DISEASES THAT MIGHT NOT BE SEEN IN AUSTRALIA: A CAUTIONARY TALE

Drury Reavill
Zoo/Exotic Pathology Service
2825 KOVR Drive
West Sacramento, CA 95605

INTRODUCTION

Despite our jet-setting life-styles and transport of pets and pathogens from continent to continent, some diseases have yet to establish themselves in all locations. This review is meant to highlight some uncommon to unknown avian diseases in Australian birds. It is just a matter of time and having the appropriate hosts and vectors before these migrate from the Americas.

ADENOVIRUS

Members of the family Adenoviridae are non-enveloped double-stranded DNA viruses with a medium-sized genome of 26 to 45 kbp. Adenoviruses are classified into four genera: Mastadenovirus, Aviadenovirus (previously classified as group I avian adenovirus), and the two recently accepted genera Atadenovirus and Siadenovirus (Benko et al., 2005). A fifth genus is proposed for fish adenoviruses (Benko et al., 2005). Group II turkey adenovirus type 3, also named turkey hemorrhagic enteritis virus, is related to members of Siadenovirus with frog adenovirus. In addition, group III egg drop syndrome virus (EDSV) has been moved to the new genera Atadenovirus.

Historically, adenovirus infections in psittacine birds have been identified based on microscopic studies. Infections with adenovirus or adenovirus-like particles have been described in a variety of psittacine birds including budgerigars (*Melopsittacus undulatus*), macaws (*Ara* spp.), Amazon parrots (*Amazona* spp.), cockatoos (*Cacatua* spp.), cockatiels (*Nymphicus hollandicus*) lovebirds (*Agapornis* spp.), parakeets (*Psittacula krameri*), eclectus parrots (*Eclectus roratus*), African grey parrots (*Psittacus erithacus*), *Poicephalus* spp, and lorikeets (*Trichoglossus* spp.) Schmidt et al., 2003; Katoh et al., 2009; Wellehan et al., 2009).

The lesions have ranged from hepatitis, conjunctivitis, interstitial pneumonia, enteritis, and splenic lymphoid depletion. The intranuclear inclusions can be seen in the liver, spleen, pancreas, kidney, brain, and/or intestines. In psittacine birds, there is a variable species susceptibility to adenovirus infection. The infection is infrequently recognized as sporadic outbreaks in small psittacine birds (cockatiels, lovebirds) and African species (African greys, Senegals).

In some birds, particularly budgerigars and cockatiels, the only lesion may be large intranuclear inclusion bodies in tubular epithelial cells (Schmidt et al., 2003; Katoh et al., 2009). In the author's experience, these have generally been immature birds, exposed to recent stressors (transportation, diet change) and have died with few other lesions or clinical signs. Adenovirus infections in lovebirds are often found as an incidental finding at necropsy. Most of these birds have only a few widely scattered inclusions (Schmidt et al., 2003).

The transmission is horizontal (bird to bird); however, the incubation period is unknown. Diagnosis in the living bird is difficult and generally requires electron microscopy to demonstrate the virus in faeces or pharyngeal secretions. Further work using PCR techniques will be necessary to fully characterize the complex relationships between adenovirus, the species of psittacine bird, and clinical disease.

PACHECO'S DISEASE

Pacheco's disease (PD) was first recognized in 1929 by Brazilian veterinarian Pacheco (Pacheco and Bier, 1930) as the cause of an acute fatal outbreak characterized by a hepatitis with intranuclear inclusion bodies in psittacine birds in Brazil. The herpesvirus is classified as psittacid herpesvirus type 1 (PsHV-1), from the subfamily avian Alphaherpesviridae (Thureen and Keeler, Jr., 2006). PsHV-1 is closely related to infectious laryngotracheitis virus but distinct from Marek's disease virus and herpesvirus of turkey. Based on UL16 gene sequence it has been classified into four genotypes. Amazon parrots are those most commonly diagnosed with PD and have been identified with all four PsHV-1 genotypes. The four PsHV-1 genotypes were also found among birds from the Pacific region such as cockatiels and cockatoos; however these species are somewhat more refractory to the disease. PsHV-1 genotypes found in African grey parrots include genotypes 2, 3, and 4, but not genotype 1. Genotype 4 is most commonly associated with Pacheco's disease in macaws and conures while genotype 3 is rarely found and genotype 1 has not been found (Tomaszewski et al., 2003, Tomaszewski et al., 2006).

