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Bearded Collies and Autoimmune Disease

Presenting Signs, Tests and Treatment
By: Linda Aronson

General: Although sex and age predilections have been noted in the literature, we find that these tend to serve as red herrings, autoimmune disease can, and does, show up in any age or sex of dog. There is genetic predisposition to many, if not all, immune-mediated diseases. Various stressors have been associated with onset - obstetrical complications; recent illness or infection; surgery, ambient temperature extremes and psychological stress (including kenneling, hormonal changes - estrous, pseudocyesis, pregnancy and parturition), environmental disruption). Drugs and environmental chemicals also appear to play a role in inducing disease in genetically susceptible animals.

Hypothyroidism:

Comments: **The most common autoimmune and endocrine problem. In and of itself, hypothyroidism is an easily treatable problem. However, it predisposes dogs to other autoimmune diseases, and attempts should be made to breed against this condition in the bearded collie.**

Signalment: **Classic signs of bilateral alopecia; obesity; lethargy; mental dullness; hyperpigmentation; dry hair coat; constant shedding; pyoderma; hypothermia (especially of the distal extremities) etc. generally only become apparent when 2/3rds of the gland has been destroyed. Earlier signs may include behavioral changes - aggression, hyperactivity, inattention, fearfulness (including thunderstorm and other sound phobias), separation anxiety; seizures; chronic ear infections; lick granuloma; skin and coat problems; dog which fatigues easily. Behavioral signs seem to occur particularly early in the course of the disease. Reproductive problems, including testicular dysgenesis, may be among the first signs observed.**

Diagnostic tests: **In order to diagnose hypothyroidism several protocols have been suggested. My preferred test panel includes: total and free thyroxine (T4) and triiodothyronine (T3), as well as T4 and T3 autoantibodies. Another recommended protocol calls for measurement of free T4 by equilibrium dialysis; canine TSH (thyroid stimulating hormone) and thryoglobulin autoantibody levels. It should be remembered that there will be significant differences between different labs, and it is recommended that the same lab should be used for all testing, particularly when comparing results on a single dog. In many, if not all cases, normal levels have been determined from animals which appear on observation to be free of disease, whereas it is probable that many of these were in the early stages of the disease. When testing animals for breeding it is recommended that thyroid levels be in the upper 50% of normal, particularly if the animal being tested is less than 15-18months of age. We have found that treating animals with thyroid levels in the lower 25% of the normal range has brought significant behavioural improvement.**

Thyroid levels are influenced by stress and other hormones, as well as by disease states (sick euthyroid syndrome). When testing intact bitches, it is best if the blood is drawn three months from the onset of the previous heat period. Animals should not be rejected for breeding on the basis of a single thyroid panel. Panels should be repeated every 12-l8 months on animals being used for reproduction.

Treatment: **Dogs should be treated with levothyroxine sodium in a nongeneric, veterinary formulation, at a dosage of 0.1mg/12 to l5lbs body weight q 12h. (Twice daily dosing is essential for optimal response to therapy.) Some dogs appear unable to convert T4 to T3, and may require additional supplementation with iodothyronine sodium, at a dose of l ug/lb body weight q8h. In our experience these are often dogs with high levels of T3 autoantibodies. Because it is extremely difficult to induce hyperthyroidism in the dog, it is recommended that any dog in the low normal range with signs of disease be treated for 6 to 8 weeks. If the problems appear to resolve, retest thyroid and continue medication.**

Hypoadrenocorticism (Addison's Disease):

Comments: **The second most common autoimmune disease in the breed. Most beardies with hypoadrenocorticism appear to also be hypothyroid. Treating the**

thyroid appears to increase life span, and make it possible to maintain the dog on lower levels of other, more expensive, medication.

Signalment: **These are typically vague and include: lethargy; depression; gastrointestinal disorders - including vomiting, diarrhea, sudden weight loss, anorexia, melena; weakness, especially in rear limbs +/- collapse; shaking; polyuria/polydypsia (PU/PD)(>50% of dogs have impaired ability to concentrate urine); bradycardia. Signs may wax and wane. Onset may be quite sudden, and dogs may just drop dead. Stress, illness or drug administration may precede onset.**

