Internal Papillomatous Disease: a Psittacine Disease Previously Exotic to Australasia

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Literature relating to internal papillomatous disease is reviewed, emphasising information relevant to the assessment of risk of dissemination of this disease in Australia and key issues in devising an eradication and prevention program.

Earlier this year internal papillomatous disease (IPD) was identified in two male green-winged macaws (*Ara chloroptera*) which had not previously been in contact with each other and had been imported in separate legal shipments into Australia in 1993. These were the first reports of this disease in Australia. In spite of representations by the Association of Avian Veterinarians (Australian Committee) against such action, the Australian Quarantine and Inspection Service, after initially holding the clinically affected birds in quarantine on the owner's property, released them and placed no restrictions on their movement or sale.

Introduction of exotic psittacine disease through live bird importation is a topical issue in Australia and New Zealand. Proventricular dilatation syndrome (PDS) was identified in a green-winged macaw dying shortly after release from quarantine in Australia in 1993, the first report of PDS in Australia. No action was taken by authorities in relation to other birds in that shipment but a moratorium was placed on subsequent importations and, to date, there have been no further reports of PDS in Australia. Pacheco's disease was identified in a shipment of exotic Psittaciformes imported into a private quarantine facility in New Zealand earlier this year and the Supreme Court ordered the destruction of the entire shipment. This paper reviews the literature on IPD with particular emphasis on information relevant to the assessment of the risk of dissemination of this disease in Australia and options for attempted eradication and prevention of further introductions.

Clinical signs and differential diagnosis

IPD, also known as cloacal papillomatosis, results in neoplastic, wart-like lesions on mucosal surfaces, most commonly observed in the cloaca and choanal cleft but lesions may also occur on other mucosal surfaces, including the oropharynx, conjunctiva, larynx, oesophagus, crop, proventriculus, ventriculus, nasal mucosa and nasolacrimal duct. Many birds will ultimately develop bile duct carcinomas, pancreatic carcinomas or both. Even though affected birds may live for years with IPD with time many will lose condition and die or are euthanased[11] Some birds with IPD exhibit no clinical signs but examination of the cloaca or choana under general anaesthesia may reveal early lesions. There are currently no screening tests for IPD and diagnosis is dependent upon clinical examination, examination under anaesthesia and histopathology of biopsy or necropsy material.

In one study involving 141 IPD cases, recorded ages of birds affected ranged from 3.5 weeks to 36 years with a mean age of 5.5 years and a median age of 4 years. There was a preponderance of females (61.1%) compared with males (38.9%).[4] In a separate study involving 40 IPD affected birds the age range, where this information was recorded, was 1.5 to 4.5 years.[8]

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IPD has been reported to be common in a wide variety of South American Psittaciformes, as well as occurring in a budgerigar (*Melopsittacus undulatus*), a Mollucan cockatoo (*Cacatua moluccensis*), an African grey parrot (*Psittacus ertihacus*) and a cockatiel (*Nymphicus hollandicus*).[4] See table 1.

In examining the cloaca for papillomas, McDonald (1988) recommended that the vent be soaked with alcohol and illuminated with a bright light. The end of a cotton bud was then introduced into the cloaca, the tip pushed to one side and slowly withdrawn to ease out the cloacal lining and allow for inspection, then the process was repeated on the opposite side. He noted that it was difficult to examine the most proximal aspect of the cloaca in this manner. The mucosa should be pink in colour (in African grey parrots the muco-cutaneous junction is pigmented), slightly moist and completely smooth in texture.

Papillomatous lesions may appear as large distinct masses or may occur as numerous small, raised lesions covering the mucosa. These friable growths may be pink or white and tend to bleed easily when bruised. On gross examination cloacal lesions resemble rectal prolapses or granulation tissue. Acetic acid (5%) will turn papillomatous tissue white, helping to identify suspect tissue. Cloacal lesions often result in prolapse of the either the papilloma or the proctodeum. Severe congestion and oedema may hinder reduction of the prolapse. Endoscopy is necessary to visualise internal lesions.

Clinical signs depend on the location of the lesions. Birds with lower intestinal or cloacal lesions may show straining, vent pasting, odoriferous or bloody droppings, recurrent enteritis, flatulence or cloacoliths. Those with oral cavity or upper gastrointestinal lesions may show dysphagia, dyspnoea, wheezing, gastrointestinal blockage, anorexia, vomiting, weight loss, dilatation of the proventriculus or ventriculus or passing whole seeds. Infertility or reduced fertility may occur because of genital tract obstruction or general ill health. Death may result from suffocation as a result of laryngeal obstruction, intestinal obstruction or debilitating systemic disease. Initially some birds do not show any clinical signs but develop problems if stressed by other illness or environmental factors. Some authors report periods of regression and recrudescence of lesions ranging from 2 to 18 months.[4]

Chronic irritation, vitamin A deficiency and environmental stress have been suggested as contributing to the development of IPD. IPD needs to be differentiated from other causes of mucosal tissue proliferation, including psittacine poxvirus (an exotic disease in Australia but widespread overseas), granulation tissue and squamous metaplasia due to hypovitaminosis A. Other gastrointestinal diseases such as PDS, bacterial infections, psittacosis or parasitic infections could mimic IPD involving the upper gastrointestinal tract, liver or pancreas.

