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SHORT PAPER

Neoplasia In Snakes At The National Zoological Park, Washington, DC (1978–1997)

J. L. Catão-Dias and D. K. Nichols*

Department of Pathology, Faculty of Veterinary Medicine and Zootechny, University of São Paulo, Av. Dr Orlando Marques de Paiva, 87 Cidade Universitária, São Paulo, SP 05508-000, Brazil and *Department of Pathology, National Zoological Park, Smithsonian Institution, Washington, DC, 20008-2598 USA

Summary

Of 291 juvenile and adult snakes examined *post mortem* over a 20-year period (1978–1997) at the National Zoological Park (NZP) in Washington, DC, 36 (24 females and 12 males) had neoplasms. Two snakes had tumours of two or three different types, but the other 34 snakes had only one type. All affected animals were adults and their average time on exhibit at the NZP was 108.9 months. Malignant neoplasms (79.5%) outnumbered benign neoplasms (20.5%). Of the malignant tumours, 19 (61.3%) were considered to have arisen in mesenchymal tissues, 11 (35.5%) were of epithelial origin, and one (3.2%) was derived from neuroectodermal tissues. All the benign neoplasms were of epithelial origin. Neoplasms of the lymphoid and haematopoietic tissues were the most common (12 cases), followed by tumours of the liver and biliary tract (seven cases) and the gastrointestinal tract (four cases).

Neoplastic diseases are among the most important causes of morbidity and mortality in domestic animals (Moulton, 1990). However, the prevalence of neoplasia in snakes and other reptiles is not well documented, the literature on this topic consisting mainly of single-case reports in animals from a wide variety of sources (Jacobson, 1981; Frye, 1991; Done, 1996). Reptile collections maintained in zoological parks are unique sources of information on neoplastic disorders because the animals are usually subjected to fairly constant environmental conditions and are allowed to live out their life span. However, there are no more than a few detailed reports on neoplasia in ophidian collections (Montali, 1980; Griner, 1983; Harshbarger and Ippen, 1991; Ramsay and Fowler, 1992; Ramsay *et al.*, 1996). The purpose of this communication is to report the neoplasms that occurred in snakes subjected to post-mortem examination at the National Zoological Park (NZP) during the 20-year period, 1978–1997.

All juvenile and adult snakes from the NZP reptile collection that died during this period (n=291) were subjected to a complete necropsy. Samples from major organs were fixed in neutral-buffered 10% formalin, processed by routine methods for histology, sectioned at 4–6 µm, and stained with

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haematoxylin and eosin (HE). Bone samples were decalcified in trichloroacetic acid before being processed for histological examination. Special stains, including periodic acid-Schiff (PAS), mucicarmine, and Alcian blue, were used on selected cases. Neoplasms detected were classified on the basis of their gross appearance, microscopical characteristics, histogenesis, invasiveness, and the presence or absence of metastases (Moulton, 1990).

Of the 291 snakes examined, 36 (12.4%) had tumours. One had three different types of neoplasm and a second snake had two, but the other 34 had only a single type. Table 1 lists the cases by snake Family, species (common and scientific names), sex, time on exhibit at the NZP, tumour type, and organ of origin. Twenty-four (66.7%) of the snakes with neoplasms were female and 12 (33.3%) were male. The exact age of most of the snakes was not known; however, all the affected animals were adults and their time of exhibition at the NZP ranged from 18–240 (mean 108.9) months.

A meaningful statistical analysis of our data is not possible due to the high diversity of species affected and variations in the composition of the snake collection at the NZP over this 20-year period. However, some trends in ophidian neoplasia are evident. Thirty-one tumours $(79\cdot5\%)$ were malignant and eight $(20\cdot5\%)$ were benign. Among the malignant neoplasms, 19 (61·3%) were derived from mesenchymal tissues, 11 (35·5%) were of epithelial cell origin, and one $(3\cdot2\%)$ was a chromatophoroma (a tumour of pigment-producing cells derived from embryonic neuroectoderm) (Frye, 1991). Of the benign tumours, seven (87·5%) were adenomas and one $(12\cdot5\%)$ was a thymoma, composed predominantly of epithelial cells.

The lymphoid and haematopoietic tissues, which were more commonly affected than other tissues, accounted for 30.8% (12/39) of all the tumours in this study (Figs 1 and 2); the liver and the biliary tract accounted for 17.9% (7/39) (Figs 3, 4 and 5) and the gastrointestinal tract for 10.3% (4/39). The oral cavity, urinary tract and cardiovascular system were each affected by three types of tumour. Two types affected the endocrine glands. The musculoskeletal, respiratory and reproductive systems, the subcutis and pigment-producing cells were each affected by one type.

Neoplastic diseases were once thought to be rare in reptiles (Lucké and Schlumberger, 1949). In the present study, 12.4% of snakes examined *post* mortem had neoplasms. This prevalence is 3–5 times higher than that reported previously in zoo reptile collections (Montali, 1980; Griner, 1983; Hubbard et al., 1983; Harshbarger and Ippen, 1991), except for a recent study in which 17.5% of all reptiles and 23.1% of snakes examined post mortem at the Sacramento Zoo had tumours (Ramsay and Fowler, 1992; Ramsay et al., 1996). The high prevalence recorded at the NZP and Sacramento Zoo may have been the result of extended life span due to improved husbandry.