Diagnosis: **Elevated serum potassium and low serum sodium levels, with a Na/ of <27 is found in 95% of cases. Azotemia is present in 85%. ECG should be taken, as hyperkalemia may be life-threatening - QRS prolongation, decreased R-wave amplitude, increased T-wave amplitude, P-R interval prolongation, absence of P waves. Radiographs may show microcardia, narrowing of the descending aorta or the vena cava, hypoperfused lung fields. ACTH stimulation test: with ACTH gel, serum cortisol levels are taken before and 2 hours after intramuscular injection of 20 U; with synthetic ACTH, serum cortisol levels are taken before and one hour after intravenous injection of 5-10 ug/kg. The ACTH response test can be done immediately or after the dog has been stabilized with parenteral fluids and dexamethasone sodium phosphate administration (this is the only glucocorticoid which doesn't affect cortisol levels). Hyperkalemia, hyponatremia and subnormal cortisol response to ACTH administration is diagnostic. About 5% of dogs do not show elevated potassium levels and diagnosis is based on the results of the ACTH stim test. Plasma ACTH levels can be used to discriminate primary (atrophy of adrenal glands - elevated ACTH) from secondary (deficient pituitary ACTH production - low or undetectable ACTH) disease.**

Treatment: **Acute presentation is life-threatening, and treatment should be instituted as soon as blood and urine have been taken for testing if the disease is suspected. Rapid administration of large volumes of intravenous fluids (60 to 80ml/kg/h for 1 to 2 hours) - preferably 0.9% NaCl, although the small amount of potassium in lactated Ringer's solution does not preclude its use if it is all that is available. Intravenous administration of dexamethasone sodium phosphate (2 to 4 mg/kg) can be repeated in 2 to 6 hours as needed. Glucocorticoids are gradually tapered to maintenance levels and may eventually be discontinued completely in the majority (>50%) of cases, (they must be continued if the dog has secondary disease). Oral administration of**

fludrocortisone acetate (Florinef) should be instituted immediately. Dogs with secondary hypoadrenocorticism may not require mineralocorticoid therapy, provided their serum electrolyte levels are normal.

For less severe presentations, fluids and glucocorticoids may be necessary. Either fludrocortisone or desoxycorticosterone pivilate (DOCP) can be used for the long term treatment of the disease. Florinef is started at a dose of 0.01 to 0.02 mg/kg daily, divided into two doses. Total daily dose is adjusted by 0.05 to 0. 1 mg increments based on serum electrolyte response. These should be monitored weekly, until the patient has stabilized, and then monthly for 3 to 6 months. BUN or creatinine should be measured at the same time. Electrolytes and BUN/creatinine should be measured every 3 to 6 months thereafter. Dosage may need to be increased, especially during the first two years of treatment due to further adrenal tissue loss. Most dogs are maintained on 0.02 to 0.03 mg/kg/24h. Most common side-effect is PU/PD. This, together with resistance to the drug, or the expense of the Florinef are among the reasons many owners choose to switch their dog to DOCP. This is given at an initial dose of 2.2mg/kg intramuscularly or subcutaneously at approximately I month intervals. After the first 2 or 3 injections, serum electrolyte levels should be determined 2, 3 and 4 weeks post injection. Once the electrolyte levels have stabilized, electrolyte levels are taken just prior to the next injection to monitor duration of effect, which is dog dependent. Most dogs do well at the above dose, but the effect lasts for a variable period (14 to 35 days), in most dogs the dose needs to be repeated every 3 to 4 weeks. It may be necessary to increase the dose of DOCP, over the life of the dog. DOCP has no glucocorticoid activity, as Florinef does, and has not been associated with PU/PD. The addition of salt to the diet has not been shown to reduce the dosage of mineralocorticoid necessary to maintain dogs with hypoadrenocorticism. Thyroid supplementation may increase longevity and reduce the dosage of mineralocorticoid required. Clients should probably be provided with prednisone to dose their dogs as needed when they are subjected to unusual stress.

Inflammatory bowel disease:

Comments: **Probably a group of diseases rather than a single disease. For this reason a multiplicity of different treatments may have to be attempted in order to control the condition.**

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Signalment: **Chronic vomiting and/or diarrhea, which is not caused by bacteria, virus, protozoa, parasite or other etiology. Type of diarrhea is determined by which areas of the gastrointestinal tract are involved. (A possible variant of this disease, seen in beardies, is episodic hemorrhagic gastroenteritis. The dogs have typical signs of HGE, most notably copious foul smelling stools which have a consistency ranging from raspberry jam to frank pools of blood, but which is generally transient, lasting <24h, and recurs when the animal is stressed - dietary indiscretion, physical or emotional stress. This does not respond to treatment as described below, and while alarming to the owner does not seem to disturb the dogs unduly. Abdominal pain before episodes is marked, and dogs often assume the bow/praying position seen in pancreatitis.)**

