected dogs may have a normal lifespan and quality without therapy. Severely affected dogs have limited lifespans and typically succumb to sudden death or CHF. In one study the average lifespan for dogs with severe SAS on atenolol was about 4.5 years.

MISCELLANEOUS

ASSOCIATED CONDITIONS
Increased risk of infective endocarditis

AGE-RELATED FACTORS
SAS is not immediately apparent at birth but appears over few weeks to months of life.

PREGNANCY/FERTILITY/BREEDING
Contraindicated

SYNONYMS
Subaortic stenosis, discrete subaortic stenosis.

SEE ALSO
• Congestive Heart Failure, Left-Sided
• Endocarditis, Infective • Cardiomyopathy, Hypertrophic—Cats • Cardiomyopathy, Hypertrophic—Dogs

ABBREVIATIONS
• AI = aortic insufficiency • CHF = congestive heart failure • HCM = hypertrophic cardiomyopathy • ECG = electrocardiogram • LV = left ventricle
• LVOT = left ventricular outflow tract
• PDA = patent ductus arteriosus • SAS = subvalvular aortic stenosis

INTERNET RESOURCES
N/A

Suggested Reading

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Client Education Handout available online

A

AORTIC THROMBOEMBOLISM

BASICS

DEFINITION
Aortic thromboembolism results from a thrombus or blood clot that is dislodged within the aorta, causing severe ischemia to the tissues served by that segment of aorta.

PATHOPHYSIOLOGY
• ATE is commonly associated with myocardial disease in cats, most commonly hypertrophic cardiomyopathy. It is theorized that abnormal blood flow (stasis) and a hypercoagulable state contribute to the formation of a thrombus within the left atrium. The blood clot is then embolized distally to the aorta. The most common site of embolization is the caudal aortic trifurcation (hind legs). Other less common sites include the front leg, kidneys, gastrointestinal tract, or cerebrum.
• ATE in dogs typically is associated with neoplasia, sepsis, infectious endocarditis, Cushing's disease, protein-losing nephropathy, or other hypercoagulable states. However, in one recent retrospective study, no concurrent condition was identified in 58% of dogs.

SYSTEMS AFFECTED
• Cardiovascular—the majority of affected cats have advanced heart disease and left heart failure.
• Nervous/Musculoskeletal—severe ischemia to the muscles and nerves served by the segment of occluded aorta causes variable pain and paresis. Gait abnormalities or paralysis results in the leg or legs involved.

GENETICS
Hypertrophic cardiomyopathy, a common associated disease, is likely heritable. Additionally, a family of domestic shorthair cats with remodeled hypertrophic cardiomyopathy who all died of ATE has been reported.

INCIDENCE/PREVALENCE
• Prevalence is not known in the general population of cats. In two large studies of cats with hypertrophic cardiomyopathy, 12–16% presented with signs of ATE. In two retrospective studies of cats with ATE, 11–25% of cats had previous evidence of heart disease.
• Rare in dogs.

GEOGRAPHIC DISTRIBUTION
N/A

SIGNALMENT
Species
Cat, rarely dog

Breed Predilections
Mixed-breed cats are most commonly affected. Abyssian, Birman, and ragdoll purebred cats were overrepresented in one study. In dogs, no breed predilection has been identified in the USA. A European study suggested that Cavalier King Charles Spaniels may be overrepresented.

Mean Age and Range
Age distribution is 1–20 years. The median age is approximately 8–9 years in cats. In dogs, the median age is 8–10 years.

Predominant Sex
Males > females (2:1) in cats. In dogs, no sex predilection in dogs in the USA. A European study suggested a male predilection.

SIGNS
The presence of the 5 "P's" is helpful to remember the classic clinical signs associated with ATE: Pain, Paralysis or Paresis, Pulselessness, Pallor, and Poikilothermic (cold).

Historical Findings
• Acute onset paralysis and pain are the most common complaints in cats. Vocalization and anxiety are also common.
• Lameness or a gait abnormality, typically of several week duration, is more common in dogs.
• Tachypnea or respiratory distress is common in cats.
• About 15% of cats may vomit prior to ATE.

Physical Examination Findings
• Usually paraparesis or paralysis of the rear legs with signs of lower motor neuron injury. Less commonly, monoparesis of a front leg. In dogs, the majority are paretic and ambulatory.
• Absent or diminished femoral pulses.
• Pain upon palpation of the legs.
• Gastrocnemius muscle often becomes firm several hours after embolization.
• Cyanotic or pale nail beds and foot pads.
• Tachypnea/dyspnea and hypothermia are common in cats.
• Since commonly associated with heart disease in cats, a cardiac murmur, arrhythmias, or gallop sound may be present.

CAUSES
• Cardiomyopathy (all types)
• Hyperthyroidism
• Neoplasia
• Sepsis (dogs)
• Hyperadrenocorticism (dogs)
• Protein-losing nephropathy (dogs)

RISK FACTORS
• In the cat, cardiomyopathy is a risk factor. Cardiomyopathic cats with a markedly enlarged left atrium, spontaneous echocardiographic contrast (smoke), or an intracardiac thrombus observed on an echocardiogram are at a higher risk for development of ATE.
• In the dog, hypercoagulable conditions, such as neoplasia, sepsis, endocarditis, protein losing nephropathies, or hyperadrenocorticism are risk factors.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Hind limb paresis secondary to other causes such as spinal neoplasia, trauma, myelitis, fibrocartilaginous infarction, or intervertebral disc protrusion. These conditions resulting in spinal cord injury present with signs of upper motor neuron disease, whereas ATE patients present with signs of lower motor neuron disease.

CBC/BIOCHEMISTRY/URINALYSIS
• High creatine kinase as a result of muscle injury.
• High aspartate aminotransferase and alanine aminotransferase as a result of muscle and liver injury.
• Hyperglycemia secondary to stress.
• Mild increases in blood urea nitrogen and creatinine due to low cardiac output and possible renal emboli.
• Electrolyte derangements, due to low output and muscle damage, such as hypocalcemia, hyponatremia, hyperphosphatemia and hyperkalemia are not uncommon.
• CBC and urinalysis changes are non-specific.

OTHER LABORATORY TESTS
Routinely available coagulation profiles typically do not reveal significant abnormalities because the hypercoagulability results from hyperaggregable platelets. In the dog, thromboelastrography may suggest a hypercoagulable state with a clot strength (increased maximum amplitude) or shortened clotting time (decreased R).

IMAGING
Radiographic Findings
• Cardiomegaly is common in cats.
• Pulmonary edema and/or pleural effusion in approximately 50% of cats.
• Rarely, a mass is seen in the lungs, suggestive of neoplasia.

Echocardiographic Findings
• In cats, changes consistent with cardiomyopathy. Hypertrophic cardiomyopathy is most common, followed by restrictive or unclassified cardiomyopathy and then dilated cardiomyopathy.
• Most cases (> 50%) have severe left atrial enlargement (i.e., left atrial to aortic ratio of ≥ 2).
• A left atrial thrombus or spontaneous echocardiographic contrast (smoke) may be seen.

Abdominal Ultrasonographic Findings
• May be able to identify the thrombus in the caudal aorta.
• Typically not necessary to reach a diagnosis in the cat but often needed to reach a diagnosis in the dog.

(CONTINUED)

AORTIC THROMBOEMBOLISM

A

Advanced Diagnostic Imaging

• Nonselective or CT angiography should identify a negative filling defect in the caudal aorta representing the thrombus.
• Typically not necessary to reach a diagnosis.

DIAGNOSTIC PROCEDURES

Electrocardiography

• Sinus rhythm and sinus tachycardia most common. Less common rhythms include atrial fibrillation, ventricular arrhythmias, supraventricular arrhythmias, and sinus bradycardia.
• Left ventricular enlargement pattern and left ventricular conduction disturbances (left anterior fascicular block) are common.

PATHOLOGIC FINDINGS

• Thrombus typically is identified at the caudal aortic trifurcation.
• Occasionally, a left atrial thrombus is seen.
• Emboli of the kidneys, gastrointestinal tract, cerebrum, and other organs also may be seen.

TREATMENT

APPROPRIATE HEALTH CARE

Initially, cats with ATE should be treated as inpatients because many have concurrent congestive heart failure and require injectable drugs, in addition to being in considerable pain and distress.

NURSING CARE

• Fluid therapy is cautiously used as most cats have advanced myocardial disease. If in congestive heart failure, IV fluid therapy may not be necessary.
• Supplemental oxygen therapy or thoracocentesis may be beneficial if in congestive heart failure.
• Initially, minimally handle the affected legs. However, as reperfusion occurs, physical therapy (passive extension and flexion of the legs) may speed full recovery.
• Do not perform venipuncture on the affected legs.
• These animals may have difficulty posturing to urinate and may need to have their bladders expressed to prevent overdistention or urine scald.

ACTIVITY

Restrict activity and stress

DIET

Initially, most cats are anorexic. Tempt these cats with any type of diet to keep them eating and avoid hepatic lipidosis.

CLIENT EDUCATION

• Short- and long-term prognosis is poor in both dogs and cats.
• Most cats will re-embolize. Most cats that survive an initial episode will be on some type of anticoagulant therapy that may require frequent re-evaluations and an indoor lifestyle.
• Most cats that survive an initial episode will recover complete function to the legs; however, if ischemia was severe and prolonged, sloughing of parts of the distal extremities or persistent neurologic deficits may result. In one study, approximately 15% of cats had permanent neuromucscular abnormalities after surviving the initial embolic event.
• Based on 3 small retrospective studies in dogs, the prognosis is generally poor but may be better in dogs presenting with chronic (vs. acute) lameness and dogs treated appropriately with warfarin.

SURGICAL CONSIDERATIONS

• Surgical embolectomy typically is not recommended because these patients are high risk for surgery because of severe heart disease.
• Rheolytic thrombectomy has been used with limited success in a small number of cats with ATE.

MEDICATIONS

DRUG(S) OF CHOICE

• Thrombolytic therapy (e.g., tissue plasminogen activator [TPA]) is used extensively in humans and infrequently in cats and dogs. These drugs are expensive and carry a significant risk for bleeding complications; to date, they have not demonstrated improved treatment efficacy and thus are rarely used in general practice. TPA is theorized to be more beneficial if given early, ideally, within the first 6 hours of the event.
• Clopidogrel is an antiplatelet aggregation drug. One may choose to give a loading dose of clopidogrel for treatment of an acute embolic event. The loading dose in the cat is 75 mg/cat PO once and then maintenance dose starting 24h later is 18.75 mg/cat (one-fourth of 75 mg tablet) PO q24h. The loading dose in the dog is approximately 10 mg/kg once and then a maintenance dose of 1 mg/kg q24h. When compared to aspirin, clopidogrel was superior in preventing re-embolization, resulting improved survival times in cats that had survived an ATE.
• Unfractionated heparin is the preferred anticoagulant drug in general practice for initial management of feline ATE. Heparin has no effect on the established clot; however, it prevents further activation of the coagulation cascade. In either a cat or dog, give an initial dose of 100–200 units/kg IV and then 200–300 units/kg SC q8h. Alternatively, heparin can be administered as a CRI, if there is concern about adequate bioavailability via the SC route, at a dose of 25–35 units/kg/h. Titrate the dose to prolong the activated partial thromboplastin time approximately two-fold.
• Aspirin is theoretically beneficial during and after an episode of thromboembolism because of its antiplatelet effects. The dose in cats is an 81 mg tablet PO q48–72h. Vomiting and diarrhea are not uncommon. Some specialists advocate a mini dose of 5 mg/cat q72h. Antithrombotic dose recommendations for dogs range from 0.5 to 2 mg/kg q24h. Always give aspirin with food.
• Buprenorphine in the cat is useful and widely available drug used for analgesia and sedation at a dose of 5–20 μg/kg IV, SC, or in cheek pouch q6–8h. For stronger analgesia, use fentanyl or hydromorphone.
• Acepromazine may be cautiously used for its sedative and vasodilatory properties at a dose of 0.01–0.02 mg SC q8–12h.
• Warfarin, a vitamin K antagonist, is the anticoagulant most widely used in humans and has been proposed for prevention of re-embolization in cats surviving an initial episode. The initial dose is 0.25–0.5 mg/cat PO q24h or 0.05–0.2 mg/kg PO q 24h in the dog. Overlap with heparin therapy for 3 days. The dose is then adjusted to prolong the prothrombin time approximately two times its baseline value or to attain an international normalized ratio of 2 to 3. Long-term management with warfarin can be challenging because of frequent monitoring and dose adjustments in addition to bleeding complications. In one study, dogs treated appropriately with warfarin had a better clinical outcome.
• Low molecular weight heparin has recently been proposed for the long-term prevention of feline ATE. LMWH has a more predictable relationship between dose and response than warfarin and does not need monitoring or dose adjustments. It also has a lower risk of bleeding complication. The main disadvantage of LMWH is high drug cost and the injectable route of administration. The two LMWHs that have been used in feline ATE are: dalteparin (100–150 units/kg SC q8–24h) and enoxaparin (1 mg/kg SC q12–24h). Best dose unknown. LMWH usually started q24h due to cost. Some studies suggest q6h dosing necessary for stable blood levels, but may increase bleeding risk.

CONTRAINDICATIONS

N/A

PRECAUTIONS

• Anticoagulant therapy with heparin, warfarin, or the thrombolytic drugs may cause bleeding complications.
• Avoid a nonselective beta-blocker such as propranolol as it may enhance peripheral vasoconstriction.

A

AORTIC THROMBOEMBOLISM (CONTINUED)

POSSIBLE INTERACTIONS
Warfarin may interact with other drugs, which may enhance its anticoagulant effects.

ALTERNATIVE DRUG(S)
N/A

FOLLOW-UP

PATIENT MONITORING
• ECG monitoring while the cat is in hospital is helpful to detect reperfusion injury and hyperkalemia related ECG changes.
• Monitoring electrolytes and renal parameters periodically may be helpful to optimize management of the cardiac disease.
• Examine the legs frequently to assess clinical response. Initially, APTT should be performed once daily to titrate the heparin dose.
• If warfarin is used, PT or INR is measured approximately 3 days after initiation of therapy and then weekly until the desired anticoagulant effect is reached. Thereafter, measure three to four times yearly or when drug regimen is altered.

PREVENTION/AVOIDANCE
Because of the high rate of re-embolization, prevention with either clopidogrel, aspirin, warfarin, or LMWH is strongly recommended.

POSSIBLE COMPLICATIONS
• Bleeding with the anticoagulant therapy.
• Permanent neurologic deficits or muscular abnormalities in the hind limbs may arise with prolonged ischemia.
• Recurrent congestive heart failure or sudden death.
• Reperfusion injury and death usually associated with hyperkalemic arrhythmias.

EXPECTED COURSE AND PROGNOSIS
• Expected course is days to weeks for full recovery of function to the legs.
• Prognosis, both short term and long term, is poor in cats.
• In two large studies, ~ 60% of cats were euthanized or died during the initial thromboembolic episode. Long-term prognosis varies between 2 months to several years; however, the average is a few months with treatment. Predictors of poorer prognosis include hypothermia (< 99°F) and congestive heart failure. One study demonstrated a median survival time of 77 days in cats with congestive heart failure and 223 days in cats without congestive heart failure. Predictors of better prognosis include normothermia, single leg affected, and presence of motor function on initial exam.
• In dogs, the disease is rare and prognosis in general is also poor. One study suggested a better prognosis if the dog had chronic clinical signs and if treated with warfarin.
• Recurrence of ATE is common.

MISCELLANEOUS

ASSOCIATED CONDITIONS
See "Causes" and "Risk Factors"

AGE-RELATED FACTORS
N/A

ZOONOTIC POTENTIAL
None

PREGNANCY/FERTILITY/BREEDING
N/A

SYNONYMS
• Saddle thromboembolism
• Systemic thromboembolism

SEE ALSO
• Cardiomyopathy, Dilated—Cats
• Cardiomyopathy, Hypertrophic—Cats
• Cardiomyopathy, Restrictive—Cats

ABBREVIATIONS
• APTT = activated partial thromboplastin time
• ATE = aortic thromboembolism
• CRI = constant rate infusion
• ECG = electrocardiogram
• INR = international normalized ratio
• LMWH = low molecular weight heparin
• PT = prothrombin time

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Client Education Handout available online

APUDOMA

BASICS

OVERVIEW

• Tumors of endocrine cells that are capable of amine precursor uptake and decarboxylation and secretion of peptide hormones; the tumors are named after the hormone they secrete.
• APUD cells are generally found in the gastrointestinal tract and CNS.
• Gastrin- and pancreatic polypeptide-secreting tumors are discussed here; insulinoma and glucagonoma are discussed separately.
• Hypergastrinemia from gastrin-secreting tumors causes gastritis and duodenal hyperacidity, which can cause gastric ulceration, esophageal dysfunction from chronic reflux, and intestinal villous atrophy.
• High concentration of pancreatic polypeptide also causes gastric hyperacidity and its consequences.

SIGNALMENT

• Gastrinoma—rare in dogs and cats; age range 3–12 years, mean 7.5 years (dogs).
• Pancreatic polypeptide—extremely rare in dogs.

SIGNS

• Vomiting
• Weight loss
• Anorexia
• Diarrhea
• Lethargy, depression
• Polydipsia
• Melena
• Abdominal pain
• Hematemesis
• Hematochezia
• Fever

CAUSES & RISK FACTORS

Unknown

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Other conditions associated with hypergastrinemia, gastric hyperacidity, and gastrointestinal ulceration
• Uremia
• Hepatic failure
• Drug-induced ulceration (e.g., NSAIDs or steroids)
• Inflammatory gastritis
• Stress-induced ulceration
• Mast cell disease

CBC/BIOCHEMISTRY/URINALYSIS

• Normal or reflect the chronic effects of general disease
• Iron-deficiency anemia secondary to gastrointestinal bleeding
• Increased BUN secondary to gastrointestinal bleeding
• Hypoproteinemia
• Electrolyte abnormalities with chronic vomiting

OTHER LABORATORY TESTS

• Serum gastrin concentration normal or high-normal in patients with gastrinoma. Treatment with H2 antagonists or proton pump inhibitors increases serum concentrations of gastrin and could lead to false-positive diagnosis of gastrinoma, but withdrawal of these drugs results in return of gastrin concentrations to baseline in dogs without gastrinoma.
• Provocative test of gastrin secretion—increased gastrin concentration after intravenous calcium gluconate or secretin administration suggests gastrinoma; see Appendix II for protocol and interpretation.

IMAGING

Abdominal ultrasound sometimes demonstrates a pancreatic mass but is usually normal.

DIAGNOSTIC PROCEDURES

• Endoscopy with gastric and duodenal biopsy.
• Aspirate any detectable masses because of suspicion of mast cell disease.
• If no detectable masses exist, examine a buffy coat smear for mast cells.

PATHOLOGIC FINDINGS

• Endoscopic biopsy reveals gastrointestinal ulceration.
• Histopathologic examination of pancreatic tumors reveals findings consistent with islet cell tumor but not specific for hormone type.
• Immunocytochemical staining can aid in the specific diagnosis.
• Histopathologic examination also can reveal metastasis to liver and regional lymph nodes.

TREATMENT

• Tell owner that most APUDomas are malignant and have metastasized by the time of diagnosis and that long-term control is often difficult.
• Aggressive medical management can sometimes palliate signs for months to years.
• Surgical exploration and excisional biopsy of a pancreatic mass are important both diagnostically and therapeutically.
• Medical management is useful for gastric hyperacidity.

MEDICATIONS

DRUG(S)

• Histamine H_2-receptor antagonists—cimetidine, ranitidine, and famotidine; decrease acid secretion by gastric parietal cells.
• Omeprazole—a proton pump inhibitor; the most potent inhibitor of gastric acid secretion available; highly effective and expensive.
• Sucralfate—adheres to ulcerated gastric mucosa and protects it from acid; promotes healing by binding pepsin and bile acids and stimulating local prostaglandins.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Because sucralfate may be less effective in an alkaline environment, and may reduce the absorption of other drugs, it should be given 1–2 hours prior to antacid drugs.

FOLLOW-UP

PATIENT MONITORING

• Physical examination and clinical signs are the most useful measures of treatment effectiveness and disease progression.
• Gastroscopy can monitor progression of gastritis but is not necessary.
• Abdominal radiography or ultrasound may detect development of abdominal masses.

EXPECTED COURSE AND PROGNOSIS

• Difficult to predict.
• Patients with gastrinoma have been controlled on medical management for months to years.
• No cure available.

MISCELLANEOUS

SEE ALSO

Gastroduodenal Ulceration/Erosion

ABBREVIATIONS

• APUD = amine precursor uptake and decarboxylation
• CNS = central nervous system
• NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

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A

ARTERIOVENOUS FISTULA AND ARTERIOVENOUS MALFORMATION

BASICS

OVERVIEW
Abnormal, low-resistance connections between an artery and vein which bypass a capillary bed; arteriovenous malformations (AVM) are typically congenital and involve a vascular nidus, or complex of communicating vessels, while arteriovenous fistulae (AVF) are often acquired direct connections. Large AVMs and AVFs allow a significant fraction of the total cardiac output to bypass the capillary bed. The resulting increase in cardiac output may lead to circulatory volume overload and congestive heart failure (CHF). The anatomic location of AVMs is variable, most often reported in the liver of dogs. The location of AVFs is also variable, occurring frequently in the limbs or at the site of previous surgery/trauma.

SIGNALMENT
• Dog and cat (rare in both). • No specific age, breed, or sex predilections known, though AVMs are typically seen in younger animals.

SIGNS
Historical Findings
• Animals with AVF often have a history of trauma to the affected area. • Owner may notice a warm, non-painful swelling at the site. • Other findings depend on the lesion location (e.g., ascites with hepatic AVM). • The shunt may cause local organ dysfunction.

Physical Examination Findings
• Vary and depend on location of the AVM/AVF. • Signs of CHF (e.g., coughing, dyspnea, tachypnea, exercise intolerance) may develop in animals with long-standing disease and high blood flow. • Bounding pulses may be present because of high ejection volume and rapid runoff through the AVM/AVF. • Continuous murmur (bruit) at the site caused by turbulent blood flow through the lesion. • Cautious compression of the artery proximal to the lesion abolishes the bruit. When blood flow is high, this compression may also elicit an immediate reflex decrease in heart rate (Branham's sign). • Edema, ischemia, and congestion of organs and tissues caused by high venous pressure in the proximity of the lesion. • If the lesion is on a limb, pitting edema, lameness, ulceration, scabbing, and gangrene may result. • Lesions near vital organs may cause signs associated with organ failure such as ascites (liver), seizures (brain), paresis (spinal cord), and dyspnea (lung).

CAUSES & RISK FACTORS
• AVMs are rare; frequently a congenital lesion. • Acquired AVFs typically result from local damage to vasculature secondary to trauma, surgery, venipuncture, perivascular injection, or tumor.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• The lesion may look like a mass if peripherally located (limb, ear). • Other differentials include an aneurysm or false aneurysm. • Atypical clinical findings, depending on location, may suggest other disease processes; AVF or AVM may be a late diagnostic consideration.

CBC/BIOCHEMISTRY/URINALYSIS
May reflect damage to systems in the vicinity of the lesion, i.e., biochemical abnormalities suggesting hepatic, renal, or other organ dysfunction are possible.

OTHER LABORATORY TESTS
N/A

IMAGING
Thoracic Radiographic Findings
Cardiac enlargement and pulmonary overcirculation in some animals with hemodynamically significant lesions.

Ultrasonographic Findings
• AVM and AVF appear as cavernous, vascular structures. • Doppler ultrasound may demonstrate high-velocity, turbulent flow within the lesion.

Cross-sectional Imaging
Computed tomography or magnetic resonance angiography can aid in the diagnosis, particularly when imaged with contrast injection to highlight the vascular anatomy.

Angiography
Selective angiography defines the lesion and may be necessary for definitive diagnosis. This is performed at the time of intervention, if transcatheter therapy is pursued. Placement of the catheter close to the lesion and rapid injection is necessary; high-volume blood flow dilutes the contrast medium quickly.

DIAGNOSTIC PROCEDURES
N/A

TREATMENT
• Surgery can be difficult and labor-intensive and may require blood transfusion, though is the traditional treatment for clinically-significant lesions. • Transcatheter therapies with coils, devices, or glue represent newer treatment options. Coils or devices are often sufficient for treatment of AVF; AVMs typically require glue embolization, as closure of the nidus is required for complete cure. Potential advantages include less invasive treatment and intravascular access to remote lesions. • AVMs and AVFs may recur. In some animals, surgical removal of the affected limb or organ (e.g., amputation, liver lobectomy) may be necessary.

MEDICATIONS

DRUG(S)
• Concurrent medical treatment depends on the site of the lesion and secondary clinical features.
• Medical treatment for CHF or other organ dysfunction may be required before surgery.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
Avoid excessive fluid administration; animals with these lesions are often volume overloaded.

FOLLOW-UP
Postoperative reevaluation is needed to determine whether the AVM or AVF has recurred and if organ dysfunction has normalized.

MISCELLANEOUS

SEE ALSO
Congestive Heart Failure, Left-Sided

ABBREVIATIONS
• AVF = arteriovenous fistula • AVM = arteriovenous malformation • CHF = congestive heart failure

Suggested Reading
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ARTERIOVENOUS MALFORMATION OF THE LIVER

BASIC

OVERVIEW

• Intrahepatic arteriovenous (AV) malformations (also referred to as AV fistulae) are communications between proper hepatic arteries and intrahepatic portal veins; this anatomic union results in hepatofugal (away from the liver) splanchnic circulation.
• Blood flows directly from a hepatic artery into portal vasculature retrograde into the vena cava through multiple acquired portosystemic shunts (APSS).
• Associated with ascites.
• Uncommon, usually congenital, but may be acquired (surgical injury, trauma, neoplasia).

SIGNALMENT

• Dogs, less common in cats
• Age-related presentation (congenital): < 2 years
• No sex or breed predilection

SIGNS

General Comments

Vague or acute illness; present for signs caused by portal hypertension and APSS: ascites and hepatic encephalopathy (HE).

Historical Findings

• Dogs may have a normal transition to growth foods, unlike PSVA that demonstrate HE.
• May have an acute onset of ascites or HE.
• Vague signs include: lethargy, anorexia, vomiting, diarrhea, weight loss, polydipsia, dementia, abdominal distention, and uroliths causing obstructive uropathy.

Physical Examination Findings

• Lethargic, poor body condition, ascites; enlarged liver lobe containing the AV malformation; rarely palpated on initial examination.
• Rarely, bruit auscultated over AV malformation.

CAUSES & RISK FACTORS

• Usually congenital vascular malformations (single or multiple vessels) reflecting failed differentiation of common embryologic anlage.
• Rare: secondary to abdominal trauma, inflammation, neoplasia, surgical interventions, or diagnostic procedures (e.g., liver biopsy).
• Portal hypertension—reflects arterialization of valveless portal system—establishing APSS.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• CNS signs—infectious disorders (e.g., distemper); toxicity (e.g., lead); hydrocephalus; idiopathic epilepsy; metabolic disorders (e.g., hypoglycemia, hypokalemia or hyperkalemia); HE (e.g., acquired liver disease or PSVA).
• Abdominal effusion:—pure transudate (ascites; protein-losing nephropathy, protein-losing enteropathy, liver disease); modified transudate (congenital cardiac malformations, right-sided heart failure, pericardial tamponade, supradiaphragmatic vena caval obstruction, neoplasia, portal vein thrombosis); hemorrhage.
• Portal hypertension—chronic hepatic disease, ductal plate malformations/congenital hepatic fibrosis, non-cirrhotic or idiopathic portal hypertension, cirrhosis, portal thrombi.

CBC/BIOCHEMISTRY/URINALYSIS

• Erythrocyte microcytosis (APSS), target cells
• Hypoalbuminemia with normal or low serum globulins; ALP and ALT activity normal or moderately increased; variable low BUN and hypocholesterolemia, and anicteric
• Hyposthenuria or isosthenuria
• Ammonium biurate crystalluria

OTHER LABORATORY TESTS

• Coagulation tests—variable, may be normal; low protein C activity reflects APSS.
• Total serum bile acids—preprandial values variable, postprandial values increased; classic shunting pattern.
• Plasma ammonia—usually increased, inferred by ammonium biurate crystalluria.
• Peritoneal fluid—pure transudate (total protein < 2.5 g/dL) or modified transudate.

IMAGING

Radiography

• Abdominal effusion
• Microhepatia or normal sized liver due to enlarged lobe with AV malformation
• Renomegaly
• Normal thorax

Abdominal Ultrasonography

• Abdominal effusion
• Liver lobe with AV malformation—large compared to most other liver lobes that are atrophied due to portal hypoperfusion.
• Tortuous anechoic tubules represent AV structure with unidirectional pulsating or turbulent flow on color-flow Doppler.
• Hepatic artery and/or portal vein branches may appear tortuous.
• Hepatofugal portal flow (away from the liver)—through APSS.
• Renomegaly.
• Urolithiasis: urinary bladder or renal pelvis.
• Rule out portal thrombosis (luminal filling defect, abrupt blood flow termination).

Radiographic Contrast Angiography

• Not indicated in most cases.
• Venous portography—only confirms APSS.
• Hepatic arteriography—required to confirm AV communication (celiac trunk or anterior mesenteric artery contrast injection).

Multi-Sector CT

Non-invasive contrast imaging of hepatic vasculature; arterial and venous phases; 3-dimensional reconstruction illustrates AV malformation, large liver lobe, atrophied liver.

Echocardiography

Rule out right-sided heart disease, pericardial disease, and vena caval occlusion.

DIAGNOSTIC PROCEDURES

• Multi-sector CT and exploratory laparotomy.
• Liver biopsy—collect samples from *affected* and *unaffected* liver lobes; "normal" liver often demonstrates severe vascular arterialization (more severe than associated with PSVA).

TREATMENT

APPROPRIATE HEALTH CARE

Inpatient— Treat HE and ascites prior to surgical approach or percutaneous selective acrylamide embolization.

NURSING CARE

• Diet—restrict nitrogen intake to ameliorate HE and hyperammonemia; restrict sodium to attenuate ascites formation.
• HE—resolve endoparasitism, electrolyte and hydration disturbances, treat infections, initiate treatments to alter enteric uptake and formation of HE toxins (see Hepatic Encephalopathy).
• Ascites—mobilize by restricting activity and sodium intake and instituting dual diuretic therapy (furosemide and spironolactone); reserve therapeutic abdominocentesis for tense ascites impairing ventilation, nutrition, sleep, or recumbent posture; (see Portal Hypertension, Portosystemic Shunting, Acquired, and below).

SURGICAL CONSIDERATIONS

• Resection of liver lobe containing AV malformation is complicated by coexistence of additional hepatic vascular malformations; clinical cure possible but unlikely.

A

ARTERIOVENOUS MALFORMATION OF THE LIVER (CONTINUED)

• Percutaneous selective acrylamide vascular embolization; complicated by risk of thromboembolism of additional vasculature; temporary improvement; but treatment may be curative.
• Multiple microscopic vascular malformations continue portal hypertension and APSS.
• Do not ligate APSS nor band the vena cava.

MEDICATIONS

DRUG(S)

Hepatic Encephalopathy
See Hepatic Encephalopathy

Ascites
• Restrict sodium intake.
• Furosemide (0.5–2 mg/kg PO IM or IV q12–24h)—combine with spironolactone.
• Spironolactone (0.5–2 mg/kg PO q12h)—double initial dose as loading dose once.
• Chronic diuretic therapy— individualized to response, 4- to 7-day assessment intervals used to titrate dose to response, avoiding hydration, electrolyte, and HE complications.
• Diuretic-resistant ascites— may require therapeutic abdominocentesis; to initiate diuresis.
• Vasopressin V_2 receptor antagonists newly available may control ascites accumulation. (See Portosystemic Shunting, Acquired.)

Bleeding Tendencies
See Coagulopathy of Liver Disease

Gastrointestinal Hemorrhage
• *Histamine type-2 receptor antagonists* (famotidine 0.5–2 mg/kg PO, IV, or SC q12–24h); or *HCl pump inhibitors* (omeprazole 1.0 mg/kg/24h PO or pantoprazole 1 mg/kg/24h IV [omeprazole may induce p450 cytochrome-associated drug interactions and may have a 24–48h delay onset of action]; some clinicians recommend chronic treatment to minimize gastrointestinal bleeding and ulceration that may be chronic problems).
• *Gastroprotectant*—sucralfate: 0.25–1.0 g/10 kg PO q8–12h; titrate to effect, beware of drug interactions as sucralfate may bind other medications, reducing bioavailability.
• *Eliminate endoparasitism.*

CONTRAINDICATIONS

Avoid drugs dependent on hepatic biotransformation or first pass hepatic extraction (reduced by APSS) or that react with GABA-benzodiazepine receptors because of propensity for HE.

FOLLOW-UP

PATIENT MONITORING

Biochemistry—initially monthly until stabilized after surgery or AV malformation embolization, thereafter quarterly; monitor for hypoalbuminemia, infection, optimization of HE management and control of ammonium biurate crystalluria.

EXPECTED COURSE AND PROGNOSIS

• Prognosis fair if patient survives surgical resection of AV malformation or embolization.
• Most patients require indefinite nutritional and medical management (HE, ascites) because of coexisting microscopic vascular malformations across the liver; APSS persists requiring continued management of HE.

MISCELLANEOUS

SEE ALSO

• Ascites
• Hepatic Encephalopathy
• Hypertension, Portal
• Portosystemic Shunting, Acquired
• Portosystemic Vascular Anomaly, Congenital

ABBREVIATIONS

• APSS = acquired portosystemic shunt
• GABA = γ-aminobutyric acid
• HE = hepatic encephalopathy
• PSVA = portosystemic vascular anomalies

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ARTHRITIS (OSTEOARTHRITIS)

BASICS

DEFINITION
Osteoarthritis or degenerative joint disease is the progressive and permanent deterioration of the articular cartilage of diarthrodial (synovial) joints due to primary (idiopathic) and secondary causes.

PATHOPHYSIOLOGY
• DJD is initiated by mechanical stress—traumatic injury, instability, abnormal conformation, abnormal activity, etc. • Metalloproteinases, serine proteases, and cysteine protease enzymes are released from damaged chondrocytes, causing collagen degradation and loss of collagen cross-linking in cartilage. • Collagen synthesis is altered, resulting in decreased collagen/proteoglycan interaction and reduced hydrophyllic matrix properties. • Cartilage matrix is further compromised by increased breakdown of proteoglycans and manufacture of poorer-quality proteoglycans. • Nitric oxide is released, which mediates cartilage breakdown and supports chronic inflammation. Chondrocyte apoptosis is facilitated by cyclooxygenase-2 enzymes. • Synovial membrane inflammation results in decreased viscosity of the synovial fluid, reducing lubrication. • Poorer-quality synovial fluid reduces oxygen and nutrient supply to the chondrocytes. • Subchondral bone becomes sclerotic, worsening loading qualities of the bone and overlying cartilage. • Pain of DJD results from stimulation of pain receptors in the tendons, ligament, subchondral bone, and joint capsule. • The result of these processes is progressive cartilage degradation ranging from fibrillation to deep fissuring of cartilage. Full-thickness cartilage loss can eventually occur. • Periarticular fibrosis occurs to reduce joint motion (and pain), leading to poorer vascularity of the synovial membrane. • Osteophytes and enthesiophytes develop around and within the joint to increase the load-bearing surface area. • These changes reduce functionality and may eventually lead to ankylosis.

