# PET BIRD ONCOLOGY

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Although neoplastic diseases occur with some frequency in the commonly kept pet birds, published information regarding prognosis and therapy of specific neoplasms is limited. Each case report or study that provides this information, helps us to improve the level of care we can offer our companion avian pets. This review will cover some basic information about select tumour types with attempted therapies and will reference the more recent reports in the avian literature. It is not intended to be all encompassing. For more information, there are extensive published reviews of the reported avian tumours (Leach 1992; Reece 1992; Reavill,2004). Table 1 provides a summary of therapies reported in pet birds. A survey of the tumours diagnosed at our service, Zoo Excotic Pathology Service (ZEPS), will be discussed.

## SELECTED PET BIRD TUMOURS

### Haemangiomas and Haemangiosarcomas

Haemangiomas are benign tumours of vascular endothelium. The malignant version is haemangiosarcoma, also known as malignant haemangioendothelioma or angiosarcoma. Haemangiomas are more commonly reported in budgerigars (*Melopsittacus undulatus*) than in other birds, and usually occur in the skin or spleen (Leach 1992; Reece 1992). Splenic and cutaneous haemangiomas have also been reported in African grey parrots (*Psittacus erithacus*) and an Indian ring-necked parakeet (*Psittacula krameri*) (Leach, 1992).

Of the haemangiomas we've seen (n=19), the majority were removed from the skin (feet, inguinal region, cloaca, side of neck, and wing); one was found in the spleen. Budgerigars were the most commonly affected species (n=5), with additional cases in conures, Amazon parrots, cockatiels, Moluccan cockatoo (*Cacatua moluccensis*), finch, duck, yellow collar macaw (*Ara auricollis*), and dove. There was no sex predilection and the average age was10.8 years (range 3 to 20 years).

Haemangiomas appear grossly as circumscribed soft red to black swellings in the skin and subcutis (Reavill, 2004). Malignant melanomas, although rare in pet birds, can have a similar appearance and are an important differential diagnosis especially in African greys (Schmidt,1992) and budgerigars (Andre et al., 1993). Haemangiomas must also be differentiated from vascular malformations (arteriovenous fistulas, aneurysms), hematomas, and highly vascular granulation tissue. Among our cases, complete surgical removal resulted in survival times ranging from 2 months to 2 years without tumour regrowth. One mass recurred one year later in an Amazon with an incompletely removed cloacal haemangioma.

Although haemangiosarcomas are reportedly uncommon, they were seen as often as haemangiomas in our case files (n=18). Haemangiosarcomas have been reported in the skin of doves (Leach 1992), the liver of a mealy Amazon (Amazona farinosa) parrot (Rossi, 1998), the ovary in an orange-winged Amazon parrot (*Amazona amazonica*) (Mickley et al., 2009), attached to the right internal carotid artery in a double yellow-headed Amazon parrot (*Amazona ochrocephala oratrix*) (Hanley et al., 2005), and the right metacarpus of a male budgerigar (Freeman et al., 1999). They are locally invasive, metastatic, and multicentric. Other sites at which haemangiosarcomas have been described include the wings, legs, dorsum of the neck, myocardium, abdominal viscera, and the diaphysis of long bones, where they have an aggressive osteolytic radiographic appearance (Turrel et al., 1987). The highly metastatic behavior of haemangiosarcomas was evident in a budgerigar that developed disseminated disease eight weeks after local therapy. The bird presented with acute swelling of the metacarpal region and was treated with local irradiation of the wing three times weekly for a total of ten 400-cGy fractions (Freeman et al., 1999).

The beak, wing, feet, leg, and cloaca were the most common sites for cutaneous haemangiosarcomas submitted to our service. One case each was seen in the heart and liver. Cockatiels (*Nymphicus hollandicus*) lead the list of species, which also included a swan (with multiple beak lesions), lovebird (*Agapornis* spp.), African grey parrot, pionus (*Pionus* sp.), parakeet, canary (*Serinus canarius*), and finches. The age range of affected birds was similar to those with haemangiomas and the sexes were evenly represented. The majority of tumours had local regrowth within days to months, which usually led to a decision to euthanize. Skin tumours tended to be inflamed and necrotic. Although metastases were not described, many birds were incompletely evaluated for metastatic disease. One swan with multiple beak tumours received local radiation therapy and has survived tumour-free for six months.

In chickens, haemangiomas and haemangiosarcomas are induced by a recently described strain of avian retrovirus, avian haemangioma virus (AHV) (Soffer et al., 1990; Sela-Donenfeld et al., 1996). The typical type C retrovirus particle was demonstrated in the tumour by electron microscopy (Soffer et al., 1990). No retrovirus or viral particles were found by electron microscopy in budgerigar haemangiomas (Gardner et al., 1981). Long term exposure to ultraviolet (UV) light and an inherited or familial predisposition are potential etiologies for tumour development in domestic dogs (Clifford et al., 2000). Both benign and malignant tumours were found on sparsely feathered regions of waterfowl in our case files, suggesting an association with exposure to sunlight. An Amazon parrot with a hepatic haemangiosarcoma, had been on long term testosterone therapy for feather loss (Rossi, 1998). Hepatic haemangiosarcoma in people is linked to androgenic-anabolic steroid use (Falk et al., 1979).