Diagnosis: **Exclusion of other causes of vomiting/diarrhea. Endoscopy and sampling of mucosal lining of the gastrointestinal tract, areas affected may include stomach, small and/or large intestine. Disease is characterized by predominant inflammatory cell type, the most common form being lymphocytic/plasmacytic followed by eosinophilic.**

Treatment: **Dogs are usually placed on hypoallergenic diets using ingredients to which the dog has not previously been exposed. While this may prove curative in the short term, the dog will generally become allergic to the new diet. If dietary management is non-curative, animals are usually given 20 to 50 mg/kg sulfasalazine to a maximum of q8h, in combination with 10 to 20mg/kg metronidazole q8 to 12h. The most common side-effect of the former is keratoconjunctivitis sicca (KCS) which is generally not responsive to cyclosporine. Vomiting can usually be limited by administering sulfasalazine with food. Neuropathy has been reported in beardies treated with metronidazole. Prednisone can be given in conjunction with the above protocol, to reduce the required dose of sulfasalazine, or in place of sulfasalazine if the drug is not tolerated and the dog's condition is not controlled by metronidazole alone. (Limited trials of some of the newer mesalamine preparations developed for human patients have been conducted in dogs which do not tolerate sulfasalazine, but they generally still produce KCS.) Prednisone or prednisolone is initiated at a dose of 1 to 2 mg/kg q 24h. This dose should be halved 4 weeks after the dog's stools have returned to normal. It should then be tapered to the lowest effective dose (usually 0.5 to 1.O mg/kg q 48h). Tylosin 5 to 100mg/kg q 12h may be curative in some patients. If none of the previously described therapies have been successful, treatment may be attempted with azathioprine at 2mg/kg q24h. It may take several months for treatment to be effective, and**

CBC and platelet counts should be monitored every I to 2 weeks for evidence of myelosuppression.

Immune-mediated hemolytic anemia:

Comments: **Immune destruction of red blood cells resulting in extravascular and occasionally intravascular hemolysis. Anemia is typically regenerative. The condition frequently occurs in conjunction with immune-mediated thrombocytopenia. May occur subsequent to vaccination or administration of the drug levamisole. Animals which recover may suffer from further episodes of disease.**

Signalment: **Sudden onset of exercise intolerance; pale mucous membranes; tachycardia; hyperpnea; fever and icterus may also be seen.**

Diagnosis: **Anemia with evidence of hemolysis (hyperbilirubinemia, bilirubinuria and/or hemoglobinuria) with a positive direct Coomb's test or persistent autoagglutination after saline washing, and/or spherocytosis. Extreme variation in RBC diameter is noted.**

Treatment: **Steroid suppression of erythrophagocytosis - prednisone or prednisolone 2 to 4 mg/kg q 24h for 2 to 3 weeks minimum and until an increasing hematocrit has been established. Dosage can then be reduced gradually, while monitoring for recurrence of disease. If the hematocrit has dropped dangerously low, the dog should receive a transfusion of whole blood (10 to 20 ml/kg). More potent cytotoxic/immunosuppressive drugs may produce more satisfactory and faster results, but may produce fatal myelosuppression in a dog which is already anemic. Cyclophosphamide (50mg/m square), given orally for 4 consecutive days/week, or azothioprine (dose given above) are frequently used. Response is generally good. Sudden death may result from acute anemia.**

Idiopathic thrombocytopenia:

Comments: **Antibodies result in the premature destruction of platelets by macrophages. ITP may occur alone or in association with IMHA- systemic lupus erythematosus (SLE), rheumatoid arthritis (RA); neoplasia; bacterial, viral, rickettsial or parasitic infection, or drug administration. Viral and other infectious agents may induce ITP by induction or alteration of host antigens, molecular mimicry, stimulation of anti-idiotypic antibody production, etc.**

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Signalment: **Anorexia; epistaxis; hematochezia; bruising; lethargy; weakness and mucosal hemorrhage are most common presenting complaints. Mucosal and cutaneous petechia, ecchymoses, hyphema, retinal hemorrhages, melena, hematemesis, epistaxis and pallor are found on physical examination. Anemia can be the result of hemorrhage or concurrent AIHA. CNS or intraoccular hemorrhage can result in neurological signs or blindness respectively. The degree of hemorrhage is not related to the platelet count, and dogs with platelets counts of <10,000/ul may not hemorrhage. This maybe because the platelets are immature and larger than normal. Fever, splenomegaly and lymphadenopathy are not usually seen.**

