NEOPLASMS OF BIRDS OF PREY

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SUMMARY

Historically, there has been a paucity of reports of neoplasms in birds of prey of the orders Falconiformes and Strigiformes. It was not clear if this accurately represented a low prevalence in these species or was merely a reflection of low level of detection and/or reporting such lesions. In this paper a survey of neoplasms and neoplasm-like lesions is reported. 122 neoplasms of 39 types were recorded from 120 birds, of 25 genera, represented by 44 species (93 falconiforms, 27 strigiforms) from several countries of the world. 50 cases were found at post-mortem, 41 were presented as clinical cases, which subsequently either died or were euthanased, whilst 29 were clinical cases which were effectively treated. The ages of affected birds ranged from 30 days to in excess of 40 years, with an average age of 10.2 years. 68% affected captive birds, 32% were in free-living birds. Of those cases where the sex was known, 68% occurred in female birds and 32% in male birds. The identity of these neoplasms, together with information about species of host and other relevant data, is discussed and attention is drawn to the difficulty in categorising accurately some of the cases, especially where the authors did not make the original diagnosis.

INTRODUCTION

Although neoplasms were described in birds of prey (Orders Falconiformes and Strigiformes) over 70 years ago (Fox 1923), reports of such lesions are still relatively few in number. To try to answer the question "Are neoplasms rare in raptors?" (Keymer 1972; Cooper 1985; Redig *et al* 1993), a survey was carried out, the results of which are presented in this paper.

MATERIALS AND METHODS

The survey was based upon 1) a note requesting information, sent by post, fax and e-mail to veterinarians and others in Europe, North America, East and North Africa and Australasia, as well as the reproduction of the same note in letter form, in various veterinary and pathology journals (producing 40 cases), 2) a literature search, using as its key words "Raptor, bird of prey, neoplasia, tumour", carried out in conjunction with the Library of the Royal College of Veterinary Surgeons (RCVS) (producing 47 cases), 3) the author's own previous cases (producing 35 cases of which 10 had been previously published).

For each unpublished case the following information was sought: - species (and, where appropriate, subspecies) of raptor, age and sex, captive or free-living, type of neoplasm diagnosed, site, whether or not considered malignant, any treatment given and outcome. Whenever possible histological section(s) of the lesion was requested, together with other material such as radiographs, 35 mm transparencies and laboratory results relating to diagnosis. Clinical histories and findings were reviewed by NAF, pathological reports by JEC and RJH.

The survey started in May 1997 and is ongoing.

RESULTS

A list of neoplasms reported by correspondents and/or recorded in the literature is given in Table I.

A total of 122 neoplasms were located in 44 species (including those described as "*Falco* sp.") of bird. The diagnoses are listed in Table 1. Where the identification of the neoplasm is given in inverted commas, this means that the authors are citing the original (sometimes, published) identity but have reservations about the diagnosis or believe the nomenclature to be outdated. Thus the number of tumour "types" in this survey is given as 39 but some of these are still under debate.

The numbers of neoplasms by genera was as follows: -

CATHARTIDAE (New World Vultures)
Genus Sarcoramphus   - 1.S. papa

ACCIPITRIDAE (Hawks and Eagles)
Genus Haliaeetus   - 1. H. leucocephalus
Genus Gypaetus   - 1. G.barbatus
Genus Gyps   - 1. G. coprotheres
Genus Torgus   1. T. tracheliotus
Genus Terathopius   - 1.T. ecaudatus
Genus Circus   -1. C. pygargus
Genus Accipiter   - 6 A. gentilis
                          - 1 A. nisus
                          - 1 A. cooperi
Genus Parabuteo   - 4 P. unicinctus
Genus Geranoaetus   1 G. melanoleucus
Genus Buteo   - 10 B jamaicensis
                          - 2 B regalis
                          - 1 B rufofuscus augur
Genus Buteo   - 7 B buteo
                          - 1 B lineatus
Genus Aquila   - 2 A rapax
                          - 3 A chrysaetos
Genus Hieraaetus   - 1 H dubius
Genus Lophaetus   - 2 L occipitalis

FALCONIDAE
Genus Polyborus   - 1 P plancus
Genus Falco   - 12 F peregrinus (including sub species)
                          - 4 F columbarius
                          - 3 F cherrug
                          - 3 F tinnunculus
                          - 2 F biarmicus
                          - 1 F ardosiaceus
                          - 1 F sparverius
                          - 3 F rusticolus
                          -2 F rusticolus x cherrug
                          - 1 F punctatus
                          - 1 F araea

STRIGIDAE
Genus Strix   - 2 S aluco
                      - 1 S uralensis
                      - 1 S varia

Genus Bubo	- 11 B virginianus
	- 2 B bubo (including sub species)
Genus Athene	- 3 A noctua
Genus Rhinoptynx	1 R clamator
Genus Nyctea	- 1 N scandiaca
Genus Speotyto	- 1 S cunicularia
Genus Asia	- 1 A flammeus
Genus Otus	- 1 O asio
Genus Aegolius	- 1 A acadicus

Analysis of tumour type

Data relating to cases are detailed below, but certain parameters may be unavailable for individual birds e.g. sex, age, free-living or captive. Where the reader requires greater details concerning any tumour type, cross reference may be made to Table 1, which includes a reference list. A selection of gross and histopathological illustrations of different tumour types is also included, where appropriate, together with a histological description.

Connective tissue tumours

Connective tissue neoplasms (fibrosarcoma, fibroma, myxosarcoma and myxoma) are of mesenchymal origin. Tumour cells are typically ovoid or spindle-like in appearance with a variable amount of intercellular collagenous or mucinous stroma which determines their sub-classification. Connective tissue tumours in poultry can sometimes arise following infection with specific strains of avian leukosis or sarcoma virus (Payne & Purchase 1991), but a viral pathogenesis has never been proved in raptors.