Based on our case submissions, complete surgical removal is curative for cutaneous haemangiomas. As in dogs and based on one report of therapy in a budgerigar, complete surgical excision followed by radiation, chemotherapy, or both is recommended for cutaneous haemangiosarcomas (Withrow and MacEwen, 1996; Clifford et al., 2000; Mickley et al., 2009). Chemotherapeutic agents used in dogs include doxorubicin as a single drug or in combination with vincristine and cyclophosphamide (Withrow and MacEwen, 1996). Birds with haemangiosarcomas should be closely evaluated for metastases to help determine the biologic behavior of these tumours.

**Myelolipomas**

Myelolipomas are well-delineated, expansile, benign extramarrow neoplasms composed of varying proportions of fat and haematopoietic cells. In mammals, focal areas of mineralization or bone formation may occur (Moulton, 1990; Rossi and Incensati, 1998). They are considered choristomatous

(histologically normal tissue in an abnormal location) haematopoietic stem cell elements (Moulton, 1990 (Latimer and Rakich, 1995). Myelolipomas are uncommon tumours. They have been reported in the subcutaneous wing tissues of a peach-faced lovebird (*Agapornis roseicollis*) (Ozaki et al., 1996), and the subcutaneous tissues of the thigh and thorax in a society finch, hyacinth macaw (Anodorhynchus hyacinthinus), and cockatiels (Leach 1992; Latimer and Rakich, 1995). A myelolipoma was also described in the spleen in a lovebird (Andreasen et al., 1995) and multifocally in the liver of a saffron toucanet (Baillonius bailloni) with concurrent mycobacterial infection (Latimer and Rakich, 1995).

Myelolipomas behave like lipomas, with slow progressive growth. They are highly vascular, so haemostasis during surgery is important. Grossly they appear as masses of fat with haemorrhage and can resemble lipomas, xanthomas, and fibrosarcomas. The differential diagnoses based on histologic examination include haemangiolipoma, osseous metaplasia, osteoma, and haematopoietic neoplasms. Haemangiolipomas are fatty neoplasms with endothelium-lined vascular channels (Latimer and Rakich, 1995). They occur as solitary tumours of the skin and ovary in fowl and as a solitary subcutaneous tumour in budgerigars (Leach 1992; Latimer and Rakich, 1995).

Six haemanioglipomas were identified in our database that originated in the subcutaneous tissue on the body and/or limbs. Species included a budgerigar, yellow collar macaw, cockatiel, lovebird, blue-fronted Amazon (*Amazona aestiva aestiva*), and canary. All affected birds were > 9 years of age. Osseous metaplasia, the formation of bone from soft tissue, is comprised of osteoid and spicules of mineralized bone associated with the haematopoietic cells (Latimer and Rakich, 1995). Osteomas are benign bony growths arising from the surface of bones and comprised of dense accumulations of well-differentiated cancellous or compact bone with delicate intervening fibrovascular stroma (Moulton, 1990). Osteomas are uncommonly described in birds (Soffer et al., 1990; Reece 1992). Haematopoietic neoplasms (eg, myelocytoma and myeloblastoma) result from proliferation of a single cell line, with a shift to immaturity. These tumours are relatively common in domestic fowl but rare in exotic birds (Latimer et al., 1994; Calnek et al., 1997; García et al., 1998). Extramedullary haematopoiesis is an non-encapsulated, dense aggregate of haematopoietic cells that lacks a fatty component. It is seen most frequently in the liver, spleen, kidney, yolk sac remnant, and bursa of Fabricius.

In published reports, the majority of birds with internal myelolipomas died of unrelated causes. Although subcutaneous masses were successfully removed, intra-operative haemorrhage resulted in the death of one cockatiel (Latimer and Rakich, 1995). Of the 21 myelolipomas in our database, the majority (n=9) occurred on the wings (some bilaterally) of adult (7 to 20 years) female cockatiels, with one hepatic tumour. In lovebirds (n=5), myelolipomas occurred as multiple masses in the subcutaneous tissues of the body and wing, with one intrathoracic tumour. A parrotlet has a myelolipoma on the capsule of its adrenal gland; an Amazon parrot had multiple hepatic masses. The remaining species (budgerigar, Quaker and Amazon parrots) had subcutaneous masses. The majority of myelolipomas (n=11) occurred in female birds (the sex was not listed for 8 birds). Complete surgical removal of discrete masses appears curative although haemorrhage can be a serious complication.

Myelolipomas are reported infrequently in man (Huang et al., 2000), domestic cats (Moulton, 1990), dogs (Moulton, 1990; Newman et al., 2000), cheetahs (Cardy and Bostrom, 1978), Goeldi's monkeys (Narama et al., 1985; Hauser and Baumgartner, 1991), rats (Moulton, 1990), and ferrets (Li et al., 1996). The majority of tumours are present within the thorax and abdomen, often involving the adrenal glands, liver, and spleen. They usually affect adult or elderly animals. Clinical signs were not apparent unless the growths become large or acquired secondary changes (Li et al., 1996).