Diagnosis: **Marked thrombocytopenia (<50,000 platelets/ul). Megathrombocytes may be seen on blood smear. Diagnostic criteria used to confirm diagnosis include: severity of thrombocytopenia; presence of microthrombocytosis/platelet fragmentation; normal to increased numbers of megakaryocytes in bone marrow (dogs which have ITP with reduced numbers of megakaryocytes have a poor prognosis); detection of antiplatelet autoantibodies (available tests have variable sensitivity); increased platelet counts subsequent to immunosuppressive glucocorticoid therapy (most dogs will have platelet counts of greater than 50,000 to 100,000/ul within 7 days of initiating treatment); exclusion of other etiologies for thrombocytopenia (splenomegaly; disseminated intravascular coagulation; hemolytic uremic syndrome; anticoagulant rodenticide poisoning; lymphoproliferative neoplasia; hemangiosarcoma; SLE; drugs including auranofin, cefazedone, trimethoprim/sulfonamide (in humans gold salts and methyl dopa induce ITP); infectious diseases (ehrlichiosis, Rocky Mountain spotted fever, dirofilariasis, bacteremia, modified live distemper vaccine or virus); poor sampling - clumping of platelets). No test is definitive, and a diagnosis of ITP is never absolutely certain.**

Treatment: **Cage rest and minimization of trauma. Fluids and drugs should preferably be given orally. Hypovolemia or anemia can be treated with crystalloid or colloid solutions, packed red blood cells -or whole blood. Platelet transfusion is rarely necessary except to control bleeding in dogs with intracranial hemorrhage until other therapies produce an increase in platelet numbers. Prednisone or prednisolone (1 to 3 mg/kg q 12h) is the drug of choice, and should be continued until platelet levels normalize. The dose should then be tapered over weeks or even months. Alternate day therapy is preferred. Platelet levels should be monitored as drug levels are tapered. If dogs fail to respond, alternate treatments include: pulse therapy with**

methylprednisolone, sodium succinate or dexamethasone; vincristine (0.01 to 0.025mg/kg) - either as vincristine loaded platelets or infused intravenously over 6 to 8 hours; cyclophosphamide (dose as for IMBA); azathioprine (dose as above); splenectomy; Danazol (1 mg/kg q l2h); cyclosporine (15 to 30 mg/kg q 24h). The efficacy of these alternate treatments has only been reported in a few cases. >70% of dogs with ITP respond to treatment, approximately 30% die or are euthanized during the initial episode or because of disease recurrence. About 40% of dogs experience a recurrence of the disease.

Systemic Lupus Erythematosus:

Comments: **Known as the great imitator due to variability of presenting signs. Onset may be sudden or insidious, and signs may wax and wane.**

Signalment: 1. **Gait abnormalities - stilted gait or shifting leg lameness is seen in approx. 75% of dogs during course of disease, and is due to polyarthritis or polymyositis. Usually there is associated muscle pain on palpation or diffluse muscle wasting. 2. Cutaneous - lesions range ftom symmetric to focal distribution and may affect limbs,body, head, ears, face, mucocutaneous junctions and oral cavity. They may include ulceration, crusting, oozing, and alopecia; cellulitis, furunculosis, scarring and leukoderma may also occur. This is probably the most common presenting complaint in the Beardie. 3. Kidney disease - glomerulonephritis, blood and protein in the urine. The disease may also result in pleuritis or meningitis, and may be accompanied by fever, ITP or INMA.**

Diagnosis: **There is no definitive test. Diagnosis is based on the presence of major (nonerosive polyarthritis, polymyositis, bullous dermatitis, proteinuria, IMHA, thrombocytopenia or leukopenia) and minor (fever of unknown origin, oral ulceration, pleuritis, myocarditis, pericarditis, peripheral lymphadenopathy, dementia and seizures) signs. Diagnosis is supported by serological testing (indirect fluorescent antinuclear antibody and lupus erythematosus cell tests). Diagnosis requires 2 major signs and a positive serological test, or 1 major and 2 minor signs and a positive serological test. Probable SLE is considered with I major signs and a positive serological test, or 2 major signs and negative serology.**

Treatment: **Prednisone or prednisolone (1 to 3 mg/kg q 12h) until clinical improvement is observed. If this has not occurred in 10 days, azathioprine (above dose) should be instituted. Once remission of signs has occurred doses**

should be tapered to the minimum schedule which will control the disease. Aspirin may be given, provided the dog is not thrombocytopenic, for additional analgesic, antipyretic and anti-inflammatory relief Additional treatment to prevent failure of affected organs is essential. About 40% of dogs die of SLE within I year from bronchopneumonia, septicemia or steroid-induced pancreatitis. Severe organ dysfunction or infection carry a grave prognosis.