Pacheco's disease is a peracute to acute fatal disease of psittacines with rare descriptions in passerine birds. It may occur in an individual bird or as an explosive outbreak among a collection. The signs of disease are often minimal to absence prior to death. If noted they include; depression, anorexia, diarrhoea, tremors, and weakness. Due to the short duration of illness, necropsy specimens are typically well muscled and have adequate body fat. If there are gross lesions, the liver is most frequently noted. The liver may be enlarged and friable with variable yellow-grey mottling and with or without haemorrhage Histologically, acute multifocal to submassive hepatic necrosis is a nearly consistent finding. The amount of inflammation present is generally minimal. Syncytial cell formation may occur but is uncommon. Intranuclear inclusion bodies (INIB) in heptatocytes and biliary epithelium are typically abundant but may be rare or absent entirely. Inclusion bodies (Cowdry type A) are typically deeply eosinophilic, but may be lightly basophilic (Schmidt et al., 2003).

Extra-hepatic lesions may be identified in the spleen and pancreas with associated necrosis and INIB. The crop is another commonly affected organ. The crop epithelium may have multifocal ballooning degeneration of the basal cell layer causing erosions, ulcers, and rarely vesicles possibly with inclusions. Intestinal lesions are relatively uncommon and are generally mild, often being confined to the presence of inclusion bodies in the nuclei of crypt epithelial cells. Rarely, a severe necrotizing tracheitis will also be observed (Schmidt et al., 2003).

The differential diagnosis based on the gross lesions and clinical signs include bacterial hepatitis, lead poisoning, avian polyomavirus, psittacine adenovirus infection, and reoviruses (Katoh et al., 2010).

Not all PsHV-1 infections cause disease and some parrots are asymptomatic. Latently infected parrots (generally Amazon parrots and certain species of conures and macaws) are potential sources for virus dissemination and PsHV-1 has been identified in the oral and cloacal mucosa at a prevalence of 92% from these birds (Tomaszewski et al., 2006). Ingestion, inhalation, and conjunctival exposure have experimentally been shown to result in infection and disease.

PsHV-1 has also been detected mucosal papillomas (papillomatosis) from new world parrots (Styles et al., 2004) and recently, another psittacid herpesvirus, PsHV-2, has been identified in three African grey parrots with cutaneous papillomas (Styles et al., 2005). PsHV-1 genotypes 1, 2, and 3, but not 4 have been found in mucosal papillomas (Styles et al., 2004).

The most common neoplasm of the oral cavity and cloaca is mucosal papillomatosis. This disease is most common in the in New World psittacine birds; Macaws, conures, Amazon parrots, and hawk-headed parrots are most susceptible to this disease. Oral lesions are particularly common in the larger macaws, but are relatively rare in Amazon parrots. Papillomas are most commonly located along the margins of the choanal fissure, at the base of the tongue, and on the glottis or in the cloaca, near the junction with the skin. Rarely the oral papillomas may become large enough to cause obstruction of the airways and cloacal papillomas frequently prolapse and ulcerate. The papillomatous lesions are white to pink, raised, and focal to locally extensive. Most have the typical cauliflower-like appearance. However, these lesions wax and wane and smaller slightly raised discolored lesions that also represent this disease may be overlooked (Schmidt et al., 2003).

In some birds there is an apparent correlation between the occurrence of cloacal papillomas and proliferative biliary, pancreatic or upper intestinal lesions and these changes should be ruled out in affected birds (Schmidt et al., 2003).

PARAMYXOVIRUS

Viruses from the large and diverse Paramyxoviridae family have been isolated from mammalian and avian species for centuries. Viruses belonging to this family are pleomorphic, enveloped, single-stranded, nonsegmented, negative-sense RNA viruses of 13-19kb. The family Paramyxoviridae is divided in to two subfamilies: Paramyxovirinae and Pneumovirinae. The subfamily Paramyxovirinae is divided into five genera: Respirovirus (including Sendai virus and human parainfluenza virus types 1 and 3), Rubulavirus (including simian virus type 5, mumps virus, and human parainfluenza virus types 2 and 4), Morbillivirus (including measles and canine distemper viruses), Henipavirus (comprising Hendra and Nipah viruses), and Avulavirus (comprising the avian paramyxoviruses [APMVs]). The Avulavirus genus contains nine distinct avian paramyxovirus (APMV) serotypes (Khattar et al., 2011).