SYSTEMS AFFECTED
Musculoskeletal—diarthrodial joints

GENETICS
• Primary DJD is rare. • Dogs—causes of secondary DJD are varied, including hip and elbow dysplasias, osteochondrosis dissecans, patellar luxations, congenital shoulder luxation, Legg-Perthes, and cranial cruciate ligament rupture. • Cats—causes of secondary DJD are patellar luxation, hip dysplasia, and arthropathy.

INCIDENCE/PREVALENCE
• Dog—very common; 20% of dogs older than 1 year have some degree of DJD. • Cat—90% of cats over 12 years of age had evidence of DJD on radiographs. • Clinical problems are more prevalent in larger, overweight, and very active animals. • Primary DJD is rare.

SIGNALMENT
Species
Dog and cat

Mean Age and Range
• Secondary DJD due to congenital disorders (OCD, hip dysplasia) seen in immature animals; some present with DJD signs when older (hip and elbow dysplasia). • Secondary to trauma—any age.

SIGNS
Historical Findings
• Dogs—decreased activity level, unwilling to perform certain tasks; intermittent lameness or stiff gait that slowly progresses; possible history of joint trauma, OCD, or developmental disorders; may be exacerbated by exercise, long periods of recumbency, and cold weather. • Cats—overt lameness may not be seen. May have difficulty grooming, jumping onto furniture, or accessing the litter box; increased irritability.

Physical Examination Findings
• Stiff-legged or altered gait (e.g., bunny hopping in hip dysplasia) or non-use of leg. • Decreased range of motion. • Crepitus. • Joint swelling (effusion and/or thickening of the joint capsule). • Joint pain. • Joint instability.

CAUSES
• Primary—no known cause. • Secondary—results from an initiating cause: abnormal wear on normal cartilage (e.g., joint instability, joint incongruity, trauma to cartilage or supporting soft tissues) or normal wear on abnormal cartilage (e.g., osteochondral defects).

RISK FACTORS
• Working, athletic, and obese dogs place more stress on their joints. • Dogs with disorders that affect collagen or cartilage (Cushing's disease, diabetes mellitus, hypothyroidism, hyperlaxity, prolonged, steroids).

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Neoplastic (synovial sarcoma; rarely, chondrosarcoma; osteosarcoma). • Septic arthritis (caused by bacteria; spirochetes; L forms in cats; *Mycoplasma; Rickettsia; Ehrlichia;* viruses, such as feline calicivirus; fungi, and protozoa). • Immune-mediated arthritis (erosive vs. non-erosive). • Other musculoskeletal conditions that cause lameness. • Neurologic conditions causing lameness or decreased activity/weakness.

OTHER LABORATORY TESTS
• Coombs' test, ANA, and rheumatoid factor may help to rule out immune-mediated arthritis. • Serum titers for *Borrelia, Ehrlichia,* and *Rickettsia* to evaluate for infectious arthritis.

IMAGING
• Radiographic changes—include joint capsular distention, osteophytosis, enthesiophytosis, soft-tissue thickening, and narrowed joint spaces; in severely affected patients: subchondral sclerosis, and intra-articular calcified bodies (joint mice). • Radiographic severity often does not correlate with clinical severity. • Stress radiography may identify underlying instability and accentuate joint incongruity (e.g., distraction index, passive hip laxity of the coxofemoral joint is predictive of hip DJD). • Bone nuclear scintigraphy can assist in localizing subtle DJD.

DIAGNOSTIC PROCEDURES
• Arthrocentesis and synovial fluid analysis—cell counts are normal or slightly increased (< 2,000–5,000 cells/mL) predominantly mononuclear (macrophages) and occasional synovial lining cells. • Bacterial culture of synovial fluid—negative. • Biopsy of synovial tissue to rule out neoplasia or immune-mediated arthritides (lymphocytic plasmacytic synovitis, SLE).

PATHOLOGIC FINDINGS
• Fibrillation or erosion of articular cartilage. • Eburnation and sclerosis of subchondral bone. • Thickening and fibrosis of the joint capsule. • Synovial fluid can be grossly normal to thin and watery, usually increased volume. • Synovial villous hypertrophy and hyperplasia. • Osteophytes and enthesiophytes at joint capsule attachments and adjacent to the joint. • Neovascularization or pannus in severe cases over joint surfaces.

TREATMENT

APPROPRIATE HEALTH CARE
• Medical—usually tried initially. • Surgical options—to improve joint geometry or remove bone-on-bone contact areas.

NURSING CARE
• Physical therapy—very beneficial. • Maintaining or increasing joint motion—passive range of motion exercises, massage, swimming. • Pain management—cold and heat therapy. • Muscle tone/strengthening—swimming (aerobic exercise with minimal weight bearing); controlled leash walks up hills or on soft surfaces, such as sand or dry or underwater treadmill.

A

ARTHRITIS (OSTEOARTHRITIS) (CONTINUED)

ACTIVITY
Limited to a level that minimizes aggravation of clinical signs.

DIET
• Weight reduction for obese patients—decreases stress placed on arthritic joints.
• Omega n-6 and n-3 fatty acids decrease the production of certain prostaglandins and modulate inflammation.

CLIENT EDUCATION
• Medical therapy is palliative and the condition is likely to progress. • Discuss treatment options, activity level, and diet.

SURGICAL CONSIDERATIONS
• Arthrotomy—used to remove aggravating causes (e.g., fragmented coronoid process, un-united anconeal process, osteochondral flaps). • Arthroscopy—used to diagnose and remove aggravating causes; flushing the joint may be beneficial. • Reconstructive procedures—used to eliminate joint instability and correct anatomic problems (patella luxation, angular deformity). • Joint removal—femoral head and neck ostectomy, temperomandibular joint arthroplasty. • Joint replacement—total hip replacement is widely used, total elbow replacement still experimental. • Joint fusion (arthrodesis)—in selected chronic cases and for joint instability, complete or partial; carpus, hock: generally excellent outcome; shoulder, elbow, stifle,: less predictable outcome.

MEDICATIONS

DRUG(S) OF CHOICE

NSAIDs
• Inhibit prostaglandin synthesis through cyclooxygenase enzymes.
• Deracoxib (3–4 mg/kg PO q24h, chewable).
• Carprofen (2.2 mg/kg PO q12h or q24h).
• Meloxicam (load 0.2 mg/kg PO, then 0.1 mg/kg PO q24h: liquid).
• Tepoxalin (load 20 mg/kg, then 10 mg/kg PO q24h).
• Cats—meloxicam (0.1 mg/kg PO q24h: liquid) or robenacoxib (1 mg/kg PO q24h for 3 days).

Chondroprotective/Regenerative Supplements
• Supply PSGAG molecules to repair and regenerate cartilage.
• Host of products, many with little production oversight so effects vary widely.
• Glucosamine and chondroitin sulfate—injectable Adequan, oral Cosequin, oral MSM, mixtures (e.g., Glycoflex II, SynFlex).
• Adequan—clinical study in dogs with hip dysplasiam; 4.4 mg/kg IM every 3–5 days for 8 injections had a positive, temporary effect.
• Cosequin—trials showed positive effects.

CONTRAINDICATIONS
• NSAIDs must not be given with steroids.
• Acetaminophen must not be given to cats.

PRECAUTIONS
• NSAIDs—may cause gastric ulceration.
• COX-2 selective drugs may interfere with liver function. • When switching NSAIDs—wait 3 days for washout before starting new drug.

POSSIBLE INTERACTIONS
Steroids and NSAIDS

ALTERNATIVE DRUG(S)
• Free-radical scavengers. • Glucocorticoids—inhibit inflammatory mediators and cytokines; however, chronic use delays healing and initiates damage to articular cartilage; potential systemic side effects documented; goal is low-dose (dogs, 0.5–2 mg/kg; cats, 2–4 mg/kg) q48h. • Prednisone—initial dose 1–2 mg/kg PO q24h for dogs and 4 mg/kg PO q24h for cats. • Triamcinolone hexacetonide—intra-articular injection of 5 mg in dogs showed a protective and therapeutic effect in one model.

FOLLOW-UP

PATIENT MONITORING
Clinical deterioration—indicates need to change drug selection or dosage; may indicate need for surgical intervention.

PREVENTION/AVOIDANCE
Early identification of predisposing causes and prompt treatment to help reduce progression of secondary conditions, e.g., surgical removal of osteochondral lesions.

EXPECTED COURSE AND PROGNOSIS
• Slow progression of disease likely. • Some form of medical or surgical treatment usually allows a good quality of life.

MISCELLANEOUS

SYNONYMS
• Degenerative arthritis • Degenerative joint disease • Osteoarthritis • Osteoarthrosis

ABBREVIATIONS
• ANA = antinuclear antibody • COX-2 = cyclooxygenase-2 • DJD = degenerative joint disease • NSAID = nonsteroidal anti-inflammatory drug • OCD = osteochondrodysplasia • PSGAGs = polysulfated glycosaminoglycans • SLE = systemic lupus erythematosus

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Client Education Handout available online

ARTHRITIS, SEPTIC

BASICS

DEFINITION
Pathogenic microorganisms within the closed space of one or more synovial joints

PATHOPHYSIOLOGY
• Usually caused by contamination associated with traumatic injury (e.g., a direct penetrating injury such as bite, gunshot wound, foreign object), a sequela to surgery, arthrocentesis or joint injection, hematogenous spread of microorganisms from a distant septic focus, or less commonly the extension of primary osteomyelitis
• Primary sources of hematogenous infection—urogenital, integumentary (including ears and anal sacs), respiratory, cardiac, and gastrointestinal systems

SYSTEMS AFFECTED
Musculoskeletal—usually affects one joint

GENETICS
N/A

INCIDENCE/PREVALENCE
Relatively uncommon cause of monoarticular arthritis in dogs and cats

GEOGRAPHIC DISTRIBUTION
May be an increased incidence in Lyme disease-endemic areas

SIGNALMENT
Species
• Most common in dogs
• Rare in cats

Breed Predilections
Any. Medium to large breeds—most commonly German shepherds, Dobermans, and Labrador retrievers.

Mean Age and Range
Any age; usually between 4 and 7 years. Hematogenous: more common in immature animals.

Predominant Sex
Male

SIGNS
General Comments
Always consider the diagnosis in patients with acute, monoarticular lameness associated with soft tissue swelling, heat, and pain.

Historical Findings
• Lameness—acute onset most common, but can present as chronic lameness
• Lethargy
• Anorexia
• May report previous trauma—dog bite, penetrating injury, prior surgery or other invasive procedure of the joint

Physical Examination Findings
• Monoarticular lameness, rarely polyarticular
• Joint pain and swelling—commonly carpus, stifle, hock, shoulder, or cubital joint
• Localized joint heat
• Decreased range of motion
• Local lymphadenopathy
• Fever

CAUSES
• Aerobic bacterial organisms—most common: staphylococci, streptococci, coliforms and *Pasteurella*
• Anaerobic organisms—most common: *Propionibacterium, Peptostreptococcus, Fusobacterium* and *Bacteroides*
• Spirochete—*Borrelia burgdorferi*
• *Mycoplasma*
• Fungal agents—*Blastomyces, Cryptococcus,* and *Coccidioides*
• *Rickettsial—Anaplasma, Ehrlichia, Rickettsia*
• *Leishmania*
• Feline calicivirus

RISK FACTORS
• Predisposing factors for hematogenous infection—diabetes mellitus; hypoadrenocorticism (Addison's disease); immunosuppression
• Penetrating trauma to the joint including surgery
• Existing osteoarthritis or other joint damage
• Intra-articular injection, particularly if steroid injected

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Osteoarthritis
• Trauma
• Immune-mediated arthropathy
• Postvaccinal transient polyarthritis
• Greyhound polyarthritis
• Feline progressive polyarthritis
• Crystal-induced joint disease
• Synovial sarcoma

CBC/BIOCHEMISTRY/URINALYSIS
• Hemogram—inflammatory left shift in some cases
• Other results normal

OTHER LABORATORY TESTS
Serologic testing for specific pathogens

IMAGING
Radiography
• Early disease—may reveal thickened and dense periarticular tissues; may see evidence of synovial effusion. Often difficult to diagnose early disease radiographically.
• Late disease—reveals bone destruction, osteolysis, irregular joint space, discrete erosions, and periarticular osteophytosis.

DIAGNOSTIC PROCEDURES
Synovial Fluid Analysis
• Increased volume
• Turbid fluid
• Decreased viscosity
• Decreased mucin clot reaction
• Make slides immediately; if additional fluid is obtained, place in EDTA tube
• Elevated WBC count—> 80% neutrophils with > 40,000/mm^3 (normal joint fluid < 10% neutrophils and < 3,000/mm^3)
• Neutrophils may show degenerative changes (chromatolysis, vacuolation, nuclear swelling, loss of segmentation)
• Neutrophils with phagocytosed bacteria—definitive diagnosis or bacteria in the synovial fluid

Synovial Fluid Culture
• Positive culture is definitive but not necessary for diagnosis.
• Must be collected aseptically; requires heavy sedation or general anesthesia.
• Place fluid sample in aerobic and anaerobic culturettes and in blood culture medium.
• Use 1:9 dilution of synovial fluid to blood culture media.
• Culturette samples—cultured immediately upon arrival to the laboratory.
• Blood culture medium—re-culturing after 24 hours of incubation increases accuracy by 50% and is the preferred method.
• *Mycoplasma*, bacterial L-forms and protozoa require specific culture procedures—contact laboratory prior to sample collection.

Other
• Synovial biopsy—to rule out immune-mediated joint disease; no more effective than incubated blood culture medium for growing bacterial organisms.
• Blood and urine cultures if hematogenous source is suspected.

PATHOLOGIC FINDINGS
• Synovium—thickened; discolored; often very proliferative
• Histology—evidence of hyperplastic synoviocytes
• Increased numbers of neutrophils, macrophages, and fibrinous debris
• Cartilage—loss of proteoglycan, destruction of articular surface, pannus formation

TREATMENT

APPROPRIATE HEALTH CARE
• Inpatient—initial stabilization; initiate systemic antibiotic therapy as soon as fluid is obtained for bacterial culture; consider joint drainage/lavage as soon as possible to minimize intra-articular injury.
• Identify and treat source if hematogenous spread is suspected.
• Outpatient—long-term management.

NURSING CARE
Alternating heat and cold packing—beneficial in promoting increased blood flow and decreased swelling.

ACTIVITY
Restricted until resolution of symptoms

DIET
N/A

A

ARTHRITIS, SEPTIC (CONTINUED)

CLIENT EDUCATION
• Discuss probable cause.
• Warn client about the need for long-term antibiotics and the likelihood of residual degenerative joint disease.

SURGICAL CONSIDERATIONS
• Acute disease with minimal radiographic changes—joint drainage and lavage via needle arthrocentesis, arthroscopic lavage or arthrotomy. An irrigation catheter (ingress/egress) can be placed in larger joints.
• Chronic disease—may require open arthrotomy with debridement of the synovium and copious lavage; if appropriate, an irrigation catheter (ingress/egress) may be placed to lavage the joint postoperatively.
• Lavage—use warmed physiologic saline or lactated Ringer's solution (2–4 mL/kg q8h) until effluent is clear. Do not add povidone/iodine or chlorhexidine to lavage fluid.
• Effluent fluid—cytologically monitored daily for existence and character of bacteria and neutrophils.
• Removal of catheters—when effluent fluid has no bacteria and the neutrophils are cytologically healthy.
• Arthroscopy allows for visual assessment of articular cartilage, lavage and biopsy, and is a less invasive method of thorough joint lavage than arthrotomy.
• Recent reports suggest there may be no difference between combined medical and surgical management and medical management alone.

MEDICATIONS

DRUG(S) OF CHOICE
• Pending culture susceptibility data—bactericidal antibiotics, such as first-generation cephalosporin or amoxicillin-clavulanic acid, preferred.
• Choice of antimicrobial drugs—primarily depends on in vitro determination of susceptibility of microorganisms; toxicity, frequency, route of administration and expense also considered; most penetrate the synovium well; need to be given for a minimum of 4–8 weeks.
• NSAIDs—may help decrease pain and inflammation.

CONTRAINDICATIONS
Avoid fluorinated quinolones in pediatric patients; they induce cartilage lesions experimentally.

PRECAUTIONS
Failure to respond to conventional antibiotic therapy—may indicate anaerobic disease or other unusual cause (fungal, spirochete).

POSSIBLE INTERACTIONS
N/A

ALTERNATIVE DRUG(S)
N/A

FOLLOW-UP

PATIENT MONITORING
• If drainage and irrigation catheters have been placed—may be removed after 4–6 days or after reassessment of synovial fluid cytology.
• Duration of antibiotic therapy—2 weeks following resolution of clinical signs. Total treatment may be 4–8 weeks or longer depending on clinical signs and pathogenic organism.
• Persistent synovial inflammation without viable bacterial organisms (dogs)—may be caused by antigenic bacterial fragments or antigen antibody deposition.
• Systemic corticosteroid therapy (after joint sepsis has been resolved) and aggressive physical therapy—may be needed to maximize normal joint dynamics.

PREVENTION/AVOIDANCE
If clinical signs recur, early (within 24–48 hours) treatment provides the greatest benefit.

POSSIBLE COMPLICATIONS
• Chronic disease—severe degenerative joint disease
• Recurrence of infection
• Limited joint range of motion
• Generalized sepsis
• Osteomyelitis

EXPECTED COURSE AND PROGNOSIS
• Acutely diagnosed disease (within 24–48 hours) responds well to antibiotic therapy.
• Delayed diagnosis or resistant or highly virulent organisms—guarded to poor prognosis.

MISCELLANEOUS

ASSOCIATED CONDITIONS
N/A

AGE-RELATED FACTORS
N/A

ZOONOTIC POTENTIAL
N/A

PREGNANCY/FERTILITY/BREEDING
N/A

SYNONYMS
• Infectious arthritis
• Joint ill

SEE ALSO
• Osteomyelitis
• Polyarthritis, Immune-mediated

ABBREVIATION
NSAIDs = nonsteroidal anti-inflammatory drugs

INTERNET RESOURCES
N/A

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Client Education Handout available online

ASCITES

BASICS

DEFINITION
The escape of fluid, either transudate or exudate, into the abdominal cavity between the parietal and visceral peritoneum.

PATHOPHYSIOLOGY
- Ascites can be caused by the following:
  - CHF and associated interference in venous return
  - Depletion of plasma proteins associated with inappropriate loss of protein from renal or gastrointestinal disease—protein-losing nephropathy or enteropathy, respectively
  - Obstruction of the vena cava or portal vein, or lymphatic drainage due to neoplastic occlusion
  - Overt neoplastic effusion
  - Peritonitis—infective or inflammatory
  - Electrolyte imbalance, especially hypernatremia
  - Liver cirrhosis.

SYSTEMS AFFECTED
- Cardiovascular
- Gastrointestinal
- Hemic/Lymph/Immune
- Renal/Urologic

SIGNALMENT
- Dogs and cats
- No species or breed predisposition

SIGNS
- Episodic weakness
- Lethargy
- Abdominal fullness
- Abdominal discomfort when palpated
- Dyspnea from abdominal distension or associated pleural effusion
- Anorexia
- Vomiting
- Weight gain
- Scrotal or penile edema
- Groaning when lying down

CAUSES
- Nephrotic syndrome
- Cirrhosis of liver
- Right-sided CHF
- Hypoproteinemia
- Ruptured bladder
- Peritonitis
- Abdominal neoplasia
- Abdominal hemorrhage

RISK FACTORS
N/A

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Differentiating Abdominal Distension without Effusion
- Organomegaly—hepatomegaly, splenomegaly, renomegaly, and hydrometra.
- Abdominal neoplasia.
- Pregnancy.
- Bladder distension.
- Obesity.
- Gastric dilatation.

Differentiating Diseases
- Transudate—nephrotic syndrome, cirrhosis of liver, right-sided CHF, hypoproteinemia, and ruptured bladder.
- Exudate—peritonitis, abdominal neoplasia, and hemorrhage.

CBC/BIOCHEMISTRY/URINALYSIS
- Neutrophilic leukocytosis occurs in patients with systemic infection.
- Albumin is low in patients with impaired liver synthesis, gastrointestinal loss, or renal loss.
- Cholesterol is low in patients with impaired liver synthesis.

Liver Enzymes
- Low to normal in patients with impaired liver synthesis.
- High in patients with liver inflammation, hyperadrenocorticism, gallbladder obstruction, and chronic passive congestion.

Total and Direct Bilirubin
- Low to normal in patients with impaired liver synthesis.
- High in patients with biliary obstruction caused by tumor, gallbladder distension, or obstruction.

BUN and Creatinine
- High in patients with renal failure.
- BUN low in patients with impaired liver synthesis or hyperadrenocorticism.

Glucose
Low in patients with impaired liver synthesis.

OTHER LABORATORY TESTS
- To detect hypoproteinemia—protein electrophoresis and immune profile.
- To detect proteinuria—urinary protein:creatinine ratio (normal < 0.5:1).
- To detect liver ascites—analysis of serum ascites albumin gradient.

IMAGING
- Thoracic and abdominal radiography is sometimes helpful.
- Ultrasonography of the liver, spleen, pancreas, kidney, bladder, and abdomen can often determine cause.
- Stages of ascites:
  - Stage I: minimal ascites. Detected by ultrasound only.
  - Stage II: moderate ascites. Abdominal distention visible and/or noted on ballottement.
  - Stage III: significant ascites. Marked abdominal distention. Patient uncomfortable, possibly with labored breathing.

DIAGNOSTIC PROCEDURES

Ascitic Fluid Evaluation
Exfoliative cytologic examination and bacterial culture and antibiotic sensitivity—remove approximately 3–5 mL of abdominal fluid via aseptic technique.

Transudate
- Clear and colorless.
- Protein < 2.5 g/dL.
- Specific gravity < 1.018.
- Cells < 1,000/mm^3—neutrophils and mesothelial cells.

Modified Transudate
- Red or pink; may be slightly cloudy.
- Protein 2.5–5 g/dL.
- Specific gravity > 1.018.
- Cells < 5,000/mm^3—neutrophils, mesothelial cells, erythrocytes, and lymphocytes.

Exudate (Non-septic)
- Pink or white; cloudy.
- Protein 2.5–5 g/dL.
- Specific gravity > 1.018.
- Cells 5,000–50,000/mm^3—neutrophils, mesothelial cells, macrophages, erythrocytes, and lymphocytes.

Exudate (Septic)
- Red, white, or yellow; cloudy.
- Protein > 4.0 g/dL.
- Specific gravity > 1.018.
- Cells 5,000–100,000/mm^3—neutrophils, mesothelial cells, macrophages, erythrocytes, lymphocytes, and bacteria.

Hemorrhage
- Red; spun supernatant clear and sediment red.
- Protein > 5.5 g/dL.
- Specific gravity 1.007–1.027.
- Cells consistent with peripheral blood.
- Does not clot.

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ASCITES (CONTINUED)

Chyle
• Pink, straw, or white.
• Protein 2.5–7 g/dL.
• Specific gravity 1.007–> 1.040.
• Cells < 10,000/mm^3—neutrophils, mesothelial cells, and large population of small lymphocytes.
• Other—fluid in tube separates into cream-like layer when refrigerated; fat droplets stain with Sudan III.

Pseudochyle
• White.
• Protein > 2.5 g/dL.
• Specific gravity 1.007–1.040.
• Cells < 10,000/mm^3—neutrophils, mesothelial cells, and small lymphocytes.
• Other—fluid in tube does not separate into cream-like layer when refrigerated; does not stain with Sudan III.

Urine
• Clear to pale yellow.
• Protein > 2.5 g/dL.
• Specific gravity 1–> 1.040.
• Cells 5,000–50,000/mm^3—neutrophils, erythrocytes, lymphocytes, and macrophages.
• Other—if the urinary bladder ruptured < 12 hours before, urinary glucose and protein could be negative; if bladder ruptured > 12 hours before, urine becomes a dialysis medium with ultrafiltrate of plasma, and urine contains glucose and protein.

Bile
• Slightly cloudy and yellow.
• Protein > 2.5 g/dL.
• Specific gravity > 1.018.
• Cells 5,000–750,000/mm^3—neutrophils, erythrocytes, macrophages, and lymphocytes.
• Other—bilirubin confirmed by urine dipstick; non-icteric patient may have gallbladder rupture, biliary tree leakage, or rupture in the proximal bowel.

TREATMENT

• Can design treatment on an outpatient basis, with follow-up or inpatient care, depending on physical condition and underlying cause.
• If patients are markedly uncomfortable when lying down or become more dyspneic with stress, consider removing enough ascites to reverse these signs.
• Dietary salt restriction may help control transudate fluid accumulation due to CHF, cirrhosis, or hypoproteinemia.
• For exudate ascites control, address the underlying cause; corrective surgery is often indicated, followed by specific therapeutic management (e.g., patient with splenic tumor: tumor removed, abdominal bleeding controlled, blood transfusion administered).

LARGE-VOLUME PARACENTESIS

• Stage III treatment.
• Pretreat patient with hetastarch (6%) @ 1–2 mL/kg for 2 hours.
• Abdominal tap (paracentesis), until drainage slows.
• Post-treat patient with hetastarch (6%) @ 1–2 mL/kg for 4 hours.

MEDICATIONS

DRUG(S) OF CHOICE

• Patients with liver insufficiency or CHF—restrict sodium and give a diuretic combination of hydrochlorothiazide (2–4 mg/kg q12h PO) and spironolactone (1–2 mg/kg q12h PO); if control is inadequate, furosemide (1–2 mg/kg q8h PO) can be substituted for the thiazide with spironolactone continued; must monitor serum potassium concentration to prevent potassium imbalances.
• Patients with hypoproteinemia, nephrotic syndrome, and associated ascitic fluid accumulation—can treat as above with the addition of hetastarch (6% hetastarch in 0.9% NaCl); administer an IV bolus (dogs, 20 mL/kg; cats, 10–15 mL/kg) slowly over ~ 1 hour; hetastarch increases plasma oncotic pressure and pulls fluid into the intravascular space for up to 24–48 hours.
• Systemic antibiotic therapy is dictated by bacterial identification and sensitivity testing in patients with septic exudate ascites.

FOLLOW-UP

PATIENT MONITORING

• Varies with the underlying cause.
• Check sodium, potassium, BUN, creatinine, and weight fluctuations periodically if the patient is maintained on a diuretic.

POSSIBLE COMPLICATIONS

Aggressive diuretic administration may cause hypokalemia, which could predispose to metabolic alkalosis and exacerbation of hepatic encephalopathy in patients with underlying liver disease; alkalosis causes a shift from NH_4 to NH_3.

MISCELLANEOUS

AGE-RELATED FACTORS

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

Abdominal effusion

SEE ALSO

• Cirrhosis and Fibrosis of the Liver
• Congestive Heart Failure, Right-Sided
• Hypoalbuminema
• Nephrotic Syndrome

ABBREVIATIONS

CHF = congestive heart failure

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Client Education Handout available online

ASPERGILLOSIS, NASAL

BASICS

DEFINITION
• Nasal disease caused by *Aspergillus* spp., primarily *A. fumigatus.* • Saprophytic fungus that is ubiquitous in the environment.
• Opportunistic pathogen.

PATHOPHYSIOLOGY
• Inhalation of fungus leads to disease in the nasal cavity and frontal sinus with destruction of turbinates, formation of plaque lesions, and overproduction of mucus causing clinical signs of nasal disease. • Rarely may be associated with underlying foreign body or previous trauma. • Causes a locally aggressive and invasive disease but does not result in systemic mycosis. • Confined to nasal cavity and frontal sinus—sinonasal form (most common in dogs). • Can result in sino-nasal or sino-orbital disease in cats.

SYSTEMS AFFECTED
Respiratory—nasal cavity, sinus, orbit (cats, rare in dogs)

GENETICS
Unknown

INCIDENCE/PREVALENCE
Unknown, but a common diagnosis in dogs with nasal discharge in many locations.

GEOGRAPHIC DISTRIBUTION
Worldwide

SIGNALMENT
Species
Dog and cat (less common)

Breed Predilections
• Dogs—dolichocephalic and mesocephalic breeds • Cats—brachycephalic breeds may be overrepresented

Mean Age and Range
• Dogs—predominantly young to middle-aged • Cats—no predilection

Predominant Sex
None identified

SIGNS
Historical Findings
• Unilateral or bilateral nasal discharge—typically mucoid, mucopurulent, or serosanguinous but may be primarily epistaxis. • Sneezing. • Typically chronic signs—several months. • Many patients will have been treated with antibiotics for a possible bacterial infection before presentation with variable response.

Physical Examination Findings
• Unilateral or bilateral nasal discharge.
• Increased nasal airflow on the affected side.
• Depigmentation with ulceration of the nasal planum—~40% of dogs. • Facial pain.
• Ipsilateral mandibular lymphadenopathy.
• Stertor, exophthalmos, hard palate ulceration, facial asymmetry, loss of nasal airflow—sino-orbital disease in cats.

CAUSES
• No underlying cause identified, although preexisting foreign body or trauma is occasionally implicated. • Likely due to inhalation of a large bolus of fungus that is ubiqutous in the environment. • Species—most commonly *A. fumigatus* in dogs, *A. felis* in cats others—*A. niger, A. flavus*.

RISK FACTORS
Unknown

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Foreign body • Oronasal fistula
• Lymphoplasmacytic rhinitis • Neoplasia
• Nasopharyngeal polyp, nasal tumor, or cryptococcus—cats only

CBC/BIOCHEMISTRY/URINALYSIS
• Often normal • Possible inflammatory leukogram

OTHER LABORATORY TESTS
Serology
• Detects fungi-specific serum antibodies.
• AGID—commercially available; 98% specificity, 67% sensitivity in dogs; 43% sensitivity in cats. Serial serology does not appear to correlate with clinical status.
• ELISA—88% sensitivity, 97% specificity in dogs, 90% sensitivity in cats. • Counter-immunoelectrophoresis—85% specificity in dogs. • Serum galactomannan—unreliable.

Culture
• Tissue fungal culture of affected area; visualized biopsy sample taken from a region of suspected fungal growth showed 100% specificity, 81% sensitivity in dogs. • Culture of nasal discharge is less specific and insensitive.

IMAGING
Computed Tomography
• Imaging method of choice. • Cavitated turbinate lysis. • Thickening of the mucosa along the nasal turbinates. • Frontal sinus proliferative mass effect. • Soft tissue mass in the choana or nasopharynx—cats.
• Necessary for evaluation of the cribriform plate before topical antifungal treatment.

Skull Radiography
• Intraoral dorsoventral radiograph of the nasal cavity shows turbinate lysis.
• Rostrocaudal or skyline frontal sinus view may show increased soft tissue density in the frontal sinus. • Cannot evaluate cribriform plate.

DIAGNOSTIC PROCEDURES
Rhinoscopy
• Flexible rhinoscopy in dogs allows examination of the nasopharynx and possibly the frontal sinus if the opening of the nasofrontal duct is destroyed by fungal infection. • Rigid rhinoscopy—examination of the nasal cavity alone; good visualization is possible due to large airspaces caused by turbinate lysis; excessive mucus and bleeding can make full examination difficult.
• Visualization of fungal plaques (white, yellow, black, or light-green) on the mucosa of the nasal cavity and/or frontal sinus confirms fungal infection. • Sinuscopy—may be required to confirm the diagnosis in dogs that lack nasal plaques.

PATHOLOGIC FINDINGS
• Biopsies obtained of affected area under direct rhinoscopic visualization using cup biopsy instruments. • Samples immersion-fixed in buffered 10% formalin, routinely processed. • Evidence supportive of a diagnosis of aspergillosis—identification of septate, branching hyphae and conidia on histopathology. Surrounding inflammation is commonly neutrophilic or lymphoplasmacytic, rarely eosinophilic.
• Blind biopsies in an unaffected area of the nasal cavity can result in a false diagnosis of inflammation.

TREATMENT

APPROPRIATE HEALTH CARE
Overnight hospitalization advised after topical treatment or surgery.

NURSING CARE
Maintain the nares free of nasal discharge.

ACTIVITY
Restriction of activity is not required if no bleeding is documented.

DIET
N/A

CLIENT EDUCATION
• Dogs—inform client that multiple topical treatments are usually necessary to cure the disease; follow-up with rhinoscopy is highly recommended to ensure resolution. • No established protocols for treatment in cats.

SURGICAL CONSIDERATIONS
Endoscopic Debridement
• Extensive curettage and removal of fungal material from the nose and frontal sinus are essential to allow efficacy of topical medication.

Trephination of the Frontal Sinus
• Can be required for dogs with frontal sinus involvement. • Performed using a Jacob's chuck and intramedullary pin. • Allows direct visualization of the frontal sinus with a rigid rhinoscope and local debridement of fungal plaques. • Allows for lavage and topical treatment of the area using a red rubber catheter.

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ASPERGILLOSIS, NASAL (CONTINUED)

Surgical Debridement and Exenteration
• Used in some cats with sino-orbital disease.

MEDICATIONS

DRUG(S) OF CHOICE

Topical Clotrimazole or Enilconazole Therapy
• 1-hour infusion into nasal cavity under anesthesia.
• Treatment is usually performed during the same anesthesia as diagnostics.
• Treatment of choice in dogs; reported efficacy 85–89% with multiple treatments.
• Foley catheters are used to occlude the nares and nasopharynx.
• Dose—Clotrimazole: 1 gram in 100 mL of polyethylene glycol 200 (1% solution) evenly divided between two 60 mL syringes slowly infused over 1 hour into each side for large dogs; if trephination is used, divide the amount between the nasal cavity and sinus on the same side; less volume in smaller dogs. Enilconazole: 100 mL of 1%, 2%, or 5% solution.
• Dog is placed in dorsal recumbency with head turned to each side every 15 minutes during the infusion.
• Dog is placed in sternal recumbency with head down at the end of the procedure to drain all medication from the nasal cavity.
• Has been used in cats without orbital involvement in combination with oral antifungal therapy with varying success.

