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# Don't think outside the square, make it bigger

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# Introduction

To be an excellent veterinary diagnostician there are several skills that are necessary. These include the ability to take a relevant history, recognize and assess often subtle signs, and select and interpret the findings of ancillary diagnostic tests. A deep understanding of the disease processes that are known to occur in the species that you are working with is also important. However, details of the disease processes in the species with which we are presented are often limited. To overcome this limitation, in unfamiliar and familiar species alike, I have found that it is best to go back to first principles. One first principle is to go through, one by one, the possible disease processes that could be causing the historical, clinical and diagnostic findings (Table). This so-called DAMNIT scheme allows one to get past the road block that one gets when dealing with a new species, reminds you, after all, that you have years of diagnostic training and for the experienced veterinarian forces you to expand your thinking past the pattern recognition behaviours that, while essential in private practice, can cause one to be blinkered to less common conditions. The following three cases illustrate how this type of thinking can result in positive diagnostic outcomes from potentially challenging cases.

DAMNIT Scheme	Differentials	Recommended Diagnostics
(D)egenerative		
(A)nomalous		
(N)utritional		
(N)eoplastic		
(M)etabolic		
(I)nfectious - viral		
(I)nfectious - bacterial		
(I)nfectious - fungal		
(I)nfectious - parasitic		
(I)mmune-mediated		
(T)rauma		
(T)oxins		

## Case 1

**Signalment**: This is a 17 year-old human male.

**History**: You are contacted by a physician who has a teenaged male patient with bilateral conjunctivitis that has progressed to keratitis. This young man has been struggling with this problem for four months. Treatment with topical antibiotics has been unsuccessful in stemming the course of the disease. The physician is concerned that the boy is about to lose his sight. The boy is a normal teenager, he plays rugby, attends a local high school, lives in a home that is ten years old, eats typical Australian fare and is otherwise healthy. One thing that stands out to the physician is that this boy works in a large indoor cockatiel, budgerigar, and lovebird breeding facility and wonders if this could be related to this boy's disease.

**Physical findings and ancillary diagnostic tests**: The patient has a severe keratoconjunctivitis with neovascularization of the cornea and increasing corneal oedema. A fluorescein stain of the eye reveals diffuse punctate staining of the cornea. Bacterial and fungal cultures of

the eye following a two week cessation in topic antibiotics were negative except for a low level of mixed bacteria that were thought to be contaminants. Cytology of the conjunctiva demonstrated increased numbers of neutrophils and a moderate number of lymphocytes. A biopsy of the conjunctiva showed a chronic active proliferative neutrophilic, lymphoplasmacytic, and monocytic conjunctivitis.

**Exercise**: Before reading the remainder of this section, fill out the DAMNIT table for possible differentials and additional diagnostic testing that you might recommend based on your knowledge of avian medicine and medicine of other species.

#### Differentials

*Degenerative:* Keratoconjunctivitis sicca (KCS) is a common cause of conjunctivitis and keratitis. The patient's Schirmer's tear test was normal.

Anomalous: Trichiasis (ingrowing eyelashes), entropion and other eyelid defects can cause abrasions of the cornea resulting in conjunctivitis and keratitis. These defects were not found in this patient. Additionally, it would be unlikely that this sort of problem would take so long to develop and should have been seen at a younger age.

*Metabolic*: KCS is commonly seen in post menopausal women, but not would not apply to this patient.

*Nutritional*: Vitamin A deficiency is the leading cause of blindness around the world. It can result in decreased tear production and squamous metaplasia of the conjunctiva and opacification of the cornea. The diet of this patient contained many orange and green vegetables. Supplementation with a multivitamin tablet had not changed the course of the disease. A biochemistry panel had not detected evidence of liver disease.

*Neoplasia:* No evidence of neoplastic disease was observed.

*Infectious (viral):* The two most common viral infections of the human conjunctiva are caused by herpesviruses and adenoviruses. Both are self-limiting in the majority of the cases, although certain human adenoviruses can cause chronic conjunctivitis and keratitis. A PCR for herpesvirus and adenovirus infections were negative. The Newcastle disease virus can cause conjunctivitis in humans. Mortality in the aviary, however, was minimal, and this lesion in humans is generally self-limiting and mild.

*Infectious (Bacterial)*: Most bacterial infections of the conjunctiva are secondary to lid malformations or immune suppression. This boy was HIV negative. Cultures of the eyes were not diagnostic, including culture for *Neisseria gonorrhoea*. *Chlamydia trachomatis* is also a common cause of conjunctivitis. It was not seen on special stains of cytological preparations of this eye and the patient's IgG titre was negative. Although rare, the aetiology of cat scratch disease (*Bartonella henselae*) can also cause conjunctivitis. A PCR assay for this organism was negative as was a specific immune fluorescent assay

of cytological preparations.