Fibrosarcoma - 17 clinical cases. (Coles 1985, Stetter & Nichols 1993, Jessup 1979, Harcourt-Brown 1994).
Age - Average age 6.9 years (range 6 months – 12 years).
Husbandry - 9 captive birds, 7 free-living birds.
Sex – 12 female birds, no male birds.
Species - Peregrine 3, Northern goshawk 3, red tail 3, miscellaneous falcons 3, miscellaneous owls 3, 1 eagle.
Sites - Six cases involved the wing, five cases affected either the head, neck or flank, and four cases affected the legs or feet. One case affected the liver, spleen, kidney and lung.

Fig 1   Well-differentiated fibrosarcoma from a saker (*Falco cherrug*) showing spindle-shaped cells.

Histology – Well differentiated lesions show spindle-shaped cells (Fig 1) but pleomorphism is a feature in less well differentiated cases. Mitotic index also varies (Fig2).

Fig 2   A higher-powered view showing mitoses. A saker (*Falco cherrug*).

Behaviour – 13 cases showed histological evidence of local invasion with multiple lesions in 4 birds. Of these four birds, one was considered have three concurrent primary sites, whilst metastasis had occurred in the other three cases. One case was benign. These findings are similar to the reported behaviour of fibrosarcoma in other avian species, which are traditionally classified as being locally invasive, with the potential to metastasise, especially to the abdominal cavity, lungs, liver, kidney, heart base and bone (Petrak & Gilmore 1982, Reece 1992. Early detection of a fibrosarcoma on an external site is essential to enable early and total surgical removal of the growth. Many cases examined in this survey primarily affected extremities and prompt surgical excision was generally curative. Intratumoral cisplatin and orthovoltage radiotherapy has been used successfully in the treatment of a fibrosarcoma in a macaw (Ramsay *et al* 1993).

Case outcomes - 7 birds underwent surgery and survived, 5 birds underwent surgery and the tumours recurred, 5 birds were euthanased.

Myxofibroma 1 clinical case affecting much of the plantar aspect of a 17 year old, captive female Cape vulture. Complete surgical removal was technically impossible, since which time (4 months) a very slow re-growth has occurred.

Histology - Essentially fibrous tissue with a pronounced, largely perivascular, myxomatous component (Fig 3).

Fig 3   Myxofibroma in a Cape vulture (*Gyps coprotheres*) showing fibrous tissue and pronounced myxomatous component.

Fibroma - 1 clinical case affecting the cere of a captive common kestrel which was surgically removed (Heidenreich 1997). Fibromas are rare avian tumours. They are

typically firm with a predilection for the skin or the subcutaneous tissues of the wing, leg, face, beak, neck or sternum (Chang *et al* 1969, Turrel *et al* 1987).
Histology - Well differentiated fibroblasts with few mitotic figures.

Histiocytic sarcoma - 2 clinical cases. (Sacre *et al* 1992).
Age – one < 1 year, one adult
Husbandry – 2 free-living birds.
Sex – 1 male, 1 female.
Species – Great horned owls
Sites – both were multicentric with one bird having lesions on the eye and foot, whilst the other involved internal viscera.
Histology - Predominantly large, highly pleomorphic, round to ovoid neoplastic cells with large, often abnormal nuclei and atypical mitosis.
Behaviour – although a retrovirus is suspected of being the cause of such neoplasms, virus isolation was negative in both cases.

Tumours of adipose tissue - 5 clinical cases.(Fox 1923, Heidenreich 1997)
Age – average age 13 years (range 9 - 16 years)
Husbandry - All cases affected captive birds.
Sex - 3 females, one male bird.
Species -. The species affected were, Northern goshawk, kestrel, saker, gyr, European eagle owl.
Sites - pedal 2, adjacent to the preen gland 1, dorsal wing 1.
Histology - Proliferation of otherwise normal adipose tissue – uniform lipocytes and flattened peripheral nuclei.
Behaviour - All these neoplasms behaved in a benign manner. Four, which were surgically excised, have shown no evidence of recurrence. Interestingly, lipomas appear to be far less common in raptors than in psittacine birds, in which they are the most frequently recorded neoplasm (Latimer 1994).

Tumours of bone / cartilage / muscle

Osteosarcoma - 2 clinical cases. (Kostka *et al* 1988, Heidenreich 1997).
Age - one bird of unknown age, the other being 20 weeks old.
Husbandry – 1 captive, one free-living bird.
Sex - 1 male, one unknown.
Species - 1 gyr x saker hybrid), the other a Eurasian buzzard.
Sites - The lesions presented in the radius and keel respectively.
Histology - Disorganised osseous tissue with proliferating osteoblasts.
Behaviour - Both tumours were slow growing but necessitated euthanasia.

Osteoma / chondroma – two cases presented clinically but subsequently died or were euthanased whilst 2 were found at necropsy. (Hahn *et al* 1998).
Age - average age was 13 years (range 6 – 15 years).
Husbandry – 2 captive, 2 free living birds.
Sex - 2 female one male bird.
Species – 1 kestrel and 3 miscellaneous owls.

Sites – Sites involved included the radius (2), the frontal bone and the tibiotarsus.
Histology - Proliferation of otherwise normal bone and cartilage.
Behaviour - osteomas are reported to be found infrequently in birds compared with osteosarcomas (Latimer 1994). Such tumours are curable, if surgical removal is technically possible.