Pathological findings

Histologic examination is necessary to confirm a diagnosis of IPD.[8] Proliferation of lining epithelial cells on thin fibrovascular stalks has been the basis for designating the lesions as papillomas. However, unlike cutaneous papillomas, IPD lesions show numerous projections covered by a hyperplastic tessellated epithelium or a non-keratinized columnar epithelium containing mucin producing cells which stain positively with Alcian blue and mucicarmine stains. The stroma may show some inflammatory cells. Subjacent fibrovascular stalks may show congestion and small aggregates of lymphocytes. Mitotic activity is generally present in the polygonal basal cells but there may also be scattering of mitotic figures in the upper layers. Cells on the luminal surface contain apical basophillic granules. Structures resembling intercellular bridges may be present in the middle layers in sections exhibiting prominent intercellular oedema.

A number of authors have reported an association between IPD and local or metastatic

neoplasia, including *in situ* carcinoma,[8] and benign or malignant neoplasia of the intrahepatic bile ducts or the pancreas.[4,5,6]. There have also been two reports of bile duct carcinoma in Amazon parrots occurring in association with cloacal prolapse where the possibility of cloacal papillomata in a temporary regressing state was not ruled out.[9]

Aetiology

IPD must be distinguished from cutaneous papillomas which affect epidermal, as opposed to mucosal surfaces. Some of the early literature failed to make this distinction. Cutaneous papillomas have been shown to be associated with papillomavirus in chaffinches, brambling finches and an African grey parrot,[10] but to date there has been no such virus identified in cases of IPD. While a viral aetiology has been assumed for epidermal proliferations, in most cases virus has not been associated with the lesions.[11] Herpesvirus has been associated with cutaneous proliferations on the feet of cockatoos.

Cases of IPD often occur in clusters following the introduction of affected birds. This suggests transmission by an infectious agent, but, to date, this agent has not been identified and other aetiologies may contribute to the occurrence of disease. Stress associated with concurrent illness, environmental or nutritional deficiencies has been suggested to be involved.[7] One report noted that moderate to heavy growths of *E. coli* are frequently isolated from birds with IPD but *E. coli* is likely to be a secondary infection.[10]

Herpesvirus-like particles were identified in a cloacal papilloma in an orange-fronted conure. These were considered coincidental, but the authors noted correlation between herpesviruses and recurrent mucosal papillomas and tumours in other species. It is interesting that Pacheco's parrot disease, which was originally reported in South American Psittaciformes and is also exotic to the Australasian region, is caused by a herpesvirus. Pacheco's disease is known to cause high mortality in Australian Psittaciformes exposed to infection.

Attempts to demonstrate papillomavirus in suspect lesions by electron microscopy, low stringency southern blot techniques or immunocytochemical procedures have all failed. So too have attempts to transmit the disease by inoculations of partially purified IPD tissue homogenates in an Amazon parrot, a macaw, a sulphur crested cockatoo and a Mollucan cockatoo.[8] The possibility of IPD being caused by a viral genome present as episomal or integrated DNA where the viral antigens are not expressed has been raised.[8] Techniques used to date in investigating the disease may not have been sufficiently sensitive and/or IPD may be caused by a virus that does not belong to the papilloma group, for example a herpes-like virus. Data suggesting that IPD and Pacheco's disease may share a common aetiology is currently being investigated.[6]

Transmission

IPD was originally reported in the early 1980s in Psittaciformes imported from South America into the USA. The disease is now widespread in Psittaciformes kept in Europe and North America and some collections experience incidences in some species of over 50%.[7] Green-winged macaws, blue and gold macaws (*Ara ararauna*) and hawk-headed parrots (*Deroptyus accipitrinus*) appear to be particularly susceptible. Anecdotal reports suggest that the incidence of the disease in North America may be dropping following the cessation of wild Psittaciforme importation in 1994 (S. McDonald, personal communication, 1997). The report this year of IPD in two green-winged macaws imported from Britain to Australia was the first report from the Australasian region.

Transmission appears to require close (probably mucosa to mucosa) contact, such as preening or mating, for spread. Rosskopf (1996) noted possible transmission between a

half-moon conure and a blue and gold macaw that had been held separate from other birds but in close contact with each other.

