ALL THOSE COCKERS CAN’T HAVE PRIMARY GLAUCOMA!

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INTRODUCTION
The popularity of cocker spaniels and the high incidence of ocular disease in the breed make cockers a very important part of an ophthalmology practice. Primary inherited glaucoma is the most devastating ocular disease seen in this breed. This breed is also a perfect ‘case study’ for glaucoma in all breeds. Two crucial determinations must be made in dealing with glaucoma. This disease must first be differentiated from other ocular diseases (some inherited) with similar clinical signs. The cocker exemplifies the value and importance of knowing the breed incidence of ocular diseases. Secondly, primary glaucoma must be differentiated from secondary glaucoma. Without these two determinations, effective therapy is impossible and a reasonable prognosis cannot be established.

This lecture emphasizes the correct diagnosis of glaucoma and the differentiation of primary vs. secondary glaucoma. The diseases most frequently misdiagnosed as glaucoma and the reasons for this error will be discussed. Several diseases, such as episcleritis, endothelial dystrophy, facial paralysis, phacolytic uveitis, keratoconjunctivitis sicca, and progressive retinal atrophy, also have a breed predisposition in cockers. Other diseases, such as anterior uveitis with multiple etiologies, serous retinal detachment, optic neuritis, chorioretinitis, sudden acquired retinal degeneration, and retrobulbar masses, when they occur in the cocker spaniel, are often misdiagnosed as glaucoma.

GLAUCOMA-DIAGNOSIS
A diagnosis of glaucoma cannot be made based solely on clinical signs. This is because in the early stages of primary glaucoma, the signs and intraocular pressure may fluctuate. It is quite possible to measure the IOP and find that it is within the normal range. However, before a definitive diagnosis of glaucoma can be made, an elevated IOP must be demonstrated.

Tonometry is the technique of determining intraocular pressure. Normal IOP in the dog is reported to be 10mmHg - 25mmHg. The normal range will also vary with instrumentation. There should be a difference of no more than 8mmHg between the two eyes. A diurnal variation in IOP in the dog results in higher IOP in the morning. Glaucomatous eyes show a greater daily variance.

Applanation tonometry is economically feasible for the general practitioner. The Tono-pen X-L (Dan Scott, 1-888-TONOPEN Columbus, Ohio) is a miniaturized tonometer slightly larger than a fountain pen. It yields an accurate digital read out of IOP. It is expensive, but in my opinion, the instrument of choice if you are going to screen animals for glaucoma or monitor the response to therapy. The Tono-pen Avia is the
latest version. It does not require calibration and is ergonomically better designed. IOP in normal dogs ranges from 10-15mmHg with these tonometers.

Even if the only technique available is digital, the IOP must be determined to make the diagnosis of glaucoma. To say that an eye "looks" hard and then treat for glaucoma will lead to frequent misdiagnoses.

Ophthalmoscopy, either direct or indirect, is important as a diagnostic procedure, but possibly even more important in determining the prognosis for vision after the IOP is controlled. If by examination, it is determined that an eye is irreversibly blind, the choice of therapy is significantly different from that of a potentially visual eye. This difference will be discussed under treatment. Gonioscopy is performed by ophthalmologists to diagnose and confirm primary glaucoma. This not a procedure the general practitioner will be performing.

MISDIAGNOSIS
The misdiagnosis of glaucoma is most frequently caused by the failure to measure the intraocular pressure of the case presented. The diagnosis is based erroneously on one or more of the "cardinal signs" of glaucoma. The following is a brief discussion of the diseases that have frequently been misdiagnosed as glaucoma.

Episcleritis/scleritis is common in the cocker spaniel as a unilateral or bilateral disease that is believed to be immune mediated. It may present as a nodular or diffuse scleral swelling. Secondary vascularization and edema of the cornea is common. Posterior scleral involvement may result in optic neuritis and retinal detachments. Involvement of the uvea may lead to anterior uveitis. Treatment consists of topical corticosteroids, cyclosporine or tacrolimus and in some cases, oral corticosteroids and azathioprine. Cases are controlled but never cured.