**Squamous cell carcinoma**

Squamous cell carcinoma (SCC) is a malignant tumour comprised of nests and infiltrative cords of moderately undifferentiated to poorly differentiated squamous cells which frequently form central cores of compressed, laminated keratin ('keratin pearls'). In pet birds, the primary sites for SCC are the skin and upper gastrointestinal tract (beak, oral cavity, oesophagus, crop, proventriculus) (Bauck, 1992; Leach 1992. SCC is a common tumour in budgerigars and has been reported in several psittacine species including elegant grass parakeet (*Neophema elegans elegans*), African grey parrot, Amazon parrot, macaw, conure, cockatiel, lovebird, Solomon eclectus parrot, and umbrella cockatoo (*Cacatua alba*) (Bauck, 1992; Leach 1992; Diaz-Figueroa et al., 2006; Beaufrère et al., 2007).

Cutaneous SCCs appear as proliferative, irregular, broad-based masses or wound-like ulcers. The differential diagnoses based on gross appearance are keratoma (keratoacanthoma; a benign follicular tumour) or chronic ulcerated dermatitis. The tumours tend to develop at sites of chronic irritation (Turrel et al., 1987). Our biopsy submissions commonly were obtained from areas of chronic feather picking, especially under the wings. It has been experimentally demonstrated that inflammation will promote neoplastic proliferation (Okada et al., 2000) and other references have noted an association between inflammation and tumour development (Klaphake et al., 2006). In mammals, prolonged exposure to UV light is an important factor in the development of multicentric squamous cell carcinoma in situ, and in some cases, in the eventual development of invasive tumours (Withrow and MacEwen, 1996; Baer and Helton, 1993). Exposure to UV light does not appear to be a common mechanism in pet bird SCC since the tumours occur in locations not typically exposed to prolonged sunlight.

When SCC involves the uropygial gland there is glandular enlargement and frequent tumour ulceration or self-trauma. These masses must be differentiated from other tumours (uropygial gland adenomas, adenocarcinomas, and carcinomas) as well as non-neoplastic conditions such as adenitis and vitamin A deficiency with glandular metaplasia. Squamous cell carcinomas of the beak can cause deformities such as overgrowth, irregular peeling, cracking, necrosis, and irregular shortening or distortion.

SCCs in the nasal sinuses and oral cavity have poorly defined borders and are associated with haemorrhage and necrosis of the surrounding tissues. They commonly are associated with chronic stomatitis, and caseous material may be found within the mass. Common clinical signs for tumours in these locations include dyspnoea, recurrent infections, dysphagia (Ramis et al., 1999), exophthalmos (Diaz-Figueroa et al., 2006), and nasal discharge. SCCs of the crop and oesophagus may present as non-specific debilitation and regurgitation. On examination, there is thickening of the crop or esophageal wall, with plaque-like masses. Frequently, dietary history points to supplemented seeds as the main food source, suggesting a role for vitamin A deficiency squamous metaplasia in the tumour development.

SCC of the oesophagus and crop was associated with *Capillaria* spp. infestation in a helmeted guinea fowl (De Rosa and Shivaprasad, 1999). Metastatic SCC in a salmon-crested cockatoo (*Cacatua moluccensis*) involved the bone, lungs, liver, and spleen; a fluke was noted in the extrahepatic bile duct (Pye et al., 1999). The association between metazoan parasite infections and tumour development is well-known in the mammals. Examples include *Spirocerca lupi* and esophageal sarcomas in domestic and wild canines; *Cysticercus fasciolaris* and hepatic sarcomas in rats; and biliary carcinoma induced by *Clonorchis* in cats (Moulton, 1990). In pheasants, caecal fibrosarcomas and leiomyomas have been reported to occur in conjunction with *Heterakis* spp. Often, the parasitic

infestation is chronic.

Cutaneous SCC and those of the oral cavity and beak are locally aggressive and tend to recur (Quesenberry 1997). There are few reports of metastases (Bauck, 1992; Leach 1992; Pye et al., 1999; Ramis et al., 1999). Tumours in the crop, oesophagus, and proventriculus, while not diagnosed ante-mortem, are also expected to be locally aggressive. SCCs frequently are associated with chronic bacterial and fungal infections (Manucy et al., 1998).

When SCC occurs in accessible areas, standard therapy includes surgical excision and/or radiation therapy. Intralesional chemotherapy has also been explored. Intralesional carboplatin treatment resulted in complete regression of SCC in the neck of an Amazon parrot (*Amazona ochrocephala*); the tumour had failed to respond to cobalt-60 teletherapy radiation (Wilson et al., 2000). An Amazon parrot with a choanal SCC received three serial radiation treatments of 8 Gy/treatment; however, the tumour recurred (Quesenberry 1997). Squamous cell carcinoma on the mandibular beak in a Buffon's macaw (Ara ambigua) failed to respond to cobalt-60 radiation therapy (total tumour dose of 5,600 cGy) after surgical debulking; the associated chronic bacterial beak infection was treated with antibiotics (Manucy et al., 1998). This macaw subsequently was given intralesional cisplatin therapy; however, this also failed to alter the tumour growth. An African grey parrot (*Psittacus erithacus erithacus*) with episodes of chronic feather picking and self-mutilation for 10 years developed squamous cell carcinomas at the right axilla and left dorsal patagium. The left patagial tumour was removed completely by electrocautery. Cisplatin was administered weekly into multiple sites on the right axillary tumour and it initially improved. One month later the bird was euthanized and the SCC had invaded local tissues (Klaphake et al., 2006).