While reports of cutaneous papillomas in South American, African and Australasian Psittaciformes date back to before the 1980s,[18] reports of IPD lesions in African and Australasian species have been more recent and less common.[4] It is possible that this reflects lack of close contact and mutual preening and mating between South American and African or Australasian species rather than non-transmissibility of an infectious agent as there have been isolated reports of IPD in a cockatiel, a budgerigar and a Mollucan cockatoo.[4,8,9] One veterinarian has noted, however, that he has not seen IPD in Australasian species kept on the same premises as South American species with IPD (S. McDonald, personal communication, 1997).

The occurrence of the disease in a 3.5 week old bird suggests that IPD may be egg transmitted or that the incubation period, in some cases, may be short.[4] In a separate study no cases of IPD were found in chicks hatched from artificially incubated eggs of IPD affected parents. However, the study only involved 24 blue and gold macaws chicks aged between one and six years at the time of publication and the basis on which the birds were determined to be 'papilloma free' was not stated. Because of the significance of possible egg transmission, follow up on these birds was sought but this was not possible as the birds had been sold. From memory the curator was not aware of any reports coming back to her from new owners of IPD in artificially incubated chicks, whereas IPD had been reported in parent reared chicks sold prior to the introduction of artificial incubation policy. Interestingly, one of the parent birds in the same group had died from bile duct carcinoma. (A. Romagnano, personal communication, 1997)

Treatment

Treatment is difficult and palliative at best, recurrence is common and birds are likely to remain infectious.[7] Repeated surgical excision followed by strictures and abnormal vent healing are common. Electrosurgery, cryosurgery, radiation therapy and the use of autogenous vaccines have been described but long term follow up of treated birds or birds showing apparent spontaneous remission have not been published.[11,]

Eradication and prevention

There are reports of eradication of IPD by careful screening and removal of affected individuals. New Psittaciformes were examined under anaesthesia for the presence of papillomas soon after purchase and three to six months later. Affected birds were returned to the seller or otherwise removed from the collection.[7,10]

Discussion

The distribution of enzootic genera, as well as more recent DNA and protein electrophoresis studies, suggest that Psittaciformes evolved in Gondwana. As the ancient continent finally split around 45 million years ago, South American, Australian, New Zealand and African Psittaciformes were isolated and the respective populations underwent separate radiations. It is likely that so too did the birds' pathogens, so that each of the southern continents appears to have unique psittacine diseases, most of which have proven to be pathogenic to Psittaciformes that have evolved in other continents. Psittacine pox virus, PDS, Pacheco's disease and IPD are all diseases which were originally reported in South American Psittaciformes imported to the USA or Europe but they have been found to be pathogenic to Australasian species when these have been housed with affected South American species.[24] Similarly a strain of reovirus from African grey parrots imported from Ghana into the United States was associated with disease in

both South American and Australian psittacine species. Circovirus, on the other hand, is known to be present in Australian wild birds but had not been reported in South American species until Australian birds were mixed with South American species in the United States. This disease is now widespread in South American and African Psittaciformes kept as pets in the northern hemisphere. Other diseases, such as psittacosis, appear to have been global in distribution even before the 1970s upsurge in international bird trade assisted the intercontinental spread of avian pathogens.

Since the nineteenth century Australia has used her position as an isolated island continent to advantage in preventing the introduction of exotic diseases and in establishing disease eradication programs. In the 1980s however there was international pressure to drop non-tariff barriers to trade and the political policy changed from one of risk minimisation to risk/benefit analysis when deciding whether to allow bird or animal importation. It was in this political climate and with pressure from the avicultural community that live bird importation, which had been banned since 1950s, was resumed in 1990.[24,] Warning of the impending risk of exotic psittacine diseases to both wild and captive psittacine populations was raised directly with AQIS (Macwhirter P,1992, unpublished correspondence) and in both avicultural and veterinary publications by avian veterinarians before and at the time importation of exotic Psittaciformes commenced in 1993.[,,] It was noted that mixing birds from different sources prior to importation and then allowing the birds released from the quarantine station to go to different parts of Australia could facilitate the introduction and spread of exotic diseases such as IPD, PDS and Pacheco's disease for which there were no suitable screening tests and incubation periods could be long. There have now been three incidents of exotic disease arising from the first two importation shipments involving exotic psittacine species.

The literature indicates that IPD has caused serious morbidity and mortality in psittacine populations overseas.[4,7,10] While there would be cost involved in an eradication program, if allowed to disseminate, IPD poses risk to both captive and wild birds in Australia. There are economic, ecological and ethical implications in this.

It would cause financial loss to aviculturists through:

- death of affected birds
- cost of veterinary care of affected individuals
- cost of preventive programs to reduce risk of disease introduction into other aviaries
- reduced reproductive performance, particularly in rare species
- reduced value of birds from known IPD affected aviaries.