Endothelial dystrophy is normally a bilateral disease in older cocker spaniels. The diffuse corneal edema may be associated with superficial vessels, epithelial bullae, and superficial and deep ulcerations. Treatment consists of topical hyperosmotics in the form of sodium chloride ointment. In many cases, topical corticosteroids are needed to control corneal vascularization. Control of the disease in early cases is usually possible. Thermokeratoplasty and superficial stromal keratectomies followed by a thin conjunctival flap are two procedures used in cases by veterinary ophthalmologists.

Facial paralysis in the cocker is most often associated with chronic otitis media. In some cases hypothyroidism has been incriminated as the cause. In addition to the lack of a blink response and the wide palpebral fissure resulting in the increase "scleral show", the lip and ear on the affected side may droop or sag. Drooling from the affected side of the mouth is common. Associated keratoconjunctivitis caused by exposure or decreased tear production is common. Treatment is aimed at correcting the primary cause and protecting the globe with tear replacements, antibiotic and anti-inflammatory drugs. Once the disease progresses to the "contracture phase" with reduced palpebral fissure, pulled lip, and deviated nose, the condition is irreversible.
Progressive retinal atrophy in the cocker spaniel is normally a slowly progressive disease. However, in some cases, the owners are unaware of the disease until late in the course when the dog’s pupils become dilated and unresponsive. When presented at this stage, they may be misdiagnosed as glaucoma.

Sudden acquired retinal degeneration (SARD) presents as an acute blindness. The dilated and often sluggish pupils and associated conjunctivitis lead to the diagnosis of glaucoma. The correct diagnosis is presumed based on history and ophthalmoscopic examination showing tapetal hyperreflectivity and sacculation of vessels. The diagnosis is confirmed by electroretinography.

Anterior uveitis in the cocker may be caused by many infectious, neoplastic and immune mediated diseases. Young cockers, often less than a year of age, can be presented with an acute onset of unilateral or bilateral lens induced or phacolytic uveitis. This is caused by the rapid maturation of the cataract and liquefaction of lens protein, followed by leakage of protein through the lens capsule. All cases of anterior uveitis have the potential to become secondary glaucoma. Intraocular pressure should be closely monitored. Treatment first consists of identifying and treating the primary etiology when possible. Topical mydriatics and cycloplegics, i.e. atropine, are usually indicated. Based on severity and etiology, topical and/or systemic corticosteroids and NSAIDS are also indicated.

Acute blindness, due to posterior segment disease, may be seen in the cocker spaniel as in any breed. Chorioretinitis from a multitude of etiologies including infectious, neoplastic, metabolic, and toxic have been seen in cocker spaniels. Optic neuritis due to cryptococcosis, scleritis, and presumed immune mediated disease has been reported. All of these cases have been misdiagnosed as glaucoma due to the acute blindness, dilated pupils, associated conjunctivitis, and the simple fact that they occur in the cocker. Treatment is dependent on the etiology and associated ocular and systemic diseases.

Keratoconjunctivitis sicca in the cocker spaniel is a common and primary disease. Cases may also be caused by any and all of the reported etiologies of KCS. Advanced cases are misdiagnosed as glaucoma due to the corneal and conjunctival involvement and decreased vision. The backbone of treatment consists of cyclosporine and/or tacrolimus, tear replacements, and antibiotics with or without corticosteroids.

Retrobulbar tumors, myositis, and abscesses can be presented in any breed. The associated exophthalmia, ocular pain, and hyperemia often lead to the incorrect diagnosis of glaucoma. Treatment and prognosis is dependent on identifying the etiology through fundic examination, ocular ultrasound, and radiographs.

**PRIMARY GLAUCOMA**

Primary glaucoma, a rise in intraocular pressure without any “obvious” prior ocular disease, is common in the cocker spaniel. Cockers have a presumed inherited defect
resulting in an abnormal development of pectinate ligaments. This condition, called goniodysgenesis, can range from a thickened ligament to a band of tissue which blocks the drainage angle. Once “clinical” glaucoma is present, evaluation of the angle in the affected eye is difficult and often not diagnostic. Histological examination is always indicted in the “first” eye with glaucoma. Goniodysgenesis in the enucleated eye tells you that the remaining “normal” eye is predisposed to a rise in IOP. Examination of the fellow eye by gonioscopy is indicated and usually diagnostic. A direct correlation between gonioscopy findings and IOP is not always present.