Pemphigus:

***Comments: Pemphigus folliaceus* is the only one of this group of autoimmune diseases which occurs commonly, and Beardies are one of the breeds of dogs most frequently affected. It is however, still a relatively uncommon disorder. Disease is gradually progressive in 75% of cases, and progresses more rapidly (< 3 months) in the other 25%. Although characterized as a bullous skin disease, pustules are seen more often. Intact vesicles or bullae are rare.**

***Signalment:* Generalized, patchy, facial or pedal skin lesions. In 80% of dogs the facial lesions are observed first, and in more than 50% of dogs these are on the dorsal aspect. However, it is my impression that pedal involvement may be more common in Beardies. Lesions are characterized by crusting, scaling and alopecia. During episodes of disease exacerbation or as a result of self-inflicted trauma, there is often skin erosion and ulceration, and erythema and exudation are frequently seen. Target lesions with peripheral colarettes are common. Less than 50% of dogs are pruritic.**

***Diagnosis:* Histological and immunological examination of skin biopsy. Because the vesiculopustules are extremely transient multiple biopsies of early lesions may be necessary to confirm diagnosis. Do not surgically prepare the skin prior to biopsy, as acanthocytes present in crusts may be lost. Vesiculopustules in the stratum corneum. or intraepidermally, and microabscesses in the external root sheath or in the hair follicle lumen together with large numbers of acantholytic keratinocytes are diagnostic. Depending on the duration of acantholysis, keratinocytes may exhibit a vesicular nucleus, prominent nucleolus and no sign of cytoplasmic degeneration, while degenerated acanthocytes show nuclear pyknosis and an eosinophilic cytoplasm. Immunoperoxidase or direct immunofluorescence should show intracellular epidermal immunoglobulin deposition.**

***Treatment:* About 40% of dogs can be treated with prednisone or prednisolone (2 to 3mg/kg q 12h) without unacceptable side-effects. If substantial**

improvement has been seen in 10 days, gradually reduce the dose over 4 weeks to lmg/kg q 48h. Generally further reduction of dosing is not possible. If significant improvement is not seen within 10 days, a combined therapy can be tried, either prednisone (1 mg/kg q 12h) and azathioprine (2mg/kg q 24h) or prednisone (lmg/kg ql2h) and cyclophosphamide (50mg/m squared q 24h for 4 consecutive days in a week for 2 to 3 weeks). Another alternative is aurothioglucose. A 5 mg intramuscular injections is administered, then a 10mg injection one week later if no toxic side-effects are seen (dermatitis, stomatitis, nephrotic syndrome, blood dyscrasia, thrombocytopenia or allergic reaction). Injections are repeated weekly at 1 mg/kg dosing until remission, then tapered to every other week and finally monthly. Prednisone should be continued during the inital phase of treatment. About 50% of dogs can be successfully managed, provided owners are willing to make the financial commitment necessary. If the dog survives the first year, it should be possible to maintain it in remission for life.

Rheumatoid Arthritis:

Comments: **Diagnosis depends on a certain number of criteria based on clincial, radiologic and laboratory assessment. None are specific, and rigid adherence to them is not recommended. Canine distemper viral antigens and antibodies have been identified in immune complexes from synovia of dogs with RA, and may have initiated the immune response.**

Signalment: **Lameness may involve a single joint or limb or be wide-spread to the point that ambulation is impossible. Often lameness is of a shifting nature, and while many joints may be affected pathologically they may not be clinically. Some animals may present acutely with fever, lethargy and inappetence. Symmetric joint involvement is typical. The joints are often swollen and painful on manipulation. In advanced cases gross deformity and crepitus is observed. Secondary stretching and rupture of associated ligaments and joint capsules is common. Any limb joint as well as spinal diarthrodial joints maybe affected. Muscle atrophy may result from favouring the painful joint. Peripheral lymphadenopathy and renal disease may be seen. Pneumonia and splenomegaly can occur, sometimes with leukopenia, and RA with KCS has also been reported.**