Systemic Therapy
• Antifungal triazole drugs should be considered if the cribriform plate is not intact; also used as primary therapy in some cats.
• Can also be used in combination with topical therapy.
• May be cost-prohibitive.
• Itraconazole 5 mg/kg PO q12h in dogs with a reported efficacy of 60–70%; 10 mg/kg PO q24h in cats.
• Voriconazole 5 mg/kg PO q12h; efficacy as sole therapy has not been established, neurotoxicity in cats.
• Posaconazole: dogs, 5–10 mg/kg PO q12–24h, cats, 5 mg/kg PO q24h or divided q12h; efficacy as sole therapy has not been established.
• Fluconazole is not recommended due to resistance.

CONTRAINDICATIONS
• Breach in the cribriform plate can allow contact of antifungal medication with brain resulting in neurologic signs and possible death. • Sino-orbital disease necessitates the use of systemic therapy. Amphotericin B should be considered.

PRECAUTIONS
• Topical clotrimazole and enilconazole are caustic to all mucosal surfaces—protective gear (gloves, goggles) should be worn by all staff that are in close contact. • Enilconazole can be associated with tissue swelling and upper airway obstruction.

ALTERNATIVE DRUG(S)

Enilconazole
• Also active in the vapor phase.

Combined Clotrimazole Irrigation and Depot Therapy
• Clotrimazole (1%) is flushed through a trephine hole in the frontal sinus over 5 minutes; 50 mL in each side in dogs > 10 kg; 25 mL in each side in dogs < 10 kg.
• Clotrimazole cream (1%) is then introduced into the front sinuses; 20 g in each side in dogs > 10 kg, 10 g in each side in dogs < 10 kg. • Reported efficacy similar to topical clotrimazole or enilconazole alone (86%).

FOLLOW-UP

PATIENT MONITORING

Dogs
• Monitor clinical signs, although reduction of clinical signs does not establish resolution of disease. • Follow-up rhinoscopy is recommended in all cases to establish response to treatment, regardless of clinical signs—histopathology and culture can help establish response. • Serial serology (AGID) appears not to correlate with clinical status.
• Repeat CT scan should be considered for reassessment of the cribriform plate before repeat topical treatment if a worsening clinical signs are seen. • Monitor liver enzymes in animals on triazole therapy. • Monitor renal parameters in animals on Amphotericin B.

Cats
• Monitor clinical signs for improvement or resolution. • Monitor liver enzymes in animals on triazole therapy. • Monitor renal parameters in animals on Amphotericin B.

PREVENTION/AVOIDANCE
N/A

POSSIBLE COMPLICATIONS
• Topical therapy—monitor after treatment for any complications such as swelling of oropharynx, neurologic signs, infection/swelling of trephine site. • Triazoles can cause anorexia and can be hepatotoxic.
• Amphotericin B can be nephrotoxic.

EXPECTED COURSE AND PROGNOSIS
• Studies have shown an 87% response rate to topical therapy in dogs after one to three treatments. • A newer study showed that recurrence or reinfection is more common than previously thought and can occur years after supposedly successful therapy. • The prognosis for cats with sinonasal aspergillosis is better than with the sino-orbital form.

MISCELLANEOUS

ASSOCIATED CONDITIONS
N/A

ZOONOTIC POTENTIAL
There are no documented cases of human infection from an affected dog or cat.

PREGNANCY/FERTILITY/BREEDING
N/A

SYNONYMS
None

ABBREVIATIONS
• AGID = agar gel immunodiffusion • CT = computed tomography • ELISA = enzyme-linked immunosorbent assay

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Consulting Editor Lynelle R. Johnson

ASPERGILLOSIS, SYSTEMIC

BASICS

OVERVIEW

• Opportunistic fungal infection caused by *Aspergillus* spp., common molds that are ubiquitous in the environment, forming numerous spores in dust, straw, grass clippings, and hay.
• Disseminated disease does not appear to be related to the nasal form of the disease, although one report of a dog developing fungal osteomyelitis 6 months after treatment for nasal aspergillosis raises the possibility.
• Disseminated disease—usually *A. terreus* or *A. deflectus*,
• Portal of entry not definitively established but possibly through the respiratory tract or gastrointestinal tract, with subsequent hematogenous spread.
• Most commonly affects intervertebral discs, bones, thoracic lymph nodes, lung and renal pelvis. May affect respiratory (bronchopulmonary) only, or rarely, cornea or ear canal only.

SIGNALMENT

Dogs

• More common in dogs than in cats.
• German shepherds, and less so Rhodesian ridgebacks, overrepresented but reported sporadically in many breeds; average age 3 years (range 2–8 years); females three times more likely to develop disease as males.

Cats

• Persians—marginally increased incidence.
• Disseminated cases mostly affect the lungs and/or gastrointestinal tract.

SIGNS

Dogs

• May develop acutely or slowly over a period of several months, usually terminally ill when first presenting.
• Lameness—fungal osteomyelitis causing pronounced swelling and discharging, fistulus tracts.
• Neurologic—fungal discospondylitis causing paraparesis, paraplegia, spinal pain. Central signs—vestibular signs, seizures, hemiparesis, mental dullness, ataxia, vision impairment, circling..
• Renal involvement—polyuria/polydipsia, hematuria.
• Respiratory—cough, hemoptysis, increased respiratory effort.
• Reproduction—pyometra.
• Cardiac—pericarditis, ascites due to right sided failure, arrhythmias.
• Gastrointestinal—abdominal distension, anorexia.
• Ocular—uveitis, chorioretinitis, hyphema, panopthalmitis.
• Nonspecific—fever, weight loss, weakness, vomiting, and lymphadenopathy.

Cats

• Usually nonspecific signs (e.g., lethargy, depression, vomiting, and diarrhea).
• Ocular—exophthalmos.

CAUSES & RISK FACTORS

• Caused by *Aspergillus* species, most commonly *A. terreus or A. deflectus*, *A. fumigates, A. niger, A. flavipes,* and *A. alabamensis* also associated. *A. felis* recently reported to cause fungal rhinosinusitis in cats, disseminated disease in dogs, and pulmonary aspergillosis in humans.
• German shepherds and immunosuppressed animals at higher risk.
• Geographic/environmental conditions—may be a factor, as some regions have a higher incidence (e.g., California, Louisiana, Michigan, Georgia, Florida, and Virginia in the United States; Western Australia; Barcelona; and Milan).
• Cats—associated with FIP, FePLV, FeLV, FIV, diabetes mellitus, and immunosuppressant use.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Bacterial osteomyelitis/discospondylitis; spinal neoplasia; intervertebral disc disease; skeletal neoplasia; bacterial pyelonephritis; bacterial pneumonia; other causes of vestibular signs/seizures; other causes of uveitis (see Anterior Uveitis—Cats, Anterior Uveitis—Dogs).

CBC/BIOCHEMISTRY/URINALYSIS

• Nonspecific.
• Dogs—mature neutrophilic leukocytosis with eosinophilia and monocytosis. One third have normocytic, normochromic nonregenerative anemia. Cats—may have nonregenerative anemia and leukopenia.
• Biochemistry—may see high globulins, ALP, ALT, amylase, creatinine, phosphate, BUN, and calcium.
• Urinalysis—may see isosthenuria, hematuria, pyuria, and possible fungal hyphae in the sediment; detection of the fungal hyphae can be improved by allowing the sample to incubate at room temperature for 24–48 hours; sediment samples may be examined unstained as wet preparations or may be air dried and stained with Diff-Quick (the hyphae branch at 45° and stain purple).

OTHER LABORATORY TESTS

• Methods of detection include: cytology, culture and histopathology.
• Definitive diagnosis by fungal culture from normally sterile body fluids and tissues, e.g., urine, bone, CSF, blood, lymph node, pleural effusions, intervertebral disc aspirates, kidney, spleen. Urine culture positive in approximately 50% of dogs.
• Culture on Sabouraud's dextrose agar (requires 5–7 days).
• Antibody serology (agar gel immunodiffusion, and ELISA) support the diagnosis but is insensitive for diagnosis of disseminated aspergillosis.
• Galactomannan antigen ELISA (urine or serum) good sensitivity (89%) and specificity (89%) in one small study. Pulmonary and ocular infections have lower sensitivity. False positive in dogs treated with Plasmalyte or with other mycotic infections (*Penicillium, Paecilomyces, Cladosporidium, Geotrichum, Histoplasma, Cryptococcus*).
• Cats—test for FeLV and FIV.

IMAGING

Radiographic Findings

• Spinal views may show end-plate lysis, attempted bony intervertebral bridging, and lysis of vertebral bodies consistent with discospondylitis; productive and destructive lesions of the vertebral bodies.
• Bony proliferation, lysis and periosteal reaction typical of osteomyelitis of the diaphyseal region of long bones.
• Pulmonary involvement rare, mixed interstitial/alveolar pattern, enlarged sternal and/or tracheobronchial lymph nodes, pleural effusion; productive and destructive lesions of sternebrae. Pulmonary cavitary lesions in dogs with chronic pulmonary localization.

Ultrasonographic Findings

• Kidneys—most common site to detect changes; changes seen include renal pelvis dilation ± echogenic debris within pelvis; loss of corticomedullary distinction; renal distortion and mottled appearance of the parenchyma; dilation of proximal ureter; renalomegaly; nodules or masses; hydronephrosis.
• Spleen—hypoechoic, lacy, sharply demarcated areas with no doppler signal suggestive of infarct are most significant finding in spleen; other findings include nodules/masses, mottled parenchyma, splenic venous thrombosis.
• Other—abdominal lymphadenomegaly; diffuse hepatic hypoechogenicity, ascites, or evidence of venous thrombosis.

MRI Findings

Useful for further defining brain lesions in animals with CNS signs; changes similar to other infectious and non-infectious inflammatory brain diseases. May help to identify subtle vertebral lesions in dogs with discospondylitis.

DIAGNOSTIC PROCEDURES

Area to collect sample relies on clinical presentation but may include CSF tap, joint aspirates, intervertebral disc space aspirates, abdominocentesis/thoracocentesis, aspirate of various organs (spleen, liver, kidney) or lymph nodes.

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ASPERGILLOSIS, SYSTEMIC (CONTINUED)

PATHOLOGIC FINDINGS

• Hyphae usually visualized, special stains assist organism detection.
• Focal osteomyelitis with multiple pale granulomas in kidneys, spleen, lymph node, myocardium, pancreas, and liver.
• Microscopic granulomas can be found in lungs, eyes, thyroid, uterus, brain, and prostate and contain numbers of septate, branching hyphae that may have characteristic lateral branching aleuriospores.
• Occasionally pulmonary congestion or GI mucosal reddening and erosions.
• Best visualized with periodic acid-Schiff, Gomori's methenamine silver, or Crocott's stain.

TREATMENT

DOGS

• Treatment rarely curative; severely ill dogs are recognized to have poor prognosis. May halt progression of clinical signs.
• Fluid therapy—indicated by the degree of renal compromise and azotemia.
• Pulmonary lobectomy followed by systemic antifungals has been successful in dogs with cavitary lesions without evidence of dissemination.

CATS

Disseminated—likely difficult to treat; limited data.

MEDICATIONS

DRUG(S)

• Combination itraconazole 5–10 mg/kg PO q24h (can be divided) and amphotericin B (dogs, 2–3 mg/kg IV 3 days per week for a total of 9–12 treatments, to cumulative dose of 24–27 mg/kg) —treatment of choice.
• Itraconazole as monotherapy has achieved long-term remission in a small number of dogs.
• New triazoles: voriconazole, posaconazole and ravuconazole all have activity against *Aspergillus*. Some dogs treated with voriconazole or posaconazole have gone into remission for many months. *Aspergillus* spp. resistant to fluconazole.
• Terbinifine (5–10 mg/kg PO q24h) used alone or in combination with triazoles has been used to treat resistant infections in humans.
• β-glucan synthase inhibitors caspofungin, micafungin, anidulafungin—limited clinical information in dogs but efficacious in invasive aspergillosis in humans.
• Combination therapy with flucytosine (dogs, 25–50 mg/kg PO q6h) and amphotericin B may prove successful, but no published reports.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

• Amphotericin B—contraindicated in dogs with pre-existing renal compromise or failure; amphotericin B lipid complex significantly reduced nephrotoxicity.
• Oral azoles—nausea, intermittent anorexia, liver enzyme elevation.
• Combination of flucytosine and amphotericin B—cutaneous drug eruptions in dogs.
• Avoid midazolam and cisapride with azoles—fatal drug reactions noted in humans.
• Hepatotoxicity and ulcerative dermatitis more likely to occur at doses of 10 mg/kg/day or higher. Discontinue itraconazole if adverse effects occur. May be able to reinstitute at lower dose once side effects have resolved.

FOLLOW-UP

Disseminated—monitor serial radiographs every 1–2 months, renal function, and urine cultures; prognosis poor, especially in German shepherds.

MISCELLANEOUS

ZOONOTIC POTENTIAL

None

ABBREVIATIONS

• ALP = alkaline phosphatase
• ALT = alanine transaminase
• BUN = blood urea nitrogen
• CSF = cerebrospinal fluid
• ELISA = enzyme-linked immunosorbent assay
• FeLV = feline leukemia virus
• FePLV = feline panleukopenia virus
• FIP = feline infectious peritonitis
• FIV = feline immunodeficiency virus
• MRI = magnetic resonance imaging

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Client Education Handout available online

ASPIRIN TOXICOSIS

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BASICS

OVERVIEW
• Given for its antipyretic, analgesic, anti-inflammatory, and antiplatelet effects.
• Aspirin inhibits cyclooxygenase, reducing the synthesis of prostaglandins and thromboxanes.
• Gastric irritation and hemorrhage can occur; dogs are especially sensitive.
• Repeated doses can produce gastrointestinal ulceration and perforation.
• Toxic hepatitis, metabolic acidosis, and anemia can occur, especially in cats.

SIGNALMENT
Cats and less commonly dogs

SIGNS
• Depression
• Anorexia
• Vomiting—vomitus may be blood-tinged
• Tachypnea
• Hyperthermia
• Muscular weakness and ataxia
• Ataxia, coma, seizures, and death in 1 or more days

CAUSES & RISK FACTORS
• Owners employing human dosage guidelines to medicate cats and dogs.
• Cats have a decreased ability to conjugate salicylate with glycine and glucuronic acid due to a deficiency in glucuronyl transferase.
• Half-life increases with dosage—cats, 22–27 hours for 5–12 mg/kg and approximately 44 hours for 25 mg/kg; dogs, 7.5 hours; responsible for higher risk in cats. Elimination is slower in neonatal and geriatric patients.
• Patients with hypoalbuminemia may be at higher risk of toxicity because aspirin is highly protein bound to plasma albumin.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Ethylene glycol or alcohol
• Anticoagulant rodenticides
• Other causes of liver failure, including acetaminophen, iron, metaldehyde, and blue-green algae

CBC/BIOCHEMISTRY/URINALYSIS
• Cats—prone to Heinz body formation
• Hyponatremia and hypokalemia
• Anemia, hypoproteinemia, elevated liver enzymes, elevated white blood cell count

OTHER LABORATORY TESTS
• Initial respiratory alkalosis followed by metabolic acidosis
• High ketones and pyruvic, lactic, and amino acid levels
• Decreased sulfuric and phosphoric acid renal clearance

DIAGNOSTIC PROCEDURES
Salicylic acid concentrations in serum or urine

TREATMENT

• Inpatient—following general principles of poisoning management
• Induced gastric emptying—gastric lavage or induced emesis
• Correction of acid-base balance—continuous intravenous fluids; assisted ventilation and supplemental oxygen for severely-affected animals
• Whole blood transfusions for severe cases of hemorrhage and hypotension
• Peritoneal dialysis, hemodialysis, or charcoal hemoperfusion—advanced procedures

MEDICATIONS

DRUG(S)
• No specific antidote available.
• Activated charcoal— 1–2 g/kg PO.
• Sodium bicarbonate 1 mEq/kg IV alkalinizes urine; must closely monitor acid-base status.
• Gastrointestinal protectants—sucralfate and a H2 blocker or proton pump inhibitor; misoprostol for patients at higher risk for gastrointestinal hemorrhage.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
N/A

FOLLOW-UP

• Maintaining renal function and acid-base balance is vital.
• Severe acid-base disturbances, severe dehydration, toxic hepatitis, bone marrow depression, and coma are poor prognostic indicators.

MISCELLANEOUS

• Be sure that history of "aspirin" medication does not refer to other available pain medications.
• Question owner about any pre-existing painful condition that may have prompted the aspirin administration.

Suggested Reading

Plumb DC. Aspirin. In: Plumb DC, ed., Plumb's Veterinary Drug Handbook, 7th ed. Ames, IA: Wiley-Blackwell, 2011, pp. 83–87.
Talcott PA, Gwaltney-Brant SM. Nonsteroidal antiinflammatories. In: Peterson ME, Talcott PA, eds. Small Animal Toxicology, 3rd ed. St. Louis, MO: Elsevier, 2013, pp. 698–700.

Author Lisa A. Murphy
Consulting Editor Lynn R. Hovda
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A

ASTHMA, BRONCHITIS—CATS

BASICS

DEFINITION
• Chronic bronchitis—inflammation in the airways (bronchi and bronchioles) lacking a specific etiology; chronic daily cough of greater than 2 months in duration. • Asthma—acute or chronic airway inflammation associated with increased airway responsiveness to various stimuli, airway narrowing due to smooth muscle hypertrophy or constriction, reversibility of airway constriction, and presence of eosinophils, lymphocytes, and mast cells within the airways. • Bronchitis is thought to result in airflow obstruction due to airway remodeling while asthma is associated with airway constriction; however, clinically the two disease processes can appear similar. No physical examination findings or biomarkers can distinguish between the two syndromes, although reversal of airflow obstruction following administration of a beta-agonist is suggestive of the asthmatic form of disease.

PATHOPHYSIOLOGY
• Lower airway inflammation likely results from inhalation of irritant substances. • Bronchiolar smooth muscle constriction—reversible spontaneously or with treatment. • Increase in mucosal goblet cells, mucus production, and edema of bronchial wall associated with inflammation. • Excessive mucus can cause bronchiolar obstruction, atelectasis, or bronchiectasis. • Smooth muscle hypertrophy implies chronicity—usually not reversible. • Chronic inflammation leads to airway remodeling and irreversible airflow obstruction.

SYSTEMS AFFECTED
• Respiratory • Cardiac—pulmonary hypertension rarely

GEOGRAPHIC DISTRIBUTION
Worldwide.

SIGNALMENT
Species
Cat

Breed Predilections
Siamese overrepresented

Mean Age and Range
Any age; more common between 2 and 8 years

Predominant Sex
One study showed females overrepresented

SIGNS
Historical Findings
• Coughing, tachypnea, labored breathing or wheezing. • Signs are typically episodic and can be acute or chronic.

Physical Examination Findings
• Severely affected cats present with open-mouth breathing, tachypnea, and cyanosis. • Increased tracheal sensitivity is common. • Chest auscultation may reveal crackles and/or expiratory wheezes, but can be normal. • Labored breathing with an abdominal push on expiration, increase in expiratory effort.

CAUSES
Triggers of airway inflammation unknown

RISK FACTORS
• Cigarette smoke, poor environmental hygiene, dusty cat litter, hair sprays, and air fresheners can exacerbate disease. • Use of potassium bromide—implicated in causing signs of bronchitis/asthma in some cats.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Rule out infectious pneumonia (*Mycoplasma, Toxoplasma*, bacterial or fungal pneumonia). • Consider *Dirofilaria immitis* and primary lung parasites (*Aelurostrongylus abstrusus, Capillaria aerophilia, Paragonimus kellicotti*). More common in southern and midwest US, and in outdoor and hunting cats in some geographic regions. • Primary or metastatic neoplasia can have similar clinical and radiographic appearance. • Clinical presentation of idiopathic pulmonary fibrosis may appear similar to feline bronchitis.

CBC/BIOCHEMISTRY/URINALYSIS
Frequently normal, ~40% of cats with bronchial disease have peripheral eosinophilia.

OTHER LABORATORY TESTS
• Fecal exams—flotation for *Capillaria,* sedimentation for *Paragonimus*, Baermann for *Aelurostrongylus.* False-negative tests common. • Heartworm antigen and antibody testing, particularly if coughing occurs in conjunction with vomiting. • Radioallergosorbent testing or intradermal skin testing—no correlation between skin allergies and respiratory disease currently documented.

IMAGING
Radiography
• Classically, diffuse bronchial wall thickening; interstitial or patchy alveolar patterns also possible. • Severity of radiographic changes does not necessarily correlate with clinical severity or duration, and normal radiographs can be found. • Hyperinflation of lung fields—flattened and caudally displaced diaphragm, increased distance between the heart and diaphragm, extension of lungs to the first lumbar vertebrae thought to reflect bronchoconstriction. • Collapse of right middle lung lobe due to mucus plugging and atelectasis reported in 11% of cases.
• Pulmonary lobar arterial enlargement is suspicious for heartworm disease.

Echocardiography
Useful to document heartworm disease or secondary pulmonary hypertension.

DIAGNOSTIC PROCEDURES
Transoral Tracheal Wash
Use a sterile endotracheal tube and polypropylene catheter to collect airway fluids at the level of the carina.

Bronchoscopy
• Allows visualization of trachea and bronchi. Excessive amounts of thick mucus are common with bronchitis. Mucosa of the airways is typically hyperemic and edematous.

Cytology of TOTW or BAL
• Eosinophils and neutrophils are most prominent cell types. • Up to 20% eosinophils on BAL cytology can be found in normal cats. • A mixed inflammatory cell population occurs in about 21% of cats.

Bacterial Cultures
• Quantitated cultures recommended; positive cultures frequently encountered but bacterial colony counts > 100–300 cfu/mL uncommon with bronchitis. • Specific *Mycoplasma* culture often needed.

Biopsy
Keyhole biopsy—can differentiate between idiopathic pulmonary fibrosis, neoplasia and bronchitis if needed.

PATHOLOGIC FINDINGS
Hyperplasia/hypertrophy of goblet cells, hypertrophy of airway smooth muscle, epithelial erosion, and inflammatory infiltrates.

TREATMENT

APPROPRIATE HEALTH CARE
• Remove patient from environment that exacerbates disease. • Hospitalize for acute respiratory distress.

NURSING CARE
Oxygen therapy, bronchodilators, and sedatives in an acute crisis. Minimize manipulation in order to lessen stress and oxygen needs of the animal.

ACTIVITY
Usually self-limited by patient.

DIET
Calorie restriction for obese cats.

CLIENT EDUCATION
• Most causes are chronic and progressive. • Do not discontinue medical therapy when clinical signs have resolved—subclinical inflammation is common and can lead to progression of disease. Lifelong medication and environmental changes usually necessary. • Some clients can be taught to give

terbutaline subcutaneously and corticosteroid injections at home for a crisis situation.

MEDICATIONS

DRUG(S) OF CHOICE

Emergency Treatment

• Oxygen and a parenteral bronchodilator. Injectable terbutaline (0.01 mg/kg IV or SC); repeat if no clinical improvement (decrease in respiratory rate or effort) in 20–30 minutes.
• A sedative can aid in decreasing anxiety (butorphanol tartrate at 0.2–0.4 mg/kg IV or IM, buprenorphine at 0.01 mg/kg IV or IM, or acepromazine at 0.01–0.05 mg/kg SC).
• A short-acting parenteral corticosteroid may also be required. Dexamethasone sodium phosphate (0.1–0.25 mg/kg, IV or SC). Can repeat if no improvement noted within 20–30 minutes.

Long-Term Management

Corticosteroids

• Decrease inflammation.
• Oral treatment is preferred over injectable for closer monitoring of dose and duration.
• Prednisolone: 0.5–1 mg/kg PO q12h. Begin to taper dose (50% each week) after 1–2 weeks if clinical signs have improved. Maintenance therapy = 0.5–1 mg/kg PO q24–48h.
• Longer-acting parenteral steroids (Vetalog or Depomedrol) should be reserved only for situations where owners are unable to administer oral or inhaled medication on a routine basis.

Inhaled Corticosteroids

• Requires a form-fitting facemask, spacer, and metered-dose inhaler (MDI). Veterinary brand: Aerokat (Trudell Medical).
• The most common corticosteroid used as an MDI is fluticasone propionate (Flovent). 110-μg Flovent MDI is recommended (1–2 actuations, 7–10 breaths q12h). In one study, use of 44-μg Flovent decreased BAL eosinophil counts in cats with experimentally induced lower airway disease.
• Flovent is used for long-term control of airway inflammation. Takes 10–14 days to reach peak effect; use oral steroids concurrently during this time.
• Results in some suppression of the hypothalamic-pituitary axis but systemic side effects appear to be limited.

Bronchodilators

• Methylxanthines: sustained-release theophylline formulations recommended, and pharmacokinetics can vary greatly. Only generic currently available. Dose at 15–20 mg/kg PO once daily in the evening.
• Beta-2 agonists (terbutaline, albuterol)—reverse smooth muscle constriction. Oral terbutaline dose is 1/4 of a 2.5 mg tablet q12h. Initial albuterol dose is 20 μg/kg PO q12h; can increase to 50 μg/kg PO q8h.

Inhaled Bronchodilators

• Albuterol—preferred inhalant bronchodilator, effect lasts less than 4 hours. Long-term use of traditional racemic form of inhaled albuterol (R and S-enantiomers) has been associated with worsened airway inflammation. Enantiomer specific R-albuterol should be used if the drug is needed in moderately to severely affected cats (q12–24h) or during respiratory distress.

Anthelminthics

• Empirical therapy is indicated for cats with clinical signs of bronchial disease and eosinophilic airway cytology in an appropriate geographic location.
• Consider fenbendazole, ivermectin, or praziquantel.

Antibiotics

Use based on a positive quantitative culture and susceptibility testing or *Mycoplasma* isolation.

CONTRAINDICATIONS

Beta-2 antagonists (e.g., propranolol) are contraindicated because of their ability to block sympathetically mediated bronchodilation.

PRECAUTIONS

• Long-term use of steroids increases risk of development of diabetes mellitus and predisposes to immunosuppression. • Use of corticosteroids in cats may precipitate congestive heart failure. • Beta agonists could cause tachycardia and exacerbate underlying cardiac disease.

ALTERNATIVE DRUG(S)

Leukotriene receptor blockers and inhibitors of generation: no evidence to support use. Anti-serotonin and antihistamine drugs: no evidence to support use. Immunotherapy: no clinical evidence to support use at this time.

FOLLOW-UP

PATIENT MONITORING

• Owners should report any increase in coughing, sneezing, wheezing, or respiratory distress. Medications should be increased appropriately or additional therapy initiated if clinical signs worsen. • Follow-up radiographs may be helpful to detect onset of new disease.
• Owner should watch for signs of PU/PD that could indicate diabetes mellitus or renal disease. Monitor blood glucose and urine cultures.

PREVENTION/AVOIDANCE

Eliminate any environmental factors that can trigger a crisis situation (see "Risk Factors"). Change furnace and air-conditioner filters on a regular basis. Consider dust-free litters.

POSSIBLE COMPLICATIONS

• Acute episodes can be life-threatening.
• Right-sided heart disease rarely develops as a result of long-term bronchitis.

EXPECTED COURSE AND PROGNOSIS

• Long-term therapy should be expected.
• Most cats do well if recurrence of clinical signs is carefully monitored and medical therapy appropriately adjusted. • A few cats will be refractory to treatment; these carry a much worse prognosis.

MISCELLANEOUS

ASSOCIATED CONDITIONS

Cor pulmonale can be a sequela to chronic lower airway disease.

PREGNANCY/FERTILITY/BREEDING

Glucocorticoids are contraindicated in the pregnant animal. Bronchodilators should be used with caution.

SYNONYMS

Allergic bronchitis, asthmatic bronchitis, feline lower airway disease, extrinsic asthma, eosinophilic bronchitis.

SEE ALSO

• Heartworm Disease—Cats • Respiratory Parasites

ABBREVIATIONS

• BAL = bronchoscopy/bronchoalveolar lavage • MDI = metered-dose inhaler
• PU/PD = polyuria/polydipsia

INTERNET RESOURCES

• www.Aerokat.com: for ordering facemasks and spacers for inhalant therapy.
• www.fritzthebrave.com: source for clients to research use of inhaled medications.

Suggested Reading

Cohn LA, DeClue AE, Cohen RL, Reinero CR. Effects of fluticasone propionate dosage in an experimental model of feline asthma. J Feline Med Surg 2010, 12(2):91–96.
Kirschvink J, Leemans J, Delvaux F, et al. Inhaled fluticasone reduces bronchial responsiveness and airway inflammation in cats with mild chronic bronchitis. J Feline Med Surg 2006, 8(1):45–54.

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Client Education Handout available online

A

ASTROCYTOMA

BASICS

OVERVIEW

• Glial cell neoplasm, most commonly affecting the brain and rarely the spinal cord. • Neoplastic cells are of astrocytic origin. • It is the most common intra-axial (situated inside of the brain parenchyma) intracranial neoplasm of dogs but is rarely diagnosed in cats. • Tumors are often located in the pyriform area of the temporal lobe, the cerebral hemispheres, the thalamus, hypothalamus, or midbrain. • Biologic behavior of this tumor is dictated by the histopathologic grade (I–IV, from best to worst prognosis) and anatomic involvement. • Tumors typically do not penetrate the ventricular system or metastasize outside of the cranial vault.

SIGNALMENT

• Dog—often brachycephalic breeds > 5 years of age; no sex predilection reported.
• Cat—usually > 9 years; no sex or breed predilection reported.

SIGNS

• Location and growth kinetic dependent • Seizures • Behavioural changes • Apathy towards normal activities including eating, playing, and societal interactions • Disorientation • Loss of conscious proprioception • Cranial nerve abnormalities • Head muscle atrophy • Upper motor neuron tetraparesis

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Other primary tumors arising from tissues of the central nervous system • Metastatic neoplasia with brain tropism such as hemangiosarcoma • Granulomatous meningoencephalitis • Trauma • Cerebrovascular infarction • Meningitis

CBC/BIOCHEMISTRY/URINALYSIS

Usually unremarkable

OTHER LABORATORY TESTS

CSF analysis may show albumin-cytologic dissociation (high protein with low number of nucleated cells). The CSF analysis is indicated to exclude infectious etiology, not to diagnose astrocytoma.

IMAGING

• MRI of brain is ideal for mass lesion confirmation, as it is superior to CT scanning for detecting lesions in the middle and caudal fossae. Additionally, MRI is more sensitive than CT for detection infarcts, bleeding, and edema. • Brain MRI may be useful in establishing a tentative differential diagnosis of a glial tumor, based on tumor characteristics highlighted in specific sequences.

DIAGNOSTIC PROCEDURES

• Neurologic exam. • Ophthalmic exam. • MRI. • CSF analysis. • Tumor biopsy for definitive diagnosis, when specific antineoplastic treatment is sought (surgery, curative-intent radiation therapy, experimental therapies).

TREATMENT

• Surgery. • Radiation therapy can be very effective in improving neurologic signs. • Chemotherapy with lomustine, procarbazine, or temozolomide might exert cytoreductive activities. • Anti-inflammatory dosing with corticosteroids to reduce peritumoral edema. • Consultation with a neurosurgeon and a radiation oncologist is essential for the appropriate patient management.

MEDICATIONS

DRUG(S)

Seizure Control

• Status epilepticus—diazepam (0.5–1 mg/kg IV, up to three times to achieve effect); if no response to diazepam, use pentobarbital (5–15 mg/kg IV slowly to effect).
• Long-term management—phenobarbital (1–4 mg/kg PO q12h) with or without adjuvant potassium bromide (20 mg/kg PO q24h).

Tumor Control

• Timely consultation with a neurosurgeon is of paramount importance for the appropriate management of the patient. • Radiation therapy may be effective, and consultation with a radiation oncologist is recommended. Stereotactic radiosurgery or intensity modulated radiation therapy may be considered as first-line treatment options. • Chemotherapy may be effective for treating dogs. Potential drugs that may exert measurable anticancer effects include CCNU (60–70 mg/m^2 PO every 3 weeks) or temozolomide (100–120 mg/m^2 PO q24h for 5 days every 3 weeks). • Prednisone (1 mg/kg q24h), may be effective in reducing peritumoral edema and improving the neurologic signs. Patients may need to be on steroids long term, even after the definitive treatment of the tumor.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

• Prednisone and phenobarbital may cause polyphagia, polydipsia, and polyuria.
• Phenobarbital may cause sedation for up to 2 weeks after initiation of treatment, and increase in hepatic enzymes on serum biochemical panel. • CBC and platelet count is recommended 7–10 days after chemotherapy and immediately before each dose of chemotherapy to monitor myelosuppression. • Chemotherapy has the potential to be synergistic with radiation therapy. Timely specialty to a referral center with neurosurgery, radiation therapy, and medical oncology capabilities is important for patients seeking more than palliative care.

FOLLOW-UP

PATIENT MONITORING

• Blood phenobarbital concentration should be assessed after 7–10 days of treatment, with modifications to dosages for achieving target plasma concentrations. • Serial MRIs should be considered for documenting response if multimodality therapy is used. • Serial CBC and platelet counts should be performed to monitor myelotoxicity associated with chemotherapy.

EXPECTED COURSE AND PROGNOSIS

• Long-term prognosis—guarded. • Median survival after chemotherapy plus medical management may be up to 7 months.
• Median survival after radiation therapy has been reported to be as high as 12 months.

MISCELLANEOUS

SEE ALSO

• Seizures (Convulsions, Status Epilepticus)—Cats • Seizures (Convulsions, Status Epilepticus)—Dogs

ABBREVIATIONS

• CSF = cerebrospinal fluid • CT = computed tomography • MRI = magnetic resonance imaging

Suggested Reading

Bentley RT, Ober CP, Anderson KL, Feeney DA, Naughton JF, Ohlfest JR, O'Sullivan MG, Miller MA, Constable PD, Pluhar GE. Canine intracranial gliomas: relationship between magnetic resonance imaging criteria and tumor type and grade. Vet J 2013, 198(2):463–471.

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Troxel MT, Vite CH, Van Winkle TJ, et al. Feline intracranial neoplasia: Retrospective review of 160 cases (1985–2001). J Vet Intern Med 2003, 17:850–859.

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ASTROVIRUS INFECTION

BASICS

OVERVIEW
An uncommon intestinal viral infection characterized by enteritis and diarrhea.

SIGNALMENT
- Cats
- No known breed, sex, or age predilection

SIGNS
- Small bowel diarrhea often green and watery.
- Kittens show more severe signs.
- May be severe and acute enough to cause dehydration and anorexia.

CAUSES & RISK FACTORS
- A small, non-enveloped, RNA virus of the genus *Astrovirus.*
- Details of the incidence, prevalence, and predisposing factors unknown.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
- Many causes of gastroenteritis
- Food allergy
- Toxin ingestion
- Inflammatory bowel disease
- Neoplasia
- Intestinal parasites
- Viral infections—panleukopenia, rotavirus, enteric coronavirus, enteric calicivirus
- Bacterial infections—salmonellosis, coliforms
- Protozoal infections—*Giardia,* cryptosporidiosis

CBC/BIOCHEMISTRY/URINALYSIS
N/A

OTHER LABORATORY TESTS
- Electron microscopy of feces—identify astrovirus particles.
- Difficult to isolate in the laboratory.