SECONDARY GLAUCOMA
Secondary glaucoma is a rise in IOP following other ocular diseases that interfere with the normal outflow pathway of aqueous. The most common causes of secondary glaucoma in the cocker include anterior uveitis due to multiple etiologies (phacolytic and sclerouveitis), and anterior lens luxations. Initially, the IOP may be low to normal due to decrease production of aqueous by the inflamed ciliary processes. As the inflammation is successfully treated, the ciliary processes again produce more aqueous. If the outflow pathway is blocked by a broad peripheral anterior synechia, a complete posterior synechia, or anterior lens luxation, the IOP will start to rise above normal. For this reason, it is mandatory to monitor the pressure during the treatment of anterior uveitis.

The differentiation of primary from secondary glaucoma is aided by the knowledge of the causes of secondary glaucoma and close examination of the fellow eye, which may include gonioscopy of the drainage angle, detection of a mild aqueous flare, or lens subluxation.

TREATMENT-EMERGENCY GLAUCOMA
Acute congestive glaucoma is frequently presented as an emergency. These individuals are presented with all of the cardinal signs of glaucoma, (steamy cornea, episcleral injection, dilated pupils & blindness) plus IOP greater than 60mmHg. Seldom does the IOP rise rapidly from normal. These cases are usually the result of chronic primary glaucoma or secondary glaucoma due to anterior uveitis or anterior lens luxation. They are true emergencies because, regardless of cause, if the IOP remains elevated in the range of 60mmHg for greater than 24 hours, the prognosis for vision is very poor. It is important to differentiate primary from secondary glaucoma, since the etiology significantly affects the treatment.

In all cases of acute glaucoma, IV flunixin meglumine (Banamine®, Schering Corp.) or sub-Q carprofen (Rimadyl® Pfizer) will reduce the signs of pain. Its most significant effect is seen in secondary glaucoma. Systemic corticosteroids are indicated in secondary glaucoma (except those cases secondary to mycotic disease). Their efficacy in primary glaucoma is questionable, but can do no harm.

Systemic hyperosmotics are one means of rapidly lowering IOP in cases of acute primary glaucoma. Hyperosmotics should not be used in the treatment of acute secondary glaucoma.
Oral glycerin (2.2ml/kg) or IV 20% mannitol (11ml/kg) is given. In secondary glaucoma, the value of these drugs may be reduced. This is especially true in cases of active inflammation since the blood vitreous barrier is not intact. In these cases, mannitol, due to its greater molecular weight, may be the hyperosmotic of choice. Hyperosmotics are beneficial in cases of anterior lens luxation. The hyperosmotics should not be repeated more than twice during a 48 hour period. Water must be withheld for two to four hours. Glycerin may cause emesis and a transient diarrhea. Hyperosmotics frequently lower the IOP in primary glaucoma in 30 to 40 minutes. Furosemide has no effect on IOP. The choice of miotic versus mydriatic is not always clear-cut and is very critical. If severe corneal edema prevents visualization of the pupil or if you cannot decide between primary and secondary glaucoma, their use should be delayed until the previous treatment response is evaluated.

In cases of known primary glaucoma, 1% pilocarpine is given every 15 minutes for one hour and then every two to four hours for the next 48 hours. The miotic effect of pilocarpine is not instantaneous. Ocular irritation, hypersalivation, and diarrhea are possible side effects.

Latanoprost (Xalatan® Upjohn; generic) and travoprost (Travatan® Alcon Lab. Inc.) are products that are being used by ophthalmologists. These drugs have been used to quickly lower the IOP in primary glaucoma. One drop has lowered IOP from a 60mmHg to less than 20mmHg in a half an hour! Severe miosis is associated with the hypotensive affect and could complicate a secondary glaucoma due to anterior uveitis or anterior lens luxation. This procedure has replaced the use of hyperosmotics and pilocarpine in the treatment of acute glaucoma.

In cases of known secondary glaucoma due to miosis with posterior synechia or primary anterior lens luxation, mydriatics are indicated. Atropine 1% every 15 minutes for one hour then every 12 to 24 hours is the drug of choice. Systemic atropinization is possible. In addition to the cardiac effect and decrease salivation, decrease tear production is possible. STT should be evaluated prior and during treatment.