Diagnosis: **Radiographs show subchondral bone destruction seen as punched out erosions on the articular surfaces. In advanced cases, extensive bone destruction and joint deformity is seen. Loss of mineralization around the**

epiphyses, soft tissue swelling or synovial effusion in the joints may be seen. Joint spaces may be decreased or increased depending upon the stage of the disease. Periostitis or secondary osteoarthritis may lead to bony proliferation. Calcification of soft tissues around the joint is quite common. Erosion may not be seen in the early (< 6 months) stage.

There are usually circulating autoantibodies against IgG, collectively known as rheumatoid factor. RF is not specific for RA (it is seen particularly in other chronic disease states with antigen-antibody interaction such as bacterial endocarditis, other arthropathies and viral infections), nor does its absence exclude diagnosis. Rheumatoid factor of IgM and IgA may also be found, the former more commonly, and latter particularly in dogs with severe erosive disease. Synovial fluid is often increased, generally discoloured and usually turbid. Viscosity is decreased. It usually contains fibrin and fibrinogen and may clot on standing.

Treatment: **Multiple possibilities. High doses of analgesic and anti-inflammatory drugs, such as aspirin, phenylbutazone, piroxicam, mefenamic acid and meclofenamic acid may be tried. As can immunosuppressive doses of prednisone, cyclophosphamide or azathioprine as described above. Oral and injectable gold preparations have also been reported to show some success. In acute cases, start on prednisolone/prednisone at Ito 2 mg/kg q 12h, and taper to alternate day treatment. For chronic cases with obvious bone-destruction, low dose steroid therapy with gold injections can be tried. (Sodium aurothiomalate 5 to 20 mg depending on size of dog intramuscularly once a week for 6 weeks, then every 2 to 3 months for maintenance. A small test dose should be given, and hematology should be checked every 7 to 14 days). Arthrodesis, synovectomy (of single joint), replacement of damaged ligaments, patellectomy or other excision arthroplasty may provide temporary relief.**

Myositis:

Comments: **Masticatory muscle myositis (MMM) is more commonly seen in Beardies, and may accompany other autoimmune diseases or occur subsequent to the administration of drugs (e.g. ivermectin). Polymyositis may accompany SLE or neoplasia. In humans it has been reported subsequent to infection with *Toxoplasma gondii,* certain viruses and drugs (D-penicillamine), and this is probably also the case in dogs.**

Signalment: **MMM: Masticatory muscles may be swollen in acute cases, and it is painful for the dog to open its mouth. In chronic cases there is a marked, and usually symmetrical atrophy of the temporaries and master muscles. Fibrosis often results in truisms. Polymyositis: Generalized muscle atrophy and weakness which is often exacerbated by exercise. Muscle palpation often elicits hyperesthesia. Frequently the condition is accompanied by pyrexia and obtundation. Megaesophagus with associated regurgitation may occur.**

Diagnosis: **MMM: Serum creatinine Chinese levels usually are only mildly elevated if at all. Electromyography of the Masticatory muscles may show spontaneous activity. Biopsy shows a principally mononuclear inflammatory infiltrate with eosinophils scattered but not the predominant cell type. Marked muscle fiber necrosis and myophagocytosis is seen in some dogs. 2M fibers are selectively affected. Immunocytochemistry and western blotting show antibodies directed against cytoplasmic and sarcolemmal proteins. In polymyositis there is a variable elevation in serum creatinine kinase, which may correlate with the severity of the clinical presentation. Multiple muscles should be biopsied. The appearance is essentially the same as for MMM, with extensive necrosis and nonsupparative inflammation. Electromyography shows increased spontaneous activity and reduced amplitude/duration of motor unit potentials.**

Treatment: **Prednisone 2 to 3mg/kg q 24h, the dose being tapered once improvement is seen. Some dogs can be removed from treatment in a few weeks, without recurrence, while others require prolonged or even lifetime treatment. Even advanced atrophy may show some improvement. If prednisone does not produce any response, some of the other immunosuppressive drug regimes described above may be tried.**

Myasthenia Gravis:

Comments: **Acquired MG is an immune-mediated disorder in which autoantibodies are produced against the nicotinic acetylcholine receptors of skeletal muscle. The resulting impairment of signal transmission from nerve to muscle results in apparent muscle weakness. Dogs may also have thymomas and other tumours.**