A single irradiation fraction of 100 Gy/8.3 mm from a Strontium-90 ophthalmic applicator after surgical debulking was successful in resolving a carcinoma and squamous cell carcinoma of the uropygial gland in two budgerigars and a papillary adenoma of the uropygial gland in a cockatiel (Nemetz and Broome, 2004). A uropygial gland squamous cell carcinoma was surgically removed from an African grey parrot (Pignon et al., 2011). Radiation therapy was started 1 week after surgery, using a strontium probe (Sr-90 Ophthalmic Applicator, Atlantic Research Corp, Gainesville, VA, USA). The treatment site was divided into 4 areas and each area was irradiated with 100 Grays (maximum depth of penetration of the radiation is about 5 mm). This fraction was repeated one more time, a week later. The surgery site appeared healed 6 months after the second radiation.

In follow-up surveys of cases in our database, intralesional carboplatin was administered to two birds (a cockatiel and budgerigar) with uropygial gland SCC. One bird had complete surgical removal of the uropygial gland but died four months later of unknown causes. The other bird had incomplete gland removal and the tumour regrew during therapy. Four of eight birds died or were euthanized because of uropygial gland SCC. Three birds with complete removal are still alive or died of unrelated causes with no evidence of regrowth. All 12 birds with SCC of the beak, oral cavity, or oesophagus died or were euthanized due to uncontrolled tumour growth and secondary infections. With wing amputation or aggressive surgical excision of cutaneous SCC, four of 17 birds survived without tumour recurrence. Nine of the birds either died or were euthanized due to tumour regrowth and four birds were lost to follow-up. Based on our submissions, there is no sex predilection for SCC. The most common species in which SCC was diagnosed were cockatiels (n=17), Amazons (n=10), and budgerigars (n=9). Other species included dove, cockatoo, conure, African grey parrot, pionus, ring-necked parakeet, and lovebird.

**Lipomas and Liposarcomas**

Lipomas are benign lumps of fat that occur are more commonly in budgerigars, rose-breasted cockatoos (*Cacatua roseicapilla*), Amazons, and cockatiels. They are soft, pale yellow, encapsulated and lobulated masses in the subcutis, most frequently over the sternum and less commonly over the abdomen and thighs. If lipomas are traumatized, they may become inflamed and necrotic. Obese birds can develop fat pads at locations typical for lipomas, such that masses at these sites maybe hyperplastic adipose tissue rather than lipomas. A possible relationship has been reported between abnormal thyroid gland function and lipomas. Lipomas can grow rapidly, develop high tumour vascularity, and result in ulceration of the overlying skin. Recurrence is common, especially with incomplete removal.

Of the 420 psittacine birds identified with a lipomas from the ZEPS database, the top four species were Amazon parrots (n=89), cockatiels (n=77), budgerigar (n=55), and cockatoos (n=45 including 14 galahs - *C. roseicapilla*).

Liposarcomas, malignant tumours of lipocytes and lipoblasts, have rarely been reported in pet birds. They have been described in budgerigars, cockatiels, a monk (Quaker) parakeet (*Myiopsitta monachus*) (Tully et al., 1994), a green-cheeked conure (*Pyrrhura molinae*) (Ritzman and Hawley, 1996), and an African grey parrot (Graham et al., 2003). They are yellow to gray masses of the subcutis and differ from lipomas in being firmer, more infiltrative and more vascular (Bauck, 1992). Because cytological examination of an aspirate may not differentiate between a liposarcoma and lipoma, surgical biopsy is recommended for diagnosis. Liposarcomas are expected to be aggressive and in the monk parakeet (Tully et al., 1994), it presented as multiple subcutaneous masses resulting in a decision to euthanize. Only a single tumour was found on the green-cheeked conure (Ritzman and Hawley, 1996) and amputation of the toe and mass proved curative. An adult African grey parrot (Graham et al., 2003) presented with bilateral periorbital swelling of 1-year duration. Bilateral periorbital and retrobulbar soft tissue swelling was identified by ultrasonographic imaging. At necropsy the liposarcoma was a soft, yellow tissue that filled the periorbital diverticuli of the infraorbital sinus and elevated the overlying skin extending into the retrobulbar spaces and the mandible.

From our records liposarcomas have been identified on 21 birds (Amazons n=2, budgerigar n=4, cockatiels n=5, cockatoos n=2, one conure, lovebirds n=2, macaws n=2, and quaker parrots n=3). When age was provided these were all adult to mature birds, distributed evenly between males and females. The most common location was the wing, n=8.

**Lymphosarcoma (Lymphoma, Malignant Lymphoma)**

Lymphoma is the most common lymphoid neoplasia in psittacine bird and passerine birds (Bauck, 1986; Coleman and Oliver, 1994; Coleman 1995). Lymphoma may be more common in canaries and with an increased prevalence in males; however, male canaries, due to their popularity as a songster, may be the most common sex presented to veterinarians. Lymphoid neoplasias have been reported in budgerigars, cockatiels, African gray parrots, mynah birds, cockatoos, pionus, lovebirds, corellas (Cacatua sanguinea), parakeets, rosellas (*Platycercus* spp.), lorikeets, macaws, and an Amazon parrot (Paul-Murphy et al., 1985; Hill et al., 1986; France and Gilson, 1993; Shivaprasad, 1993; Coleman and Oliver, 1994; Coleman 1995; Ramos-Vara et al., 1997; Gamble, 1999). In addition, we have recognized lymphoma in caiques (*Pionites* spp.), doves, and grey-cheeked parakeet (*Brotogeris pyrrhopterus*). The reported ages of birds at the time of diagnosis ranged from 8 months to 18 years. Pet birds with

lymphoma submitted to our service (n=41) ranged in age from 5 months to 30 years, with an average of 8 years.