Rhabdomyosarcoma – A single case affecting a male 19 year old Lappet-faced vulture which died suddenly. The neoplasm was found at necropsy as a discrete lesion in the myocardium.
Histology - Large cells with extensive eosinophilic cytoplasm and pleomorphic nuclei. Immunohistochemistry confirmed that the tumour was of muscle origin.

Leiomyoma – A single clinical case affecting the toe of a captive 17year old female golden eagle subsequently cured by surgical removal.
Histology - Swathes and interlacing bundles of plump fusiform cells with eosinophilic, slightly vacuolated, cytoplasm and no evidence of mitoses, as illustrated in Fig 4.

Fig 4   Leiomyoma from a golden eagle (*Aquila chrysaetos*). Note bundles of fusiform muscle cells.

Leiomyoma more typically arises from the smooth muscle of the gut, female reproductive tract (and hence present as a slowly growing abdominal distension), or occasionally vessels or ducts of the pancreas or spleen (Latimer 1994).

Mixed cell tumour – A single post mortem case in a free-living female Seychelles kestrel of 30 days of age (Cooper *et al* 1978). Multiple lesions were found in the chest and head. Although the tumour was considered to be of embryonal origin 2 clutch mates were apparently unaffected.
Histology - A mixture of tissues, including lymphangiomatous, epithelial and chondromatous elements (see Fig 5).

Fig 5   Mixed cell tumour from a Seychelles kestrel (*Falco araea*) showing different elements.

Tumours of Glandular tissues

Adenocarcinoma - 15 cases were identified. Nine of these were found post mortem, 4 were clinical cases which were euthanased, whilst two cases were cured by surgically excision. (Dillehay *et al* 1985, Cooper 1978, Cooper 1979, Appleby & Keymer 1971, Swayne & Weisbrode 1990, Blackmore 1965, Heidenreich 1997, Cooper *et al* 1993).
Age - average age of 21.4 years (i.e. significantly greater than the overall average age incidence), (range 6 – 26 years).
Husbandry – 5 cases were recorded in captive birds, five were free-living birds.
Sex - six birds were female and 2 birds were male.
Species - miscellaneous Buteo 5, miscellaneous falcons 2, miscellaneous eagles 2, miscellaneous owls 3, goshawk 1, Lammergeier 1.
Sites - The primary tumour involved a variety of glandular organs (oviduct, liver, preen gland, tongue, lung), with secondaries in many other tissues but particularly the liver.
Histology - Epithelial components, often in well formed acini, as in the case of the adenocarcinoma of a European buzzard (Fig 6).

Fig 6 Gross appearance of adenocarcinoma in the liver of a Eurasian buzzard (*Buteo buteo*).

Some cases are very poorly differentiated and the tissue of origin can be difficult to determine as in the oviduct adenocarcinoma in a Mauritius kestrel (Fig 7).

Fig 7 A poorly-differentiated oviduct adenocarcinoma from a Mauritius kestrel *(Falco punctatus*).

Behaviour - Most cases were fatal. The only two birds that survived had tumours of the preen gland, where early detection of the lesion by the owner or clinician enabling curative surgery to be performed. A higher incidence in females may be anticipated due to adenocarcinoma of the reproductive tract.

Adenoma – one clinical case, with two additional cases found post mortem. (Heidenreich 1997, Morishita *et al* 1998).

Age - average age incidence of 13.5 years (range 7 – 20 years)
Husbandry - One was a captive bird, two were free-living.
Sex - All affected birds were female.
Species - gyr hybrid, long crested eagle, and red tail buzzard.
Sites - One clinical case affected the nasolacrimal duct but the lesion could not be completely excised (Heidenreich 1997). The two other cases were incidental lesions found in the kidney at necropsy.
Histology - Proliferation of otherwise normal glandular tissue.

Carcinoma - 5 post mortem cases. (Wadsworth & Jones 1980)
Age - average age of 8 years (range 18 months – 10 years).
Husbandry - Four were captive birds.
Sex - 3 birds were male, none was female.
Species - Miscellaneous hawks and falcons were affected.
Sites - Lesions were located in the kidney, the air sac with secondaries in the liver.
Histology - Not always distinguishable from adenocarcinoma (see earlier). They are of epithelial origin, often poorly differentiated with bizarre cells (cytoplasm and nucleus) and high mitotic index. Necrosis can be a feature in rapidly growing carcinomas (Fig 8).

Fig 8 A rapidly growing carcinoma from a merlin (*Falco columbarius*). Central necrosis is present.

Behaviour - One case was localised (kidney) but the other four showed histological evidence of more aggressive growth (3) or metastasis (1).

Bile Duct Carcinoma – three cases were found post mortem. (Hartup *et al* 1995, Mikaelian *et al* 1998).
Age – average age incidence 23 years (range 13 – 33 years)
Husbandry - two birds were captive.
Sex – two birds were male.
Species - red tail buzzard (1) golden eagle (1)
Sites - In all cases the lesions originated from the liver.
Histology – Usually replaces hepatic tissue, causing liver enlargement (Fig 9).

Fig 9 Gross appearance of a bile duct carcinoma (cholangiocarcinoma) in a red tail hawk (*Buteo jamaicensis*).

Acinar structures lined by cuboidal on columnar cells which show pleomorphic and excess mitosis (Fig 10).

Fig 10 Histological view of the previous tumour showing glandular structures

All cases were highly malignant with multiple secondaries. There is no effective treatment for this neoplasm (Latimer 1994), which is rarely diagnosed before extensive metastatic spread has occurred.

Endocrine Tumours – no clinical evidence of disease was observed in any of the following cases, which were all found as incidental findings post mortem. This observation is similar to that of Latimer (1994).