*Infectious (Fungal):* Fungal infections of the eye are generally rare in most species. Special stains of cytological preparations of the patient's eyes and a conjunctiva biopsy were negative for fungal organisms.

*Infectious (Parasitic):* Gross parasites were not seen. Acid fast stains of cytological preparations and a conjunctival stain were negative for crytosporidiosis. Additionally, microsporidia were not seen, although the histopathologist suggested that the microscopic changes observed were consistent with microsporidiosis.

*Immune-mediated:* KCS can be caused by an immune-mediated disease, but KCS had been ruled out. Systemic immune-mediated diseases of the skin can affect the lids, conjunctiva, and cornea, but these were not present in this patient. Chronic systemic allergies can also cause inflammation of the cornea, but rarely to this extent and this patient did not have a history of season or non-seasonal allergies.

Trauma: There was no history of trauma.

*Toxins:* Makeup, topical antibiotics and eye drops have all been associated with irritation of the cornea and conjunctiva. However, this patient had not had any exposure to these prior to the onset of signs. Hygiene was not featured highly in the aviary and there was considerable dust and the possibility of increased concentrations of ammonia. Because of the persistent problem the patient had quit his job at the aviary 1 month previous. This had not resulted in any change to the ocular condition.

#### **Diagnosis and outcome**

Given that *Encephalitozoon hellem* is commonly shed in the droppings of lovebirds and at times budgerigars and infection in immunosuppressed people results in a bilateral and severe keratoconjunctivitis, and the biopsy was consistent with this infection, a PCR assay was used on a conjunctival swab and it was positive. Topical treatment for *Enc. hellem* successfully resolved the lesions.

## Case 2

**Signalment:** Adult male willie-wagtail (*Rhipidura leuco-phrys*).

**History:** Found unable to fly in the front yard of a concerned citizen.

**Physical findings:** The bird was bright, alert and feisty, and readily ate meal worms provided. It used its left wing normally, but was unable to flap its right wing, although it held it in a normal position. The left pectoral muscle was severely atrophied (pectoral muscle score 1/5). The right pectoral muscle was of normal mass (pectoral muscle score 5/5).

**Ancillary diagnostic tests**: A complete blood count demonstrated a marked leucocytosis, heterophilia,

monocytosis, mild hypoproteinemia, and a mild nonregenerative anaemia. A biochemistry profile was unremarkable.

**Exercise**: Before reading the remainder of this section, fill out the DAMNIT table for possible differentials and additional diagnostic testing that you might recommend based on your knowledge of avian medicine and medicine of other species.

#### **Differentials:**

*Degenerative:* A degenerative cause of this bird's condition seemed unlikely.

*Anomalous:* Given the age of this bird, an anomalous disorder seemed unlikely.

*Metabolic:* Given the otherwise apparent good health of this bird and the normal biochemistry of this bird, a metabolic cause of the signs was not considered to be likely. *Nutritional:* While there are multiple nutritional diseases that can cause muscle disease, asymmetrical involvement would not be considered likely. However, in rapidly growing poultry, infraction of the supracoracoideus muscle occurs commonly. However, it is generally bilateral.

*Neoplastic:* Neoplasia originating from muscle and bone can be highly invasive and could have infiltrated the right pectoral muscle and not the left.

*Infectious (Viral):* Viral infections were not considered likely in this case.

*Infectious (Bacterial):* The elevated white blood cell count was consistent with either psittacosis or mycobacteriosis. There were, however, no other signs consistent with these diseases.

*Infectious (Fungal):* The elevated white blood cell count and monocytosis is consistent with a chronic inflammatory disease such as a mycotic infection. *Aspergillus* infections often invade vessels resulting in the formation of emboli and thrombi.

*Infectious (Parasitic):* The microfilaria filarial nematodes have been associated with pulmonary emboli. It is possible that they could cause an infarction of the right pectoral muscle. Microfilaria were not seen in the blood smear, but this is not a sensitive means of detecting them.

*Immune-mediated:* An immune-mediated vasculitis with thrombosis could not be ruled out, but was considered unlikely.

*Trauma:* A very common injury that results in a bird holding its wing in a normal position at rest but not being able to use it for flight is a coracoid fracture. It might be possible that trauma could have caused swelling of the right pectoral muscle preventing flight. Broken bones were not seen radiographically. However, a significant round- to irregular-soft tissue mass was seen to the right of the heart base within the coelomic cavity.