Clinical signs associated with lymphoma include periorbital or cutaneous swelling, depression, anorexia, weight loss, paresis, lameness, abdominal swelling, diarrhoea, blindness, scant droppings, dyspnoea, polydipsia, regurgitation, feather loss, and folliculitis. Canaries usually present with abdominal enlargement, lack of singing, and dyspnoea.

A leukaemic blood profile is uncommon in psittacine birds with lymphoid neoplasia (Campbell, 1984; France and Gilson, 1993; Latimer et al., 2000). We observed a lymphocytosis in three birds (a budgerigar, lovebird, and cockatoo) of eight birds with CBC results. Anemia (PCV<35%) was commonly reported, and two African grey parrots had a heterophilia. Of nine canaries, only three listed blood work and all had leukocytosis and lymphocytosis.

Diffuse or nodular involvement is characteristic of pet bird lymphoma. Organs typically infiltrated include liver, spleen, kidneys, skin, bone, gastrointestinal tract, thyroid gland, oviduct, lungs, sinus, thymus, testes, brain, mesentery, trachea, fat, periorbital muscles, and pancreas (Leach 1992; Shivaprasad, 1993). The liver is most frequently involved followed by involvement of the spleen and kidneys. These organs generally are enlarged and pale. Other diseases that grossly resemble visceral lymphoma are amyloidosis, fatty liver syndrome, atoxoplasmosis (in mynahs and canaries), hepatitis, systemic mycobacteriosis and other neoplasms. Four of five Amazons examined by our service presented with a mass in the choana. Two of three budgerigars, two caiques, a lovebird, a parakeet, and a cockatiel presented with a mass on the side of the neck. The mass most likely was the thymus, although the gland was effaced by neoplastic lymphocytes.

Cutaneous lymphoma is most commonly reported on the head and neck (Schmidt, 1997). The lesions are usually grayish-yellow, multifocal or diffuse thickenings, which must be differentiated from xanthomas and inflammatory lesions. In our cases, all birds with cutaneous lesions eventually progressed to multiorgan involvement. All African grey parrots presented with a periorbital mass, as was previously described in an African grey (Paul-Murphy et al., 1985), Amazon (Campbell, 1984), and scarlet macaw (*Ara macao*) (Ramos-Vara et al., 1997). Both Umbrella cockatoos in our files presented with multiple cutaneous masses, similar to what was previously reported in cockatoos (France and Gilson, 1993; Latimer et al., 2000).

Diagnosis of lymphoma relies on biopsy or aspiration cytology of the affected areas or organs, and bone marrow evaluation, if indicated. In the literature and in our experience, cutaneous presentations usually have a more pleomorphic neoplastic cell population consisting of large lymphoblasts, small well differentiated lymphocytes, and scattered plasma cells (Latimer et al., 2000).

Although lymphoma in chickens commonly is associated with retrovirus (avian leukosis virus) or herpesvirus (Marek's) infection, there is no evidence to date of a viral link to the tumour formation in pet birds (Coleman 1995; Ramos-Vara et al., 1997; Latimer et al., 2000). Electron microscopic examination of two cases from the service (a caique and umbrella cockatoo - Madewell, 1999) did not demonstrate viral particles. Recent molecular investigations suggested a retroviral cause for multicentric lymphoma in a starling (Wade et al., 1999). Retroviral-induced lymphoma has been suspected in other passerine birds, but remains to be proven. Transmissible viruses cause lymphomas and leukaemias in a wide variety of mammalian species, including humans, cattle, cats, and most recently, ferrets (Moulton, 1990; Erdman et al., 1995). In dogs and people, chromosome abnormalities are associated with lymphoma (Hahn et al., 1994).

Few birds with lymphoma have responded favorably to treatment, which has included prednisolone, orthovoltage X-ray, vincristine sulfate, and chlorambucil. An African grey exposed to 4,000 rads of orthovoltage radiation survived 2 months before tumour recurrence (Paul-Murphy et al., 1985). Multidrug chemotherapy was used in a Moluccan cockatoo, and included prednisone, vincristine, cyclophosphamide, doxorubicin, L-asparaginase, and alpha-interferon, with diphenhydramine and dexamethasone to minimize anaphylactic reactions (France and Gilson, 1993). The solid tumours slowly regressed; however, the bird remained leukemic. L-asparaginase treatment was associated with weight loss, lethargy, anorexia, and regurgitation (France and Gilson, 1993). Prednisone alone was given for 32 weeks to an Amazon with lymphoma (Coleman 1995). An adult Fischer's lovebird (*Agapornis fischeri*) with surgical removal of lymphoma from the neck has survived two years with no signs of tumour regrowth (Gamble, 1999). A young blue and gold macaw with cutaneous pseudolymphoma responded to two courses of chlorambucil with no recurrence 2.5 years later (Kollias et al., 1992). Prednisone, cyclophosphamide, vincristine, L-asparaginase, and doxorubicin are the mainstay of most modern chemotherapy protocols for canine lymphoma (Madewell, 1999). A case of nonepitheliotropic cutaneous B-cell lymphoma with a leukemic blood picture in an umbrella cockatoo (*Cacatua alba*) resolved with aggressive therapy of vincristine and chlorambucil for 17 weeks (Rivera et al., 2009).