IMAGING
N/A

DIAGNOSTIC PROCEDURES
None

PATHOLOGIC FINDINGS
None described; similar to mild enteritis, rotavirus, or coronavirus enteritis.

TREATMENT
- Control diarrhea.
- Reestablish fluid and electrolyte balance.

MEDICATIONS

DRUG(S)
No specific antiviral drugs.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
None

FOLLOW-UP

PATIENT MONITORING
Monitor fluid and electrolytes.

PREVENTION/AVOIDANCE
Isolate infected cats during acute disease.

POSSIBLE COMPLICATIONS
Secondary intestinal viral and bacterial infections.

EXPECTED COURSE AND PROGNOSIS
- Illness usually < 1 week.
- Mortality—appears low.
- Prognosis—good.
- If diarrhea persists, investigate other causes.

MISCELLANEOUS

ZOONOTIC POTENTIAL
Sequence analysis of human and animal astroviruses suggests human-to-animal transmission does not occur.

Suggested Reading
Barr MC, Olsen CW, Scott FW. Feline viral diseases. In: Ettinger SJ, Feldman EC, eds., Veterinary Internal Medicine. Philadelphia: Saunders, 1995, pp. 409–439.
Lukashov VV, Goudsmit J. Evolutionary relationships among Astroviridae. J Gen Virol 2002, 83:1397–1405.

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A

ATAXIA

BASICS

DEFINITION

• A sign of sensory dysfunction that produces incoordination of the limbs, head, and/or trunk.
• Three clinical types—sensory (proprioceptive), vestibular, and cerebellar; all produce changes in limb coordination, but vestibular and cerebellar ataxia also produce changes in head and neck movement.

PATHOPHYSIOLOGY

Sensory (Proprioceptive)

• Proprioceptive pathways in the spinal cord (i.e., fasciculus gracilis, fasciculus cuneatus, and spinocerebellar tracts) relay limb and trunk position to the brain.
• When the spinal cord is slowly compressed, proprioceptive deficits are usually the first signs observed, because these pathways are located more superficially in the white matter and their larger sized axons are more susceptible to compression than are other tracts.
• Generally accompanied by weakness owing to early concomitant upper motor neuron involvement; weakness not always obvious early in the course of the disease.
• Ataxia can occur with spinal cord, brainstem, and cerebral lesions; mild to absent with unilateral brainstem lesions, and subtle to absent with unilateral cerebral lesion.

Vestibular

• Changes in head and neck position are relayed through the vestibulo-cochlear nerve to the brainstem.
• Vestibular receptors or the nerve in the inner ear are considered part of the peripheral nervous system, whereas nuclei in the brainstem are part of the central nervous system.
• Localize the vestibular signs to peripheral or central vestibular nervous system because prognosis and rule-outs differ for these two locations.
• Both locations of vestibular disease cause various degrees of disequilibrium with ensuing vestibular ataxia.
• Affected animal leans, tips, falls, or even rolls toward the side of the lesion; accompanied by head tilt.
• Central vestibular signs usually have changing types of nystagmus or vertical nystagmus; somnolence, stupor, or coma (due to involvement of the nearby ascending reticular activating system); multiple cranial nerve signs; proprioceptive deficits and quadriparesis or hemiparesis.
• Peripheral vestibular signs do not include changes in mental status, vertical nystagmus, proprioceptive deficits, quadriparesis or hemiparesis.
• Bilateral vestibular involvement, peripheral or central in origin, has characteristic exaggerated head motion with often poor to absent physiologic nystagmus.

Cerebellar

• The cerebellum regulates, coordinates, and modulates motor activity.
• Proprioception is normal because the ascending proprioceptive pathways to the cortex are intact; weakness does not occur because the upper motor neurons are intact.
• Inadequacy in the performance of motor activity; strength preservation; no proprioceptive deficits.
• Affected animal shows uncoordinated motor activity of limbs, head, and neck; hypermetria; dysmetria; head tremors; intention tremors; and truncal sway. Menace responses may be absent without visual dysfunction.

SYSTEMS AFFECTED

Nervous—spinal cord (and brainstem and cortex), cerebellum, vestibular system.

SIGNALMENT

Any age, breed, or sex

SIGNS

• Important to define the type of ataxia to localize the problem.
• Only one limb involved—consider a lameness problem.
• Only hind limbs affected—likely a spinal cord disorder affecting the spinocerebellar tracts.
• All or both ipsilateral limbs affected—cervical spinal cord, or cerebellar localization.
• Head tilt and/or nystagmus—vestibular localization.

CAUSES

Neurologic

Cerebellar

• Degenerative—abiotrophy (Kerry blue terrier, Gordon setter, rough-coated collie, Australian kelpie, Airedale, Bernese mountain dog, Finnish harrier, Brittany spaniel, border collie, beagle, Samoyed, wirehaired fox terrier, Labrador retriever, Great Dane, chow chow, Rhodesian ridgeback, domestic shorthair cats); storage diseases often have cerebellomedullary involvement.
• Anomalous—hypoplasia secondary to perinatal infection with panleukopenia virus (cats); malformed cerebellum due to herpesvirus infection (newborn puppies); arachnoid or epidermoid cyst located near fourth ventricle.
• Neoplastic—any CNS tumor (primary or secondary) localized to the cerebellum.
• Infectious—canine distemper virus; FIP; and any other CNS infection affecting the cerebellum.
• Inflammatory, idiopathic, immune-mediated—granulomatous meningoencephalomyelitis.
• Toxic—metronidazole.

Vestibular—Central Nervous System

• Infectious—FIP; canine distemper virus; rickettsial diseases.
• Inflammatory, idiopathic, immune-mediated—granulomatous meningoencephalomyelitis, meningoencephalomyelitis of unknown origin.
• Nutritional—thiamine deficiency.
• Toxic—metronidazole.

Vestibular—Peripheral Nervous System

• Infectious—otitis media interna; *Cryptococcus* granuloma (cats).
• Inflammatory—nasopharyngeal (middle ear) polyps (cats).
• Idiopathic—geriatric vestibular disease (dogs); idiopathic vestibular syndrome (cats).
• Metabolic—hypothyroidism.
• Neoplastic—squamous cell carcinoma, bone tumors.
• Traumatic.

Spinal Cord

• Degenerative—degenerative myelopathy (old German shepherd, Welsh corgi).
• Vascular—fibrocartilaginous embolic myelopathy.
• Anomalous—hemivertebrae; dens hypoplasia with atlantoaxial subluxation-luxation; Chiari-like malformation; cervical spondylomyelopathy; spinal sub-arachnoid diverticulum; other spinal cord and vertebral malformation.
• Neoplastic—primary bone tumors; multiple myeloma and metastatic tumors that infiltrate the vertebral body; meningioma; others.
• Infectious—discospondylitis; myelitis.
• Traumatic—intervertebral disc herniation; fracture or luxation; atlantoaxial subluxation-luxation.

Metabolic

• Anemia
• Polycythemia
• Electrolyte disturbances—especially hypokalemia, hypocalcemia, and hypoglycemia

Miscellaneous

• Drugs—acepromazine; antihistamines; antiepileptic drugs
• Respiratory compromise
• Cardiac compromise—reverse PDA, aortic thromboembolism

RISK FACTORS

• Intervertebral disc disease—dachshund, poodle, cocker spaniel, and beagle.
• Cervical spondylomyelopathy—Doberman pinscher and Great Dane.
• Fibrocartilaginous embolism—young, large-breed dogs and miniature schnauzers.
• Dens hypoplasia and atlantoaxial luxation—small-breed dogs, poodles.
• Chiari-like malformation—Cavalier King Charles spaniel, small-breed dogs.

(CONTINUED) # ATAXIA A

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Differentiate the types of ataxia.
• Differentiate from other disease processes that can affect gait—musculoskeletal, metabolic, cardiovascular, respiratory.
• Musculoskeletal disorders—typically produce lameness, pain, and a reluctance to move; degenerative joint disease signs often improve with increased movements.
• Systemic illness and endocrine, cardiovascular, and metabolic disorders—can cause intermittent ataxia, especially of the pelvic limbs; with fever, weight loss, murmurs, arrhythmias, hair loss, or collapse with exercise, suspect a non-neurologic cause; obtain minimum data from hemogram, biochemistry, and urinalysis.
• Head tilt or nystagmus—likely vestibular localization.
• Intention tremors of the head or hypermetria—likely cerebellar localization.
• All four limbs affected—lesion is in the cervical spinal cord, cerebellum or is multifocal to diffuse.
• Only pelvic limbs affected—lesion is anywhere below the second thoracic vertebra.

CBC/BIOCHEMISTRY/URINALYSIS
Normal unless metabolic cause (e.g., hypoglycemia, electrolyte imbalance, anemia, polycythemia).

OTHER LABORATORY TESTS
• Hypoglycemia—determine serum insulin concentration on sample that has low glucose value; low glucose and higher than expected insulin value suggest insulin-secreting tumor.
• Anemia—differentiate as nonregenerative or regenerative on the basis of the reticulocyte count.
• Electrolyte imbalance—correct the problem; see if ataxia resolves.
• Antiepileptic drugs—if being administered, evaluate serum concentration for toxicity.

IMAGING
• Spinal radiography, myelography, CT or MRI—if spinal cord dysfunction suspected.
• Bullae radiography—if peripheral vestibular disease suspected; CT or MRI superior; for inner ear disease, MRI superior to CT.
• Thoracic radiography—for older patients and patients suspected to have neoplasia or systemic fungal infection.
• CT or MRI—if cerebellar disease suspected;. MRI superior to CT.
• Abdominal ultrasonography—if hepatic, renal, adrenal, or pancreatic dysfunction suspected.

DIAGNOSTIC PROCEDURES
Cerebrospinal fluid—helps confirm nervous system etiology.

TREATMENT
• Usually outpatient, depending on severity and acuteness of clinical signs.
• Exercise—decrease or restrict if ataxia originates from spinal cord disease.
• Client should monitor gait for increasing dysfunction or weakness; if paresis worsens or paralysis develops, other testing is warranted.
• Avoid drugs that could contribute to the problem; may not be possible in patients on antiepileptic drugs for seizures.

MEDICATIONS

DRUG(S) OF CHOICE
Not recommended until the source or cause of the problem is identified.

FOLLOW-UP

PATIENT MONITORING
Periodic neurologic examinations to assess condition.

POSSIBLE COMPLICATIONS
• Spinal cord—progression to weakness and possibly paralysis
• Hypoglycemia—seizures
• Cerebellar disease—head tremors and bobbing
• Brainstem disease—stupor, coma, death

MISCELLANEOUS

AGE-RELATED FACTORS
N/A

SEE ALSO
• See specific causes
• Cerebellar Degeneration
• Head Tilt
• Paralysis

ABBREVIATIONS
• CNS = central nervous system
• CT = computed tomography
• FIP = feline infectious peritonitis
• MRI = magnetic resonance imaging

INTERNET RESOURCES
https://www.vetlearn.com/_preview?_cms.fe.previewId=1f98fff0-caa9-11e1-aa85-005056ad4736&WT.mc_id=newsletter%3BPV07111

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Consulting Editor Joane M. Parent

Client Education Handout available online

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ATHEROSCLEROSIS

BASICS

OVERVIEW
Thickening of the inner arterial wall in association with lipid deposits. Chronic arterial change characterized by loss of elasticity, luminal narrowing, and proliferating and degenerative lesions of the intima and media.

SIGNALMENT
- Rare in dogs.
- Not described in cats.
- Higher prevalence in miniature schnauzer, Doberman pinscher, poodle, and Labrador retriever.
- Geriatric patients (> 9 years).

SIGNS
Historical Findings
- None in some animals
- Lethargy
- Anorexia
- Weakness
- Dyspnea
- Collapse
- Vomiting
- Diarrhea

Physical Examination Findings
- Dyspnea
- Irregular rhythm
- Heart failure
- Disorientation
- Blindness
- Circling
- Coma
- Episodic lameness

CAUSES & RISK FACTORS
- Severe hypothyroidism
- Increasing age
- Hyperlipidemia in miniature schnauzers
- Male gender (male dogs may have predisposition)
- High total cholesterol
- Diabetes
- Glomerulonephritis

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Arteriosclerosis

CBC/BIOCHEMISTRY/URINALYSIS
- Hypercholesterolemia
- Hyperlipidemia
- High BUN and creatinine
- High liver enzymes

OTHER LABORATORY TESTS
- Low T_3 and T_4.
- High values for alpha-2 and beta fractions on protein electrophoresis.

IMAGING
Radiography
Thoracic and abdominal radiographs may reveal cardiomegaly and hepatomegaly.

DIAGNOSTIC PROCEDURES
Electrocardiography
- Conduction abnormalities and notched QRS complexes.
- Atrial fibrillation.
- ST segment elevation or depression with myocardial infarction.

TREATMENT
- Treat the underlying disorder and clinical signs (e.g., dyspnea if congestive heart failure develops).
- Diet—low-fat diet, weight loss program, and high soluble fiber intake to control hyperlipidemia.

MEDICATIONS

DRUG(S)
- Treat conduction disturbances and arrhythmias if clinically indicated.
- Thyroid replacement if hypothyroidism is confirmed.
- Antihypertensive therapy if hypertension is documented.
- Blood cholesterol-reducing medications if hyperlipidemic.
- Treat diabetes.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS
N/A

FOLLOW-UP
- Monitor T_4 concentration 4–6 hours post-administration after the first 6 weeks of treatment and adjust dosage accordingly.
- Monitor blood triglyceride and cholesterol levels.
- Monitor ECG for conduction disturbances and ST segment changes.

MISCELLANEOUS

ASSOCIATED CONDITIONS
- Hypothyroidism
- Diabetes
- Mitral valve disease (myxomatous)
- Glomerulonephritis

AGE-RELATED FACTORS
Geriatric patients (> 9 years)

SEE ALSO
Myocardial Infarction

INTERNET RESOURCES
www.vetgo.com/cardio

Suggested Reading

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Consulting Editors Larry P. Tilley and Francis W.K. Smith, Jr.

ATLANTOAXIAL INSTABILITY

BASICS

OVERVIEW

• Results from malformation or disruption of the articulation between the first and second cervical vertebrae (atlas and axis, respectively); causes spinal cord compression.
• AA instability can result in spinal cord trauma or compression at the junction between the atlas and axis—may cause neck pain and/or varying degrees of general proprioceptive (GP) ataxia /upper motor neuron (UMN) tetraparesis, tetraplegia (with or without nociception), and death from respiratory arrest.

Etiology

• Congenital: anomaly of the dens (aplasia, hypoplasia, or malformation [dorsal angulation] of the dens) and its ligamentous attachments.
• Acquired: may be a consequence of traumatic injury.

SIGNALMENT

• Congenital—toy-breed dogs (Yorkshire terrier, miniature or toy poodle, Chihuahua, Pekingese, and Pomeranian).
• Age at onset—usually before 12 months of age.
• Uncommon in larger-breed dogs, dogs > 1 year old, and cats.
• No sex predilection.

SIGNS

• Intermittent or progressive ambulatory tetraparesis, usually with neck pain—most common.
• Neurologic signs vary from mild to moderate GP/UMN ambulatory tetraparesis to non-ambulatory GP/UMN tetraparesis, or tetraplegia depending on degree of spinal cord compression and secondary pathology (i.e., edema, hemorrhage, or gliosis).
• Animals may have only neck pain without concurrent neurologic deficits.
• Episodes of collapse secondary to weakness.
• Abnormal postural reactions with spinal reflexes that are normal to exaggerated with normal to increased muscle tone in all four limbs.
• Acute death may occur when accompanied by trauma and respiratory arrest (uncommon).

CAUSES & RISK FACTORS

• Usually caused by abnormal development of the dens and/or ligamentous support structures, resulting in subluxation of the atlantoaxial joint.
• Fracture of the axis.
• Clinical signs often occur as a result of mild or insignificant trauma (e.g., jumping or playing).
• Clinical signs may be exacerbated by activity such as flexion of the neck.
• Toy-breed dogs—at risk for congenital malformation of the dens.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Differential diagnoses are consistent with various causes of cervical myelopathies, including:
  ◦ Other congenital malformation.
  ◦ Trauma.
  ◦ Meningitis or meningomyelitis (i.e., infectious or non-infectious [granulomatous meningoencephalomyelitis]).
  ◦ Fibrocartilaginous embolic myelopathy.
  ◦ Disk herniation.
  ◦ Neoplasia.

CBC/BIOCHEMISTRY/URINALYSIS

Normal

IMAGING

• Plain radiography of the cervical vertebral column:
  ◦ Lateral view—caudal and dorsal displacement of the axis in relationship to the atlas, resulting in an increased distance between vertebrae.
  ◦ Ventral dorsal or oblique view—may reveal absence, hypoplasia, or malformation (dorsal angulation) of the dens.
• Cross-sectional imaging:
  ◦ MRI.
  ◦ Diagnosis based on observation of caudal and dorsal displacement of the axis in relationship to the atlas as evidenced by the following features of the atlantoaxial articulation: (1) Dorsal: displacement of the spinous process of the axis; (2) Ventral: increased size of the occipito-atlas-axis joint cavity.
  ◦ Allows identification of spinal cord compression.
  ◦ Allows recognition of secondary spinal cord pathology such as edema, hemorrhage, or gliosis, which may impact prognosis.
• Computed tomography:
  ◦ May provide detailed visualization of bony structures, which allows for the creation of three-dimensional reconstructed image to help surgical planning.
• Precautions:
  ◦ Proper positioning will require sedation or general anesthesia.
  ◦ Sedation or general anesthesia carries significant risk for iatrogenic trauma.
  ◦ Care needs to be exercised when positioning animals.
  ◦ AVOID EXCESSIVE FLEXION OF THE NECK!!
  ◦ Flexion may exacerbate compression, which may worsen clinical signs or cause death due to spinal cord trauma.
  ◦ To protect against neck flexion during recovery, affected animals should be closely monitored until they are capable of maintaining normal head and neck carriage.

TREATMENT

• Prior to treatment, consultation with a board-certified neurologist or surgeon should be pursued.
• Improper treatment can lead to irreversible deterioration in neurologic function.

MEDICAL

• Neck brace (splint) to stabilize the cervical vertebral column in extension.
  ◦ Fiberglass cast material is positioned ventrally from the rostral aspect of mandible to the xiphoid and incorporated into bandage material, which immobilizes the head and neck.
  ◦ Strict exercise restriction (cage confinement) for a minimum of 8 weeks.
  ◦ Frequent bandage/splint changes are needed.
• Adjunctive medication (see below).

Overall Prognosis

• Successful outcome observed in 62.5% of dogs.
• Improved prognosis was associated with an acute onset and short duration of clinical signs (< 30 days).
• Surgery is recommended to treat animals that fail to improve or experience recurrence of signs following medical treatment.

SURGERY

• Treatment of choice in the majority of cases.
• Surgical approach; **ventral method is preferred**.
• Ventral approach—variety of methods:
  ◦ Transarticular pinning or lag screw technique; ventral tips of the pins incorporated in polymethylmethacrylate to prevent pin migration.
  ◦ Transarticular pinning and ventral cortical screws or K-wires in the bodies of the atlas and axis ± K-wires applied longitudinally and wired to the screws; screw heads and K-wires are incorporated in polymethylmethacrylate to provide fixation.
• Dorsal approach—use wire or synthetic suture material to fix the spinous process of the axis to the dorsal arch of the atlas; provides less rigid fixation and may be associated with greater implant failure.
• Strict exercise restriction is required for the first month postoperatively, followed by a gradual return to activity over an additional month.
• Adjunctive medication (see below).
• Overall prognosis ranges from 63% to 91% success: improved prognosis was associated with young (< 24 months) dogs, duration of clinical signs < 10 months, and mild neurologic deficits.

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ATLANTOAXIAL INSTABILITY (CONTINUED)

- Complications:
  - Failure to improve/worsening of neurologic deficits.
  - Implant failure/infection.
  - Respiratory—respiratory arrest, dyspnea, cough, and aspiration pneumonia.
  - Death.

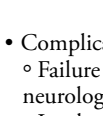
MEDICATIONS

DRUG(S)

- Anti-inflammatory medication:
  - Corticosteroids: prednisone 0.5–1.0 mg/kg PO divided twice daily for 2 weeks, followed by a tapering regime. Suggested protocol following initial dose: 0.5 mg/kg PO daily for 5 days, followed by 0.5 mg/kg PO every other day for 5 days.
  - NSAID: 1- to 4-week course.
- Analgesia:
  - Tramadol 2.0–4.0 mg/kg PO q6–8h.
  - Gabapentin 10–20 mg/kg PO q6–8h.
  - Pregabalin 3–4 mg/kg (begin with 2 mg/kg) PO q8–12h.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Corticosteroid—use caution when given in conjunction with medical treatment; may reduce pain, resulting in increased activity and spinal cord trauma.
- Avoid NSAIDs in combination with corticosteroids in all patients—increases risk of life-threatening gastrointestinal hemorrhage.



FOLLOW-UP

- Dogs treated medically require frequent (weekly) bandage changes for associated soft tissue trauma.
- All dogs should be reevaluated at 1 and 3 months (postoperatively or after neck brace removal) and monthly until neurologic deficits resolve or remain static over 2–3 months.
- More frequent rechecks may be needed for dogs experiencing complications or recurrence of signs.
- Untreated animals may experience deterioration in neurologic function, catastrophic acute spinal cord trauma, respiratory arrest, and death.

MISCELLANEOUS

- Rehabilitation may play a significant role in the ultimate neurologic functional level of the patient.
- Rehabilitation should only be considered in dogs > 30 days postoperatively or after neck brace (splint) removal.

ABBREVIATIONS

- GP = general proprioceptive
- MRI = magnetic resonance imaging
- NSAID = nonsteroidal anti-inflammatory drug
- UMN = upper motor neuron

INTERNET RESOURCES

http://www.acvs.org/AnimalOwners/HealthConditions/SmallAnimalTopics/AtlantoaxialInstability/.

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ATOPIC DERMATITIS

BASICS

DEFINITION

• A genetically predisposed hypersensitivity reaction to normally innocuous substances. • Manifests as an inflammatory, chronically relapsing, non-contagious and pruritic skin disease.

PATHOPHYSIOLOGY

• Atopic dermatitis (AD) has a multifactorial etiology involving genetic, structural, and immunologic factors. • Classical theory describes the pathway through which susceptible animals become sensitized to environmental allergens producing allergen-specific IgE, followed by mast cell degranulation upon re-exposure to allergens via epicutaneous absorption (extrinsic AD). • A subset of AD patients does not have increased allergen-specific IgE (intrinsic AD). • Current focus on the pathogenesis of AD includes abnormalities in barrier function and T-cell dysregulation or imbalance. • Barrier function impairment, shown as increased transepidermal water loss and decreased fillagrin expression, in affected dogs has been demonstrated. • Acute lesions of AD are characterized by increased T_H2 lymphocyte activity while T_H1 cytokines predominate in chronic lesions. Thus a T_H2:T_H1 imbalance in AD has been proposed. • Recently, aberrant regulatory T-cell function has been reported. • Following repeat epicutaneous absorption of allergens, mast cell degranulation results in the release of histamine, proteolytic enzymes, cytokines, chemokines, and other chemical mediators. • Bacterial superantigens, auto-antigens released via keratinocyte damage, and *Malassezia* may play a role in perpetuating the inflammation.

SYSTEMS AFFECTED

• Ophthalmic • Respiratory • Skin/Exocrine

GENETICS

• Dogs—inherited predisposition; polygenetic with environmental influences important for disease development. • Cats—inherited predisposition less clear.

INCIDENCE/PREVALENCE

• Canine—true prevalence is unknown; estimated at 3–15% of the canine population. • Feline—unknown; generally believed to be lower than that for dogs.

GEOGRAPHIC DISTRIBUTION

Canine—recognized worldwide; local environmental factors (temperature, humidity, and flora) influence the seasonality, severity, and duration of signs.

SIGNALMENT

Species

Dogs and cats

Breed Predilections

• Canine—any breed, including mongrels; recognized more frequently in certain breeds or families (can vary geographically). • United States—Boston terrier, boxer, cairn terrier, Chinese Shar-Pei, cocker spaniel, Dalmatian, English bulldog, English and Irish setter, French bulldog, American pit bull terrier, Lhasa apso, miniature schnauzer, pug, Sealyham terrier, Scottish terrier, West Highland white terrier, wirehaired fox terrier, Labrador retriever, and golden retriever. • Feline—none reported.

Mean Age and Range

• Canine—mean age at onset 1–3 years; range 3 months–6 years; signs may be mild the first year but usually progress and become clinically apparent before 3 years of age. • Feline—6 months to 2 years.

Predominant Sex

None reported

SIGNS

General Comments

• Pruritus—itching, scratching, rubbing, licking. • Most cutaneous changes caused by self-induced trauma; primary lesions usually unrecognized.

Historical Findings

• Facial, pedal, or axillary pruritus • Early age of onset • History in related individuals • May be initially seasonal • Recurring skin or ear infection • Temporary response to glucocorticosteroids • Symptoms progressively worsen with time • Feline—face and neck pruritus

Physical Examination Findings

• Areas most commonly affected—interdigital spaces, carpal and tarsal areas, muzzle, periocular region, axillae, groin, and pinnae. • Lesions—vary from none to broken hairs or salivary discoloration to erythema, papules, and, alopecia, to crusts, hyperpigmentation, lichenification. The skin may become excessively oily or dry seborrhea, and hyperhidrotic (apocrine sweating). • Secondary bacterial and yeast skin infections (common). • Chronic relapsing otitis externa. • Conjunctivitis, blepharitis, and rhinitis may occur.

CAUSES

• Pollens (grasses, weeds, and trees) • Mold spores (indoor and outdoor) • *Malassezia* • House dust and storage mites • Animal dander • Insects

RISK FACTORS

• Temperate environments with long allergy seasons and high pollen and mold spore levels. • Concurrent pruritic dermatoses, such as flea bite hypersensitivity and adverse food reaction (summation effect).

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Adverse food reaction—may cause identical symptoms; may occur concurrently with atopic dermatitis; differentiation is made by noting response to hypoallergenic diet. • Flea bite different lesion distribution and response to flea control. • Sarcoptic mange—causes severe pruritus of the ventral chest, lateral elbows, lateral hocks, and pinnal margins; differentiation by multiple skin scrapings and/or complete response to a trial of miticidal therapy. • Secondary pyoderma—follicular papules, pustules, crusts, and epidermal collarettes. • Secondary yeast infections—erythematous, scaly, crusty, greasy, and malodorous body folds and intertriginous areas; differentiation by demonstration of numerous budding yeast organisms on skin cytology. • Contact dermatitis (allergic or irritant)—severe erythema and pruritus of the feet and thinly haired areas of the flank and axillae.

CBC/BIOCHEMISTRY/URINALYSIS

Eosinophilia—rare in dogs without concurrent flea infestations; common in cats.

DIAGNOSTIC PROCEDURES

• Diagnosis of AD is made by history, physical examination, and ruling out of differential diagnoses; not by either serologic or intradermal allergy testing. • Greatest treatment success noted when immunotherapy is based on results of both serum and intradermal testing.

Serologic Allergy Tests

• Measures the amount of allergen-specific IgE antibody in the patient's serum. • Advantages over IDT—availability; hair coat does not require clipping; sedation is not required. • Disadvantages—cannot distinguish between allergic and normal patients; frequent false-positive or false-negative reactions; limited number of allergens tested; inconsistent assay validation, quality control, and reliability (may vary with the laboratory used); a subset of AD patients does not have elevated levels of circulating allergen-specific IgE.

Intradermal Test (Preferred)

• Small amounts of test allergen are injected intradermally causing localized reactions; wheal formation is measured and evaluated subjectively. • Advantages—more physiologically-appropriate determination of allergens for immunotherapy; potentially higher success rate of immunotherapy versus allergens chosen based on serum testing. • Disadvantages—results more difficult to interpret in cats owing to the relatively small wheals produced; requires sedation and clipping a small patch of hair coat; false

A

ATOPIC DERMATITIS (CONTINUED)

positive and false negative reactions may occur.

PATHOLOGIC FINDINGS
Skin biopsy—rule out other differential diagnoses; results not pathognomonic; acanthosis, mixed mononuclear superficial perivascular dermatitis, sebaceous gland metaplasia, with secondary superficial bacterial folliculitis.

TREATMENT

APPROPRIATE HEALTH CARE
Outpatient

ACTIVITY
Avoid offending allergens when possible

DIET
Diets rich in essential fatty acids may be beneficial

CLIENT EDUCATION
• Explain the inheritable and progressive nature of the condition. • Rarely goes into remission and cannot be cured. • Ongoing therapy may be necessary to maintain quality of life.

MEDICATIONS

DRUG(S) OF CHOICE
Immunotherapy (Hyposensitization)
• Subcutaneous or sublingual administration of gradually increasing doses of the causative allergens to reduce sensitivity. • Allergen selection—based on allergy test results, patient history, and/or knowledge of local exposure. • Immunotherapy formulation procedures and administration protocols are not standardized and vary widely between clinicians. • Preferred treatment in most cases; especially indicated when it is desirable to avoid or reduce the amount of corticosteroids required to control signs, when signs last longer than 4–6 months per year, or when non-steroid forms of therapy are ineffective. • Successfully reduces pruritus in 60–80% of dogs and cats. • Response is slow, requiring at least 3 months and up to 1 year for full effect.

Cyclosporine
• Cyclosporine, modified (name brand preferred—Atopica 5 mg/kg/day) effective in controlling pruritus associated with chronic atopic dermatitis. • Response is similar to that of glucocorticosteroids. • Slow onset of activity (1–4 weeks). • Many patients can be adequately controlled with less frequent dosing (every 2–4 days). • Patient monitoring is recommended. • Drug blood level monitoring recommended in cats.

Corticosteroids
• May be given for short-term relief and to break the itch-scratch cycle. • Should be tapered to the lowest dosage that adequately controls pruritus. • Prednisolone (0.25–0.5 mg/kg PO q48h). • Cats—oral steroids or very infrequent methylprednisolone acetate by injection (2–4 mg/kg).

Antihistamines
• Less effective than corticosteroids.
• Dogs—hydroxyzine (1–2 mg/kg PO q12h), chlorpheniramine (0.2–0.4 mg/kg PO q12h), diphenhydramine (2.2 mg/kg PO q12h), fexofenadine (2–5 mg/kg PO q12–24h), and clemastine (0.04–0.10 mg/kg PO q12h).
• Cats—chlorpheniramine (0.5 mg/kg PO q12h); efficacy estimated at 10–50%.

Oclacitinib
Oclacitinib Apoquel (0.4–0.6 mg/kg q12h for 14 days then q24h). Dogs—effective in controlling pruritus associated with chronic atopic dermatitis. Onset time and response similar to glucocorticoids. Long-term safety and efficacy undetermined.

PRECAUTIONS
• Cyclosporine—may affect glucose homeostasis; may increase incidence of urinary tract infection. • Corticosteroids—use judiciously in dogs to avoid iatrogenic hyperglucocorticism and associated problems, aggravation of pyoderma, and induction of demodicosis. • Antihistamines—can produce drowsiness, and rarely anorexia, vomiting, diarrhea, increased pruritus; use with caution in patients with cardiac arrhythmias.
• Oclacitinib—not for use in dogs under 1 year of age; insufficient long-term experience.

POSSIBLE INTERACTIONS
Concurrent use of cyclosporine and ketoconazole permits a 50% dose reduction of each drug

ALTERNATIVE DRUG(S)
• Frequent bathing (once to twice weekly) in cool water with antipruritic shampoos is very beneficial and should be strongly encouraged.
• Fatty acids: ω-3 (eicosapentaenoic acid 66 mg/kg/day) may be more effective than ω-6 (linoleic acid 130 mg/kg/day) fatty acids.
• Tricyclic antidepressants: dog—(doxepin 1–2 mg/kg PO q12h; or amitriptyline 1–2 mg/kg PO q12h); overall effectiveness is unclear; not extensively studied in the cat.
• Gabapentin (dogs, 10–30 mg/kg q6–12h; cats, 3–8 mg/kg q6–8h) • Pentoxifylline 10 mg/kg q8–12h. • Topical triamcinolone spray 0.015% can be used over large body surfaces to control pruritus with minimal side effects.

FOLLOW-UP

PATIENT MONITORING
• Examine patient every 2–8 weeks when a new course of therapy is started. • Monitor pruritus, self-trauma, development of bacterial folliculitis, and possible adverse drug reactions. • Once an acceptable level of control is achieved, examine patient every 3–12 months. • CBC, serum chemistry profile, and urinalysis with culture—recommended every 3–12 months for patients on chronic corticosteroid, cyclosporine or Oclacitinib therapy.

PREVENTION/AVOIDANCE
• If offending allergens have been identified through allergy testing, avoidance may help to reduce the level of pruritus; this is seldom possible. • Minimizing other sources of pruritus (e.g., flea infestation, adverse food reaction, and secondary skin infection) permits better response to therapy.

POSSIBLE COMPLICATIONS
• Secondary bacterial folliculitis or *Malassezia* dermatitis. • Concurrent flea bite hypersensitivity and/or adverse food reaction.

EXPECTED COURSE AND PROGNOSIS
• Not life-threatening unless intractable pruritus results in euthanasia. • Degree of pruritus usually worsens and the duration of signs last longer each year without intervention. • Some cases spontaneously resolve.

MISCELLANEOUS

ASSOCIATED CONDITIONS
• Flea bite hypersensitivity • Adverse food reaction/food hypersensitivity • Bacterial folliculitis • *Malassezia* dermatitis • Otitis externa

AGE-RELATED FACTORS
Severity worsens with age

PREGNANCY/FERTILITY/BREEDING
• Corticosteroids—contraindicated during pregnancy • Affected animals should not be used for breeding

SYNONYMS
• Atopy • Canine atopic disease

SEE ALSO
• Flea Bite Hypersensitivity and Flea Control • Food Reactions, Dermatologic • Otitis Externa and Media • Pyoderma

ABBREVIATION
IDT = intradermal test

Suggested Reading
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Consulting Editor Alexander H. Werner

Client Education Handout available online

ATRIAL FIBRILLATION AND ATRIAL FLUTTER

BASICS

DEFINITION

• Atrial fibrillation—rapid, irregularly irregular supraventricular rhythm. Two forms recognized: primary atrial fibrillation, an uncommon disease that occurs mostly in large dogs with no underlying cardiac disease, and secondary atrial fibrillation, which occurs in dogs and cats secondary to underlying cardiac disease. • Atrial flutter is similar to atrial fibrillation, but the atrial rate is generally slower and is characterized by saw-toothed flutter waves in the baseline of the ECG. The ventricular response is generally rapid but may be regular or irregular.