The presence of this disease in Australia poses a threat to both exotic, and to a lesser extent, native Psittaciformes, particularly those species with low numbers. Studies have not been carried out to determine what effect this disease may have in previously naive psittacine populations. Failing to take action to prevent dissemination may establish a precedent for future exotic avian disease introductions.

Allowing dissemination of IPD increases the risk of suffering in affected birds.

Based on overseas experience, features of IPD which need to be considered in devising an eradication scheme include:

- the disease appears to require close contact for transmission.
- many affected birds are likely to remain infectious for life, regardless of treatment.
- amelioration of symptoms may be temporarily effected in some birds with surgery and autogenous vaccine but recurrence is likely.

- anaesthesia may be needed to detect early signs of the disease and birds with low grade infections.
- overseas experience indicates that if birds who are not showing any abnormalities on physical examination are held in quarantine away from affected birds for twelve months and do not show papillomatous lesions when examined under anaesthesia, then the risk of the birds having the disease is very low. There have not been reports of birds so assessed subsequently developing or transmitting the disease.
- while the incubation period may be long, carrier birds able to transmit the disease but never developing lesions have not been demonstrated.
- egg transmission, if it occurs, does not appear to be a common mode of spread.
- certain species, particularly green-winged macaws, blue and gold macaws and hawk-headed parrots appear to be particularly susceptible. Australiasian species may have lower susceptibility.

The owner of the only two birds which have so far been reported with disease has apparently not been willing to euthanase the clinically affected birds voluntarily. This points to the legal, economic and political difficulties that must be addressed if an eradication scheme is to succeed. In this author's opinion, based on the literature, key elements in a scheme to eradicate IPD from Australia would need to include the following:

- Close involvement and cooperation of the avicultural community, including a general education program to advise bird owners about the clinical signs of IPD and means of reducing risk of dissemination. Compensation for legally imported, clinically affected birds euthanased would be needed to gain this support.

- Euthanasia or removal from Australia of clinically affected birds.

- Making IPD a notifiable disease and maintaining a central register of reported cases. It is not known how widespread IPD is in Australia Trace backs would need to be applied in order to quantify the occurrence of the disease and to identify the likely source of any infection.

- Holding birds which have been in direct contact with IPD affected birds in quarantine for 12 months and ensuring that birds are free of lesions on close clinical examination under anaesthesia before release from quarantine.

- Regulatory requirement for vendors of exotic Psittaformes to notify new owners if the bird may have been in contact with an IPD affected bird and supply of information regarding steps to adopt to minimise the risk of dissemination to other aviaries. (e.g., depending on circumstances, quarantine for a prescribed period and physical examination under general anaesthesia to check for IPD lesions)

- A notification/eradication program should consider exotic psittacine diseases generally.

When considering future exotic bird importation, the community cost, effectiveness and aviculturalist co-operation in dealing with the occurrence of exotic disease in these imported birds should be considered.

Table 1

Species in which IPD has been reported in the literature

Hawk-headed parrot (*Deroptyus accipitrinus*)[4,7,8,10,28]
Green-winged macaw (*Ara chloroptera*)[5,7,8,10,28]
Yellow-collared macaw (*Ara auricollis*)[7]
Blue and gold macaw (*Ara ararauna*)[7,10,28]
Severe macaw (*Ara severa*)[7,8]
Illiger's macaw (*Ara maracana*)[7]
Scarlet macaw (*Ara macao*)[7,10,28]
Military macaw (*Ara militaris*)[7,10]
Noble macaw (*Ara nobilis*)[7]

Ara spp[4,5,7,8,9,10,28]
Yellow-headed Amazon (*Amazona ochrocephala*)[7,8]
Blue-fronted Amazon (*Amazona aestiva)*[7,8]
Red-lored Amazon (*Amazona autumnalis*)[7]
Lilac-crowned Amazon (*Amazona finschi*)[7]
Oranged-winged Amazon (*Amazona amazonica*)[7,8]
Black-headed caique (*Pionites melanocephala*)[7]
Festive Amazon (*Amazona festiva*)[7]
Green-cheeked Amazon (*Amazona viridigenalis*)[7,8]
Amazona spp [4,7, 8,9,10,28]

Peach-fronted conure (*Aratinga canicularis*)[4,7,8,10,23]
Half-moon conure (*Aratinga canicularis eburniostrum*)[28]
Aratinga spp[4,7,8,10,23,28]

White-capped pionus (*Pionus senilus*)[7]

Orange-cheeked parrot (*Pionopsitta barrabandi*)[8]

Budgerigar (*Melopsittacus undulatus*)[8]

Mollucan cockatoo (*Cacatua moluccensis*)[9]

African grey parrot (*Psittacus erithacus*)[4]

Cockatiel (*Nymphicus hollandicus*)[4]

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