*Toxin:* While there are toxins that can cause muscle disease, it would be unlikely that they would inpact one side and not the other.

#### **Diagnosis and outcome**

Because of the guarded prognosis, the bird was euthanized. Post-mortem examination revealed a relatively large thrombosis and associated granuloma of the right brachiocephalic trunk. Microscopically the right brachiocephalic trunk was thrombosed and the thrombus and surrounding granuloma contained fungal hyphae. Fungal lesions were not found in any other part of the body.

### Case 3

**Signalment:** Juvenile fully fledged galah (*Cacatua galer*-*ita*).

**History:** Concerned citizens found this bird next to the side of the road. It was weak and they picked it up and brought it to the clinic for your examination. The well-trained receptionist put it in the wildlife isolation room until you could examine it.

**Physical findings:** The bird is thin (pectoral muscle score of 2/5). It is alert and responsive, but weak. There are numerous stress bars on all feathers. Its vent is soiled with urates and faeces. There is a mild serpentine deviation to the keel. The urates are yellow.

**Exercise**: Before reading the remainder of this section, fill out the DAMNIT table for possible differentials and additional diagnostic testing that you might recommend based on your knowledge of avian medicine and medicine of other species.

#### Differentials:

*Degenerative:* This is a young bird, a degenerative condition would be unlikely.

Anomalous: Given that it is a young bird, a storage disease, possibly of the liver, could be considered, but would be very rare indeed.

*Metabolic:* Given the condition of this bird, it is likely that is dehydrated and may have some electrolyte imbalances and could be hypoglycaemic. A primary metabolic cause for this condition seems unlikely.

*Nutritional:* If this bird was still being fed by its parents, it is possible that they stopped feeding it and it was starving. The stress bars on the feathers would be consistent with an unbalanced diet as a nestling. The serpentine deviation of the keel shows that this bird did not get adequate calcium when developing. It might still be calcium deficient and could have a pathological fracture preventing it from flying.

*Neoplastic:* Neoplasia of a very young bird would be unlikely, but still possible. None of the physical findings point to a neoplastic disorder.

*Infectious (Viral):* Psittacine beak and feather disease virus is everywhere in Australia. This bird could be infected with it and have a secondary bacterial or parasitic infection. The feather lesions are not consistent with psitta-

cine beak and feather disease.

*Infectious (Bacterial):* The weight loss, weakness, soiled feathers around the vent and the yellow urates are consistent with this bird having a systemic bacterial infection. A complete blood count reveals a moderate nonregenerative anaemia, a moderate hypoproteinemia, and a marked leucocytosis, heterophilia, and monocytosis. These findings are consistent with a chronic inflammatory disease and could be consistent with either psittacosis or mycobacteriosis.

*Infectious (Fungal):* The poor condition of the bird and the haematological changes could also be consistent with either primary or secondary aspergillosis.

*Infectious (Parasitic):* Parasitic infections would have to be high on the differential. Nematodes could cause a bird to be debilitated, especially a young bird, and *Spironucleus* is well documented to cause a chronic wasting disease and diarrhoea in juvenile galahs. A faecal wet prep is negative for *Spironucleus*. A faecal float is negative for worm eggs.

*Immune-mediated:* Very few immune-mediated diseases are known in birds. An immune-mediated vasculitis, myositis or myocarditis, as well as an immune-mediated anaemia could be included in a differential, but would be unlikely.

*Trauma:* Given that this bird was found down by the side of the road, trauma, likely resulting in a fracture of the coracoid, clavicle or scapula is highly likely. Bruising and fractures were not found on physical examination but a coracoid or clavicular fracture could still be present. Internal bruising of the heart, lung or liver could also be preventing this bird from flying.

*Toxin:* A toxin would be less likely, but possible, given that this bird has evidence of liver disease.

#### **Diagnosis and outcome**

Radiographs demonstrated a prominent hepatomegaly and splenomegaly consistent with a systemic infectious disease. The Immunocomb (Biogal, Kibbutz Galed, Israel) was strongly positive for anti-chlamydial antibodies. The bird was euthanized. Post mortem also revealed a pericarditis and diffuse airsacculitis.

#### **Recommended Readings**

Yanoff, M. 2014. Ophthalmology, 4th Ed., Chatsworth, NSW, Elsevier.

Schmidt, R. E., Reavill, D., Phalen, D. N. 2015. Pathology of Cage and Pet Birds, 2<sup>nd</sup> ed. Ames, Iowa, Wiley.