ECG FEATURES

Atrial Flutter

• Atrial rhythm usually regular; rate approximately 300–400 bpm. • P waves usually discerned as either discrete P waves or a "saw-toothed" baseline. • Ventricular rhythm and rate generally depend on the atrial rate and AV nodal conduction, but are generally regular or regularly irregular and rapid. • Conduction pattern to the ventricles is variable—in some cases every other atrial depolarization produces a ventricular depolarization (2:1 conduction ratio), giving a regular ventricular rhythm; other times the conduction pattern appears random, giving an irregular ventricular rhythm that can mimic atrial fibrillation.

Secondary Atrial Fibrillation

• No P waves present—baseline may be flat or may have small irregular undulations ("f" waves); some undulations may look like P waves. • Ventricular rate high—usually 180–240 bpm in dogs and > 220 bpm in cats. • Interval between QRS complexes is irregularly irregular; QRS complexes usually appear normal.

Primary Atrial Fibrillation

Similar to secondary atrial fibrillation except ventricular rate usually in the normal range.

PATHOPHYSIOLOGY

• Atrial fibrillation—caused by numerous small reentrant pathways creating a rapid (> 500 depolarizations/minute) and disorganized depolarization pattern in the atria that results in cessation of atrial contraction. Depolarizations continuously bombard the AV nodal tissue, which acts as a filter and does not allow all depolarizations to conduct to the ventricles. Many atrial depolarizations activate only a part of the atria because the rapid rate renders portions of the atria refractory, and thus they cannot reach the AV junction. Other atrial impulses penetrate into the AV junctional tissue but are not robust enough to penetrate the entire length. Blocked impulses affect the conduction properties of the AV junctional tissue and alter conduction of subsequent electrical impulses; electrical impulses are conducted through the AV junction irregularly, producing an irregular ventricular rhythm. • Atrial flutter—probably originates from one site of reentry that moves continuously throughout the atrial myocardium and frequently and regularly stimulates the AV node. When the atrial rate becomes sufficiently fast, the refractory period of the AV node exceeds the cycle length (P to P interval) of the SVT, and some atrial depolarizations are blocked from traversing the AV node (functional second-degree AV block).

SYSTEMS AFFECTED

Cardiovascular

Loss of atrial contraction may result in decreased stroke volume and cardiac output depending on heart rate; high heart rate may result in deterioration in myocardial function (tachycardia-induced myocardial failure).

GENETICS

No breeding studies available

SIGNALMENT

Species

Dog and cat

Breed Predilections

Large- and giant-breed dogs are more prone to primary atrial fibrillation.

Mean Age and Range

N/A

Predominant Sex

N/A

SIGNS

General Comments

• Generally relate to the underlying disease process and/or CHF rather than the arrhythmia itself, but previously stable animals may decompensate. • Patients with primary atrial fibrillation are generally asymptomatic but may demonstrate mild exercise intolerance.

Historical Findings

• Coughing/dyspnea/tachypnea. • Exercise intolerance. • Rarely syncope. • Dogs with primary atrial fibrillation are typically asymptomatic.

Physical Examination Findings

• On auscultation, patients with atrial fibrillation have an erratic heart rhythm that sounds like "tennis shoes in a dryer." • First heart sound intensity in atrial fibrillation is variable; second heart sound only heard on beats with effective ejection, not on every beat. • Third heart sounds (gallop sounds) may be present. • Patients with atrial fibrillation have pulse deficits and variable pulse quality. • Signs of CHF often present (e.g., cough, dyspnea, cyanosis).

CAUSES

• Chronic valvular disease • Cardiomyopathy • Congenital heart disease • Digoxin toxicity • Idiopathic • Ventricular preexcitation (atrial flutter)

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Frequent atrial (supraventricular) premature depolarizations • Supraventricular tachycardia with AV block • Multifocal atrial tachycardia (irregular)

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

• Echocardiography and radiography may characterize type and severity of the underlying cardiac disease; moderate to severe left atrial enlargement common. • Typically normal in patients with primary atrial fibrillation, although mild left atrial enlargement may accompany the hemodynamic alterations imposed by the arrhythmia.

DIAGNOSTIC PROCEDURES

A baseline 24-hour Holter is recommended to determine if the arrhythmia is chronic or paroxysmal. If it is chronic, drug therapy is indicated.

TREATMENT

APPROPRIATE HEALTH CARE

• Patients with fast (secondary) atrial fibrillation are treated medically to slow the ventricular rate. Converting the atrial fibrillation to sinus rhythm would be ideal, but such attempts in patients with severe underlying heart disease or left atrial enlargement are generally futile because of a low success rate and high rate of recurrence. Consider electrical cardioversion to sinus rhythm for a dog with primary atrial fibrillation and only mild structural heart disease. • Patients with primary atrial fibrillation may be converted back to normal sinus rhythm. The success rate depends on chronicity. Patients that have been in atrial fibrillation for > 4 months generally have a lower success rate and a higher rate of recurrence. In these patients, rate control, if necessary, is the recommended treatment. • Electrical (DC) cardioversion—application of a transthoracic electrical shock at a specific time in the cardiac cycle; requires special equipment, trained personnel, and general anesthesia. Using a monophasic defibrillator: Start with 4 J/kg; if no conversion occurs,

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ATRIAL FIBRILLATION AND ATRIAL FLUTTER (CONTINUED)

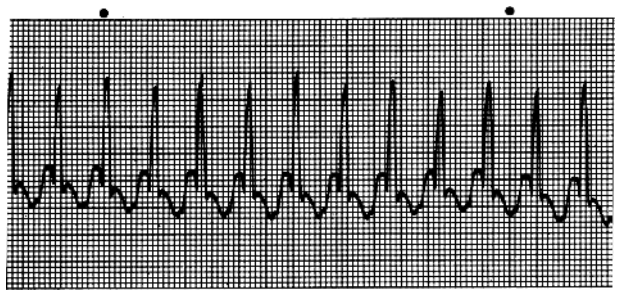

Figure 1.

Atrial flutter with 2:1 conduction at ventricular rate of 330/minute in a dog with an atrial septal defect. This supraventricular tachycardia was associated with a Wolff-Parkinson-White pattern. (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)

increase dose by 50 J and repeat until a max of 360 J. Using a biphasic defibrillator: Start with 1 to 2 J/kg; if no cardioversion occurs, increase dose by 50 J and repeat until max of 360 J. • For atrial flutter, conversion to sinus rhythm can be done by drug therapy, electrical cardioversion, or rapid atrial pacing (transvenous pacing electrode).

NURSING CARE
As indicated for CHF.

ACTIVITY
Restrict activity until tachycardia is controlled.

DIET
Mild to moderate sodium restriction if CHF.

CLIENT EDUCATION
• Secondary atrial fibrillation and atrial flutter is usually associated with severe underlying heart disease; goal of therapy is to lower heart rate and control clinical signs. • Sustained conversion to sinus rhythm is unlikely with secondary atrial fibrillation.

SURGICAL CONSIDERATIONS
N/A

MEDICATIONS

DRUG(S) OF CHOICE
• Digoxin, β-adrenergic blockers, esmolol, and calcium channel blockers (diltiazem) are frequently used to slow conduction through the AV node; definition of an adequate heart rate response varies among clinicians, but in dogs is generally 140–160 bpm.
• For atrial flutter, therapy is aimed at suppressing the atrial re-entry circuit using sotlalol, amiodarone or procainamide.

Dogs
• Digoxin—maintenance oral dose 0.005–0.01 mg/kg PO q12h; to achieve a therapeutic serum concentration more rapidly, the maintenance dose can be doubled for the first day. If digoxin is administered alone and the heart rate remains high, check the digoxin level and adjust the dose to bring the level into the therapeutic range. If the heart rate remains high, consider adding a calcium channel blocker or a β-adrenergic blocker.
• Diltiazem—initially administered at a dose of 0.5 mg/kg PO q8h, then titrated up to a maximum of 1.5 mg/kg PO q8h or until an adequate response is obtained.
• Therapy for atrial fibrillation is aimed at suppressing the atrial reentry circuit using sotalol, amiodarone, or procainamide. The conversion to normal sinus rhythm is usually unsuccessful.

Cats
• Diltiazem (1–2.5 mg/kg PO q8h) or atenolol (6.25–12.5 mg/cat PO q12–24h) are the drugs of choice in most cats.
• If the heart rate is not sufficiently slowed with these drugs or if myocardial failure is present, digoxin (5 μg/kg PO q24–48h) can be added.

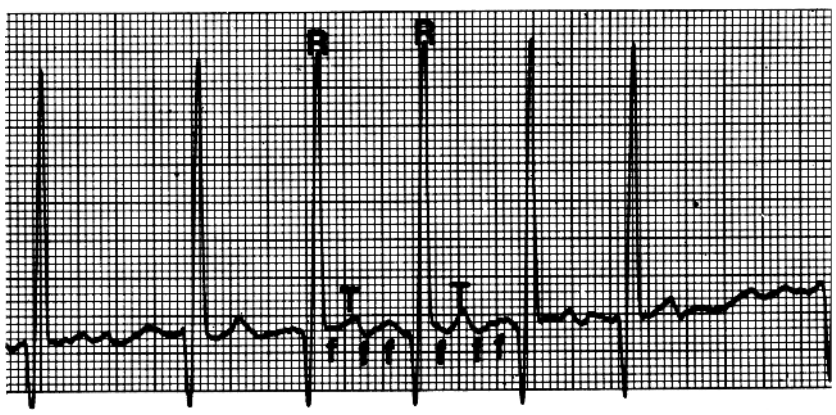

Figure 2.

"Coarse" atrial fibrillation in a dog with patent ductus arteriosus. The f waves are prominent. (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)

(CONTINUED)

ATRIAL FIBRILLATION AND ATRIAL FLUTTER

CONTRAINDICATIONS

• Digoxin, diltiazem, propranolol, and atenolol should not be used in patients with preexisting AV block. • Use of calcium channel blockers in combination with beta blockers should be avoided because clinically significant bradyarrhythmias and/or AV block can develop.

PRECAUTIONS

• Calcium channel blockers and β-adrenergic blockers, both negative inotropes, should be used cautiously in animals with myocardial failure. • Using high-dose oral quinidine for conversion into sinus rhythm carries a risk of quinidine toxicity (e.g., hypotension, weakness, ataxia, and seizures)—administration of diazepam intravenously controls seizures; other signs abate within several hours of discontinuing quinidine administration.

POSSIBLE INTERACTIONS

Quinidine raises the digoxin level, generally necessitating a digoxin dose reduction.

FOLLOW-UP

PATIENT MONITORING

• Monitor heart rate and ECG closely. • As heart rates in the hospital and those measured on the surface ECG may be inaccurate (due to patient anxiety and other environmental factors), Holter monitoring provides a more accurate means for assessing the need for heart rate control and/or the efficacy of medical therapy for heart rate control.

POSSIBLE COMPLICATIONS

Worsening of cardiac function with onset of arrhythmia.

EXPECTED COURSE AND PROGNOSIS

• Secondary atrial fibrillation—associated with severe heart disease, so a guarded-to-poor prognosis. • Primary atrial fibrillation with normal ultrasound findings—generally a good prognosis.

MISCELLANEOUS

ABBREVIATIONS

• AV = atrioventricular • CHF = congestive heart failure • ECG = electrocardiogram • SVT = supraventricular tachycardia

Suggested Reading

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Client Education Handout available online

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ATRIAL PREMATURE COMPLEXES

BASICS

DEFINITION
Premature atrial beats that originate outside the sinoatrial node and disrupt the normal sinus rhythm for 1 or more beats

ECG FEATURES
• Heart rate usually normal; rhythm irregular due to the premature P wave (called a P′ wave) that disrupts the normal P wave rhythm (Figure 1).
• Ectopic P′ wave—premature; configuration differs from that of the sinus P waves and may be negative, positive, biphasic, or superimposed on the previous T wave.
• QRS complex—premature; configuration usually normal (same as that of the sinus complexes). If the P′ wave occurs during the refractory period of the AV node, ventricular conduction does not occur (non-conducted APCs), so no QRS complex follows the P′ wave. If there is partial recovery in the AV node or intraventricular conduction systems, the P′ wave is conducted with a long P′–R interval or with an abnormal QRS configuration (aberrant conduction). The more premature the complex, the more marked the aberration.
• In the P–QRS relationship, the P′–R interval is usually as long as, or longer than, the sinus P′–R interval.
• A non-compensatory pause—when the R–R interval of the two normal sinus complexes enclosing an APC is less than the R–R intervals of three consecutive sinus complexes—usually follows an APC (Figure 2). The ectopic atrial impulse discharges the sinus node and resets the cycle.

PATHOPHYSIOLOGY
• Mechanisms—an increase in automaticity of atrial myocardial fibers or a single reentrant circuit.
• May be normal finding in aged dogs; commonly seen in dogs with atrial enlargement secondary to chronic mitral valvular insufficiency; may also be observed in dogs or cats with any atrial disease.
• May not cause hemodynamic problems; the clinical significance relates to their frequency, timing relative to other complexes, and the underlying clinical problems.
• Can presage more serious rhythm disturbances (e.g., atrial fibrillation, atrial flutter, or atrial tachycardia).

SYSTEMS AFFECTED
Cardiovascular

GENETICS
N/A

INCIDENCE/PREVALENCE
Not documented

SIGNALMENT
Species
Dog and cat

Breed Predilections
Small-breed dogs

Mean Age and Range
Geriatric animals, except those with congenital heart disease

SIGNS
Historical Findings
• No signs
• CHF
• Coughing and dyspnea
• Exercise intolerance
• Syncope

Physical Examination Findings
• Irregular heart rhythm
• Cardiac murmur
• Gallop rhythm
• Signs of CHF

CAUSES & RISK FACTORS
• Chronic valvular disease
• Congenital heart disease
• Cardiomyopathy
• Atrial myocarditis
• Electrolyte disorders
• Neoplasia
• Hyperthyroidism
• Toxemias
• Drug toxicity (e.g., digitalis)
• Normal variation in aged animals

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Marked sinus arrhythmia.
• Ventricular premature complexes when aberrant ventricular conduction follows an APC.

CBC/BIOCHEMISTRY/URINALYSIS
N/A

OTHER LABORATORY TESTS
N/A

IMAGING
Echocardiography and Doppler ultrasound may reveal the type and severity of the underlying heart disease.

DIAGNOSTIC PROCEDURES
• Electrocardiography
• Holter monitor to quantify APC frequency and event monitor/Holter ECG to correlate symptoms with rhythm.

PATHOLOGIC FINDINGS
Atrial enlargement; other features vary depending on underlying cause.

TREATMENT

APPROPRIATE HEALTH CARE
• Treat animal as inpatient or outpatient.
• Treat the underlying CHF, cardiac disease, or other causes.

NURSING CARE
Usually not necessary; varies with underlying cause.

ACTIVITY
Restrict if symptomatic.

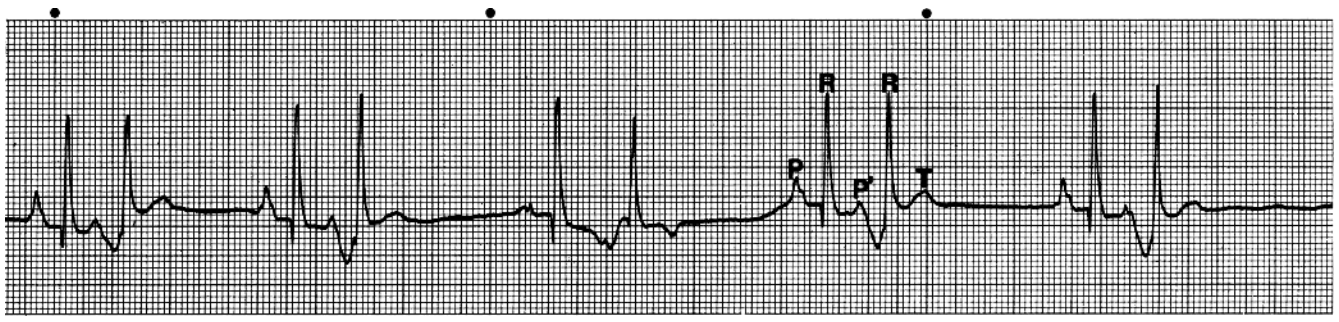

Figure 1.

APCs in a dog. P′ represents the premature complex. The premature QRS resembles the basic QRS. The upright P′ wave is superimposed on the T wave of the preceding complex. (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Blackwell Publishing, 1992, with permission.)

(CONTINUED) ATRIAL PREMATURE COMPLEXES A

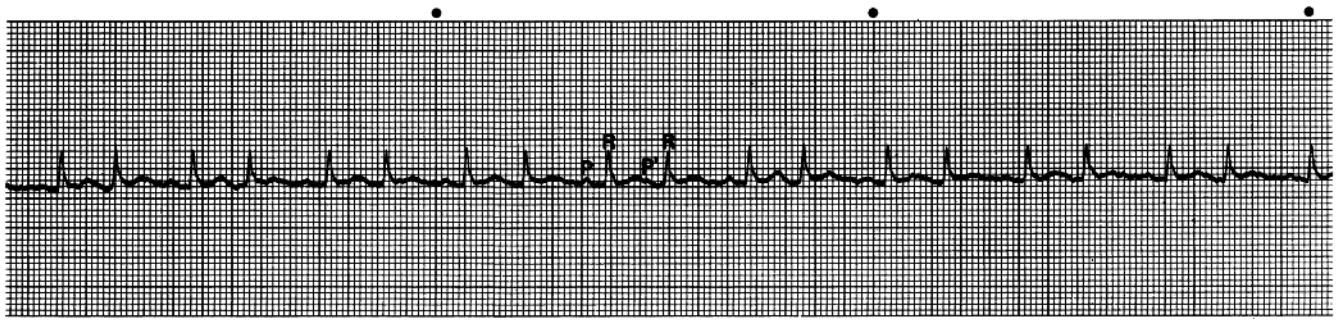

Figure 2.

APCs in bigeminy in a cat under general anesthesia. The second complex of each pair is an APC, where the first is a sinus complex. The abnormality in rhythm disappeared after the anesthetic was stopped. (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Blackwell Publishing, 1992, with permission.)

DIET
No modifications unless required for management of underlying condition (i.e., low-salt diet).

CLIENT EDUCATION
APCs may not cause hemodynamic abnormalities; may be precursors of serious arrhythmias.

SURGICAL CONSIDERATIONS
N/A

MEDICATIONS

DRUG(S) OF CHOICE
Treat CHF and correct any electrolyte or acid/base imbalances.

Dogs
- Digoxin (0.005–0.01 mg/kg PO q12h, maintenance dosage), diltiazem (0.5–1.5 mg/kg PO q8h), or atenolol (0.25–1 mg/kg PO q12h) are used to treat clinically significant arrhythmias.
- Digoxin—treatment of choice; also indicated to treat the cardiac decompensation that is usually present.
- CHF is treated with appropriate dosage of diuretic, angiotensin converting enzyme inhibitor, and pimobendan; appropriate management of CHF may reduce APC frequency.

Cats
- Cats with hypertrophic cardiomyopathy—diltiazem (1–2.5 mg/kg PO q8h) or atenolol (6.25–12.5 mg PO q12–24h).
- Cats with dilated cardiomyopathy—digoxin (one-fourth of a 0.125 mg digoxin tablet q24h or q48h).

CONTRAINDICATIONS
Negative inotropic agents (e.g., propranolol) should be avoided in animals with CHF.

PRECAUTIONS
Use digoxin, diltiazem, atenolol, or propranolol cautiously in animals with underlying atrioventricular block or hypotension.

POSSIBLE INTERACTIONS
N/A

ALTERNATIVE DRUG(S)
N/A

FOLLOW-UP

PATIENT MONITORING
Monitor heart rate and rhythm with serial ECG.

PREVENTION/AVOIDANCE
N/A

POSSIBLE COMPLICATIONS
Frequent APCs may further diminish cardiac output in patients with underlying heart disease and worsen clinical symptoms.

EXPECTED COURSE AND PROGNOSIS
Even with optimal antiarrhythmic drug therapy some animals have an increased frequency of APCs or deteriorate to more severe arrhythmia as the underlying disease progresses.

MISCELLANEOUS

ASSOCIATED CONDITIONS
None

AGE-RELATED FACTORS
Typically occurs in geriatric dogs

PREGNANCY/FERTILITY/BREEDING
N/A

SYNONYMS
Atrial extrasystoles, atrial premature contractions, atrial premature impulses

SEE ALSO
Supraventricular Tachycardia

ABBREVIATIONS
- APC = atrial premature complex
- AV = atrioventricular
- CHF = congestive heart failure

INTERNET RESOURCES
www.vetgo.com/cardio.

Suggested Reading

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Client Education Handout available online

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ATRIAL SEPTAL DEFECT

BASICS

OVERVIEW

• Congenital defect in which the interatrial septum fails to develop normally, resulting in communication between the atria. Unknown cause; genetic basis suspected. Acquired ASD secondary to atrial rupture reported in dogs with degenerative mitral valve disease.
• Comprises 0.7–3.7% of congenital heart defects in dogs and < 10% of congenital heart defects in cats. Significantly higher incidence (37.7%) noted in a more recent study.
• 3 major types of ASD classified based on the location of the defect within the interatrial septum: ostium primum ASD (most apical portion of septum, adjacent to the atrioventricular valves), ostium secundum ASD (central portion of the septum, region of fossa ovalis), and sinus venosus ASD (upper portion of septum, junction of cranial vena cava).
• Secundum ASD with left-to-right shunting is most common (98.7% in one study of dogs and cats).
• Ostium primum ASDs typically large; may be component of atrioventricular (AV) canal defect.
• Sinus venosus ASDs typically located at the junction of the cranial vena cava (less commonly the caudal vena cava) and right atrium. Right pulmonary veins may be directed at the right atrium through the defect. May be associated with anomalous pulmonary venous connections of some or all pulmonary veins.
• Isolated ASDs typically shunt left-to-right. Magnitude of flow dependent on size (ostium) of defect, relative systemic and pulmonary resistance, and relative compliance of the ventricles. Small defects allowing atria to maintain normal differential pressure are termed restrictive. Large defects more likely to cause significant left-to-right shunting and volume overload to the right heart and pulmonary vessels. Development of secondary pulmonary hypertension can lead to reverse (right-to-left) shunting, termed Eisenmenger's physiology. ASDs may occur with concurrent defects; conditions increasing right atrial pressure (i.e., pulmonic stenosis, tricuspid valve dysplasia, tricuspid valve stenosis) can also cause balanced or reverse shunting.

SIGNALMENT

• Dog and cat
• Various breeds affected; higher prevalence in boxer and standard poodle
• No sex predisposition

SIGNS

General Comments

• Most commonly asymptomatic (73.7% in one study).
• Severe cases may present with signs of CHF.
• Signs related to generalized cyanosis may occur with right-to-left shunting.

Historical Findings

Clinical signs related to concurrent heart disease or cyanosis; exercise intolerance, syncope, cough, and dyspnea.

Physical Examination Findings

• Soft systolic murmur over the pulmonic valve due to relative pulmonic stenosis (increased blood flow across a normal pulmonic valve).
• Rarely a diastolic murmur over the tricuspid valve due to relative tricuspid stenosis.
• Split S2 (fixed) due to delayed closure of the pulmonic valve.
• Cyanosis with right-to-left shunting.
• Ascites and jugular vein distension with right heart failure.

DIAGNOSIS

CBC/BIOCHEMISTRY/URINALYSIS

• Typically normal.
• Polycythemia in some patients with right-to-left shunting.

IMAGING

Radiographic Findings

• None with small defects.
• Right-sided heart enlargement and pulmonary overcirculation with significant shunting.

Echocardiographic Findings

• Right atrial and/or right ventricular dilation
• Septal dropout (not artifactual septal dropout in the region of the fossa ovalis)
• Shunting across ASD by color-flow or spectral Doppler
• Increased pulmonic flow velocity
• Dilation of the pulmonary trunk

OTHER

Electrocardiography

• Usually normal.
• Right atrial and ventricular enlargement (tall P wave, right axis deviation, deep S waves in lead II).
• Arrhythmias and intraventricular conduction disturbances possible.

TREATMENT

GENERAL

• Long-term prognosis for small ASDs is good; treatment is not typically required.
• Large ASDs with hemodynamically significant shunting and right-sided enlargement warrant closure.

MEDICAL THERAPY

• Standard treatment of CHF (furosemide, pimobendan, ACE inhibitor).
• Treatment of polycythemia (right-to-left shunting) if clinically indicated.

SURGICAL THERAPY

• Open heart surgery under cardiopulmonary bypass- direct surgical closure using patch graft.
• Pulmonary artery banding as palliative measure to limit left-to-right shunting.

CATHETER-BASED THERAPY

• Amplatzer® atrial septal occluder (ASO) device delivered percutaneously through the jugular vein for secundum-type defects; requires adequate atrial diameter, ostium diameter, ASD rim tissue, and vessel size for venous access.
• Hybrid procedure involving surgical access to right atrium, transatrial delivery of ASO device, and active device fixation under inflow occlusion reported.

FOLLOW-UP

PATIENT MONITORING

Recheck when decompensation or other clinical signs develop.

EXPECTED COURSE AND PROGNOSIS

• Dependent on defect size and co-existing abnormalities.
• Small, isolated defects unlikely to cause clinical signs.
• Defects > 12 mm more likely to cause heart failure.

MISCELLANEOUS

ABBREVIATIONS

• ASD = atrial septal defect
• CHF = congestive heart failure

Suggested Reading

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ATRIAL STANDSTILL

BASICS

DEFINITION
ECG rhythm characterized by absence of P waves; condition can be temporary (e.g., associated with hyperkalemia or drug-induced), terminal (e.g., associated with severe hyperkalemia or dying heart), or persistent.

ECG Features
Persistent Atrial Standstill
- P waves absent.
- Heart rate usually slow (< 60 bpm).
- Rhythm regular with supraventricular type QRS complexes.
- Heart rate does not increase with atropine administration.

Hyperkalemic Atrial Standstill
- Heart rate normal or slow.
- Rhythm regular or irregular.
- QRS complexes tend to be wide and become wider as the potassium level rises; with severe hyperkalemia (potassium > 10 mEq/L), the QRS complexes are replaced by a smooth biphasic curve.
- Heart rate may increase slightly with atropine.

PATHOPHYSIOLOGY
Persistent Atrial Standstill
Caused by an atrial muscular dystrophy; skeletal muscle involvement common.

Hyperkalemic Atrial Standstill
Generally occurs with serum potassium levels > 8.5 mEq/L; value influenced by serum sodium and calcium levels and acid-base status. Hyperkalemic patients with atrial standstill have sinus node function, but impulses do not activate atrial myocytes; thus, the associated rhythm is termed a sinoventricular rhythm. Since the sinus node is functional, an irregular rhythm may be due to sinus arrhythmia.

SYSTEMS AFFECTED
Cardiovascular

GENETICS
None

INCIDENCE/PREVALENCE
Rare rhythm disturbance

GEOGRAPHIC DISTRIBUTION
None

SIGNALMENT
Species
Dog and cat

Breed Predilections
Persistent atrial standstill—most common in English springer spaniels; other breeds occasionally affected.

Mean Age and Range
Most animals with persistent atrial standstill are young; animals with hypoadrenocorticism are usually young to middle-aged.

Predominant Sex
Hypoadrenocorticism more common in females (69%).

SIGNS
Historical Findings
- Vary with underlying cause.
- Lethargy common; syncope may occur.
- Patients with persistent atrial standstill may show signs of congestive heart failure.

Physical Examination Findings
- Vary with underlying cause.
- Bradycardia common.
- Patients with persistent atrial standstill may have skeletal muscle wasting of the antebrachium and scapula.

CAUSES
- Hyperkalemia.
- Atrial disease, often associated with atrial distension (e.g., cats with cardiomyopathy).
- Atrial myopathy (persistent atrial standstill).

RISK FACTORS
- Hyperkalemic atrial standstill
- Hypoadrenocorticism
- Conditions leading to obstruction or rupture of the urinary tract
- Oliguric or anuric renal failure

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
- Slow atrial fibrillation
- Sinus bradycardia with small P waves lost in the baseline

CBC/BIOCHEMISTRY/URINALYSIS
Persistent Atrial Standstill
Normal

Hyperkalemic Atrial Standstill
- Hyperkalemia.
- Hyponatremia and sodium:potassium ratio < 27 if atrial standstill secondary to hypoadrenocorticism.
- Azotemia and hyperphosphatemia with hypoadrenocorticism, renal failure, and rupture or obstruction of the urinary tract.

OTHER LABORATORY TESTS
ACTH stimulation test if hypoadrenocorticism suspected

IMAGING
Echocardiogram and electromyography if persistent atrial standstill suspected—cardiomegaly and depressed contractility may be seen.

DIAGNOSTIC PROCEDURES
Skeletal muscle biopsy in animals with persistent atrial standstill.

PATHOLOGIC FINDINGS
Persistent Atrial Standstill
- Greatly enlarged and paper-thin atria; usually biatrial involvement, although one case of only left atrial involvement was reported.
- Severe scapular and brachial muscle wasting in some dogs.
- Marked fibrosis, fibroelastosis, chronic mononuclear cell inflammation, and steatosis throughout the atria and interatrial septum.

TREATMENT

APPROPRIATE HEALTH CARE
Persistent Atrial Standstill
Not life-threatening condition; animal can be treated as an outpatient.

Hyperkalemic Atrial Standstill
Potentially life-threatening; often requires aggressive treatment.

NURSING CARE
Aggressive fluid therapy with 0.9% saline often required to correct hypovolemia and lower serum potassium levels (see Hyperkalemia) in patients with hyperkalemic atrial standstill.

ACTIVITY
Restrict activity in patients with persistent atrial standstill and signs of CHF or syncope.

DIET
N/A

CLIENT EDUCATION
Persistent Atrial Standstill
Clinical signs generally improve after pacemaker implantation; signs of CHF may develop, and weakness and lethargy may persist even after heart rate and rhythm are corrected with the pacemaker.

SURGICAL CONSIDERATIONS
Persistent Atrial Standstill
Implant permanent ventricular pacemaker to regulate rate and rhythm.

Hyperkalemic Atrial Standstill
Hyperkalemia secondary to urinary tract obstruction or rupture may require surgery.

MEDICATIONS

DRUG(S) OF CHOICE
Persistent Atrial Standstill
Treat with diuretics and ACE inhibitor (e.g., enalapril or benazepril) if CHF develops.

Hyperkalemic Atrial Standstill
- Treat the underlying cause (e.g., oliguric renal failure, hypoadrenocorticism).
- Aggressive fluid therapy with 0.9% saline and possibly sodium bicarbonate or insulin

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ATRIAL STANDSTILL (CONTINUED)

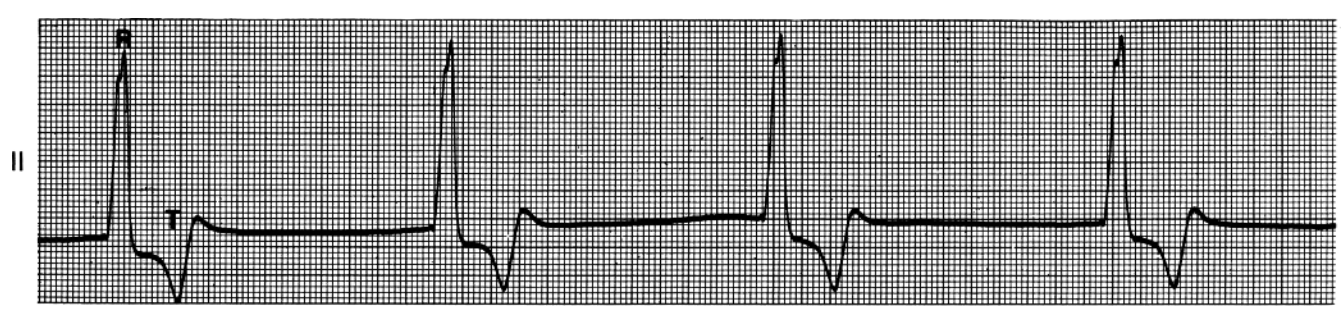

Figure 1.
Atrial stand still in a dog with a potassium of 9 mEq/L. Note the absence of P waves and wide QRS complexes.

with dextrose as discussed under Hyperkalemia.
• Calcium gluconate—counters the cardiac effects of hyperkalemia; can be used in life-threatening situations to reestablish a sinus rhythm while instituting treatment to lower potassium concentration.

CONTRAINDICATIONS
Avoid potassium-containing fluids or medications that increase potassium concentration in hyperkalemic patients.

PRECAUTIONS
Diuretics lower preload and may worsen weakness in dogs with persistent atrial standstill and CHF unless a pacemaker has been implanted.

POSSIBLE INTERACTIONS
N/A

ALTERNATIVE DRUG(S)
N/A

FOLLOW-UP

PATIENT MONITORING
• Monitor ECG during treatment of hyperkalemia and periodically in animals with a permanent ventricular pacemaker.
• Monitor electrolytes in patients with hyperkalemic atrial standstill.
• Monitor patients with persistent atrial standstill for signs of CHF.

PREVENTION/AVOIDANCE
N/A

POSSIBLE COMPLICATIONS
CHF in patients with persistent atrial standstill

EXPECTED COURSE AND PROGNOSIS
Persistent Atrial Standstill
Clinical signs generally improve after pacemaker implantation. Signs of CHF may develop, and weakness and lethargy persist even after heart rate and rhythm are corrected with the pacemaker. There may be persistence of signs related to muscular dystrophy.

Hyperkalemic Atrial Standstill
Long-term prognosis is excellent if underlying cause can be corrected and hyperkalemia reversed.

MISCELLANEOUS

ASSOCIATED CONDITIONS
Diseases causing hyperkalemia (e.g., hypoadrenocorticism, urethral obstruction or urinary tract tear, acidosis, and drugs).

AGE-RELATED FACTORS
Persistent atrial standstill—usually diagnosed in young animals; hypoadrenocorticism—usually diagnosed in young to middle-aged animals.