Thyroid follicular cystadenoma – A single case in a captive 7 year old female cara cara.
Histology - A benign proliferation of areas of thyroid follicles.

Thyroid cystic fibroadenoma – one case in a captive > 27 year old Chilean Eagle.
 (Hamerton 1943)
Histology - Similar to thyroid follicular cystadenoma but with a pronounced fibrous component.

Adrenal cortical carcinoma: one case in a 20 year-old free living female long crested eagle. **Histology** - Neoplastic transformation of adrenal cortical cells.

Integumental Tumours
Squamous cell carcinoma - 13 cases. (Cooper *et al* 1993, Halliwell & Graham 1978, Ramis *et al* 1997).
Age – average age incidence of 8.7 years (range 4 – 15 years).
Husbandry – 9 captive, three free-living birds.
Sex - 4 male and 4 female birds.

Species – peregrine (7) (6 female, 1 male), miscellaneous owls (2), miscellaneous species (4). **Sites** – sites affected were predominantly the flank or thigh (8), with single cases affecting the palate, the metatarsus, the cloaca, and the base of the tail.

Outcome – 2 cases were cured by surgical excision, eight were clinical cases which either died or were euthanased as a consequence of their tumours, one case was found at post mortem.

Histology – The diagnostic feature is keratinised "prickle cells" forming "keratin pearls" (Fig 11).

Fig 11 Squamous cell carcinoma in a peregrine. (*Falco peregrinus*). "Keratin pearls" are evident.

Less well differentiated areas show little keratinisation only dark-staining epithelial cells (Fig 12).

Fig 12 A less well-differentiated area showing absence of keratin but proliferation of epithelium

Ulceration of overlying skin, with secondary infection, is often a feature and may be seen in clinical or post-mortem cases (Fig 13).

Fig 13 Gross appearance of a squamous cell carcinoma in a Barbary *falcon (Falco peregrinoides*) illustrating ulceration and secondary ulceration.

Metastasis to lung, bone and elsewhere are not uncommon. In this survey all squamous cell carcinoma were classified as locally invasive with potential to slowly metastasise. Although Latimer (1994) states that cutaneous squamous cell carcinoma rarely infiltrates the underlying skeletal muscle, this feature was not observed in some of these cases. Laminated keratin pearls were typically present within the better differentiated tumours, as has been noted in other companion and free living birds (Reece 1992). Paterson (1997) has described the use of topical 5-fluorouracil (Efudix; Roche Products), for the control of squamous cell carcinoma in other species. In view of the relatively slow rate of local infiltrative growth of cases in this survey the authors suggest that this drug has potential in the treatment of avian squamous cell carcinoma cases.

Epidermoid carcinoma – one clinical case and one additional post mortem case. (Kern *et al* 1996).
Husbandry - one bird was free-living.
Species - both cases affected red tail hawks.
Sites - Lesions were situated in the pharynx (1), and the nictitans (1).
Histology – Neoplastic epithelial cells are noted within the epidermis. The case involving the nictitans was cured by surgical excision.

Papillomas - 6 clinical cases. (Cooper 1978, Halliwell & Graham 1978, Wallach *et al* 1993).
Age – average age 4 years (range 6 months – 9 years).
Husbandry - 3 captive birds were affected.
Sex - two female and one male bird.
Species – peregrine (2), king vulture, goshawk, and tawny eagle.
Sites – Lesions involved the crop (3), glottis (1), cloaca (1) and digit (1).
Outcome - The digit, cloaca and glottis cases were cured by surgical excision.
Histology – Proliferation of epithelial cells, often with fibrovascular stalks (Fig 14).

Fig 14 Skin papilloma from a lanner (*Falco biarmicus*). This is essentially a benign proliferation of epithelium. This section shows minimal stalk.

Mitosis are usually seen but not in large numbers. In psittacine bird's hepatic (bile

duct carcinoma) and pancreatic (carcinoma) lesions may be secondary to cloacal or choanal papilloma. Cutaneous papilloma have been shown to be virus-induced in some avian species including, Amazon parrots, African grey parrots (Jacobson *et al* 1983), Chaffinches (Moreno-Lopez *et al* 1984) and Bramblings (Osterhaus *et al* 1977).
In this survey all cases not treated surgically were self-limiting.

Haemangioma - 1 case, in a 15 year old captive female peregrine, emanating from the skin of the dorsal cranium. This neoplasm was successfully excised surgically removed with no recurrence to date (4 years).
Histology - Dilated blood filled, spaces with no sign of malignant cells.

Mast cell tumours - 2 were clinical cases; a further case was found post mortem. (Schmidt & Okimoto 1992, Swayne & Weisbrode 1990).
Age - all cases affected adult birds of unknown age.
Husbandry - 2 were free-living, one was a captive bird.
Sex - 1 bird was male.
Species – All affected birds were owls.
Sites - Lesions were limited to the oral cavity or the head.
Histology – Proliferation of mast cells which usually contain granules that stain well with toluidine blue or Giemsa stain. Electron microscopical examination can help to identify the cells.
Outcome - One case was cured by surgical excision. In the other clinical case, the lesion re-grew three times following surgery, eventually necessitating euthanasia.

Tumours of the eye and neural tissue

Melanoma - two clinical cases were presented, one further case was found post mortem. (Fournier *et al* 1983, Kufou-Mensch & Watson 1992).
Age – average age 20 years (range 10 – 31 years).
Husbandry – two captive and one free-living birds were affected.
Sex – all affected birds were female.
Species – great horned owl (1), striped owl (1), red tail hawk (1).
Sites - Both clinical cases were affecting the eye, the post mortem (red tail) lesions were present in the lung and adrenal gland.
Histology – Usually a sheet of deeply pigmented (melanistic) cells-epithelioid, round to oval nuclei and prominent nucleoli.
One (striped owl) was euthanased as the tumour was highly malignant, in the other case (great-horned owl) the eye was enucleated. The tumour was found to be benign and there was no recurrence. In the one post mortem case, (a red tailed buzzard) the bird was euthanased on account of its clinical condition.