**Xanthomas**

Xanthomas are not neoplasms, but are locally invasive and appear as masses in the skin. They rarely occur in internal organs. These masses of foamy macrophages, multinucleated giant cells, and cholesterol clefts produce thickened, dimpled skin that is yellow to orange in color. Xanthomas have been reported most frequently in psittacine bird and gallinaceous birds. They are considered common in cockatiels and female budgerigars. In the 44 cases in our files, we found 13 cockatiels, six Amazons, five macaws, and four budgerigars, with fewer cockatoos, doves, Quaker parrots, eclectus parrots, pionus, and African grey parrots. The average age was 10 years (range 3 to 30 years).

Xanthomas most commonly occur over the ventral abdomen, hip, thigh, wing, and around the face. Wing masses were more commonly observed among our cases, as were a number of masses from the eyelids of Amazons. The lesions may be pruritic. Xanthomas often are associated with other pathologic findings such as lipomas, hernias and sites of chronic irritation (Schmidt, 1997). We found three xanthomas with intralesional granulomatous mycobacterial infections. Therapy includes surgical resection, although diffuse tissue involvement may result in insufficient tissue to close the defect. Amputation is recommended for xanthomas on the wing tip. Xanthomas covering large areas or with indistinct borders have a guarded prognosis. The majority of xanthomas in our database that were surgically removed (n=18) did not recur. Dietary modification was commonly used as an adjunctive therapy.

**ANTI-TUMOUR THERAPY REPORTED IN PET BIRDS**

There are a few specific reviews of tumour therapy and appropriate surgical intervention for pet birds listed in the references (Filippich, 2004; Filippich and Charles, 2004; Mehler and Bennett, 2004; Mauldin and Shiomitsu, 2005).

Cisplatin (Platinol, New York, NY, Bristol-Myers Squibb) and Carboplatin (Paraplatin, New York, NY, Bristol-Myers Squibb)

Cisplatin (cis-dichlorodiamineplatinum [II]) is an inorganic, platinum-containing chemotherapeutic

drug (Filippich et al., 1999). Anti-tumour activity is effected through binding and cross linking of DNA, with interference of DNA replication and cell-cycle-independent tumour lysis (Fox, 2000). Carboplatin is a second-generation, platinum containing chemotherapeutic agent that is less nephrotoxic and emetogenic than cisplatin in dogs and cats (Fox, 2000).

Cisplatin in human medicine is used either alone or in combination with other drugs against a variety of solid tumours, especially those of gonadal or urinary bladder origin, and tumours of the head and neck (Filippich et al., 1999). In domestic mammals, cisplatin is reported to be effective for the treatment of osteosarcoma, SCC, bladder tumours, and mesotheliomas (Withrow and MacEwen, 1996). Toxic side effects include myelosuppression, alopecia, gastrointestinal toxicity, and, rarely, neurotoxicity and nephrotoxicity (Withrow and MacEwen, 1996). Aggressive fluid diuresis, and pretreatment with butorphanol or serotonin antagonists to control vomiting are suggested (Withrow and MacEwen, 1996). Cisplatin can cause fatal pulmonary haemorrhage in domestic cats (Fox, 2000).

In one study, cisplatin was evaluated in eight healthy sulfur-crested cockatoos (Filippich et al., 1999). The suggested dosage of 1 mg/kg infused over one hour was well-tolerated, and plasma platinum levels were in the therapeutic range. Side effects included regurgitation, weight loss, and bone marrow depression. One bird receiving a high dose developed substantial renal tubular damage with visceral and articular urate deposition. Intratumoural cisplatin and orthovoltage radiotherapy was used to treat fibrosarcoma in a macaw (Ramsay et al., 1993). Intralesional cisplatin was used unsuccessfully against SCC in the mandibular beak of a Buffon's macaw (*Ara ambigua*); the tumour had also failed to respond to cobalt-60 radiation therapy (Manucy et al., 1998). Carboplatin has been used successfully for the treatment of a bile duct carcinoma in a yellow-naped Amazon parrot (*Amazona ochrocephala*) (Zantop, 2000) and pancreatic duct adenocarcinoma in a green-winged macaw (*Ara chloroptera*) (Speer and Eckermann-Ross, 2001.

**Vincristine (Oncovin, Indianapolis, Indiana, Eli Lilly)**

Vincristine is a vinca alkaloid that acts directly on the mitotic spindle and results in metaphase arrest. Vincristine is one of the few cytotoxic drugs that are not myelosuppressive. It causes local tissue necrosis following perivascular injection or intravenous extravasation. In domestic mammals, vincristine is commonly used to treat transmissible venereal tumours (TVTs), lymphomas, mast cell tumours and sarcomas. Except when treating TVT, it is usually used in combination with doxorubicin, cyclophosphamide, chlorambucil, and/or prednisone. Vincristine was used in the chemotherapeutic regime of an African gray parrot with malignant lymphoreticular neoplasia (Paul-Murphy et al., 1985), a Moluccan cockatoo with lymphoma (France and Gilson, 1993), and a Pekin duck with lymphoma and leukemia (Newell et al., 1991).