Systemic corticosteroids are continued in secondary glaucoma if not contraindicated due to a specific infectious disease. Topical prednisolone or dexamethasone products are started every four to six hours.

Antiprostaglandin therapy is continued in secondary glaucoma using carprofen (Rimadyl® Pfizer). Topical .03% flurbiprofen sodium (Ocufen® Allergen Lab., generic) or diclofenac (Voltaren® Ciba Vision) is instituted in severe cases every 4-6 hours.

After the initial therapy, treatment will continue for the next 48 hours based on etiology of the glaucoma. Carbonic anhydrase inhibitors are given orally in primary glaucoma. Their use in secondary glaucoma is greatly reduced since they only act on the active production of aqueous, which is already reduced in cases of active inflammation.
Surgery is seldom indicated on an emergency basis. Paracentesis of aqueous is never indicated.

**MEDICAL TREATMENT OF PRIMARY GLAUCOMA**

Carbonic anhydrase inhibitors (C.A.I.) are used to reduce the active production of aqueous by no more than 50%. Since the total production of aqueous is approximately 50% active and 50% passive, C.A.I. can reduce total production by only ~25%. Seldom do they alone control an elevated IOP. Maximal effect is seen 4-8 hours after administration. Dichlorphenamide and methazolamide are chosen primarily due to decreased incidence of side effects. The side effects of C.A.I. include polyuria and polydipsia and gastric irritation and emesis. Acidosis manifested by rapid breathing, emesis, diarrhea, and salivation; uneasiness is also possible. This, if it occurs, is usually transient and requires no specific treatment, but the dosage of the C.A.I. should be reduced. Hypokalemia is also possible and this is manifested primarily by muscular weakness and mental confusion. This can be treated by salting the animal's food with a potassium salt, feeding bananas, or giving a potassium replacement such as potassium gluconate (Koan® Elixir, Adrea Lab., 20mEq/15ml or Tumil-K® tab., 2mEq, Daniels Pharm, Inc.). This hypokalemia is not life threatening but the C.A.I dosage may have to be reduced. Urticaria has also been reported in dogs.

Two topical C.A.I., 2% dorzolamide hydrochloride (Trusopt® Merck and Co., Inc.,generic) and 1% brinzolamide (Azopt®, Alcon), are now available. Topical administration should eliminate the side effect of gastric irritation. Whether the hypotensive effect is due to direct action at the nonpigmented ciliary epithelium or through systemic adsorption is not clear. Both drugs are used t.i.d. A severe blepharitis has been seen rarely with the use of these drugs.

Parasympathomimetics are used in the treatment of primary glaucoma because they increase the coefficient of outflow or the rate at which aqueous leaves the drainage angle. Their miotic effect is not directly correlated with their ability to increase aqueous outflow but can be used as a rough indicator. In the case of greatly elevated pressures, the miotic effect of these drugs is limited until the pressure is lowered with hyperosmotics. Pilocarpine 1% or 2% is used initially every four to six hours. Higher concentrations show little to no additive hypotensive effect and can be very irritating. A 4% pilocarpine gel (Pilopine® HS Gel, Alcon) has been used at bedtime in place of the lower concentration solutions. The clients should be advised that in most cases initial irritation from topical pilocarpine will be manifested by chemosis, hyperemia, and blepharospasms. A severe miosis and aqueous flare may be detected. In the vast majority of cases, this is transient and the owners are requested to continue the medication for 72 hours before a decision is made to switch or discontinue the drug. Diarrhea, even hemorrhagic, and hypersalivation are also possible side effects that will have to be monitored and dealt with accordingly. Pilocarpine is not routinely used today by veterinary ophthalmologists in either acute or chronic glaucoma due in part to the popularity of the prostaglandins.
Demecarium bromide (Wedgewood Pharmacy), is a cholinesterase inhibitor with similar action to pilocarpine. Its primary use is in the control of I.O.P. following initial treatment with pilocarpine. It is also used in treating the "normal" eye with gonioscopically-affected angles, as in many cocker spaniels. It has been used successfully in cases in which pilocarpine was not tolerated. Demecarium bromide is effective when used twice daily. The owners are instructed that the pupil should be miotic every time they treat. Although this is not an absolute, the pupil getting large between treatments may indicate a rise in I.O.P.