Astrocytoma – a single case was detected in the brain stem of a female great-horned owl post mortem. (Halliwell & Graham 1978). No histological description has been traced (Halliwell and Graham 1978), but it is assumed that the features are similar to those of an astrocytoma in other species.

Lymphoid tumours

Malignant lymphoma – one clinical case, 3 further cases were found post mortem. (Rosskopf *et al* 1987, Hruban *et al* 1992).
Age – average age 12 years (range >8 to 18 years).
Husbandry - All cases involved captive birds.
Sex - 3 females, 1 male
Species - peregrine (2), gyr (1), snowy owl (1)
Sites - Lesions were detected in the bone marrow, lungs, liver, pericardium, kidney, lymph node, spleen, small intestine, testes, fat.
Histology - Neoplastic lymphocytes infiltrating visceral organs (Figs 15 & 16).

Fig 15 Liver of a peregrine (*Falco peregrinus*) showing infiltration by neoplastic lymphocytes characteristic of malignant lymphoma.

Fig16 The same case as above at a higher magnification.

These tumours autolyse rapidly after death. The tumours could have been of viral origin but limited virus isolation attempts were not successful.

Malignant Thymoma – One case was discovered post mortem in a 12-year-old saker falcon. Lesions were found in the lungs, suggesting metastatic spread from the thymus. Death was attributed to vagal inhibition as a result of pressure. Histology was not described in detail.

Lymphoid leukosis – Four cases, of which 3 were found post mortem. (Higgins & Hannam 1985, Appleby 1952, Appleby & Keymer 1971).
Age - average age was 2.5 years (range 3 months to 3 years).
Husbandry – three were captive birds.

Sex – one case was male, one was female.
Species - merlin (1), one grey kestrel (1), Harris' hawk (1), Eagle owl (1).
Sites - Lesions were found in the liver and other viscera.
Histology – Sheets of neoplastic lymphoid infiltrating visceral organs, resulting in complete loss of normal lobular architecture (Fig 17).

Fig 17 Lymphoid leukosis in a merlin (*Falco columbarius*). The hepatic architecture has been completely lost.

In this survey, virus isolation, where attempted, was negative. Lymphoid leukosis is the commonest virus-induced neoplasm of chickens. Lymphoid leukosis is associated with tumour formation throughout the body, but particularly in the liver. In chickens less than 3% of infected birds develop tumours (Payne & Purchase 1991). In chickens disease most commonly occurs between four and nine months of age. Tumours typically form slowly over a period of more than 16 weeks (Fadley 1989). Antigenically distinct subgroups of avian leukosis-sarcoma viruses have been documented in a number of non poultry species, including pheasant, quail, partridges (Frisby *et al* 1979), whilst lesions similar to those seen in gallinaceous birds with lymphoid leukosis have been reported in a variety of other species (Ritchie 1995). The commonest gross post mortem finding is an enlarged yellowish-white liver and spleen.

Erythroblastosis – One case was detected in a gyr. (Halliwell & Graham 1978).
This form of erythrocytic leukaemia has been shown to be caused by retrovirus in poultry (Payne & Purchase 1991). No histological description has been traced (Halliwell and Graham 1978).

Myeloproliferative disease – was reported in two cases, affecting a bald eagle and unspecified falcons. No histological description has been traced (Halliwell & Graham 1978).

Lymphosarcoma – 3 cases were identified.
Age - one case affected a 22 year-old bird, the other cases were in birds of unknown age.
Husbandry - 1 free-living and one captive bird
Sex – one of the birds was male.
Species – Harris' hawk (1), great horned owl (1), miscellaneous hawks (1).
Sites – adjacent to the sternum (1), not specified (2).
Histology - Neoplastic lymphocytic cells infiltrating other tissues.

Lymphosarcoma, otherwise known as 'malignant lymphoma', is a lymphoid neoplasm originating from the peripheral lymphoid neoplasia. Tumours are commonly disseminated multisystemic neoplasms, affecting all tissues of the body, including the bone marrow (Bauck 1986, Calnek & Witter 1991, Palmer & Stauber 1981, Reece 1992). Clinical cases may present with swellings of the skin or retrobulbar masses (Bauck 1986), or abdominal enlargement and hepatomegaly. A variable number of immature (neoplastic) lymphocytes may be observed in the blood film (if the bird is leukaemic).

Marek's disease – 3 clinical cases were reported. (Woodford & Glasier 1955, Halliwell 1971, Halliwell & Graham 1978, Jennings 1954, Jennings 1978).
Age - average age of 3.5 months (range 2 – 5 months).
Husbandry – all affected birds were free-living.
Species – sparrow hawk (3 all from one clutch), great horned owl (1), little owl (1).
Sites – neural (sparrow hawks), sciatic nerve, liver, spleen, kidneys, pancreas, mesentery (great horned owl), unspecified viscera (little owl).
Outcome - All cases died or were euthanased.
Histology – Must be differentiated from lymphoid leukosis (see earlier). Involvement of nervous tissue is a feature of some cases of Marek's and the cells are more heterogenous. The sparrow hawks were presented with progressive wing and leg weakness, the great horned owl with leg paralysis. Mareks disease is a virus-induced neoplasm, can give rise to similar clinical and gross signs to lymphoid leukosis, although it generally affects younger birds and primarily affects the neural system (Ritchie 1995). In psittacine birds with Marek's disease cutaneous neoplasms may develop under the skin of the face or neck, often in association with generalised or systemic lymphosarcoma (Bauck 1986).