APMV-1 (NDV) strains are divided into three pathotypes: highly virulent (velogenic) strains that cause severe respiratory and neurologic diseases in chickens; moderately virulent (mesogenic) strains that cause milder disease in chickens, and nonpathogenic (lentogenic) strains that cause inapparent infection. This strain is monitored at US quarantine stations and in outbreaks of disease within the poultry industry. It rarely is of concern to the pet bird owning public unless an outbreak has occurred and steps are taken to control the outbreaks by isolation, quarantine, and 'scorched earth' policy (primarily for poultry) (Hietala et al., 2004; Soberano et al., 2009). Because of this disease and the availability to obtain free diagnostics, ranging from those poultry kept as pets to small production flocks, most, if not all chickens are submitted to state diagnostic labs. This strain will result in neurologic clinical signs in pet birds and a variable mortality (Erickson et al.,1977). Canaries and mynahs show some resistance and will be asymptomatic (Erickson et al., 1977). A closely related APMV-1 is a common cause of encephalitis in racing pigeons (Dortmans et al., 2011).

Less is known about the biological characteristics and pathogenicity of APMV-2 to -9. APMV-2 has been associated with severe respiratory disease and drop in egg production in turkeys. APMV-6 and -7 cause mild respiratory disease in turkeys and are associated with a drop in egg production. APMV-

4, -8, and -9, isolated from ducks, waterfowl, and other wild birds did not produce any clinical signs of viral infection in chickens.

APMV-3 has been associated with encephalitis and high mortality in some caged birds, respiratory diseases in turkeys and stunted growth in young chickens (Jung et al., 2009). It is particularly pathogenic to *Neophema* species resulting in neurologic clinical signs of torticollis and circling. Chronic infection may lead to a chronic pancreatitis. Budgerigars and *Forpus* species seem resistant (Jung et al., 2009). APMV-3 infections rarely cause gross lesions and histologically the disease process is variable. Some birds have no inflammatory changes and others have perivascular cuffing by lymphocytes and plasma cells, minimal necrosis, gliosis and endothelial hypertrophy (Schmidt et al., 2003).

APMV-5 causes disease in budgerigars that is characterized by depression, dyspnoea, diarrhoea and high mortality (Nerome et al., 1978). This strain has claim to the longest APMV genome and as yet, has not been identified in the US (Samuel et al., 2010).

WEST NILE VIRUS

The author's service has monitored West Nile virus from when it was first recognized in the USA in 1999 through case submissions across the USA and Canada. Some of the early diagnostic test material came from raptors submitted to ZEPS, confirmed by Dr. Tracey MacNamara, Wildlife Conservation Society at the Bronx Zoo as having lesions typical for this emerging viral infection and identified as West Nile Virus by the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID).

West Nile virus is a vector-borne flavivirus (RNA virus) transmitted between avian hosts by mosquitoes. This virus, which causes systemic disease as well as central nervous system lesions, has infected a variety of pet and wild birds. Actual disease is uncommon in psittacine birds unlike other species (eg. corvids, raptors) based on the rare documented cases in the literature and case submissions to the author's service (Carboni et al., 2008; Stockman et al., 2010). The clinical signs are neurologic with paresis, opisthotonus, and seizures. Grossly, meningeal and brain congestion and hemorrhage can be found although in psittacines no gross lesions are more typical. Histologically there is lymphoplasmacytic meningitis and variable encephalitis. In mild cases, lesions are more common in the cerebellum and brain stem but may be generalized in the more severe disease. Cuffing of vessels by lymphocytes and plasma cells, gliosis or glial nodule formation and neuronal necrosis are seen (Schmidt et al., 2003; Carboni et al., 2003; Stockman et al., 2010).

West Nile virus can also cause a peripheral neuritis in some avian species that is morphologically similar to PDD. The species of bird and the characteristics of other lesions must be evaluated in making a distinction between the two diseases.

SARCOCYSTIS

Sarcocystis species are protozoa with an obligate two-host life cycle. At least six species of sarcocystis infect birds. Sarcocystis falcatula appears to be the most significant in susceptible pet birds that are inadvertent hosts. The North American opossum is the definitive host and cowbirds and grackles are the intermediate hosts. Asexual reproduction of the protozoa occurs within the intermediate host's endothelium. This stage can result in serious or fatal disease in aberrant hosts. In the normal host schizogony is followed by formation of sarcocysts in muscles. The cysts are 20-25µm long and may be macroscopically visible. They are packed with banana-shaped bradyzoites. The definitive host is

infected when it eats the cysts within the muscle tissues. American or neotropical (Mexico, South and Central America) psittacines are usually resistant to disease as adults, but clinical disease sometimes occurs. Old World psittacine birds of Australia, Asia, and Africa, are highly susceptible to the disease (Schmidt et al., 2003).