ZOONOTIC POTENTIAL
None

PREGNANCY/FERTILITY/BREEDING
N/A

SYNONYMS
Silent atrial

SEE ALSO
• Digoxin Toxicity
• Hyperkalemia
• Hypoadrenocorticism (Addison's Disease)
• Urinary Tract Obstruction

ABBREVIATIONS
• ACE = angiotensin converting enzyme
• ACTH = adrenocorticotropic hormone
• CHF = congestive heart failure
• ECG = electrocardiogram

Suggested Reading
Kittleson MD. Electrocardiography. In: Kittleson MD, Kienle RD, eds., Small Animal Cardiovascular Medicine. St. Louis, MO: Mosby, 1998, pp. 72–94.
Kraus MS, Gelzer ARM, Moise S. Treatment of cardiac arrhythmias and conduction disturbances. In: Smith FWK, Tilley LP, Oyama MA, Sleeper MM, eds., Manual of Canine and Feline Cardiology, 5th ed. St. Louis, MO: Saunders Elsevier, 2015 (in press).
Tilley LP, Smith FWK, Jr. Electrocardiography. In: Smith FWK, Tilley LP, Oyama MA, Sleeper MM, eds., Manual of Canine and Feline Cardiology, 5th ed. St. Louis, MO: Saunders Elsevier, 2015 (in press).
Author Francis W.K. Smith, Jr.
Consulting Editors Larry P. Tilley and Francis W.K. Smith, Jr.

Client Education Handout available online

ATRIAL WALL TEAR

BASICS

DEFINITION

• Endocardial splitting is a linear defect limited to the endocardial layer of the atrium (typically the left atrium) resulting from distension of the atrial wall beyond its elastic limits. • An atrial tear may result if the split extends through the myocardium and epicardium, resulting in a full thickness defect in the atrial wall and hemorrhage into the pericardial space.

PATHOPHYSIOLOGY

• Endocardial splitting typically results from increased left atrial volume and pressure secondary to severe mitral regurgitation and mechanical trauma from the regurgitant jet; primary endocardial degeneration may also play a role. • If the split is incomplete, fibrin may seal the defect temporarily; this either heals as a linear depression in the endocardial surface or subsequently extends through the myocardium resulting in a complete left atrial tear. • A left atrial tear results in peracute bleeding into the pericardial sac and severe, life-threatening hemodynamic compromise secondary to acute cardiac tamponade. • If a tear occurs in the interatrial septum, an acquired atrial septal defect may form. • Tearing of either atrium may also rarely occur secondary to blunt trauma, or iatrogenically during pericardiocentesis.

SYSTEMS AFFECTED

• Cardiovascular • Respiratory

INCIDENCE/PREVALENCE

Atrial tear is a rare cause of hemorrhagic pericardial effusion in the dog encompassing approximately 2% of pericardial effusion cases.

SIGNALMENT

Species

Dog; uncommon in cat

Breed Predilections

• Same as endocardiosis breeds; more common in small- to medium-sized dogs. • Poodle, dachshund, cocker spaniel, and Shetland sheepdog may be overrepresented. • If trauma is the cause, any breed may be represented.

Mean Age and Range

Middle-aged to older dogs are predisposed.

SIGNS

Historical Findings

• Acute onset of weakness and collapse that may progress quickly to respiratory or cardiopulmonary arrest; episode may follow a period of increased excitement or activity. • History of long-standing cardiac disease with signs of CHF described in most patients. • Acute worsening of cough or dyspnea are commonly observed. • Possible history of blunt trauma.

Physical Examination Findings

• Collapse. • Tachycardia. • Weak arterial pulses or pulsus paradoxus. • Pale, muddy, or ashen mucous membranes; prolonged CRT. • Other signs of significant cardiac disease (e.g., murmur, gallop rhythm, arrhythmia, cough, or dyspnea) are typically present. • Signs of right heart failure (e.g., ascites and jugular venous distension) may also be seen in some patients. • Heart sounds may be muffled, or if a murmur was heard before the atrial wall tear occurred, it may be reduced in intensity.

CAUSES

• Mitral valve endocardiosis • Chordae tendinae rupture • Cardiac neoplasia, most commonly hemangiosarcoma • Chest trauma • Cardiac catheterization

RISK FACTORS

• Severe mitral regurgitation, left atrial enlargement. • May be precipitated by an episode of excitement, stress, or activity.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Other causes of acute cardiovascular collapse or syncope • Pericardial effusion from other causes (e.g., neoplastic and idiopathic) • Heart failure • Severe cardiac arrhythmias

CBC/BIOCHEMISTRY/URINALYSIS

• Anemia is uncommon unless pericardiocentesis is performed since volume of blood loss is relatively small. • Hypoproteinemia is common. • Elevations in serum lactate, metabolic acidosis. • Increased ALT, AST in some patients. • Prerenal azotemia; hyponatremia or other electrolyte derangements may be seen.

OTHER LABORATORY TESTS

NT-proBNP and TnI levels may be elevated.

IMAGING

Radiographic Findings

• Moderate to severe left atrial enlargement is expected. • Comparison with previous thoracic radiographs may show rounding and further enlargement of cardiac silhouette; characteristic globoid cardiac silhouette associated with pericardial effusion may be more obvious on the DV view. • Interstitial to alveolar pulmonary infiltrates if concomitant left-sided CHF is present. • Small volume pleural effusion, ascites, hepatomegaly, and large caudal vena cava may be seen due to right-sided CHF.

Echocardiographic Findings

• Pericardial effusion is evidenced by a hypoechoic space between the heart and pericardial sac; the volume of pericardial effusion identified may be relatively small as the pericardium remains inelastic due to the acute nature of the bleed; a characteristic linear, hyperechoic blood clot may be seen within the pericardial sac. • The actual tear is often not identified though an associated thrombus is occasionally visualized within the left atrium. • Cardiac tamponade is evidenced by diastolic collapse of the right atrium and/or ventricle. • Signs of advanced mitral endocardiosis, including mitral valve thickening and prolapse, moderate to severe mitral regurgitation, moderate to severe left atrial enlargement and often one or more ruptured chordae tendineae.

DIAGNOSTIC PROCEDURES

Electrocardiographic Findings

• Sinus tachycardia • Atrial or ventricular arrhythmias • Possible dampened QRS complexes • Electrical alternans • ST-segment abnormalities • Possible left ventricular or left atrial enlargement pattern

PATHOLOGIC FINDINGS

• Endocardial splitting is noted grossly as a pale linear depression in the atrial endocardium. • Atrial wall tears appear as full thickness defects extending through the atrial endocardium, myocardium and epicardium; an associated thrombus may or may not be present. The caudolateral aspect of the left atrium is most commonly affected, with many tears occurring at the atrio-auricular junction. • Hemorrhagic pericardial effusion or pericardial thrombus are seen with acute tears. • Mitral endocardiosis characterized by thickened mitral valve leaflets with rolled edges; chordae tendinae rupture may be seen; atrial jet lesions are possible. • Cardiomegaly with severe left atrial enlargement expected.

TREATMENT

APPROPRIATE HEALTH CARE

• If a left atrial tear is strongly suspected, perform pericardiocentesis only if the effusion is causing symptomatic, life-threatening cardiac tamponade, since further hemorrhage into the pericardial sac or exsanguination may occur once pericardial fluid is removed. • If pericardiocentesis is performed, remove only enough fluid to improve clinical signs. • Pericardiocentesis will likely be difficult given the small volume of effusion typically identified, severe cardiac enlargement, and the small size of most dogs with left atrial rupture; ultrasound guidance and continuous ECG monitoring are highly recommended. • Best practices for management of left atrial tears have not been clearly established; however, aggressive medical management to lower left atrial pressure using afterload and preload reducers is recommended based on the author's clinical experience. • If a fibrin clot

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ATRIAL WALL TEAR (CONTINUED)

forms over the defect, the patient may stabilize and recover.

NURSING CARE
• Administer oxygen to dogs with dyspnea or signs of hemodynamic instability.
• Administer IV fluids or blood products only if evidence of hypovolemia is present; most dogs remain in a volume overloaded state and further intravascular volume expansion will increase left atrial pressure and potentially worsen tamponade.

ACTIVITY
Strict cage rest in the acute period should be followed by chronic exercise restriction.

CLIENT EDUCATION
Left atrial tear typically accompanies advanced cardiac disease and chronic medical therapy will be necessary; though the prognosis is guarded for surviving the acute event some dogs with left atrial tear have lived more than a year after the incident.

SURGICAL CONSIDERATIONS
• Exploratory thoracotomy may be considered if hemorrhage persists or recurs but should be undertaken cautiously given the advanced state of cardiac disease typically present. • Transcatheter septal puncture and balloon tear of the fossa ovalis may also be considered to decompress the left atrium; however, right heart failure or hypoxemia due to right-to-left shunting may result.

MEDICATIONS

DRUG(S) OF CHOICE
• Atrial tears occur secondary to elevated left atrial pressure; thus medical therapy should be focused on lowering of left atrial pressures in order to reduce continued hemorrhage into the pericardial space and permit fibrin clot formation at the site of the tear; this may be accomplished with preload (e.g., diuretics, nitroglycerin paste) and/or afterload reducers (arterial vasodilators).
• Preload and afterload reduction must be undertaken cautiously to avoid worsening of hemodynamic compromise.
• Afterload reduction may be achieved by conservative doses of sodium nitroprusside; a low starting CRI dose of 0.5–1 μg/kg/min is recommended to achieve a decrease in LA pressure without precipitating significant hypotension; blood pressure monitoring is recommended and the dose may be uptitrated as necessary every 15–30 minutes up to a maximum of 10 μg/kg/min to achieve an improvement in clinical signs and/or a reduction in blood pressure of 10–15 mmHg.
• Alternatively, amlodipine may be started at 0.1–0.2 mg/kg PO q24h; chronic amlodipine therapy may be implemented in normotensive or hypertensive animals to reduce regurgitant fraction and lower left atrial pressure.
• Diuretics should be used cautiously if needed to treat dyspnea associated with concomitant congestive heart failure (e.g., 1–2 mg/kg of furosemide IV as needed); signs of left-sided congestive heart failure may worsen as cardiac tamponade resolves due to augmentation of preload; more aggressive diuretic therapy may then be required.
• Pimobendan (0.2–0.3 mg/kg PO q12h) may result in a further reduction in left atrial pressure though studies have not specifically examined its use in the setting of left atrial rupture and the author typically delays starting inotropes for several days so as not to disrupt stability of the fibrin clot.
• Once the patient is stable, ACE inhibitors (e.g., enalapril 0.5 mg/kg q12–24h) should be implemented for chronic management of accompanying heart failure.

PRECAUTIONS
• Aggressive fluid therapy is not warranted in these patients; further volume expansion may increase left atrial pressure, worsen cardiac tamponade, and contribute to hemodynamic compromise. • Best practices for management of left atrial tear have not been clearly established; the choice of whether to perform pericardiocentesis, and whether to administer preload and/or afterload reducers should be made based on assessment of the volume status, blood pressure and clinical stability of the patient.

POSSIBLE INTERACTIONS
Sodium nitroprusside should never be administered concurrently with phosphodiesterase-V inhibitors (e.g., sildenafil or tadalafil) due to the potential for life-threatening systemic hypotension.

FOLLOW-UP

PATIENT MONITORING
• Recommend close monitoring of respiratory rate and effort, mucous membrane color and CRT, pulse quality, and heart rate; blood pressure monitoring is recommended if arterial vasodilators are implemented.
• Follow-up examination with echocardiography helps determine resolution of pericardial effusion and resorption of an atrial or pericardial clot. • Close follow-up every 2–3 months thereafter is recommended for repeat pericardial fluid checks and medication adjustments as deemed appropriate.

PREVENTION/AVOIDANCE
Recommend avoidance of strenuous physical activity and excitement.

POSSIBLE COMPLICATIONS
• Even if the tear seals, the patient is prone to further tears because of underlying cardiac disease. • Most dogs have or will develop concurrent CHF.

EXPECTED COURSE AND PROGNOSIS
Prognosis for survival is guarded to poor; however, some animals can do well for several months or longer with close monitoring, exercise restriction and optimal medical management of cardiac disease.

MISCELLANEOUS

ASSOCIATED CONDITIONS
• Chronic valvular disease • CHF
• Mainstem bronchial compression

SYNONYMS
• Atrial rupture • Atrial splitting

SEE ALSO
• Atrial Septal Defect • Atrioventricular Valve (Myxomatous) Disease • Congestive Heart Failure • Pericardial Effusion • Syncope

ABBREVIATIONS
• ACE = angiotensin converting enzyme
• ALT = alanine aminotransferase • AST = aspartate aminotransferase • CHF= Congestive heart failure

INTERNET RESOURCES
James Buchanan Cardiology Library: http://www.vin.com/MEMBERS/CMS/Misc/Default.aspx?id=7703.

Suggested Reading

Peddle GD, Buchanan JW. Acquired atrial septal defects secondary to rupture of the atrial septum in dogs with degenerative mitral valve disease. J Vet Cardiol 2010, 12:129–134.
Reineke EL, Burkett DE, Drobatz KJ. Left atrial rupture in dogs: 14 cases (1990–2005). J Vet Emerg Crit Care 2008, 18:158–164.
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Sadanaga KK, MacDonald MJ, Buchanan JW. Echocardiography and surgery in a dog with left atrial rupture and hemopericardium. J Vet Intern Med 1990, 4:216–221.

Author Suzanne M. Cunningham
Consulting Editors Larry P. Tilley and Francis W.K. Smith, Jr.

ATRIOVENTRICULAR BLOCK, COMPLETE (THIRD DEGREE)

BASICS

DEFINITION
• All atrial impulses are blocked at the AV junction; atria and ventricles beat independently. A secondary "escape" pacemaker site (junctional or ventricular) stimulates the ventricles.
• Atrial rate normal.
• Idioventricular escape rhythm slow.

ECG Features
• Ventricular rate slower than the atrial rate (more P waves than QRS complexes)—ventricular escape rhythm (idioventricular) usually < 40 bpm; junctional escape rhythm (idiojunctional) 40–60 bpm in dogs and 60–100 bpm in cats.
• P waves—usually normal configuration (Figure 1).
• QRS complex—wide and bizarre when pacemaker located in the ventricle, or in the lower AV junction in a patient with bundle branch block; normal when escape pacemaker in the lower AV junction (above the bifurcation of the bundle of His) in a patient without bundle branch block.
• No conduction between the atria and the ventricles; P waves have no constant relationship with QRS complexes; P–P and R–R intervals relatively constant (except for a sinus arrhythmia).

PATHOPHYSIOLOGY
Slow ventricular escape rhythms (< 40 bpm) result in low cardiac output and eventual heart failure, often when animal is excited or exercised, since demand for greater cardiac output is not satisfied. As the heart fails, signs increase with mild activity.

SYSTEMS AFFECTED
Cardiovascular

GENETICS
Can be an isolated congenital defect

INCIDENCE/PREVALENCE
Not documented

GEOGRAPHIC DISTRIBUTION
N/A

SIGNALMENT
Species
Dog and cat

Breed Predilections
• Cocker spaniel—can have idiopathic fibrosis.
• Pug and Doberman pinscher—can have associated sudden death, AV conduction defects, and bundle of His lesions.

Mean Age and Range
Geriatric animals, except congenital heart disease patients. Median age for cats—14 years.

Predominant Sex
Intact female dogs

SIGNS
Historical Findings
• Exercise intolerance
• Weakness or syncope
• Occasionally, CHF

Physical Examination Findings
• Bradycardia
• Variable third and fourth heart sounds
• Variation in intensity of the first heart sounds
• Signs of CHF
• Intermittent "cannon" A waves in jugular venous pulses

CAUSES & RISK FACTORS
Isolated congenital defect
• Idiopathic fibrosis
• Infiltrative cardiomyopathy (amyloidosis or neoplasia)
• Hypertrophic cardiomyopathy in cats
• Digitalis toxicity
• Hyperthyroidism in cats
• Myocarditis
• Endocarditis
• Electrolyte disorder
• Myocardial infarction
• Other congenital heart defects
• Lyme disease
• Chagas disease

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Advanced second-degree AV block
• Atrial standstill
• Accelerated idioventricular rhythm

CBC/BIOCHEMISTRY/URINALYSIS
• Abnormal serum electrolytes (e.g., hyperkalemia, hypokalemia) possible.
• High WBC with left shift in animals with bacterial endocarditis.

OTHER LABORATORY TESTS
• High serum digoxin concentration if AV block is due to digoxin toxicity.
• Lyme titer and accompanying clinical signs if AV block due to Lyme disease.

IMAGING
Echocardiography and Doppler ultrasound to assess cardiac structure and function.

DIAGNOSTIC PROCEDURES
• Electrocardiography
• His bundle electrogram to determine the site of the AV block.
• Long-term (Holter) ambulatory recording if AV block is intermittent.

PATHOLOGIC FINDINGS
Degeneration or fibrosis of the AV node and its bundle branches, associated with endocardial and myocardial fibrosis and organized endomyocarditis.

TREATMENT

APPROPRIATE HEALTH CARE
• Temporary or permanent cardiac pacemaker—only effective treatment in symptomatic patients.

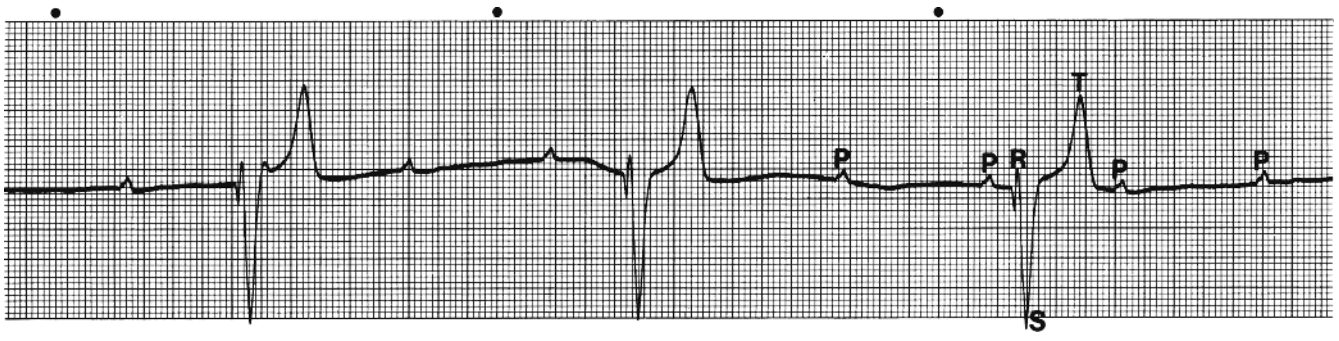

Figure 1.

Complete heart block. The P waves occur at a rate of 120, independent of the ventricular rate of 50. The QRS configuration is a right bundle branch block pattern. The regular rate and stable QRS indicate that the rescuing focus is probably near the AV junction. (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Blackwell Publishing, 1992, with permission.)

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ATRIOVENTRICULAR BLOCK, COMPLETE (THIRD DEGREE) (CONTINUED)

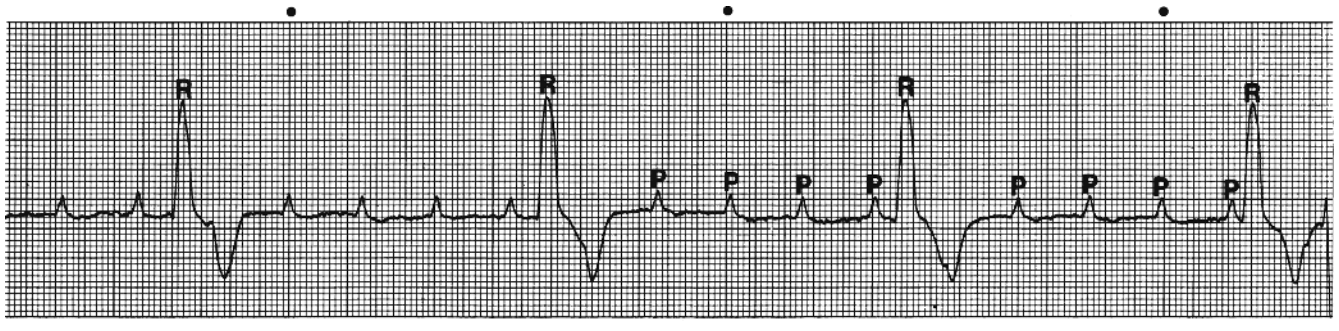

Figure 2.

Complete heart block in a cat. The P waves rate is 240/minute, independent of the ventricular rate of 48/minute. QRS configuration is a left bundle branch block pattern. (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Blackwell Publishing, 1992, with permission.)

• Carefully monitor asymptomatic patients without a pacemaker for development of clinical signs.

NURSING CARE
Cage rest prior to pacemaker implantation; when the pulse generator is put into a subcutaneous pocket, a non-constricting bandage is required around the ventral neck or abdomen for 3–5 days to prevent seroma formation or pacemaker movement.

ACTIVITY
Restrict if symptomatic

DIET
No modifications unless required to manage underlying condition (e.g., low-salt diet).

CLIENT EDUCATION
• Temporary or permanent cardiac pacemaker—only effective treatment in symptomatic patients.
• Asymptomatic patients without a pacemaker—must be carefully monitored for development of clinical signs.

SURGICAL CONSIDERATIONS
• Most patients—at high anesthetic cardiopulmonary risk; usually paced preoperatively with a temporary external pacemaker system.
• The small size of cats makes pacemaker implantation more difficult than in dogs.

MEDICATIONS

DRUG(S) OF CHOICE
• Treatment with drugs—usually of no value. Traditionally used to treat complete AV block: atropine, isoproterenol, corticosteroids, and dobutamine.
• Intravenous isoproterenol infusion may help increase the rate of the ventricular escape rhythm to stabilize hemodynamics.
• If CHF—diuretic and vasodilator therapy may be needed before pacemaker implantation.

CONTRAINDICATIONS
Avoid digoxin, xylazine, acepromazine, beta blockers (e.g., propranolol and atenolol), and calcium channel blockers (e.g., verapamil and diltiazem); ventricular antiarrhythmic agents are dangerous because they suppress lower escape foci.

PRECAUTIONS
Vasodilators—may cause hypotension in animals with complete AV block; monitor closely if used, especially prior to pacemaker implantation.

FOLLOW-UP

PATIENT MONITORING
• Monitor—pacemaker function with serial ECGs.
• Radiographs—following pacemaker implantation, to confirm the position of the lead and generator.

PREVENTION/AVOIDANCE
N/A

POSSIBLE COMPLICATIONS
Pulse generators—broad range of clinical life; pacemaker replacement necessary when battery is depleted, pulse generator malfunction occurs, or exit block develops; pacemaker leads can become dislodged and infected.

EXPECTED COURSE AND PROGNOSIS
Poor long-term prognosis if no cardiac pacemaker implanted, especially when the animal has clinical signs. Cats can sometimes survive > 1 year.

MISCELLANEOUS

ASSOCIATED CONDITIONS
None

ABBREVIATIONS
• AV = atrioventricular
• CHF = congestive heart failure
• ECG = electrocardiogram
• WBC = white blood cell

INTERNET RESOURCES
www.vetgo.com/cardio

Suggested Reading

Bright JM. Pacemaker therapy. In: Smith FWK, Tilley LP, Oyama MA, Sleeper MM, eds., Manual of Canine and Feline Cardiology, 5th ed. St. Louis, MO: Saunders Elsevier, 2015 (in press).
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Schrope DP, Kelch WJ. Signalment, clinical signs, and prognostic indicators associated with high-grade second or third-degree atrioventricular block in dogs: 124 cases (January 1, 1997–December 31, 1997). J Am Vet Med Assoc 2006, 228:1710–1717.
Tilley LP, Smith FW. Essentials of Electrocardiography. Interpretation and Treatment, 4th ed. Ames, IA: Wiley Blackwell Publishing, 2016 (in preparation).

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Client Education Handout available online

ATRIOVENTRICULAR BLOCK, FIRST DEGREE

BASICS

DEFINITION
Refers to a delay in conduction that occurs between atrial and ventricular activation.

ECG Features
- Rate and rhythm—usually normal.
- Usually there are regularly occurring normal P waves and QRS complexes (Figures 1 and 2).
- Prolonged, consistent PR intervals—dogs, > 0.13 sec; cats, > 0.09 sec (Figures 1 and 2).

PATHOPHYSIOLOGY
- Virtually never causes clinical signs.
- May become a more severe AV conduction disturbance in some animals.
- Normally the PR interval tends to shorten with rapid heart rates.
- May be the result of intra-atrial conduction delay (prolongation of the PA interval on surface ECG and simultaneous His bundle electrogram) or delay of conduction within the AV node itself (prolongation of the AH interval on His bundle electrogram).

SYSTEMS AFFECTED
Cardiovascular

GENETICS
N/A

INCIDENCE/PREVALENCE
Common

GEOGRAPHIC DISTRIBUTION
None

SIGNALMENT
Species
Dog and cat

Breed Predilections
American cocker spaniel, dachshund, brachycephalic dogs, Persian cats

Mean Age and Range
- May occur in young, otherwise healthy dogs as a manifestation of high vagal tone.
- Intra-atrial conduction delay involving the right atrium may be seen with congenital heart disease, especially atrioventricular septal defects.
- May be noted in aged patients with degenerative conduction system disease, particularly cocker spaniels and dachshunds.
- Persian cats of any age with high vagal tone and in cats of any age with hypertrophic cardiomyopathy.

SIGNS
Historical Findings
- Most animals are asymptomatic.
- If drug-induced, may have a history of clinical signs related to drug toxicity—anorexia, vomiting, and diarrhea with digoxin; weakness with calcium channel blockers or β-adrenergic antagonists.

Physical Examination Findings
- Normal—unless also signs of more generalized myocardial disease, drug toxicity, or non-cardiac disease.

CAUSES
- May occur in normal animals.
- Enhanced vagal stimulation resulting from non-cardiac diseases—usually accompanied by sinus arrhythmia, sinus arrest, and/or Mobitz type I second-degree AV block.
- Pharmacologic agents (e.g., digoxin, β-adrenergic antagonists, calcium channel blocking agents, propafenone, amiodarone, α_2-adrenergic agonists, parasympathomimetic agents [bethanechol, physostigmine, pilocarpine] and severe procainamide or quinidine toxicity).
- Degenerative disease of the conduction system.
- Hypertrophic cardiomyopathy.
- Myocarditis (*especially Trypanosoma cruzi, Borrelia burgdorferi, Rickettsia rickettsii*).
- Infiltrative diseases (tumors, amyloid).
- Atropine administered intravenously may briefly prolong the PR interval.

RISK FACTORS
Any condition or intervention that raises vagal tone

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
P waves superimposed upon preceding T waves because of first-degree AV block should be differentiated from bifid T waves.

CBC/BIOCHEMISTRY/URINALYSIS
- Serum electrolytes—hypokalemia and hyperkalemia may predispose to AV conduction disturbances.
- Leukocytosis—may be noted with bacterial endocarditis or myocarditis.

OTHER LABORATORY TESTS
- Serum digoxin concentration—may be high.
- *T. cruzi, B. burgdorferi, R. rickettsii* titers—may be high.
- T_4—may be high in cats if associated with thyrotoxic myocardial disease.

IMAGING
Echocardiographic examination—may reveal hypertrophic or infiltrative myocardial disorder.

DIAGNOSTIC PROCEDURES
May be needed to identify causes of high vagal tone—upper airway disease, cervical and thoracic masses, gastrointestinal disorders, and high intraocular pressure.

PATHOLOGIC FINDINGS
Variable—depend on underlying cause

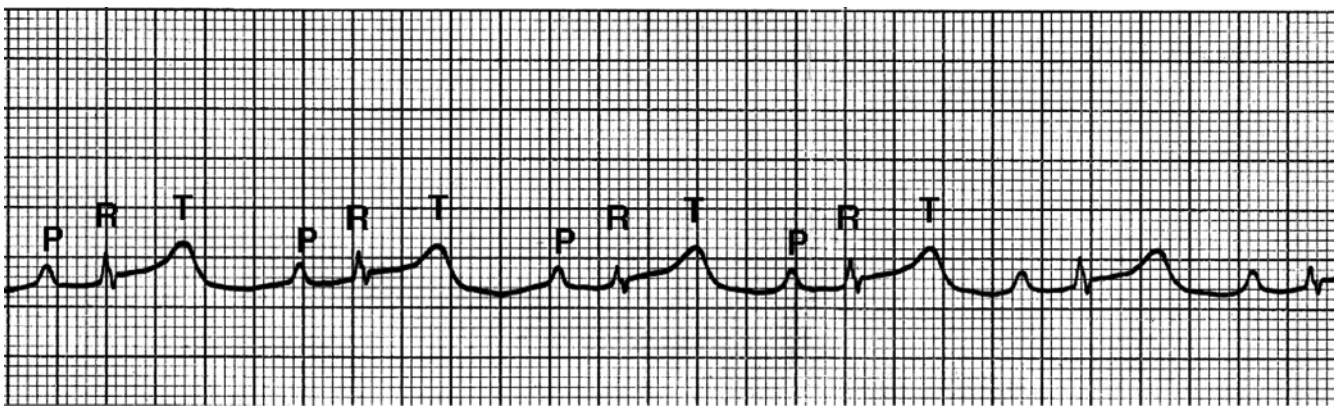

Figure 1.

Lead II ECG rhythm strip recorded from a cat with hypertrophic cardiomyopathy. There is sinus bradycardia (120 bpm) and first-degree atrioventricular conduction block. The PR interval is 0.12 second (paper speed = 50 mm/s).

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ATRIOVENTRICULAR BLOCK, FIRST DEGREE (CONTINUED)

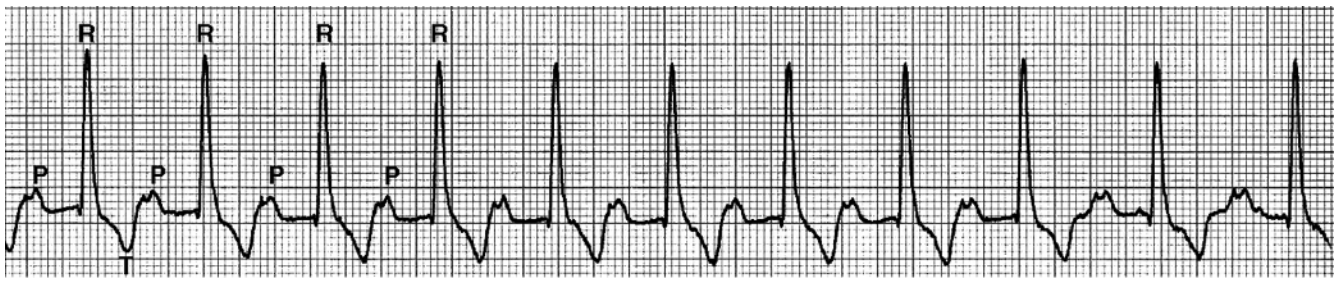

Figure 2.
Lead II ECG rhythm strip recorded from a dog showing sinus tachycardia (175 bpm) and first-degree atrioventricular conduction block. Because the heart rate is rapid, P waves are superimposed on the downslope of the preceding T waves. The PR interval exceeds 0.16 second (paper speed = 50 mm/s).

TREATMENT

APPROPRIATE HEALTH CARE
• Remove or treat underlying cause(s).
• Hospitalization may be necessary to manage the underlying cause (e.g., cardiomyopathy, gastrointestinal disease, airway disease).

NURSING CARE
N/A

ACTIVITY
Unrestricted; unless restriction required for an underlying condition.

DIET
No modifications or restrictions unless required to manage an underlying condition.

CLIENT EDUCATION
Generally unnecessary

SURGICAL CONSIDERATIONS
None unless required to manage an underlying condition.

MEDICATIONS

DRUG(S) OF CHOICE
Medications used only if needed to manage an underlying condition.

CONTRAINDICATIONS
• Avoid hypokalemia—increases sensitivity to vagal tone; may potentiate AV conduction delay.
• Avoid drugs likely to impair impulse conduction further (calcium channel blocking agents, β-adrenergic antagonists, α_2-adrenergic agonists, amiodarone, propafenone).

PRECAUTIONS
Drugs with vagomimetic action (e.g., digoxin, bethanechol, physostigmine, pilocarpine) may potentiate first-degree block.

POSSIBLE INTERACTIONS
N/A

ALTERNATIVE DRUG(S)
N/A

FOLLOW-UP

PATIENT MONITORING
Except in healthy young animals, monitor ECG to detect any progression in conduction disturbance.

PREVENTION/AVOIDANCE
N/A

POSSIBLE COMPLICATIONS
N/A

EXPECTED COURSE AND PROGNOSIS
• Depends on underlying cause.
• Prognosis usually excellent if no significant underlying disease is present.

MISCELLANEOUS

ASSOCIATED CONDITIONS
None

AGE-RELATED FACTORS
PR interval—tends to lengthen with advancing age

ZOONOTIC POTENTIAL
None

PREGNANCY/FERTILITY/BREEDING
N/A

SEE ALSO
• Atrioventricular Block, Complete (Third Degree)
• Atrioventricular Block, Second Degree—Mobitz I
• Atrioventricular Block, Second Degree—Mobitz II

ABBREVIATIONS
• AV = atrioventricular
• ECG = electrocardiogram
• T_4 = thyroxine

Suggested Reading

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Consulting Editors Larry P. Tilley and Francis W.K. Smith, Jr.

Client Education Handout available online

ATRIOVENTRICULAR BLOCK, SECOND DEGREE—MOBITZ I

BASICS

DEFINITION
Second-degree AV block refers to failure of one or more P waves but not all P waves to be conducted. Mobitz Type I second-degree AV block occurs when AV transmission is progressively delayed prior to a blocked P wave.

ECG Features
• PR interval—becomes progressively longer prior to the appearance of a P wave that is not followed by a QRS complex (Figure 1).
• Heart rate and QRS morphology—usually normal.
• Often cyclical.

PATHOPHYSIOLOGY
• Frequently associated with high resting vagal tone and sinus arrhythmia in dogs.
• Generally not pathologic or hemodynamically significant.
• This type of AV block usually results from conduction delay within the AV node itself (rather than delay in other segments of the AV conducting system) and is characterized by a progressive increase in AH interval with eventual block between the A and H deflections on a His bundle recording.

SYSTEMS AFFECTED
Cardiovascular

GENETICS
N/A

INCIDENCE/PREVALENCE
Radiotelemetry studies have shown that this arrhythmia occurs in 64% of healthy adult dogs and 100% of healthy puppies 8–12 weeks of age.

GEOGRAPHIC DISTRIBUTION
N/A

SIGNALMENT
Species
Dog; uncommon in cat

Breed Predilections
N/A

Mean Age and Range
• Usually occurs in young, otherwise healthy dogs as a manifestation of high vagal tone.
• Occasionally occurs in older dogs with abnormally strong vagal tone.
• Rarely noted in old dogs with degenerative conduction system disease.

SIGNS
Historical Findings
• Most animals are asymptomatic.
• If drug-induced, owner may report signs of drug toxicity—anorexia, vomiting, and diarrhea with digoxin; weakness with calcium channel blockers or β-adrenergic antagonists.
• If heart rate is abnormally slow, syncope or weakness may occur.

Physical Examination Findings
• May be normal unless signs of more-generalized myocardial disease or non-cardiac disease are present.
• Intermittent pauses in the cardiac rhythm.
• First heart sound may become progressively softer, followed by a pause.
• An audible S4 may be heard unaccompanied by S1 and S2 when block occurs.