Lymphoid tumours - Discussion

Viruses in the family Retroviridae have been shown to cause neoplasms in poultry and possibly other species. The avian type C retroviruses of importance to birds are avian leukosis/sarcoma virus (ALSV), as well as reticuloendotheliosis virus (REV) group. ALSV as a group have been associated with a range of tumours including lymphoid leukosis, erythroblastosis, myeloblastosis, renal neoplasms (adenomas and carcinomas), haemangiomas and osteopetrosis in chickens (Payne & Purchase 1991). Similar viruses may cause different neoplasms in different birds depending on the age and route of infection as well as the species affected. The REV group induce tumours principally of the lymphoreticular or reticuloendothelial cells (Gerlach 1994). Occasionally these viruses are associated with other neoplasms such as histiocytic sarcoma, osteomas, chondrosarcomas, mesotheliomas, fibrosarcoma or myxosarcoma (Witter *et al* 1979, Witter *et al* 1981). Horizontal virus transmission occurs particular among young birds when viraemic birds shed virus via faeces or in any other body fluids. Mosquitoes, particularly *Culex annulirostis*, are reported to be capable of transmitting the virus after feeding on a viraemic bird (Gerlach 1994). Vertical transmission is possible, although not common. Most REV-induced neoplasms occur following horizontal spread in young. In raptors fed on avian (especially poultry) derived food, infection by ingestion may also occur.

Teratoma – A single clinical case in a 10 year old, male captive Eurasian buzzard. The bird was in poor body condition on presentation, with a firm distended abdomen. Following radiography, the bird was euthanased.

Grossly these primordial germ cell neoplasms may be large and cystic; originating from a variety of sites (Ritchie 1995).

Histology - The case in the survey is difficult to differentiate from an adenocarcinoma. The lesions showed a variety of tissues, including glandular components (Fig 18).

Fig 18 Part of a neoplasm from a Eurasian buzzard (*Buteo buteo*) diagnosed as a teratoma. Osseous, connective tissue and gland are visible.

Xanthoma – 3 cases, one of which was found post mortem.
Age - average age of 18 years (range 2 to > 40 years).
Husbandry – all affected birds were in captivity.
Sex - Two male and one female bird were affected.
Species - Eurasian buzzard, Bateleur eagle, and merlin.
Sites - pre orbital diverticulum of the infra orbital sinus (1), (a position where trauma was unlikely to have been a factor), the abdomen (1), spleen and liver (1).
Outcome – one case (buzzard – sinus) was cured by surgical excision, the other clinical case was euthanased.
Behaviour - xanthoma is not a true neoplasm, but an inflammatory intumescence resulting from lipid-laden macrophages, giant cells, free cholesterol and variable degrees of fibrosis. Xanthomas appear as single or multiple, subcutaneous nodules or yellowish thickenings of the skin, which may be featherless, ulcerated or haemorrhagic (Turrel *et al* 1987). Xanthomas are on occasions found overlying other neoplasms, or at a site of repeated chronic trauma or inflammation.

Mesothelioma - 2 cases, one of which was found post mortem. (Cooper & Pugsley 1984, Cooper *et al* 1993).
Age - average age 4.5 years (range 4 – 5 years)
Husbandry – both birds were captive.
Sex – one bird was female.
Species – both were ferruginous buzzards.
Sites - the lesions were the triosseum, pneumatic humerus and lung in one case and the distal humerus in the other.
Histology – A papillomatous, branching tumour with cuboidal lining cells (Fig 19).

Fig 19 Histological appearance of a mesothelioma from a ferruginous hawk (*Buteo regalis*). The papillomatous appearance is typical

The bone is often involved (Fig 20).

Fig 20 Humerus of the above case showing bone involvement

Outcome – the single clinical case involving the distal humerus was cured following amputation of the wing proximal to the lesion.
Behaviour - The neoplasms were described as being infiltrative. No viruses were isolated.

DISCUSSION

MANAGEMENT OF AVIAN TUMOURS

Little is known about the aetiology, pathogenesis, incidence and biological behaviour of neoplasms affecting captive and free living birds. Turrel *et al* 1987, suggested that most external tumours are benign, whilst most internal neoplasms are malignant. The authors would, however, urge clinicians not to accept this generalisation particularly in view of the frequent occurrence of fibrosarcoma and squamous cell carcinoma, both of which are usually obvious and invasive. Some forms of neoplasia do appear to be commoner in certain species. Greater awareness of these species' susceptibilities should enable clinicians to make earlier and more accurate diagnosis, thus improving case prognosis. When presented with a possible case of neoplasia the clinician is advised to carry out a thorough examination, assessing the bird as a whole, then concentrating on the tumour itself. In this way inter-current disease, and any additional tumour lesions may be detected, influencing the overall outcome of the case.   Although fine needle aspirates and cytology are very valuable, they should be complemented wherever possible by histological examination by an experienced avian pathologist. Although there is

some historical information on the diagnosis and treatment of avian neoplasms (Turrel *et al* 1987, Schmidt 1992), clinicians should be aware of the great advances in comparative oncology in recent years and consider using therapeutic regimes that have proved effective in other species.

Clinical investigation of cases in the series ranged from simple examination and taking of cytological preparations or biopsies, through radiography and ultrasonography to surgical intervention. In some instances follow-up was possible, in others not. Some clinical cases were subsequently examined post mortem. Other cases were first seen at necropsy.