The primary gross lesion and cause of death in susceptible species is severe pulmonary congestion, edema, or hemorrhage. Histologically the lungs will be congested with some fibrin deposition, edema, and hemorrhage within tertiary bronchi. Lymphocytes and plasma cells accumulate around blood vessels and bronchi. Multiple aggregates or clusters of small elliptical or crescent-shaped structures compatible with protozoal merozoites can be seen throughout the pulmonary vessels. The clusters formed are long and sinuous and may resemble microfilaria. The merozoites do not stain well with Brown and Brenn, Periodic acid-Schiff (PAS), or Giemsa (Schmidt et al., 2003).

Two other forms have been recognized; muscular disease and a neurological disease. In the muscular form, they birds initially present with severe lethargy and weakness. They will also have elevations of muscle enzyme activities (creatine phosphokinase, aspartate aminotransferase) and beta and gamma globulins concentrations. For those examined, the cysts can be found in the skeletal muscle with a lymphoplasmacytic myositis (Villar et al., 2008). These birds may be positive by IFA serology (Cray et al., 2005).

In the neurologic form, the birds present with severe ataxia and incoordinated head movements. Schizonts are identified in the cerebellum and brainstem with a lymphoplasmacytic meningoencephalitis (Siegal-Willott et al., 2005; Villar et al., 2008).

The drug pyrimethamine may be of benefit in some cases with early diagnosis or high suspicion. Control of the opossum and cockroach population is important.

REFERENCES

Benko M, Harrach B, Both GW, Russell WC, Adair BM, Adam E, et al. 2005. Family Adenoviridae. In Fauquet CM, Mayo MA, Maniloff J, Desselberger U, Ball LA (Eds.), Virus Taxonomy. Eighth Report of the International Committee on Taxonomy of Viruses. San Diego, CA: Academic Press., pp. 213-228.

Carboni DA, Nevarez JG, Tully TN, Evans DW. 2008. West Nile virus infection in a sun conure (*Aratinga solstitialis*). Journal of Avian Medicine and Surgery 22, 240-245.

Cray C, Zielezienski-Roberts K, Bonda M, Stevenson R, Ness R, Clubb S, Marsh A (2005). Serologic diagnosis of sarcocystosis in psittacine birds: 16 Cases. Journal of Avian Medicine and Surgery 19, 208-215.

Dortmans JCFM, Koch G, Rottier PJM, Peeters BPH. 2011. A comparative infection study of pigeon and avian paramyxovirus type 1 viruses in pigeons: evaluation of clinical signs, virus shedding and seroconversion. Avian Pathology 40,125-130.

Erickson GA, Marac CJ, Gustafson GA, Miller LD, Proctor SJ, Carbrey EA. 1977. Interactions between viscerotropic velogenic Newcastle diseases virus and pet birds of six species. I. Clinical and serologic responses, and viral excretion. Avian Diseases 21, 642-654.

Gilardi KVK, Lowenstine LJ, Gilardi JD, Munn CA. 1995. A survey for selected viral, chlamydial, and parasitic diseases in wild dusky-headed parakeets (*Aratinga weddelli*) and tui parakeets (*Brotogeris sanctithomae*) in Peru. Journal of Wildlife Diseases 31,523-528.

Grund CH, Werner O, Gelderblom HR, Grimm F, Kasters J. 2002. Avian paramyxovirus serotype 1 isolates from the spinal cord of parrots display a very low virulence. Journal of Veterinary Medicine. B, Infectious Diseases and Veterinary Public Health 49, 445-451.

Hietala S, Kinde H, Crossley BM, Ardans A. 2004. Exotic Newcastle disease in California: laboratory response to an animal health emergency. Canadian Veterinary Journal 45, 1022.

Jung A, Grund C, Muller I, Rautenschlein S. 2009. Avian Paramyxovirus Serotype 3 Infection in *Neopsephotus, Cyanoramphus, and Neophema* Species. Journal of Avian Medicine and Surgery 23, 205-208.