Sympathomimetics decrease aqueous production and increase aqueous outflow. They are synergistic with the parasympathomimetics and C.A.I. and are especially used in combination with these drugs. Epinephrine and dipivefrin solutions are available. Personal preference is .1% dipivefrin HCL (Propine®, Allergan or Dipivefrin HCL Ophthalmic Solution USP, O.1%, Falcon). Dipivefrin is an epinephrine prodrug that penetrates the cornea 17 times as readily as epinephrine and is converted to epinephrine in the uvea. It has minimal mydriatic effect. Like pilocarpine, these normally cause transient irritation. Superficial neovascularization of the cornea can be a problem with long-term therapy and may result in discontinuation of the drug. These drugs are usually used twice daily. Due to their decreased use in human glaucoma therapy, these drugs may soon be discontinued and are seldom used.

Prostaglandin analogues (Latanoprost, Xalatan® Pfizer, generics; Travoprost, Travatan®, Alcon Lab; Bimatoprost, Lumigan®, Allergan) are also available for the treatment of glaucoma. Various generic forms of latanoprost have been purchased out of Canada, but their efficacy has been questioned. The generic drug, now available from MWI has been proven to be effective and very economical. They are prostaglandin F analogues, and increase uveoscleral outflow. Severe miosis is associated with their use and a post-application rise in IOP caused by pupillary block has been reported. These drugs are used once or twice daily and are extremely expensive when generics are not dispensed. Using these drugs in cases of secondary glaucoma can have severe sequelae due to the potent miotic effect of the drugs.

Drugs from different classes are frequently used together in the control of glaucoma. However, two drugs from the same class show little additive hypotensive effect. Ideally, the IOP should be less then 20mmHg when reevaluated to be considered well controlled. I like to measure the IOP just prior to treatment assuming the IOP will be at its highest level. I personally do not use combination drugs such as P2EI, etc. The beta-adrenergic blocking agents have limited efficacy in the dog, in my opinion.

**MEDICAL TREATMENT OF SECONDARY GLAUCOMA**

These cases are usually controlled as described under emergency treatment. Controlling the inflammation prevents a return of the transient rise in intraocular pressure. Broad peripheral synechia and narrowing of the drainage angle may be the result of anterior uveitis. In this case, if the inflammation is under control and the IOP rises, C.A.I. may be of benefit. Topical pilocarpine and other miotic are contraindiicted
and will usually cause increase inflammation which may indirectly reduce IOP, but will not help control the uveitis or prevent recurrence of glaucoma.

SURGICAL TREATMENT
Surgery is indicated in the visual eye that cannot be controlled with medication. Surgery is also indicated in the irreversibly blind eye regardless of its response to medical therapy. The choice of surgery depends on the cause of glaucoma, the potential for vision, general health of the animal, and the owners' personal preference. Secondary glaucoma may require an iridectomy or lens extraction. Filtering procedures such as a cyclodialysis and iridencleisis have a poor success rate in the dog with primary glaucoma. Implants to aid in filtering of aqueous are used by some veterinary ophthalmologists. Transcleral cyclophotocoagulation and transcleral cyclocryosurgery, have been used to selectively destroy ciliary processes in the visual eye that is not controlled with medication. Selective destruction of the ciliary body reduces the production of aqueous. The newest procedure, called endoscopic cyclophotocoagulation (ECP) is currently being used at limited facilities. This procedure is much more invasive and expensive but appears to have fewer complications than previous procedures.

The blind eye is operated on to reduce ocular pain and, hopefully, to discontinue or reduce treatment depending on the other eye. Enucleations, cyclocryosurgery, injections into the vitreous to destroy the ciliary processes or an intraocular prosthesis are the options available to the owner. Personal preference is an intraocular prosthesis if the owner wants a cosmetic globe. In addition to the consideration of comfort of the animal, all of these procedures are economically feasible when you consider the cost of drugs to control IOP in a middle-age dog for the remainder of his life.