It is not possible on the limited data available to calculate the true prevalence of neoplasms of birds of prey, nor any specific species, sex or age incidence. Our search, does however, indicate that such tumours are not uncommon and that failure to report is a more likely explanation for their apparent scarcity. As a consequence of more raptors being kept in captivity, some of which are likely to survive longer than in the wild, clinicians may well be presented with an increasing number of raptor neoplasia cases in the future.

The literature search yielded over 40 references and added weight to the argument that neoplasms occur more frequently than had previously been supposed. Most of the references located were in English, a small number in German: nothing relevant was found in the French literature. Others undoubtedly exist in other languages not covered by the RCVS database.

Tumour nomenclature is sometimes confusing in cases reported in the literature and malignancy has not always been clearly defined. "Benign" neoplasms were defined by Willis (1960) as those that "grow only slowly, remaining quite local, do not invade neighbouring tissues and cause no harm except by virtue of the position or some accidental complication". "Malignant" neoplasms, on the other hand, "grow rapidly, invade neighbouring tissues, spread by metastases, and, unless extirpated at an early stage, inevitably prove fatal".

Identifying and determining the origin of a neoplasm is not always easy, especially for the clinician, even with recourse to biopsy examination. A superficial or palpable lesion is not necessarily primary as it may have metastasised from elsewhere; likewise secondary neoplasms often occur in sites and tissues far removed from the primary tumour. A detailed thorough necropsy is therefore essential to determine likely primary and secondary deposits. Metastases can grow larger than the primary tumour if in a good tumour bed.

In some cases the primary lesion is never found, either because necropsy has not been performed or was incomplete or because histological sections were unrepresentative of the suspect lesion. The authors also have reservations about some of the earlier reports where laboratory investigations were limited- the cases of "Marek's disease", for instance. Multicentric tumours, e.g. lymphoma, must be distinguished from those involving multiple metastases seeding a variety of organs.

Critical review of reports and pathological material in this survey enabled re-assessment of a number of original diagnoses: for example, the "renal adenocarcinoma" in a *Buteo buteo* reported by Cooper (1978) was probably an adrenal tumour since it is most unlikely that both kidneys of the bird would have been simultaneously involved if it was of primary renal origin.

A variety of factors will influence whether or not a suspect neoplasm is correctly categorised but histological examination by an experienced avian pathologist is essential. Cytology is a useful tool in some circumstances but has limitations so the provisional diagnosis should be backed up by conventional histology where possible. A good morphological description of the tumour is necessary, supported by illustrations if possible for comparative purposes both retrospectively and prospectively. In some malignancies the cell type is difficult to determine – especially if it is primitive, anaplastic or poorly differentiated. Superimposed secondary factors such as necrosis, trauma, infection or autolysis may further complicate the lesion. Even when a morphological description is given, pathologists will sometimes disagree on their interpretation or conclusions. Sometimes it is difficult to decide whether or not a lesion is a true neoplasm. Some hyperplastic, metaplastic and chronic inflammatory changes may mimic neoplasia, as will developmental abnormalities.

Although taxonomically quite distinct, data from Falconiformes and Strigiformes have been combined in this paper since both Orders are considered to be "birds of prey" or "raptors", sharing many similarities in terms of anatomy, behaviour and nutrition and generally being subject to similar management.

Treatment of neoplasia in birds relied largely on surgery. The use of chemotherapy and radiation therapy is a new and unexplored field (Quesenbery 1997). A number of chemotherapeutic agents have recently been used in birds, including prednisolone (Bauck 1992, Turrel 1987, Campbell 1984), doxorubicin (Doolen 1994), cisplatin (Ramsay *et al* 1993), chlorambucil (Kollias *et al* 1992), combination therapy involving prednisolone, cyclophosphamide, vincristine, doxorubicin, asparginase and alpha interferon (France & Gilson 1993), often with good responses. The authors encourage clinicians to study current avian and comparative literature prior to treatment of raptor neoplasia cases, as this is a rapidly developing field.

CONCLUSIONS

A number of conclusions have been drawn from this survey: -

1) neoplasms in birds of prey are not as rare as previously surmised. The survey has uncovered many individual cases not previously published. Greater publicity should encourage the reporting of further cases and more rigour in description and diagnosis.

Substantial numbers of raptors are now kept and bred in long-term captivity. Longevity, inbreeding (Latimer 1994) and exposure to potential carcinogens, may well increase the likelihood of neoplasia, including hitherto unrecorded tumour types, enabling a more accurate assessment of incidence and prevalence.

2) as a corollary to the above, neoplasia should always be considered as a differential diagnosis when a bird of prey is presented with clinical signs that could be consistent with localised or generalised neoplastic disease. A full range of investigative tests should be carried out, including both cytological and histological examination. Transmission electron microscopy should be considered where facilities and funding permit. This co-ordinated approach must involve clinicians and pathologists liaising closely with bird owners/keepers.

3) much remains to be learned about neoplasms of the Orders Falconiformes and Strigiformes. The establishment and maintenance of an international reference collection would be a starting point. With this in mind, the authors plan to continue their present study and, where possible, to retain relevant materials and supporting case histories, radiographs, laboratory results etc. as a database which will be made available to others. In addition, the search for relevant literature continues. The references cited at the end of this paper are not a complete list and more could be added.

4) in contrast to captive birds, there is still a dearth of information on the frequency and type of neoplasia in free-living birds of prey. Some species of raptors, especially those in small numbers that have been through a population "bottleneck", possibly exposed to toxic chemicals in their environment and other stressors, may be particularly at risk, (Cooper 1979, 1984). Biologists working with free-living raptors should, therefore, be encouraged to carry out routine health monitoring and to involve veterinarians in investigations into morbidity and mortality.

cases.