Signalmeni: **Episodic, generalized muscle weakness most obvious in the appendicular muscles, worsened by activity and ameliorated with rest is the most common presentation. Megaesophagus is a common finding. More rarely**

dogs have selective involvement of esophageal, facial and pharyngeal muscles without appendicular involvement. In some dogs, onset is acute, while in most the clinical signs develop more gradually. Aspiration pneumonia, secondary to regurgitation as a result of megaesophagus is a common complication. Other signs may include lameness; collapse; drooling, ventroflexion of the head and tremours. Neurological examination is usually normal.

Diagnosis: **Amelioration of signs within 30 seconds of administration of the short-acting anticholinesterase edrophonium chloride (1 to 2 mg intravenously). Signs of disease return within a few minutes. Repeated nerve stimulation produces a decremental response in muscle action potential. Serological testing for acetylcholine receptor autoantibodies. Antibody bound to neuromuscular junctions can be demonstrated via immunocytological staining.**

Treatment: **Long-acting anticholinesterases such as pyridostigmine bromide 0.2 to 2 mg/kg q 8 to 12 h. Start at lower dose range and titrate to effect. Higher doses are necessary for more severe illness as the disease progresses. Overdosage produces signs of cholinergic crisis (muscarinic - hypersalivation, lacrimation, urination, defecation, pupillary constriction, bradycardia, respiratory paralysis; nicotinic - muscle fasciculations, tremors stiff gait; CNS - anxiety, hyperactivity, anorexia, generalized seizures) which is generally managed by reducing the dose 25%, atropine is rarely needed. Some dogs respond well to pyridostigmine initially and then become refractory. Concurrent treatment with prednisone/prednisolone (2mg/kg q 12h) or azathioprine (as above) seems to improve longevity, despite the fact that immuno suppression appears contraindicated in animals with aspiration pneumonia. Acute fulminating MG is almost invariably fatal within 1 to 2 weeks as a result of respiratory failure secondary to aspiration pneumonia. About 40% of dogs with MG survive for at least a year, but aspiration pneumonia ultimately proves fatal in most cases.**

Bibliography:

Dewey CW, Bailey CS, Shelton GD, Kass PH, Cardinet GH. Clinical forms of acquired myasthenia gravis in dogs: 25 cases (1988-1995). JVetIntMedl997;ll:50-57.

Duval D, Giger U. Vaccine-associated immune-mediated hemolytic anemia in the dog. J Vet Int Med 1996; 10: 290-295.

Library Article

Kintzer PP, Peterson ME. Treatment and long-term follow-up of 205 dogs with hypoadrenocorticism. J Vet Int Med 1997; 11: 43 -49

Kintzer PP, Peterson ME. Primary and secondary canine hypoadrenocorticism. Vet Clinics of North America: Small Animal Practice 1997;27(2) 349-357.

Leib MS, Matz ME. Diseases of the large intestine: Inflammatory bowel disease. In Ettinger SJ, Feldman EC (eds) Textbook of Veterinary Internal Medicine, diseases of the dog and cat. Fourth edition Philadelphia, WB Saunders Co, 1995: 1241-1247.

Lewis DC, Meyers KM. Canine idiopathic thrombocytopenia purpura. J Vet Int Med 1996;10:207-218.

Refsal KR, Nachreiner RF. Monitoring thyroid hormone replacement therapy. In: Bonagura JD, Kirk RW (eds) Kirk's Current Veterinary Therapy)GI, Small Animal Practice, Philadelphia, 1v1, WB Saunders Co, 1095.

Thompson JP. Immunological diseases. In Ettinger SJ, Feldman EC (eds) Textbook of Veterinary Internal Medicine, diseases of the dog and cat. Fourth edition Philadelphia, WB Saunders Co, 1995:2002-2029.

Weiser MG. Erythrocyte responses and disorders: immune-mediated hemolytic anemia. In Ettinger SJ, Feldman EC (eds) Textbook of Veterinary Internal Medicine, diseases of the dog and cat. Fourth edition Philadelphia, WB Saunders Co, 1995:1879-1881.

International Symposium on Canine Hypothyroidism August 2-4, 1996, University of California, Davis

Werner & Ingbar's The Thyroid a fundamental and clinical text. Seventh edition. Philadelphia Lippincott-Raven, 1996