**Cyclophosphamide (Cytoxan, Evansville, IN, Mead Johnson)**

Cyclophosphamide is an alkylating agent that acts by cross-linking DNA. Alkylating agents are considered cell cycle-nonspecific. Cyclophosphamide is one of the most common and effective antineoplastic drugs in veterinary medicine. It is used alone or in combination to treat lymphoma, soft tissue sarcoma, feline mammary tumours, synovial cell sarcoma, haemangiosarcoma, thyroid carcinoma, and TVT. Common side effects include leukopenia, vomiting, diarrhoea, hair loss, and occasionally, sterile haemorrhagic cystitis. Cyclophosphamide was used to treat lymphoma in a Moluccan cockatoo (France and Gilson, 1993).

**Chlorambucil (Leukeran, Research Triangle Park, NC, Burroughs Wellcome)**

Chlorambucil is also an alkylating agent. In domestic mammals, it is used to treat lymphoma and as a substitute for cyclophosphamide when sterile haemorrhagic cystitis has been induced (Withrow and MacEwen, 1996). Chlorambucil was used successfully to treat cutaneous pseudolymphoma in a young blue and gold macaw; an increase in alanine aminotransferase (ALT) was noted in association with treatment (Kollias et al., 1992).

**L-asparaginase (Elspar, Singapore, Merck Sharp and Dohme)**

L-asparaginase is an enzyme that inhibits asparaginase synthetase and depletes asparagine levels in tumour cells. It is primarily used in combination with other drugs to treat lymphoma and lymphoblastic leukemia in domestic animals (Withrow and MacEwen, 1996). L-asparaginase was used in combination with other drugs to treat lymphoma in a Moluccan cockatoo, but was associated with weight loss, lethargy, anorexia, and regurgitation (France and Gilson, 1993).

**Doxorubicin (Adriamycin, Kalamazoo, MI, Adria laboratories)**

Doxorubicin belongs to a class of antibiotics used as cancer chemotherapeutics. It forms stable complexes with DNA, and inhibits DNA and RNA synthesis. Doxorubicin has broad-spectrum activity against a variety of tumours in domestic animals. Side effects and toxicity include myelosuppression, acute or chronic cardiac toxicity, and perivascular tissue necrosis. Hypersensitivity reactions are common, such that tumour patients are routinely pretreated with diphenhydramine and glucocorticoids. Using doxorubicin, complete remission was obtained for ~20 months in a blue-front Amazon with osteosarcoma (Doolen, 1994). Doxorubicin also was used (unsuccessfully) in combination therapy for lymphoma in a Moluccan cockatoo (France and Gilson, 1993).

**Radiation Therapy**

Radiation therapy is increasingly used in exotic animal medicine (Mauldin and Shiomitsu, 2005). Ionizing radiation kills cells by depositing energy on or near DNA, that eventually causes cell death. Proliferating cells such as tumour cells are more radiosensitive than quiescent cells. The goal of radiation treatment is to destroy the proliferative capability of the tumour without causing excessive damage to surrounding tissues. This is commonly achieved by dividing the total dose into a number of fractions, given over a period of time. Radiation doses are delivered in units known as Gray or Gy (1 Joule/kg or 100 rad). Ionizing radiation is administered by an external source (teletherapy) or through placement of radioactive isotopes, such as iodine-131, within the animal (brachytherapy). External beam teletherapy is classified as orthovoltage or megavoltage, depending on the energy of the photon. Megavoltage radiation (photons >1 MeV) is most commonly used at human medical facilities with linear accelerators or cobalt machines. Some centers still offer cesium treatment, which provides more uniform dose distribution than orthovoltage radiation, but which has limited skin-sparing effect. Orthovoltage is low energy radiation (150-400kVp) that distributes the maximum dose of radiation to the skin surface (Withrow and MacEwen, 1996).