TABLE 1
Occurrence of neoplasms in different species
(Bold numbers in brackets indicate number of different neoplasms: number of different birds)

Species	Neoplasms	Relevant references
Falconiformes		
Falco peregrinus (including subspecies)	Haemangiosarcoma, squamous cell carcinoma (4), lymphoma (2), oesophageal papillomatosis, "adenocarcinoma", haemangioma, fibrosarcoma (**7/11**)	Halliwell & Graham 1978; Heidenreich 1997; Rosskopf *et al* 1987
Falco cherrug	Thymoma, fibrosarcoma, lipoma (**3/3**)	
Falco tinnunculus	Osteoma, fibroma, fibrosarcoma (**3/3**)	Heidenreich 1997
Falco biarmicus	Squamous cell carcinoma, carcinoma (**2/2**)	
Falco columbarius	Lymphoma, carcinoma, fibrosarcoma, xanthoma (**4/4**)	Higgins *et al* 1985
Falco ardosiaceus	Lymphoma (**1/1**)	Appleby & Keymer 1971
Falco sparverius	Lipoma (**1/1**)	Fox 1923
Falco rusticolus	Erythroblastosis, lipoma (**2/2**)	Halliwell & Graham 1978
Falco peregrinoides	Squamous cell carcinoma (**1/1**)	Cooper *et al* 1993
Falco rusticolus x *cherrug*	Adenoma (**1/1**)	Heidenreich 1997
Falco punctatus	Adenocarcinoma (**1/1**)	Cooper 1978
Falco araea	"Mixed cell tumour" (**1/1**)	Cooper *et al* 1978
Falco cherrug	Fibrosarcoma, lipoma (**2/2**)	Heidenreich 1997
Falco sp.	Squamous cell carcinoma, oesophageal papillomatosis, "myeloproliferative disease" (**3/3**)	Cooper 1985; Halliwell & Graham 1978

Gypaetus barbatus	Tubular adenocarcinoma (**1/1**)	
Buteo jamaicensis	"Epidermoid carcinoma", malignant melanoma, fibrosarcoma (2), "cholangiocarcinoma", renal carcinoma, renal tubularadenoma, adenocarcinoma of the uropygial gland. (**7/8**)	Kern *et al* 1996; Kufou-Mensch *et al* 1992; Stetter & Nichols 1993; Hartup *et al* 1995
Buteo regalis	Mesothelioma (**1/1**)	Cooper & Pugsley 1984
Buteo buteo	Adenocarcinoma (2), "teratoma/adenocarcinoma", osteosarcoma (**3/4**)	Kostka *et al* 1988; Cooper *et al* 1993; Cooper 1978
Buteo linetus	Retroperitoneal sarcoma (**1/1**)	Fox 1923
Buteo rufofuscus augur	Clear cell carcinoma (**1/1**)	Wadsworth & Jones 1980
Accipiter gentilis	Fibrosarcoma, lipoma, bile duct carcinoma, "spindle cell sarcoma" (2), "adenocarcinoma" (**5/6**)	
Aquila rapax	Fibropapilloma, granuloma/fibroma (**2/2**)	
Aquila chrysaetos	Leiomyoma (**1/1**)	
Hieraaetus dubius	Adenocarcinoma (**1/1**)	Appleby & Keymer 1971
Circus pygargus	Squamous cell carcinoma (**1/1**)	Ramis *et al* 1997
Geranoaetus melanoleucus	Cystic fibroadenoma (**1/1**)	Hamerton 1943
Parabuteo unicinctus	Renal carcinoma, lymphoma (**2/2**)	
Accipiter nisus	"Marek's" (**1/1**)	Woodford & Glasier 1955
Haliaeetus leucocephalus	"Myeloproliferature disease", squamous cell carcinoma (**2/2**)	Halliwell & Graham 1978
Lophaetus occipitalis	"Adrenal cortical carcinoma", "renal tubular adenoma" (**2/2**)	
Polyborus plancus	"Thyroid follicular cystadenoma" (**1/1**)	

Rhinoptynx clamator	Malignant melanoma of eye (**1/1**)	
Terathopius ecaudatus	Xanthoma (**1/1**)	
Sarcoramphus papa	Papillomatosis (**1/1**)	Wallach & Boever 1983
Gyps caprotheres	Myxofibroma (**1/1**)	Griner 1983

<u>Strigiformes</u>

Strix aluco	"Chondroma/osteoma", fibrosarcoma (**2/2**)	
Strix uralensis	Osteoma (**1/1**)	
Bubo virginianus	Iris melanoma, astrocytoma, mast cell tumour, adenocarcinoma, malignant histiocytoma, "Marek's", (**6/6**)	Fournier *et al* 1983; Halliwell 1971; Halliwell & Graham 1978; Howard *et al* 1996; Sacre *et al* 1987; Swayne & Weisbrode 1990; Dillehay *et al* 1985
Bubo bubo (including subspecies)	Leukosis, "testicular tumour", squamous cell carcinoma (**3/3**)	Cooper *et al* 1993; Appleby 1952; Fiennes 1960
Nyctea scandiaca	Lymphoma, fibrosarcoma, (**2/2**)	Hruban *et al* 1992
Speotyto cunicularia	Mast cell tumour, fibrosarcoma (**2/2**)	Schmidt & Okimoto 1992; Jessup 1979
Asio flammeus	Mast cell tumour (**1/1**)	Schmidt & Okimoto 1992
Athene noctua	Adenocarcinoma, "visceral lymphomatosis/Marek's" (**2/2**)	Blackmore 1965; Jennings 1954; Graham & Halliwell 1978

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