Katoh H, Ogawa H, Ohya K, Fukushi H. 2010. A Review of DNA Viral Infections in Psittacine Birds. Journal of Veterinary Medical Science 72, 1099–1106.

Katoh H, Ohya K, Kubo M, Murata K, Yanai T, Fukushi H. 2009. A novel budgerigar-adenovirus belonging to group II avian adenovirus of Siadenovirus. Virus Research 144, 294-297.

Khattar SK, Kumar S, Xiao S, Collins PL, Samal SK. 2011 Experimental Infection of Mice with Avian Paramyxovirus Serotypes 1 to 9. PLoS ONE 6, e16776.

Murray KO, Mertens E, Despres P. 2010. West Nile virus and its emergence in the United States of America. Veterinary Research 41,67.

Nerome K, Nakayama M, Ishida M, Fukumi H. 1978. Isolation of a new avian paramyxovirus from budgerigar (*Melopsittacus undulatus*). Journal of General Virology 38, 293-301.

Pacheco G, Bier O. 1930. Epizootie chex les perroquets du Brésil. Relations avec le psittacose. Comptes Rendus de la Societe de Biologie (Paris) 105,109–111.

Samuel AS, Paldurai A, Kumar S, Collins PL, Samal SK. 2010. Complete genome sequence of avian paramyxovirus (APMV) serotype 5 completes the analysis of nine APMV serotypes and reveals the longest APMV genome. PLoS ONE 5, e9269.

Schmidt RE, Reavill DR, Phalen D. 2003. eds. Pathology of Pet and Aviary Birds. Ames, IA: Iowa State Press.

Senne DA, Pearson JE, Miller LD, Gustafson GA. 1983. Virus isolations from pet birds submitted for importation into the United States. Avian Diseases 27, 731-744.

Siegal-Willott JL, Pollock CG, Carpenter JW, Nietfeld J. 2005. Encephalitis Caused by Sarcocystis falcatula-like Organisms in a White Cockatoo (*Cacatua alba*). Journal of Avian Medicine and Surgery 19,19-24.

Soberano G, Carpenter TE, Cardona C, Charlton B. 2009. Spatial distribution of free-of-charge pathology submissions to the California Animal Health and Food Safety laboratories during the exotic Newcastle outbreak in 2002-2003. Avian Diseases 53, 2-6.

Stockman J, Hawkins MG, Burns RE, Fang Y, Brault AC, Lowenstine LJ. 2010. West Nile virus infection in a green-winged macaw (*Ara chloropterus).* Avian Diseases *54,164-169.*

Styles DK, Tomaszewski EK, Jaeger LA, Phalen DN. 2004. Psittacid herpesviruses associated with mucosal papillomas in neotropical parrots. Virology 325,24-35.

Styles DK, Tomaszewski EK, Phalen DN. 2005. A novel psittacid herpesvirus found in African grey parrots (*Psittacus erithacus erithacus*). Avian Pathology 34, 150-154.

Thureen DR, Keeler CL Jr. 2006. Psittacid herpesvirus 1 and infectious laryngotracheitis virus: Comparative genome sequence analysis of two avian alphaherpesviruses. Journal of Virology 80, 7863-7872.

Tomaszewski EK, Kaleta EF, Phalen DN. 2003. Molecular phylogeny of the psittacid herpesviruses causing Pacheco's disease: correlation of genotype with phenotypic expression. Journal of Virology 77, 11260-11267.

Tomaszewski EK, Wigle W, Phalen DN. 2006. Tissue distribution of psittacid herpesviruses in latently infected parrots, repeated sampling of latently infected parrots and prevalence of latency in parrots submitted for necropsy. Journal of Veterinary Diagnostic Investigation 18, 536-544.

Villar D, Kramer M, Howard L, Hammond E, Cray C, Latimer K. 2008. Clinical Presentation and Pathology of Sarcocystosis in Psittaciform Birds: 11 Cases. Avian Diseases 52,187-194.

Wellehan JFX, Johnson AJ, Latimer KS, Bischoff K, Lafortune M, Jacobson ER. 2005. Identification and Initial Characterization of an Adenovirus Associated With Fatal Hepatic and Lymphoid Necrosis in a Meyer's Parrot (*Poicephalus meyeri*). Journal of Avian Medicine and Surgery 19,191-197.

Wellehan, JFX, Greenacre CB, Fleming GJ, Stetter MD, Childress AL, Terrell SP. 2009. Siadenovirus infection in two psittacine bird species. Avian Pathology 38, 413-417.