CAUSES
• Occasionally noted in normal animals.
• Enhanced vagal stimulation resulting from non-cardiac diseases—usually accompanied by sinus arrhythmia, sinus arrest.
• Pharmacologic agents—digoxin, β -adrenergic antagonists, calcium channel blocking agents, propafenone, amiodarone, α_2-adrenergic agonists, opioids.

RISK FACTORS
Any condition or intervention that enhances vagal tone.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Non-conducted P waves from supraventricular premature impulses or supraventricular tachycardias should be distinguished from second-degree AV block.
• Type II second-degree AV block (no variation in PR intervals).

CBC/BIOCHEMISTRY/URINALYSIS
Hypokalemia may predispose to AV conduction disturbances

OTHER LABORATORY TESTS
Serum digoxin concentration—may be high

IMAGING
N/A

DIAGNOSTIC PROCEDURES
• May be necessary to identify specific causes of enhanced vagal tone (e.g., upper airway disease, cervical and thoracic masses, gastrointestinal disorders, and high intraocular pressure).
• Atropine response test—administer 0.04 mg/kg atropine IM and repeat ECG in 20–30 minutes; may be used to determine whether AV block is due to vagal tone; resolution of AV block with atropine supports vagal cause.
• Electrophysiologic studies are generally unnecessary but will confirm this type of second-degree AV block if surface ECG is equivocal.

PATHOLOGIC FINDINGS
Generally, no gross or histopathologic findings

TREATMENT

APPROPRIATE HEALTH CARE
• Treatment usually unnecessary
• Treat or remove underlying cause(s)

NURSING CARE
Generally unnecessary

ACTIVITY
Unrestricted

DIET
Modifications or restrictions only to manage an underlying condition.

CLIENT EDUCATION
Explain that any treatment is directed toward reversing or eliminating an underlying cause.

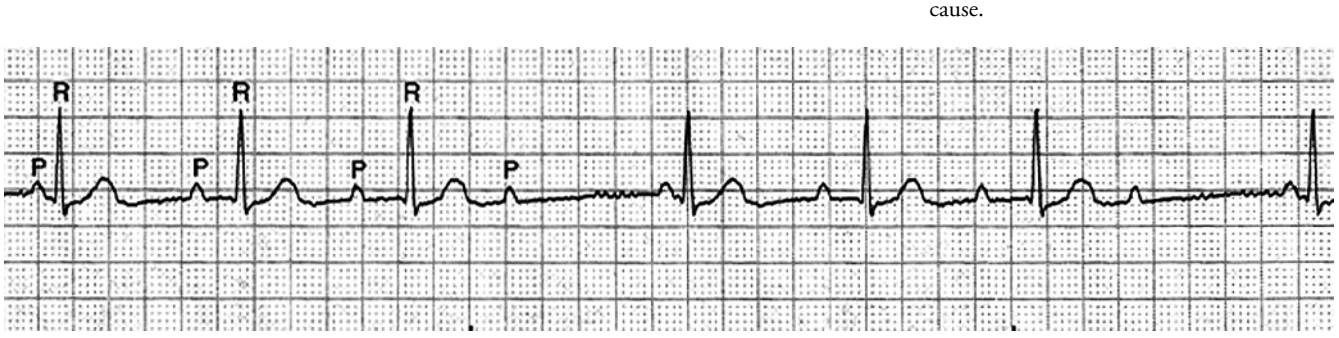

Figure 1.

Lead II ECG strip recorded from a dog with Mobitz type I, second-degree AV block. The PR intervals become progressively longer with the longest PR intervals preceding non-conducted P waves (typical Wenkebach phenomenon) (paper speed = 50 mm/s).

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ATRIOVENTRICULAR BLOCK, SECOND DEGREE—MOBITZ I (CONTINUED)

SURGICAL CONSIDERATIONS
N/A except to manage an underlying condition

MEDICATIONS

DRUG(S)
Only as needed to manage an underlying condition

CONTRAINDICATIONS
Drugs with vagomimetic action (e.g., digoxin, bethanechol, physostigmine, pilocarpine) may potentiate block.

PRECAUTIONS
Hypokalemia increases the sensitivity to vagal tone and may potentiate AV conduction delay.

POSSIBLE INTERACTIONS
N/A

FOLLOW-UP

PATIENT MONITORING
Typically not necessary

PREVENTION/AVOIDANCE
N/A

POSSIBLE COMPLICATIONS
N/A

MISCELLANEOUS

ASSOCIATED CONDITIONS
N/A

AGE-RELATED FACTORS
N/A

PREGNANCY/FERTILITY/BREEDING
N/A

SYNONYMS
- Wenckebach periodicity
- Wenckebach phenomenon

SEE ALSO
- Atrioventricular Block, Complete (Third Degree)
- Atrioventricular Block, First Degree
- Atrioventricular Block, Second Degree—Mobitz II

ABBREVIATIONS
- AV = atrioventricular
- ECG = electrocardiogram

Suggested Reading

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Client Education Handout available online

ATRIOVENTRICULAR BLOCK, SECOND DEGREE—MOBITZ II

BASICS

DEFINITION
Second-degree AV block refers to failure of one or more P waves but not all P waves to be conducted. Mobitz Type II second-degree AV block occurs when one or more P waves are blocked without a preceding progressive delay in AV transmission.

ECG Features
• One or more P waves not followed by a QRS complex; PR interval is constant but may be either normal or consistently prolonged (Figure 1).
• Ventricular rate—usually slow.
• Fixed ratio of P waves to QRS complexes may occur (e.g., 2:1, 3:1, 4:1 AV block).
• High-grade (advanced) second-degree AV block is characterized by two or more consecutive blocked P waves.
• In second-degree AV block with a 2:1 conduction ratio or higher, it is impossible to observe prolongation of the PR interval before the block, so a designation of Mobitz is not appropriate.
• QRS complexes may appear normal but may also be wide or have an abnormal morphology due to aberrant intraventricular conduction or to ventricular enlargement.
• Abnormally wide QRS complexes may indicate serious, extensive cardiac disease.

PATHOPHYSIOLOGY
• Rare in healthy animals.
• May be hemodynamically important when ventricular rate is abnormally slow.
• Frequently progresses to complete AV block, particularly when accompanied by wide QRS complexes.
• Typically this type of AV block results from conduction delay within the AV node itself (rather than delay in another segment of the AV conducting system) that is characterized by normal or prolonged AH intervals with intermittent block between A and H deflections on a His bundle electrogram).

SYSTEMS AFFECTED
• Cardiovascular.
• Central nervous or musculoskeletal systems if inadequate cardiac output.

GENETICS
May be heritable in pugs

INCIDENCE/PREVALENCE
Unknown

GEOGRAPHIC DISTRIBUTION
N/A

SIGNALMENT
Species
Dog and cat

Breed Predilections
American cocker spaniel, pug, dachshund, Airedale terrier, Doberman pinscher.

Mean Age and Range
Generally occurs in older animals

Predominant Sex
N/A

SIGNS
Historical Findings
• Presenting complaint may be syncope, collapse, weakness, or lethargy.
• Some animals are asymptomatic.
• Animals may show signs of the underlying disease process.

Physical Examination Findings
• ± weakness.
• Bradycardia common.
• May be intermittent pauses in the cardiac rhythm.
• An S4 may be audible in lieu of the normally expected heart sounds (i.e., S1, S2) when the block occurs.
• If associated with digoxin intoxication, there may be vomiting, anorexia, and diarrhea.
• May be other abnormalities reflecting the underlying etiology.

CAUSES
• Heritable in pugs.
• Enhanced vagal stimulation from non-cardiac diseases.
• Degenerative change within the cardiac conduction system—replacement of AV nodal cells and/or Purkinje fibers by fibrotic and adipose tissue in old cats and dogs.
• Pharmacologic agents (e.g., digoxin, β-adrenergic antagonists, calcium channel blocking agents, propafenone, α_2-adrenergic agonists, muscarinic cholinergic agonists, or severe procainamide or quinidine toxicity).
• Infiltrative myocardial disorders (neoplasia, amyloid).
• Endocarditis (particularly involving the aortic valve).
• Myocarditis (viral, bacterial, parasitic, idiopathic).
• Cardiomyopathy (especially in cats).
• Trauma.
• Atropine administered intravenously may cause a brief period of first- or second-degree heart block before increasing the heart rate.

RISK FACTORS
Any condition or intervention that enhances vagal tone

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• High-grade (advanced) form must be distinguished from complete AV block.
• Non-conducted P waves arising from refractoriness of the conduction system during supraventricular tachycardias must be differentiated from pathologic conduction block.

CBC/BIOCHEMISTRY/URINALYSIS
• Serum electrolytes—hypokalemia and hyperkalemia may predispose to AV.
• Conduction disturbances.
• Leukocytosis—may be noted with bacterial endocarditis or myocarditis.
• Electrolyte abnormalities (e.g., severe hypokalemia, hyperkalemia, or hypercalcemia) may predispose to AV block.

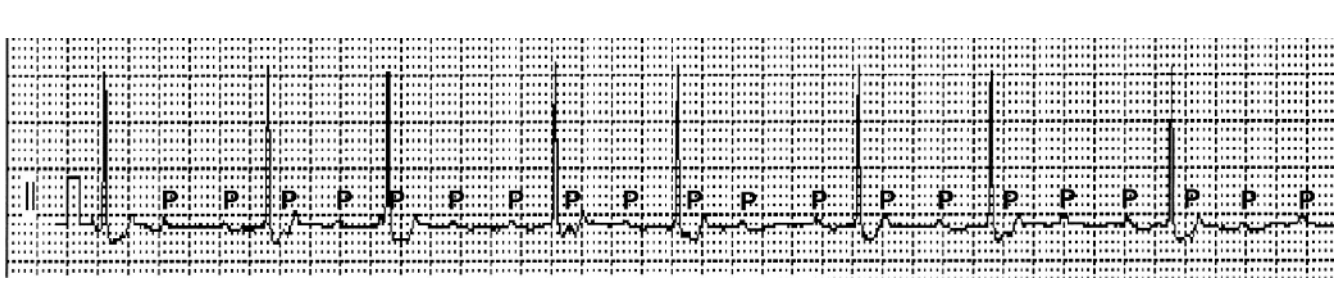

Figure 1.

Lead II ECG rhythm strip recorded from a dog with both first- and second-degree atrioventricular block. The second-degree AV block is high grade with both 2:1 and 3:1 block resulting in variation in the RR intervals. The PR interval for the conducted beats is prolonged but constant (0.28 second) (paper speed = 25 mm/s).

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ATRIOVENTRICULAR BLOCK, SECOND DEGREE—MOBITZ II (CONTINUED)

OTHER LABORATORY TESTS
• Serum digoxin concentration—may be high.
• High T_4 in cats—if associated with hyperthyroidism.
• High arterial blood pressure—if associated with hypertensive heart disease.
• Positive *Borrelia, Rickettsia,* or *Trypanosoma cruzi* titers—if associated with one of these infectious agents.
• Blood cultures may be positive in patients with vegetative endocarditis.

IMAGING
Echocardiographic examination may reveal structural heart disease (e.g., endocarditis, neoplasia, or cardiomyopathy).

DIAGNOSTIC PROCEDURES
• Atropine response test—administer 0.04 mg/kg atropine IM and repeat ECG in 20–30 minutes; may be used to determine whether AV block is due to high vagal tone.
• Electrophysiologic testing is generally unnecessary but can be done to confirm this type of AV block if surface ECG findings are equivocal.

PATHOLOGIC FINDINGS
• Variable—depend on underlying cause.
• Old animals with degenerative change of the conduction system may have focal mineralization of the interventricular septal crest visible grossly; chondroid metaplasia of the central fibrous body and increased fibrous connective tissue in the AV bundle is noted histopathologically.

TREATMENT

APPROPRIATE HEALTH CARE
• Treatment—may be unnecessary if heart rate maintains adequate cardiac output.
• Positive dromotropic interventions are indicated for symptomatic patients.
• Treat or remove underlying cause(s).

NURSING CARE
Generally unnecessary

ACTIVITY
Cage rest advised for symptomatic patients.

DIET
Modifications or restrictions only to manage an underlying condition.

CLIENT EDUCATION
• Need to seek and specifically treat underlying cause.
• Pharmacologic agents may not be effective long term.

SURGICAL CONSIDERATIONS
Permanent pacemaker may be required for long-term management of symptomatic patients.

MEDICATIONS

DRUG(S) OF CHOICE
• Atropine (0.02–0.04 mg/kg IV, IM) or glycopyrrolate (5–10 μ–g/kg IV, IM) may be used short term if positive atropine response.
• Chronic anticholinergic therapy (propantheline 0.5–2 mg/kg PO q8–12h or hyoscyamine 3–6 μg/kg q8h)—indicated for symptomatic patients if improved AV conduction with atropine response test.
• Isoproterenol (0.04–0.09 μg/kg/minute IV to effect) or dopamine (2–5 μg/kg/minute IV to effect) may be administered in acute, life-threatening situations to enhance AV conduction and/or accelerate an escape focus.

CONTRAINDICATIONS
• Drugs with vagomimetic action (e.g., digoxin, bethanechol, physostigmine, pilocarpine) may potentiate block.
• Avoid drugs likely to impair impulse conduction further or depress a ventricular escape focus (e.g., procainamide, quinidine, lidocaine, calcium channel blocking agents, β-adrenergic blocking agents).

PRECAUTIONS
Hypokalemia—increases sensitivity to vagal tone and may potentiate AV conduction delay.

POSSIBLE INTERACTIONS
N/A

ALTERNATIVE DRUG(S)
N/A

FOLLOW-UP

PATIENT MONITORING
Frequent ECG because often progresses to complete (third-degree) AV block.

PREVENTION/AVOIDANCE
N/A

POSSIBLE COMPLICATIONS
Prolonged bradycardia may cause secondary congestive heart failure or inadequate renal perfusion.

EXPECTED COURSE AND PROGNOSIS
Variable—depends on cause. If degenerative disease of the cardiac conduction system, often progresses to complete (third-degree) AV block.

MISCELLANEOUS

ASSOCIATED CONDITIONS
May be noted in cats with primary or secondary myocardial disease.

AGE-RELATED FACTORS
N/A

ZOONOTIC POTENTIAL
N/A

PREGNANCY/FERTILITY/BREEDING
N/A

SEE ALSO
• Atrioventricular Block, Complete (Third Degree)
• Atrioventricular Block, Second Degree—Mobitz I

ABBREVIATIONS
• AV = atrioventricular
• ECG = electrocardiogram
• T_4 = thyroxine

Suggested Reading

Kittleson MD. Electrocardiography. In: Kittleson MD, Kienle RD, eds., Small Animal Cardiovascular Medicine. St. Louis, MO: Mosby, 1998, pp. 72–94.
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Acknowledgment The editors acknowledge the prior contribution of Janice McIntosh Bright.

Client Education Handout available online

ATRIOVENTRICULAR VALVE DYSPLASIA

BASICS

DEFINITION
A congenital malformation of the mitral or tricuspid valve apparatus.

PATHOPHYSIOLOGY
• Atrioventricular valve dysplasia can result in valvular insufficiency, valvular stenosis, or dynamic outflow tract obstruction, depending on the anatomic abnormality. AVVD may occur alone or in association with abnormalities of the ipsilateral outflow tract (e.g., valvular or subvalvular aortic or pulmonic stenosis). It is not uncommon for mitral and tricuspid valve dysplasia to occur together in the same patient. • Valvular insufficiency results in dilation of the ipsilateral atrium, eccentric hypertrophy of the associated ventricle, and, if sufficiently severe, signs of CHF. Cardiomyopathy of chronic volume overload and elevated atrial pressures are the end result culminating in pulmonary congestion if the mitral valve is affected and systemic congestion if the tricuspid valve is affected. • Valvular stenosis results in atrial dilation and hypertrophy and, when severe, hypoplasia of the receiving ventricle. Tricuspid valve stenosis results in elevated right atrial pressure and systemic congestion if pressures exceed 15–20 mmHg. Right-to-left shunting may occur if there is an atrial septal defect or patent foramen ovale. Mitral valve stenosis results in elevated pulmonary capillary pressure and pulmonary edema if pressures exceed 25–30 mmHg. Pulmonary hypertension is a common complicating condition in animals with mitral valve stenosis. • Outflow tract obstruction may develop from defects that translocate the anterior leaflet to a position closer to the interventricular septum. Concentric left ventricular hypertrophy develops in proportion to the severity of the obstruction.

SYSTEMS AFFECTED
• Cardiovascular—inflow obstruction due to valvular stenosis and chronic volume overload from valvular insufficiency result in elevated pulmonary (left AV valve) or systemic (right AV valve) venous pressures. Signs of low cardiac output develop if the lesion is sufficiently severe. Concentric left ventricular hypertrophy develops secondary to dynamic outflow obstruction. • Respiratory—pulmonary edema may develop secondary to mitral stenosis or mitral valve insufficiency. Pulmonary hypertension is a common complication in animals with mitral stenosis. • Neurologic—collapse and loss of consciousness, most often during physical exertion, may occur with severe disease due to low cardiac output and hypotension. Collapse in animals with dynamic outflow obstruction is most often due to ventricular arrhythmia.

GENETICS
Tricuspid valve dysplasia is inherited as an autosomal recessive trait in Labrador retrievers. Heritability and pattern of inheritance not established in other breeds.

INCIDENCE/PREVALENCE
These are common congenital cardiac anomalies in cats (17% of reported congenital cardiac defects in one study). Less frequently diagnosed in dogs.

SIGNALMENT
Species
Dog and cat

Breed Predilections
• Tricuspid valve dysplasia—increased risk for Labrador retriever, German shepherd dog, Great Pyrenees, possibly Old English sheepdog. Also common in cat. • Mitral valve dysplasia—increased risk in bull terrier, Newfoundland, Labrador retriever, Great Dane, golden retriever, Dalmatian, and Siamese cat. Perhaps the most common congenital heart defects of cats. Mitral valve malformations often are noted in cats with hypertrophic cardiomyopathy.

Mean Age and Range
Variable; signs are most often manifest within the first few years after birth.

Predominant Sex
Males are more likely to evidence heart failure.

SIGNS
Historical Findings
• Exercise intolerance is the most common problem in dogs and cats with AV valve dysplasia. • Abdominal distention, weight loss, and stunting may be observed with severe tricuspid valve dysplasia. • Labored respiration is common in dogs or cats with mitral valve dysplasia. • Syncope and collapse if critical mitral or tricuspid valve stenosis, severe outflow tract obstruction, an associated arrhythmia, or heart failure from AV valvular insufficiency.

Physical Examination Findings
Mitral Valve Dysplasia
• A holosystolic murmur is heard over the cardiac apex on the left. With severe disease the murmur is accompanied by a thrill or gallop heart sounds. A soft diastolic murmur may be present in the same location in animals with mitral stenosis but many affected animals have no audible murmur. A systolic ejection murmur that intensifies with exercise or excitement is audible in animals with dynamic outflow tract obstructions. • Evidence of left heart failure—tachypnea, increased respiratory efforts, pulmonary crackles, and cyanosis in animals with severe defects.

Tricuspid Valve Dysplasia
• A holosystolic murmur is heard over the cardiac apex on the right. With severe disease the murmur is accompanied by a thrill or gallop heart sounds. Silent tricuspid regurgitation is well documented in cats and is attributable to a large regurgitant orifice and laminar regurgitant flow. Distention and pulsation of the external jugular veins may be evident. • Evidence of right heart failure—ascites and, more rarely, peripheral edema with severe malformations.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• With the noted exception of the age of onset, congenital AV valvular insufficiency resembles acquired degenerative AV valve insufficiency with respect to historical findings, physical examination abnormalities, and clinical sequelae. • The right-sided murmur of tricuspid insufficiency is sometimes confused with the right-sided murmur of a ventricular septal defect. • Ascites caused by silent tricuspid regurgitation or tricuspid valve stenosis is often attributed to pericardial effusion, hepatic disease, or obstruction of the caudal vena cava. • Dogs and cats with cor triatriatum share many of the clinical features of AV valve stenosis. • There is no certain way to distinguish mitral valve dysplasia producing outflow tract obstruction and the obstructive form of cardiomyopathy. If the obstruction can be abolished with a beta blocker and left ventricular hypertrophy resolves, it is likely that the primary abnormality was mitral valve dysplasia.

IMAGING
Radiographic Findings
Mitral Valve Dysplasia
• Left atrial and left ventricular enlargement with valvular insufficiency. Isolated left atrial enlargement with valvular stenosis. Mild left atrial enlargement with dynamic outflow obstruction. • Evidence of left heart failure—distended pulmonary veins, interstitial or alveolar edema in severe cases.

Tricuspid Valve Dysplasia
• Right atrial and right ventricular enlargement with valvular insufficiency. Cardiac silhouette may appear globoid with pronounced enlargement. Isolated right atrial enlargement with valvular stenosis. • Evidence of right heart failure—dilated caudal vena cava, hepatosplenomegaly, or ascites in severe cases.

Echocardiography
Mitral Valve Dysplasia
• Valvular insufficiency results in left atrial dilation and eccentric hypertrophy of the left ventricle. The papillary muscles are typically flattened and displaced dorsally. Chordae tendineae are often short and thickened. Doppler echocardiography demonstrates a high velocity retrograde systolic transmitral jet

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ATRIOVENTRICULAR VALVE DYSPLASIA (CONTINUED)

and modestly increased transmitral inflow velocities. • Mitral stenosis results in left atrial dilation while the left ventricular dimensions are normal or small. The valve leaflets are often thickened, relatively immobile, and often fused. Doppler echocardiography demonstrates a high velocity transmitral diastolic jet with a reduced EF slope. There may also be evidence of concurrent mitral insufficiency and/or secondary pulmonary hypertension. Exclude the possibility of cor triatriatum sinister. • Dynamic left ventricular outflow obstruction is characterized by systolic motion of the anterior mitral valve leaflet toward the interventricular septum, increased LV outflow tract velocities, and concentric left ventricular hypertrophy.

Tricuspid Valve Dysplasia

• Valvular insufficiency results in right atrial dilation and eccentric hypertrophy of the right ventricle. The papillary muscles and chordae tendineae may be fused, creating a curtain-like appearance of the tricuspid valve. Doppler echocardiography demonstrates a high velocity retrograde systolic trans-tricuspid jet and modestly increased transtricuspid inflow velocities. • Tricuspid stenosis results in right atrial dilation with normal or small right ventricular dimensions. The valve leaflets do not open completely. Doppler echocardiography demonstrates a high velocity diastolic trans-tricuspid jet with a reduced EF slope. There may be evidence of concurrent tricuspid valve insufficiency and/or right-to-left shunting across a patent foramen ovale or associated atrial septal defect. Exclude the possibility of cor triatriatum dexter.

Cardiac Catheterization

• Indicated only in those cases in which the diagnosis cannot be confirmed by echocardiography or if surgical correction is anticipated. • Mitral dysplasia—hemodynamic measurements should include left ventricular pressures, pulmonary capillary wedge pressure or direct measurement of LA pressure, pulmonary artery pressures, and, in cases of dynamic obstruction, simultaneous recording of aortic and left ventricular pressures with medical provocation. Contrast studies are best accomplished with a left ventricular injection in cases of valvular insufficiency, and direct left atrial injection via trans-septal catheterization in cases of valvular stenosis. • Tricuspid dysplasia—hemodynamic measurements should include right ventricular and right atrial pressures. Contrast studies are best accomplished with a right ventricular injection in cases of valvular insufficiency, and right atrial injection in cases of valvular stenosis.

DIAGNOSTIC PROCEDURES

Electrocardiographic Findings

• Usually reflect pattern of chamber enlargement. • Severe defects may be accompanied by a variety of arrhythmias, particularly atrial premature beats, supraventricular tachycardia, or atrial fibrillation.

TREATMENT

APPROPRIATE HEALTH CARE

Inpatient treatment required for CHF.

CLIENT EDUCATION

Owners should be informed of heritability and advised against breeding.

DIET

Sodium-restricted if overt or pending CHF.

SURGICAL CONSIDERATIONS

• Valve repair or replacement is available in a few centers. • Balloon valvuloplasty is sometimes effective for valvular stenosis.

MEDICATIONS

DRUG(S) OF CHOICE

• Mitral or tricuspid dysplasia with insufficiency—diuretics, angiotensin converting enzyme inhibitors, and pimobendan (0.3 mg/kg q12h) for patients with imminent or overt congestive heart failure. Furosemide (2–4 mg/kg q12–24h), enalapril (0.5 mg/kg q12h) are used to control congestion. Digoxin (2–4 μg/kg q12h) is used to control supraventricular tachyarrhythmias. • Mitral or tricuspid stenosis—diuretics to control edema. Furosemide (2–4 mg/kg q12–24h) dose adjusted to resolve congestion. Heart rate should be maintained near 150 bpm using digoxin (2–4 μg/kg q12h), a calcium channel blocker such as diltiazem (1–1.5 mg/kg q8h), or a beta-receptor blocking drug, such as atenolol (0.5–1.5 mg/kg q12–24h). • Dynamic outflow tract obstruction—titrate a beta-receptor blocking drug, such as atenolol (0.5–1.5 mg/kg q12–24h), to abolish or diminish severity of outflow obstruction.

PRECAUTIONS

Standard patient monitoring for cardiac medication side effects (e.g., digitalis toxicity, azotemia).

FOLLOW-UP

PATIENT MONITORING

• Recheck yearly if no signs of heart failure. • Recheck at a minimum of every 3 months if signs of CHF (thoracic radiographs, ECG, and echocardiography advisable).

PREVENTION/AVOIDANCE

Do not breed affected animals.

POSSIBLE COMPLICATIONS

• Congestive heart failure—left-sided with mitral valve dysplasia; right-sided with tricuspid valve dysplasia. • Collapse or syncope with exercise. • Paroxysmal supraventricular tachycardia or atrial fibrillation with severe disease.

EXPECTED COURSE AND PROGNOSIS

• Depends on severity of underlying defect • Guarded to poor with serious defects

MISCELLANEOUS

ASSOCIATED CONDITIONS

• Mitral valve dysplasia commonly accompanies valvular or subvalvular aortic stenosis as well as TVD. • Tricuspid valve dysplasia commonly accompanies pulmonic stenosis as well as MVD.

PREGNANCY/FERTILITY/BREEDING

Should be avoided—heritable defect and possibility of causing decompensated or worsening heart failure.

SEE ALSO

• Congestive Heart Failure, Left-Sided
• Congestive Heart Failure, Right-Sided

ABBREVIATIONS

• AV = atrioventricular • AVVD = atrioventricular valve dysplasia • CHF = congestive heart failure • ECG = electrocardiogram • MVD = mitral valve dysplasia • TVD = tricuspid valve dysplasia

Suggested Reading

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ATRIOVENTRICULAR VALVE (MYXOMATOUS) DISEASE

BASICS

DEFINITION
Myxomatous mitral valve disease is characterized by progressive myxomatous degeneration, which refers to a characteristic pathologic weakening and disturbance in the organization of the connective tissue of the AV valve (mitral and tricuspid) apparatus.

PATHOPHYSIOLOGY
• Lesions characterized by pathologic weakening and disorganization of valvular connective tissue, in which the spongiosa component is unusually prominent with accumulation of mucopolysaccharides and glycosaminoglycans.
• The valve leaflets become thickened and elongated with disease progression.
• Degenerative changes in the chordae tendineae lead to thickening and elongation of these structures; thereby contributing to systolic atrial displacement of the valve leaflets (valve prolapse).
• With progression, the valve lesions cause insufficient coaptation of the leaflets during systole, leading to backward regurgitation of blood from the ventricle into the atrium.
• Severity and progression of AV valve regurgitation depends on severity and progression of valve lesions (leaflets and/or tendinous chords).
• Compensatory mechanisms include cardiac dilatation and eccentric hypertrophy, increased force of contraction, increased heart rate, increased pulmonary lymphatic drainage (left-sided AV valve regurgitation), fluid retention, and neurohormonal modulation of cardiovascular function.
• With progression, the valvular regurgitation can no longer be compensated, leading to reduced cardiac output and increased venous pressures (leading to pulmonary edema if left-sided congestive heart failure [CHF] and to ascites if right-sided). With atrial tear, acute cardiac tamponade may result.

SYSTEMS AFFECTED
• Cardiovascular—both AV valves are commonly affected, but semilunar valves less commonly affected.
• Hepatobiliary—passive congestion.
• Renal/Urologic—prerenal azotemia.
• Respiratory—if edema and/or pulmonary hypertension develops.

GENETICS
Etiology currently unknown, but the current leading scientific hypothesis is that a genetically determined dystrophic process initiates the valve degeneration. The age at which the disease develops is inherited as a polygenetic threshold trait (i.e., multiple genes influence the trait and a certain threshold has to be reached before the disease develops).

INCIDENCE/PREVALENCE
The most common cardiac disease in dogs. The prevalence is strongly influenced by age. It is uncommon in young individuals but common in old dogs. The prevalence reaches
> 90% in some affected dog breeds
> 10 years.

SIGNALMENT
Species
Mainly dogs. Extremely rare in cats.

Breed Predilections
Typically small breeds (< 20 kg but may be encountered in larger dogs), such as Cavalier King Charles spaniels, Chihuahuas, Miniature schnauzers, Maltese, Pomeranians, Cocker spaniels, Pekingese, Poodles, and others.

Mean Age and Range
Murmur may be detected from 2 years of age with a peak incidence at 6–8 years in affected breeds, such as Cavalier King Charles spaniels. Onset of CHF from 8–12 years.

Predominant Sex
Males develop the disease at a younger age than females, which means a higher prevalence at a given age in males.

SIGNS
Signs depend on the stage of disease. The descriptions here align with the grading system described in the ACVIM consensus statement on myxomatous mitral valve disease.

Clinically Healthy Patients but Belonging to a Risk Group (ACVIM Stage A)
No abnormal findings

Patients Without Overt Clinical Signs (ACVIM Stage B)
• Systolic click (early stage).
• Systolic murmur best heard over the mitral or tricuspid areas.
• Murmurs may range from being of soft, low intensity to loud holosystolic. With progression, the murmur typically gets louder and radiates more widely.
• Initially patients have no obvious radiographic or echocardiographic changes in cardiac chamber size (ACVIM stage B1). As the disease progresses, evidence of cardiomegaly will be seen (ACVIM stage B2), often before obvious clinical signs of heart failure are recognized.

Patients with Overt Clinical Signs or Stabilized by CHF Therapy (ACVIM stages C and D)
• Usually loud heart murmur.
• Tachycardia and loss of respiratory sinus arrhythmia.
• Arrhythmia and pulse deficit may be present, most commonly supraventricular premature beats or atrial fibrillation.
• Weak femoral pulse, prolonged capillary refill time and pale mucous membranes in case of low output failure.
• Tachypnea/dyspnea/orthopnea in case of decompensated CHF.
• Respiratory crackles/rales in case of decompensated CHF.
• Pink froth, i.e., pulmonary edema may be evident in the nostrils and oropharynx in cases with severe decompensated CHF.
• Ascites if right-sided CHF.
• Diagnostic imaging invariably shows left atrial (LA) and ventricular (LV) dilatation and eccentric hypertrophy, sometimes bilateral enlargement, and evidence of pulmonary congestion/edema.

CAUSES
Primary (inciting) factor unknown, but the disease is influenced by genetic factors in affected breeds.

RISK FACTORS
• Breed
• Sex (males have an earlier onset)

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
• Dilated cardiomyopathy
• Congenital heart disease
• Bacterial endocarditis
• Chronic airway or interstitial lung disease
• Pneumonia
• Pulmonary embolism
• Pulmonary neoplasia
• Heartworm disease

CBC/BIOCHEMISTRY/URINALYSIS
• CBC/Biochemistry usually unremarkable unless severe disease and ongoing CHF therapy
• Prerenal azotemia secondary to impaired renal perfusion; urinary specific gravity is high unless complicated by underlying renal disease or previous diuretic administration.
• High liver enzyme activity in many patients with right-sided CHF.

OTHER LABORATORY TESTS
• Natriuretic peptides—concentrations are often unremarkable unless moderate to severe disease.
• Serum troponin I—concentrations unremarkable unless severe disease.

IMAGING
Radiographic Findings
• Heart size ranges from normal to left-sided or generalized cardiomegaly.
• LA enlargement is usually the earliest finding.
• Left-sided CHF—pulmonary congestion; increased interstitial pattern ± air bronchograms; initially, congestion and edema are perihilar, with all lung fields eventually showing changes.

Echocardiographic Findings
• Thickening and distortion of the AV valve leaflets.

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ATRIOVENTRICULAR VALVE (MYXOMATOUS) DISEASE (CONTINUED)

• Elongation and rupture of the chordae tendineae, causing mitral valve prolapse.
• Atrial dilatation (uni- or bilaterally).
• The LV might be distended and is hyperdynamic if the regurgitant flow is high and myocardial function intact; as the ventricle becomes more grossly distended, it may become normo- or, less commonly, hypodynamic because of myocardial failure.
• Pericardial effusion (usually mild) is rarely seen.
• Doppler studies document a jet of regurgitation into the left atrium.
• Doppler evaluation for the presence of pulmonary hypertension should be routinely performed.

DIAGNOSTIC PROCEDURES

• Systemic blood pressure should be monitored in patients with severe disease or receiving diuretics to check for hypotension. Hypertension is not common.
• Arterial/venous blood gases can be used to quantify hypoxemia and monitor treatment response.
• Abdominocentesis/Pleurocentesis—a modified transudate is characteristic of CHF.

Electrocardiographic Findings

• Sinus tachycardia is common in patients with CHF.
• May show evidence of LA enlargement (P mitrale) or LV enlargement (tall and wide R waves).
• Supraventricular, most commonly atrial fibrillation, or ventricular arrhythmias may develop in severe disease.

PATHOLOGIC FINDINGS

• Gross valvular changes range from only a few discrete nodules at the line of closure to gross distortion of the valve by gray-white nodules and plaques causing contraction of the cusps and rolling of the free edge; the chordae are irregularly thickened, with regions of tapering and rupture.
• Mild disease—normal cardiac size. More progressed cases—LA and LV dilation. Degree of right-sided dilatation variable.
• The degree of LV hypertrophy may be apparent only on weighing the heart.
• Jet lesions—irregular thickening and opacity of the atrial endocardium.
• Recent and healed LA splits or tears in some patients.
• Small thrombi in the LA are rarely seen.

TREATMENT

APPROPRIATE HEALTH CARE

Treat patients that need oxygen support as inpatients; if stable, patients may be managed at home.

NURSING CARE

Oxygen therapy as needed for hypoxemia.

ACTIVITY

• Absolute exercise restriction for symptomatic patients.
• Stable patients receiving medical treatment—avoid strenuous exercise.