**Table 1. Selected Tumours and Therapy**

| Tumour | Therapy | Outcome | Species and reference |
|---|---|---|---|
| Basal cell carcinoma | Surgical removal | Six weeks postoperatively, the masses recurred and tumour emboli found in pulmonary vessels | Blue-fronted amazon parrot (*Amazona aestiva*) (Tell et al., 1997) |
| Basal cell carcinoma | Surgical removal, incomplete | A squamous cell carcinoma occurred at the same site nine months later | Conure (Kern et al., 1996) |
| Bile Duct Carcinoma | Carboplatin | No reported recurrence | Yellow-naped Amazon parrot (*Amazona ochrocephala*) (Zantop, 2000) |
| Nonepitheliotropic cutaneous B-cell lymphoma | Vincristine and chlorambucil for 17 weeks | Resolved | Umbrella cockatoo (*Cacatua alba*) (Rivera et al., 2009) |
| Cutaneous pseudolymphoma | Chlorambucil | Recurred 3 months later. Treated again with no recurrence for 2.5 years | Blue and gold macaw (*Ara ararauna*) (Kollias et al., 1992) |
| Fibrosarcoma, cutaneous | Debulking orthovoltage radiotherapy and intratumoural cisplatin | Remission ~29 months with subsequent slow regrowth | Blue and gold macaw (*Ara ararauna*) (Ramsay et al., 1993) |
| Myxoid fibrosarcoma, wing | Radiation therapy and intratumoural chemotherapy with cisplatin | Complete tumour remission lasted 15 months until the macaw died of an unrelated causes | Blue and gold macaw (*Ara ararauna*) (Lamberski and Theon, 2002) |
| Granular cell tumour, cutaneous | Surgical removal | No recurrence in one year | Puerto Rican Amazon parrot (*Amazona vittata*) (Quist et al., 1999) |
| Haemangiomas, cloacal | Surgical removal | Mass recurred one year later in an incompletely removed | Amazon (Reavill, 2001) |
| Haemangiosarcoma, beak | Local radiation therapy | Tumour-free for six months | Swan (Reavill, 2001) |
| Haemangiosarcoma, wing | Cesium radiation | Died in 8 weeks due to disseminated haemangiosarcoma | Budgerigar (Freeman et al., 1999) |
| Liposarcoma, multiple cutaneous | Surgical removal | Multiple subcutaneous masses, euthanized | Monk parakeet (Myiopsitta monachus) (Tully et al., 1994) |
| Liposarcoma, single site on toe | Surgical removal | No recurrence or metastasis at six months | Green cheeked conure (Pyrrhura molinae) (Ritzman and Hawley, 1996) |

| Tumour | Therapy | Outcome | Species and reference |
|---|---|---|---|
| Lymphosarcoma, cutaneous with leukosis | Multiple drug chemotherapy: prednisone, vincristine, cyclophosphamide, doxorubicin, L-asparaginase, and alpha interferon with diphenhydramine and dexamethasone to minimize anaphylactic reactions | The solid tumours slowly regressed; however, the bird has remained leukaemic | Moluccan cockatoo (France and Gilson, 1993) |
| Lymphosarcoma, periocular | 4,000 orthovoltage radiation | Survived 2 months before recurrence | African grey parrot (Paul-Murphy et al., 1985) |
| Myelolipoma | Surgical removal | No recurrence | Peach-faced lovebird (Ozaki et al., 1996) |
| Myelolipoma | Surgical removal | No recurrence | Hyacinth macaw (Anodorhynchus hyacinthinus) (Latimer and Rakich, 1995) |
| Myelolipoma | Surgical removal | Died due to intra-operative haemorrhage | Cockatiel (Latimer and Rakich, 1995) |
| Osteosarcoma | Debulking and Doxorubicin | Remission ~20 months | Blue-fronted Amazon parrot (Doolen, 1994) |
| Pancreatic Duct Adenocarcinoma | Carboplatin was administered via intraosseous catheter at 5 mg/kg. Three doses of carboplatin were given, at four-week intervals. | Still alive | Green-Winged Macaw (Ara chloroptera) (Speer and Eckermann-Ross, 2001) |
| Squamous cell carcinoma of the mandibular beak | Cobalt-60 radiation, surgical debulking, antifungal therapy, and intralesional cisplatin | Ataxia and haematologic abnormalities were recorded before the bird died, no metastases | Buffon's Macaw (Ara ambigua) (Manucy et al., 1998) |
| Squamous cell carcinoma, choanal | Three 8 Gy radiation treatments | Mass recurred in 2 months | Amazon (Quesenberry 1997) |
| Squamous cell carcinoma, neck | Cobalt-60 teletherapy radiation and intralesional carboplatin treatment | Intralesional carboplatin treatment resulted in complete regression after the tumour failed to respond to cobalt-60 teletherapy radiation | Amazon parrot (Amazona ochrocephala) (Wilson et al., 2000) |

| Tumour | Therapy | Outcome | Species and reference |
|---|---|---|---|
| Squamous cell carcinoma, skin | The left patagial tumour was removed completely by electrocautery. Cisplatin was administered weekly into multiple sites on the right axillary tumour | Improved but locally invasive, euthanized | African grey parrot (Klaphake et al., 2006) |
| Squamous cell carcinoma, Uropygial gland | Intralesional carboplatin and surgical removal | One bird had complete surgical removal of the uropygial gland but died four months later of unknown causes. The other bird had incomplete gland removal and the tumour regrew during therapy. | Cockatiel and budgerigar (Reavill, 2001) |
| Squamous cell carcinoma, Uropygial gland | A single irradiation fraction of 100 Gy/8.3 mm from a Strontium-90 ophthalmic applicator | Resolved | Two budgerigars (Nemetz and Broome, 2004) |
| Squamous cell carcinoma, Uropygial gland | A strontium probe (Sr-90 Ophthalmic Applicator) at 100 Grays, Twice | Resolved | African grey Parrot (Pignon et al., 2011) |
| Synovial cell sarcoma | Surgical removal amputation | Metastases within 6 months | Sulphur crested cockatoo (Van Der Horst et al., 1996) |
| Thymoma | Surgical removal | No recurrence | Java Sparrow (Maeda et al., 1994; Rae and Shafer, 1996) |
| Thymoma | Surgical removal | Died of intra or post-operative haemorrhage, no metastases | Cockatiel, budgie, lovebird (Rae and Shafer, 1996) |

Acknowledgment: Drs. Angie Piccoli and Robert Schmidt for the original reviews and VIN for reference support.

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