DIET

• Prevent cardiac cachexia by ensuring adequate calorie intake.
• Avoid food with high sodium content.

CLIENT EDUCATION

• Discuss the progressive nature of the disease.
• Mild disease severity is suggestive of a long period without clinical signs; moderate to severe indicates a shorter period.
• If the client is a breeder, inform him/her about the genetics of the disease and impact of the finding on future breeding.
• Appropriate level of exercise, but at the same time maintain quality of life.
• Common signs of CHF listed above.
• How to medicate (if indicated)—consistent dosing and that doses of diuretics should be adjusted in collaboration with the veterinarian.
• Possible adverse side reactions of medications.
• How to monitor resting/sleeping respiratory rates at home, and at which rate new contact with the clinician should be initiated.
• Diet (if indicated)—emphasize the importance of avoiding cardiac cachexia by paying close attention to appetite and using an appropriate diet.

SURGICAL CONSIDERATIONS

Surgical valve replacement and purse-string suture techniques to reduce the area of the mitral valve orifice have been used; experience with these techniques and access usually limited.

MEDICATIONS

DRUG(S) OF CHOICE

Recommended treatment depends on the stage of the disease; these recommendations follow the guidelines set by the consensus statement developed by the ACVIM.

Patients Without Overt Clinical Signs (ACVIM Stage B)

• If no cardiac enlargement, no treatment is currently recommended.
• Administering ACE inhibitors to Stage B2 patients is of unproven efficacy (despite two clinical trials). Administration of pimobendan to Stage B2 patients is of unknown value at this time.

Patients Showing Overt Clinical Signs (ACVIM stage C and D)

Signs of Acute CHF (Often Treated as Inpatient)

• Furosemide IV, SC, IM, or PO. Dose is dependent on severity of CHF.
  ◦ Mild to moderate CHF: 2–4 mg/kg q8–24h.
  ◦ Severe or fulminant CHF: 4–8 mg/kg q2–6h, preferably IV, IM, or SC.
  ◦ Monitor outcome of treatment by respiratory rate and general clinical status. Dosages can often be reduced when the patient has stabilized.
• Oxygen supplementation and cage rest to patients with significant dyspnea. 40% in O_2 cage (can go as high as 100%) up to 24 hours; nasal O_2 in may be used in large-breed dogs, 50–100 mL/kg/minute through humidifier.
• Pimobendan at 0.25 mg/kg q12h PO.
• Additional options in cases with severe fulminant CHF:
  ◦ Nitroglycerin: ointment (one-fourth inch/5 kg up to 2 inches percutaneously) or injectable (1–5 μg/kg/minute CRI).
  ◦ Arterial vasodilator to decrease afterload rapidly, such as hydralazine at 0.5 mg/kg q12h titrated up to 2 mg/kg if necessary), or sodium nitroprusside at 1–10 μg/kg/minute. Both drugs require blood pressure monitoring and should be considered only in hospitalized dogs when monitored by a specialist.
  ◦ Dobutamine (dogs, 1–10 μg/kg/minute; cats, 1–5 μg/kg/minute).
  ◦ Dopamine (1–10 μg/kg/minute).
• Antiarrhythmics—as needed.
• Severe ascites may require abdominal paracentesis.

Chronic CHF (Typically Treated as Outpatient)

• Exact composition of medical therapy depends on disease severity and clinical signs. All dogs with CHF require life-long treatment with a diuretic, such as furosemide.
  ◦ Mild to moderate CHF: 1 mg/kg q24h to 3–4 mg/kg q8h PO.
  ◦ Moderate to severe CHF: 2–3 mg/kg q12h or higher.
• Pimobendan at 0.25 mg/kg q12h PO.
• ACEI (i.e., enalapril, benazepril, ramipril). Dose and dose interval dependent on ACE inhibitor used (enalapril [0.5 mg/kg q12–24h], benazepril [0.25–0.5 mg/kg q24h]).
• Spironolactone at 2 mg/kg q12–24h PO and/or hydrochlorothiazide at 2–4 mg/kg q12h PO.
• Digoxin at 0.22 mg/m^2 q12h PO, or lower.
• Adequate antiarrhythmic treatment if significant arrhythmia is present.
• Sildenafil at 0.5–2 mg/kg in case of pulmonary hypertension.

PRECAUTIONS

• Use digoxin, diuretics, and ACE inhibitors with caution in patients with renal disease.
• Nitrate tolerance may develop if appropriate 12-hour nitrate-free intervals are omitted from the dosing schedule.
• Beta-blockers are negative inotropes and may have an acute adverse effect on myocardial function and clinical status.

(CONTINUED) ATRIOVENTRICULAR VALVE (MYXOMATOUS) DISEASE

POSSIBLE INTERACTIONS

• Furosemide potentiates the effects of an ACE-inhibitor, spironolactone, or a thiazide.
• Nonsteroidal anti-inflammatory drugs should be used with caution in patients receiving furosemide and ACEI.

ALTERNATIVE DRUG(S)

• Diuretics—add thiazide and/or potassium sparing diuretic (e.g., spironolactone) in refractory animals.
• Torsemide and bumetanide are alternatives to furosemide.
• Vasodilators—isosorbide dinitrate can be used in place of nitroglycerin ointment in patients requiring long-term nitrate administration.

FOLLOW-UP

PATIENT MONITORING

• Frequency of reexaminations depends on severity of myxomatous valve disease and severity of CHF (if present).
• Dogs without signs of CHF.
  ◦ Slight to moderate disease severity: Perform echocardiography when a murmur is first detected and every 6-12 months thereafter to document progressive cardiomegaly. A baseline radiograph may be useful.
  ◦ Moderate to severe disease severity may require more frequent monitoring.
• Dogs with signs of CHF:
  ◦ Once acute CHF has been successfully treated, dogs can be treated at home.
  ◦ Reexamination after 1 to 2 weeks of therapy (check for signs of decompensated CHF, dehydration, electrolyte imbalance, renal dysfunction, and presence of a complication). Moderate to severe disease severity may require more frequent monitoring.
  ◦ Thereafter once every 3-6 months if the patient is stable on the medication. More severe cases may require more frequent monitoring.
• Monitor BUN and creatinine when diuretics and ACE inhibitors are used in combination. Monitor potassium levels, especially when combinations of spironolactone, ACE inhibitors and digoxin are used.

POSSIBLE COMPLICATIONS

• Asymptomatic patients may develop CHF
• Recurrent CHF in patients stabilized by medical therapy
• Pulmonary hypertension
• Biventricular CHF in patients with initial left-sided CHF
• Mild pleural and/or pericardial effusion
• Arrhythmia, most commonly atrial fibrillation
• Rupture of first-order tendinous chord(s), leading to a flail valve leaflet
• Atrial tear leading to acquired atrial septal defect or cardiac tamponade
• Formation of intracardiac thrombus and/or myocardial infarction.

EXPECTED COURSE AND PROGNOSIS

The lesions on the AV valves are progressive in nature and myocardial function may worsen, necessitating increasing drug dosages; long-term prognosis depends on response to treatment and stage of heart failure.

MISCELLANEOUS

SYNONYMS

• Chronic valvular disease (CVD)
• Chronic mitral valve disease
• Degenerative valvular disease
• Degenerative mitral valve disease (DMVD)
• Myxomatous mitral valve disease (MMVD)
• Endocardiosis

SEE ALSO

• Atrial Wall Tear
• Congestive Heart Failure, Left-Sided
• Congestive Heart Failure, Right-Sided

ABBREVIATIONS

• ACE = angiotensin converting enzyme
• AV = atrioventricular
• CHF = congestive heart failure
• LA = left atrium
• LV = left ventricle
• MAVD = myxomatous mitral valve disease

Suggested Reading

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ATRIOVENTRICULAR VALVULAR STENOSIS

BASICS

DEFINITION
Atrioventricular valvular stenosis is a pathologic narrowing of the mitral or tricuspid valve orifice due to valvular dysplasia or an obstructive, supravalvular ring.

PATHOPHYSIOLOGY
• Atrioventricular stenosis increases the resistance to ventricular filling.
• Ventricular filling in clinically significant disease requires a persistent diastolic pressure gradient between atrium and ventricle.
• Concomitant valvular regurgitation is common.
• The increased atrial pressure leads to atrial dilation, venous congestion, and often to CHF. Pulmonary edema occurs with mitral stenosis; whereas ascites, pleural effusion and chylothorax can develop in cases of severe tricuspid stenosis.
• The foramen ovale can remain patent (PFO) in patients with tricuspid stenosis, allowing right-to-left shunting with signs of cyanotic heart disease.
• Partial atrioventricular septal defect (primum ASD and abnormal atrioventricular valve) is observed in some cats with supravalvular mitral (ring) stenosis.
• Cardiac output and therefore exercise capacity are limited with atrioventricular valvular stenosis.
• The atrial pressure increases disproportionally with faster heart rates, thereby creating the risk for "flash" pulmonary edema in dogs or cats with mitral stenosis.
• Development of atrial tachyarrhythmias, especially atrial fibrillation, is associated with cardiac decompensation.
• Pulmonary hypertension can develop consequent to MS, leading to exercise intolerance and right ventricular hypertrophy. This can be severe, especially in cats with mitral stenosis.

SYSTEMS AFFECTED
• Respiratory—with MS—bronchial compression from enlarged left atrium, pulmonary edema from left heart failure; potential for hemoptysis due to rupture of pulmonary venous–bronchial venous connections; pleural effusion with atelectasis in tricuspid stenosis or in long-standing MS complicated by pulmonary hypertension or atrial fibrillation.
• Hepatobiliary—with TS—hepatic congestion, ascites.

GENETICS
• Uncertain in most cases.
• Tricuspid valve dysplasia in Labrador retrievers has been localized to a defect in dog chromosome 9 inherited as an autosomal dominant trait with reduced penetrance.

INCIDENCE/PREVALENCE
Rare

GEOGRAPHIC DISTRIBUTION
Worldwide

SIGNALMENT
Species
Dog and cat

Breed Predilections
• MS is overrepresented in bull terriers and Newfoundlands, and in Siamese cats.
• TS has been reported most often in Old English sheepdogs and Labrador retrievers.

Mean Age and Range
Most patients are presented at a young age, although exceptions occur, especially in cats.

Predominant Sex
N/A

SIGNS
Historical Findings
• Exercise intolerance
• Syncope
• Exertional dyspnea or tachypnea
• Cough—MS
• Cyanosis
• Abdominal distention—TS
• Acute posterior paresis—cats with MS and arterial thromboembolism
• Stunted growth
• Hemoptysis from rupture of intrapulmonary vessels—MS

Physical Examination Findings
• Soft diastolic murmur with point of maximal intensity over the left apex (MS) or right hemithorax (TS).
• Holosystolic murmur of mitral or tricuspid regurgitation is more often detected.
• Tachypnea, dyspnea from pulmonary edema or pleural effusion.
• Crackles from pulmonary edema.
• Jugular distention, jugular pulses, ascites, hepatomegaly with TS or biventricular CHF associated with pulmonary hypertension and atrial fibrillation in chronic MS.
• Cyanosis from right to left shunting with TS or from venous admixture and pulmonary edema with MS.

CAUSES
• Usually due to congenital dysplasia of the mitral or tricuspid valve.
• Supravalvular obstructing rings of tissue have been associated with atrioventricular stenosis; this is especially important in cats.
• Infective endocarditis, intracardiac neoplasia, and hypertrophic cardiomyopathy with scarring are rare causes of acquired AV valve stenosis.
• Acquired tricuspid stenosis has been observed due to fibrous scarring of the tricuspid valve in dogs with transvenous pacing leads.

RISK FACTORS
Breed predispositions (see above); see "Risk Factors" for Endocarditis, Infective; permanent transvenous pacing.

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS
Atrioventricular valvular stenosis must be differentiated from the more common causes of mitral and tricuspid regurgitation in the absence of stenosis. These include both congenital and acquired lesions of the atrioventricular valves and support apparatus. Acquired lesions that obstruct the inflow tracts (see "Causes"). Cor triatriatum dexter and cor triatriatum sinister can mimic some of the clinical findings of pure tricuspid and mitral valve stenosis, respectively.

CBC/BIOCHEMISTRY/URINALYSIS
May be normal or reflect changes related to CHF or drug therapy for CHF.

IMAGING
Thoracic Radiography
• Atrial enlargement is the most consistent and outstanding feature; may see generalized cardiomegaly, especially with atrioventricular valve regurgitation.
• MS—may see pulmonary venous congestion and pulmonary edema; intrapulmonary hemorrhage can be misinterpreted as pneumonia or another parenchymal disease.
• TS—may see hepatomegaly; increased diameter of caudal vena cava.

Echocardiography
• Diagnostic test of choice.
• Two-dimensional echocardiography reveals a markedly dilated atrium and attenuated valve excursion during diastole, often with thickened, irregular AV valve leaflets; valve leaflets may appear to "dome" during diastole. A supravalvular obstructing ring also may be evident as well as other lesions (see "Causes" above).
• M-mode studies show an enlarged atrium and concordant motion of the AV valve leaflets indicating commissural fusion; the E-to-F slope is decreased.
• Color-flow imaging reveals a turbulent diastolic jet that originates proximal to the stenotic valve and projects toward the apex of the ventricle; AV valve regurgitation is often present.
• Spectral Doppler studies show increased diastolic transvalvular flow velocities; prolonged calculated pressure half-time is a hallmark feature; E-wave/A-wave amplitude reversal is often evident in cases still in normal sinus rhythm.
• Right-sided chamber enlargements in MS with pulmonary hypertension or with chronic atrial fibrillation.

(CONTINUED) ATRIOVENTRICULAR VALVULAR STENOSIS

• Concurrent defects such as patent foramen ovale, ASD, or bridging septal leaflet.

Angiography

• Right atrium: injection demonstrates a markedly dilated atrium in TS; with concurrent PFO or ASD, opacification of the left atrium is also observed following right atrial injection.
• Might visualize thickened, irregular valve leaflets or a stenotic valve funnel.
• Ventricular injection often reveal valvular regurgitation.
• There can be delayed opacification of the ventricles and great vessels.

Cardiac Catheterization

• A diastolic pressure gradient is identified between the atrium and ventricle. A large "A" wave is common if atrial function is preserved.
• High left atrial, pulmonary capillary wedge, and pulmonary artery pressures occur in MS.
• High right atrial and central venous pressures are present in TS.
• Ventricular pressure may be normal in the absence of concurrent defects.

DIAGNOSTIC PROCEDURES

Electrocardiography

• Variable enlargement and ventricular conduction patterns are observed. Widened or tall P-waves are commonly observed.
• Splintered R-waves are present in some dogs with tricuspid dysplasia.
• Axis deviation due to hypertrophy or ventricular conduction disturbances is relatively common in cats with mitral valve malformation.
• Ectopic rhythms, especially of atrial origin, are often observed. Atrial fibrillation is the most important rhythm disturbance as atrial contribution to filling is lost and the R to R intervals vary with short cycles increasing the mean diastolic gradient.

PATHOLOGIC FINDINGS

• The atrioventricular valve is abnormal, with thickened leaflets and fused commissures. Other lesions may be identified such as a supra-mitral ring (see "Causes").
• Many cases also have abnormal chordae tendineae and papillary muscles.
• Atrial dilation and hypertrophy are common.
• Patent foramen ovale with TS or partial atrioventricular septal defect (primum ASD and bridging septal leaflet) with supravalvular mitral (ring) stenosis.

TREATMENT

APPROPRIATE HEALTH CARE

Patients in overt CHF should be treated with inpatient medical management. Surgical or catheter-based interventions can be considered once heart failure has been stabilized. Control of heart rhythm disturbances, especially AF, is also important. These patients are typically complicated and consultation with a cardiologist is highly recommended. Electrocardioversion of atrial fibrillation should be considered but advanced atrial disease can render the procedure less effective or limit the duration of sinus rhythm.

NURSING CARE

Sedation with butorphanol is appropriate for dyspneic patients. Oxygen therapy should be administered to the patient with dyspnea or hypoxemia from left-sided congestive heart failure. Fluid therapy is typically contraindicated in the patient with overt CHF except in cases of moderate to severe azotemia, renal compromise, or severe dehydration. Therapeutic paracentesis may be considered in the patient with pleural effusions or tympanic ascites.

ACTIVITY

Exercise restriction is important recommended for any animal with this condition because tachycardia increases the mean gradient across the stenotic valve predisposing to pulmonary edema or venous congestion. Cage rest for patients with CHF.

DIET

Feed a sodium-restricted diet to patients in CHF.

CLIENT EDUCATION

The client must be advised of symptoms associated with CHF and the urgency of treatment, particularly with left-sided CHF. The likelihood of recurrent bouts of CHF should also be discussed. Development of atrial fibrillation can lead to marked dcompensation.

SURGICAL CONSIDERATIONS

• Surgical valve replacement or repair requires cardiopulmonary bypass or hypothermia; cost, availability, and high complication and mortality rates are greatly limiting factors.
• Balloon valvuloplasty is an alternative referral treatment and has been used successfully for managing some cases of AV stenosis.

MEDICATIONS

DRUG(S) OF CHOICE

CHF

• Furosemide—dogs, 2–6 mg/kg IV, IM, SC, PO q8–24h; cats, 1–4 mg/kg IV, IM, SC, PO q8–24h.
• ACE inhibitor—enalapril—dogs, 0.25–0.5 mg/kg PO q12h; cats, 0.25–0.5 mg/kg PO q12–24h; see below under "Follow-Up" for patient monitoring.
• Nitroglycerin paste (1/4 to 1 inch topically q12h) to reduce pulmonary venous pressures, but this has not been evaluated critically.

Atrial Tachyarrhythmias

• Digoxin—dogs, 3–5 μg/kg PO q12h; cats, one-fourth of a 0.125-mg tablet PO q24–48h; adjust dosage based on serum concentrations.
• Beta-blockers such as atenolol or the calcium channel blocker diltiazem for suppression of frequent atrial premature complexes and for heart rate control in atrial tachyarrhythmias such as atrial tachycardia/flutter/fibrillation. Beware: using these drugs in uncontrolled CHF.
• Typical atenolol dosages: dogs, 0.25–1.0 mg/kg q12h; cats, 6.25–12.5 mg/cat q12–24h; start low and titrate to effect.
• Diltiazem dosages: dogs, 2–6 mg/kg daily in two (long-acting diltiazem) or three divided dosages; start low and titrate to effect); cats, 7.5 mg diltiazem HCl PO q8h.. Higher dosages are sometimes needed.
• Sotalol for intractable/recurrent arrhythmias—dogs, 1–2 mg/kg PO q12h; cats, 10–20 mg/cat q12h.
• Dogs can be referred for electrocardioversion to convert AF to sinus rhythm (with follow-up therapy with sotalol or amiodarone); however, reversion back to AF is common owing to marked atrial dilatation.

Pulmonary Hypertension

• Sildenafil—dogs, 0.5–3 mg/kg PO q8–12 hours.

PRECAUTIONS

• As a general rule pimobendan is relatively contraindicated in pure valvular stenosis; however, many dogs and cats with advanced CHF have been treated with this drug with apparent success, especially when there is combined stenosis/regurgitation of the valve.
• Use ACE inhibitors or other vasodilators judiciously in patients with CHF; cardiac output is limited and vasodilation may induce hypotension. Monitor arterial blood pressure and renal function.

POSSIBLE INTERACTIONS

• Furosemide and ACE inhibitors can affect kidney function, alter blood electrolytes, and reduce blood pressure; these parameters should be monitored.
• Sildenafil can also reduce systemic blood pressure and should not be used with nitroglycerin paste or other nitrates.

ALTERNATIVE DRUG(S)

Spironolactone (2 mg/kg PO q12–24h) should be considered as an ancillary diuretic and for its antifibrotic benefit (as an aldosterone antagonist).

FOLLOW-UP

PATIENT MONITORING

• Thoracic radiographs for pulmonary edema or pleural effusion.

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ATRIOVENTRICULAR VALVULAR STENOSIS (CONTINUED)

• Echocardiography with Doppler studies—to estimate pulmonary pressures and subjectively assess right heart function if on sildenafil.
• Digoxin level—check 7–10 days following institution of therapy; 8- to 12-hour trough should be 0.8–1.5 ng/mL.
• Renal function, electrolyte status, and arterial blood pressure when on diuretic and/or ACE inhibitor.
• Standard rhythm ECG or Holter (ambulatory ECG) if arrhythmias are present.

POSSIBLE COMPLICATIONS

• CHF
• Atrial fibrillation
• Syncope
• Arterial thromboembolism—cats with MS
• Pulmonary hemorrhage with MS

EXPECTED COURSE AND PROGNOSIS

• Morbidity is high; except for mild cases, prognosis is generally poor once an animal becomes symptomatic. However, some animals will live for many years even with relatively severe stenosis of the mitral or tricuspid valve.
• Surgical intervention or balloon valvuloplasty might alter course of disease, but data are limited.

MISCELLANEOUS

ASSOCIATED CONDITIONS

Concurrent congenital defects are common (e.g., subaortic stenosis in MS, PFO in TS; primum ASD in cats with supravalvular mitral (ring) stenosis).

PREGNANCY/FERTILITY/BREEDING

The possibility that this may be a heritable defect must be considered in assessing suitability of the animal for breeding, particularly in breeds with a predilection for this defect. The additional hemodynamic burden of gestation may be poorly tolerated by an already compromised heart. In general breeding is strongly discouraged.

SYNONYMS

Atrioventricular valve dysplasia with stenosis; supravalvular mitral ring.

SEE ALSO

• Atrioventricular Valve Dysplasia
• Endocarditis, Infective

ABBREVIATIONS

• ACE = angiotensin converting enzyme
• AF = atrial fibrillation
• AV = atrioventricular
• CHF = congestive heart failure
• ECG = electrocardiogram
• MS = mitral stenosis
• PFO = patent foramen ovale
• TS = tricuspid stenosis

Suggested Reading

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AZOTEMIA AND UREMIA

BASICS

DEFINITION

• Azotemia is an excess of urea, creatinine, or other non-protein nitrogenous substances in blood, plasma, or serum.
• Uremia is the polysystemic toxic syndrome that results from marked loss in kidney functions. Uremia occurs simultaneously in animals with increased quantities of urine constituents in blood (azotemia), but azotemia may occur in the absence of uremia.

PATHOPHYSIOLOGY

• Azotemia can be caused by (1) increased production of non-protein nitrogenous substances, (2) decreased glomerular filtration rate, or (3) reabsorption of urine that has escaped from the urinary tract into the bloodstream. High production of non-protein nitrogenous waste substances may result from high intake of protein (diet or gastrointestinal bleeding) or accelerated catabolism of endogenous proteins. Glomerular filtration rate may decline because of reduced renal perfusion (prerenal azotemia), acute or chronic kidney disease (renal azotemia), or urinary obstruction (post-renal azotemia). Reabsorption of urine into the systemic circulation may also result from leakage of urine from the excretory pathways (also a form of post-renal azotemia).
• Pathophysiology of uremia—incompletely understood; may be related to (1) metabolic and toxic systemic effects of waste products retained because of renal excretory failure, (2) deranged renal regulation of fluids, electrolytes, and acid-base balance, and (3) impaired renal production and degradation of hormones and other substances (e.g., erythropoietin and 1,25-dihydroxycholecalciferol).

SYSTEMS AFFECTED

• Uremia affects virtually every body system.
• Cardiovascular—arterial hypertension, left ventricular hypertrophy, heart murmur, cardiomegaly, cardiac rhythm disturbances.
• Endocrine/Metabolic—renal secondary hyperparathyroidism, inadequate production of 1,25-dihydroxycholecalciferol (calcitriol) and erythropoietin, hypergastrinemia, weight loss.
• Gastrointestinal—anorexia, nausea, vomiting, diarrhea, uremic stomatitis, xerostomia, uremic breath, constipation.
• Hemic/Lymph/Immune—anemia and immunodeficiency.
• Neuromuscular—dullness, drowsiness, lethargy, fatigue, irritability, tremors, gait imbalance, flaccid muscle weakness, myoclonus, behavioral changes, dementia, isolated cranial nerve deficits, seizures, stupor, coma, impaired thermoregulation (hypothermia).
• Ophthalmic—scleral and conjunctival injection, retinopathy, acute-onset blindness.
• Respiratory—dyspnea.
• Skin/Exocrine—pallor, bruising, increased shedding, unkempt appearance, loss of normal sheen to coat.

SIGNALMENT

Dog and cat

SIGNS

General Comments

Azotemia may not be associated with historical or physical abnormalities. Unless patient has uremia, clinical findings are limited to the disease responsible for azotemia. Findings described here are those of uremia.

Historical Findings

• Weight loss
• Declining appetite or anorexia
• Reduced activity
• Depression
• Fatigue
• Weakness
• Vomiting
• Diarrhea
• Halitosis
• Constipation
• Polyuria
• Changes in urine volume (increase or decrease)
• Poor haircoat or unkempt appearance

Physical Examination Findings

• Muscle wasting: sarcopenia/cachexia
• Mental depression
• Dehydration
• Weakness
• Pallor
• Petechiae and ecchymoses
• Dull and unkempt haircoat
• Uremic breath
• Uremic stomatitis (including oral ulcers, infarctions of the tongue)
• Scleral and conjunctival injection
• Relative hypothermia

CAUSES

Prerenal Azotemia

• Reduced renal perfusion due to low blood volume or low blood pressure.
• Accelerated production of nitrogenous waste products because of enhanced catabolism of tissues in association with infection, fever, trauma, corticosteroid excess, or burns.
• Increased gastrointestinal digestion and absorption of protein sources (diet or gastrointestinal hemorrhage).

Renal Azotemia

Acute or chronic kidney diseases (primary kidney disease affecting glomeruli, renal tubules, renal interstitium, and/or renal vasculature) that impair at least 75% of kidney function (glomerular filtration rate).

Post-renal Azotemia

Urinary obstruction; rupture of the excretory pathway.

RISK FACTORS

• Medical conditions—kidney disease, hypoadrenocorticism, low cardiac output, hypotension, fever, sepsis, polyuria, liver disease, pyometra, hypoalbuminemia, dehydration, acidosis, exposure to nephrotoxic chemicals, gastrointestinal hemorrhage, urolithiasis, urethral plugs in cats, urethral trauma, and neoplasia.
• Advanced age may be a risk factor.
• Drugs—potentially nephrotoxic drugs, nonsteroidal anti-inflammatory drugs, diuretics, antihypertensive medications; failure to adjust dosage of drugs primarily eliminated by the kidneys to correspond with decline in renal function.
• Toxins—ethylene glycol, grapes (dogs), lilies (cats).

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Dehydration, poor peripheral perfusion, low cardiac output, history of recent fluid loss, high protein diet, or black, tarry stools—rule out prerenal azotemia.
• Recent onset of altered urine output (high or low), clinical signs consistent with uremia, exposure to possible nephrotoxicants or ischemic renal injury, or kidney size normal or enlarged—rule out acute renal failure.
• Progressive weight loss, polyuria, polydipsia, small kidneys, disparate kidney size (cats—big kidney and little kidney), pallor, and signs of uremia that have developed over several weeks to months—rule out chronic renal failure.
• Abrupt decline in urine output and onset of signs of uremia; disparate kidney size (cats—big kidney and little kidney), occasionally dysuria, stranguria, and hematuria; large urinary bladder or fluid-filled abdomen—rule out post-renal azotemia.

CBC/BIOCHEMISTRY/URINALYSIS

CBC

• Nonregenerative anemia (normocytic, normochromic)—often present with chronic renal failure.
• Hemoconcentration—often present with prerenal azotemia; can also be seen with acute renal failure and post-renal azotemia.

Biochemistry

• Serial determinations of serum urea nitrogen and creatinine concentrations may help differentiate the cause of azotemia. Appropriate therapy to restore renal perfusion typically yields a dramatic reduction in azotemia in patients with prerenal azotemia (typically within 24–48 hours). Correcting

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AZOTEMIA AND UREMIA (CONTINUED)

obstruction to urine flow or a rent in the excretory pathway typically is followed by a rapid reduction in the magnitude of azotemia.
• Concurrent hyperkalemia may be consistent with post-renal azotemia, primary renal azotemia due to oliguric renal failure, or prerenal azotemia associated with hypoadrenocorticism.
• Increased serum albumin and globulin concentration suggest prerenal azotemia or a prerenal component.***s***

Urinalysis

• A urine specific gravity value ≥ 1.030 in dogs and ≥ 1.035 in cats supports a diagnosis of prerenal azotemia. Administration of fluid therapy before urine collection may interfere with interpretation of low specific gravity values.
• Azotemic patients that have not been treated with fluids and have urine specific gravity < 1.030 in dogs and < 1.035 in cats typically have primary renal azotemia. A notable exception to this rule is dogs and cats with glomerular disease. Glomerulopathy is sometimes characterized by glomerulotubular imbalance in which adequate urine-concentrating ability may persist despite sufficient renal glomerular damage to cause primary renal azotemia; these patients are recognized by moderate to marked proteinuria in the absence of hematuria and pyuria.
• Urine specific gravity is not useful in identifying post-renal azotemia.

OTHER LABORATORY TESTS

Endogenous or exogenous creatinine, iohexol, or inulin clearance tests or other specific tests of glomerular filtration rate may be used to confirm that azotemia is caused by reduced glomerular filtration rate.

IMAGING

• Abdominal radiographs—used to determine kidney size (small kidneys consistent with chronic kidney disease; mild-to-moderate enlargement of kidneys may be consistent with acute renal failure or urinary obstruction) and to rule out urinary obstruction (marked dilation of the urinary bladder or mineral densities within the excretory pathway).
• Ultrasonography—may detect changes in echogenicity of the renal parenchyma and size and shape of kidneys that support a diagnosis of primary renal azotemia; useful to rule out post-renal azotemia characterized by distension of the excretory pathway and uroliths or masses within or impinging on the excretory pathway and intra-abdominal fluid accumulation (with rupture of the excretory pathway).
• Excretory urography, pyelography, or cystourethrography—may help establish the diagnosis of post-renal azotemia due to urinary obstruction or rupture of the excretory pathway.

DIAGNOSTIC PROCEDURES

Renal biopsy can be used to confirm the diagnosis of primary kidney disease, to differentiate acute from chronic kidney disease, and to attempt to establish the underlying disease process responsible for primary kidney disease.

TREATMENT

• Prerenal azotemia caused by impaired renal perfusion—correct the underlying cause of renal hypoperfusion; aggressiveness of treatment depends on the severity of the underlying condition and the probability that persistent renal hypoperfusion will lead to primary renal injury or failure.
• Primary renal azotemia and associated uremia—(1) specific therapy directed at halting or reversing the primary disease process affecting the kidneys, and (2) symptomatic, supportive, and palliative therapies that ameliorate clinical signs of uremia; minimize the clinical impact of deficits and excesses in fluid, electrolyte, acid-base balances; minimize the effects of inadequate renal biosynthesis of hormones and other substances, and maintain adequate nutrition.
• Post-renal azotemia—eliminate urinary obstruction or repair rents in the excretory pathway; supplemental fluid administration is often required to prevent dehydration that may develop during the solute diuresis that follows correction of post-renal azotemia.
• Fluid therapy—indicated for most azotemic patients; preferred fluids include 0.9% saline or lactated Ringer's solution. Determine fluid volume to administer on the basis of severity of dehydration or volume depletion. If no clinical dehydration is evident, cautiously assume that the patient is less than 5% dehydrated and administer a corresponding volume of fluid. Generally provide 25% of calculated fluid deficit in the first hour. Thereafter, serially monitor perfusion (capillary refill time, pulse pressure, heart rate, and temperature of feet), blood pressure and urine output to assess adequacy of fluid therapy. If perfusion has not improved, additional fluid should be administered. Provide the remaining fluid deficit over the next 12–24 hours. Fluid therapy should be cautiously administered to patients with overt or suspected cardiac failure and patients that are oliguric or anuric.
• Treat patients in shock appropriately.
• Consider feeding diets formulated for kidney disease to reduce the magnitude of azotemia, hyperphosphatemia, and acidosis.

MEDICATIONS

DRUG(S) OF CHOICE

• Symptomatic therapy may be indicated for uremia in patients with kidney disease.
• Famotidine (0.5–1.0 mg/kg PO, SC, IM, IV q12–24h) or other H_2-receptor antagonists may be used to reduce gastric hyperacidity and nausea (dogs).
• Antiemetics such as maropitant (1 mg/kg q24h PO or SC for 5 days) are indicated for vomiting.

CONTRAINDICATIONS

Administration of nephrotoxic drugs

PRECAUTIONS

• Use caution when administering drugs requiring renal excretion. Consult appropriate references concerning dose-reduction schedules or adjustments of maintenance intervals.
• Use caution in administering fluids to patients that are oliguric or anuric. Monitor urine production rates and body weight during fluid therapy to minimize the likelihood of inducing overhydration.
• Stop fluid therapy in overhydrated oliguric/anuric patients. Use caution in administering drugs that may promote hypovolemia or hypotension (e.g., diuretics); carefully monitor the response to such drugs by assessing hydration status, peripheral perfusion, and blood pressure, with serial evaluation of renal function tests.
• Corticosteroids may worsen azotemia by increasing catabolism of endogenous proteins.

ALTERNATIVE DRUG(S)

N/A

FOLLOW-UP

PATIENT MONITORING

Serum urea nitrogen and creatinine concentrations 24 hours after initiating fluid administration; also urine production, body weight, and hydration status.

POSSIBLE COMPLICATIONS

• Failure to correct prerenal azotemia caused by renal hypoperfusion rapidly could result in ischemic primary kidney disease.
• Primary renal azotemia can progress to uremia.
• Failure to restore normal urine flow in patients with post-renal azotemia can result in progressive renal damage or death due to hyperkalemia and uremia.

MISCELLANEOUS

ASSOCIATED CONDITIONS

An association may exist between hypokalemia and azotemia in cats. Preliminary findings suggest that hypokalemia may be associated with functional or structural renal changes leading to azotemia.

AGE-RELATED FACTORS

Primary renal failure may occur in animals of any age, but geriatric dogs and cats appear to be at substantially higher risk for both acute and chronic kidney disease. However, do not assume that azotemia in geriatric dogs and cats indicates primary kidney disease; these patients are also at higher risk for prerenal and post-renal causes for azotemia.

ZOONOTIC POTENTIAL

Leptospirosis

PREGNANCY/FERTILITY/BREEDING

- Data on azotemia and pregnancy in dogs and cats are very limited. Humans may tolerate minimal renal disease well during pregnancy; however, ability to sustain a viable pregnancy declines as renal function declines.
- Pregnant azotemic animals—pharmacologic agents excreted by non-renal pathways are preferred.

SEE ALSO

- Chapters on acute and chronic kidney disease
- Urinary Tract Obstruction

INTERNET RESOURCES

International Renal Interest Society (IRIS): www.iris-kidney.com.

Suggested Reading

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