The higher proportion of malignant than benign tumours seen in the snakes of this study has also been noted in reptiles by others (Effron *et al.*, 1977; Hubbard *et al.*, 1983; Ramsay and Fowler, 1992; Ramsay *et al.*, 1996). Of the malignant neoplasms that we saw, most (61.5%) were derived from mesenchymal tissues and 35.5% were of epithelial origin. In contrast, ophidian malignant tumours reported in the Registry of Tumours of Lower Animals

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Table 1

Snakes with neoplasia at the National Zoological Park, Washington, DC 1978-1997

Animal	Sex	Time on exhibition (months)	Neoplasm (and site)
BOIDAE			
Brazilian rainbow boa	Μ	31	Lymphosarcoma (multiple organs)
Brazilian rainbow boa	Μ	240	Adenoma (pancreas)
Brazilian rainbow boa	F	70	Myelomonocytic leukemia
Brazilian rainbow boa	F	163	Squamous cell carcinoma (mouth)
Emerald tree boa	Μ	193	Leiomyosarcoma (testis)
Emerald tree boa	F	65	Lymphosarcoma (multiple organs)
Emerald tree boa	F	80	Adenocarcinoma (adrenal)
Green tree python	Μ	124	Lymphoid leukemia (multiple organs)
Green tree python	Μ	130	Fibrosarcoma (mouth)
			Chromatophoroma (small intestine)
Green tree python	F	104	Thymoma (thymus)
Green tree python	F	109	Myeloid leukemia (multiple organs)
Green tree python	F	168	Lymphosarcoma (multiple organs)
Yellow anaconda	F	165	Cystadenoma (kidney)
COLUBRIDAE			· · · · · ·
Black ratsnake	М	34	Rhabdomyosarcoma (maxilla)
Black ratsnake	F	67	Rhabdomyosarcoma (heart)
Cornsnake	M	18	Adenocarcinoma (lung)
Cornsnake	F	65	Adenocarcinoma (cloaca)
Cornsnake	F	90	Myeloid leukemia (multiple organs)
Cornsnake	F	111	Leiomyosarcoma (duodenum)
Cornsnake	F	137	Adenocarcinoma (adrenal)
Eastern milksnake	M	101	Adenocarcinoma (colon)
Eastern milksnake	M	151	Adenoma (biliary tract)
Rufous beaked snake	M	128	Haemangiosarcoma (lung, muscle)
Rufous beaked snake	F	34	
Rufous beaked snake	F	183	Lymphosarcoma (multiple organs)
Eastern kingsnake	г F	165	Fibrosarcoma (subcutis) Tubular adenoma (kidney)
Sinaloan milksnake	F	76	
	г F	49	Hepatocellular adenoma (liver) Hepatocellular carcinoma (liver)
Taiwan beauty snake	T,	чJ	riepatotentulai carenionia (nver)
ELAPIDAE			
Asian cobra	F	134	Hepatocellular carcinoma (liver)
Asian cobra	F	151	Hepatocellular carcinoma (liver)
King cobra	F	174	Tubular adenoma (kidney)
VIPERIDAE			
Gaboon viper	М	48	Lymphosarcoma (multiple organs)
Gaboon viper	F	38	Lymphosarcoma (multiple organs)
1	г F	30 124	
Gaboon viper	г F	124	Squamous cell carcinoma (mouth) Myeloid leukemia (multiple organs)
Copperhead	г	100	Cholangiocarcinoma (liver)
			Haemangiosarcoma (vena cava)
Saw-scale viper	М	34	0
Saw-scale viper	1/1	34	Hepatocellular carcinoma (liver)

Brazilian rainbow boa – Epicrates cenchria cenchria; Emerald tree boa – Corallus caninus; Green tree python – Chondropython viridis; Yellow anaconda – Eunectes notaeus; Black ratsnake – Elaphe obsoleta obsoleta; Cornsnake – Elaphe guttata; Eastern milksnake – Lampropeltis triangulum triangulum; Rufous-beaked snake – Rhamphiophis oxyrhynchus; Eastern kingsnake – Lampropeltis g. getulus; Sinaloan milksnake – Lampropeltis triangulum sinaloae; Taiwan beauty snake – Elaphe taeniura; Asian cobra – Naja naja; King cobra – Ophiophagus hannah; Gaboon viper – Bitis gabonica; Copperhead – Agkistrodon contortrix; Saw-scale viper – Echis carinatus.

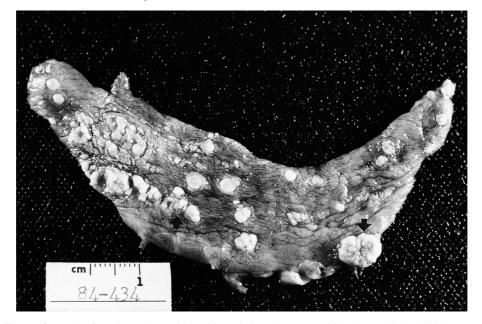


Fig. 1. Stomach of a gaboon viper with multicentric lymphosarcoma. Note the multiple, whitish masses of variable size scattered throughout the mucosa (arrows).

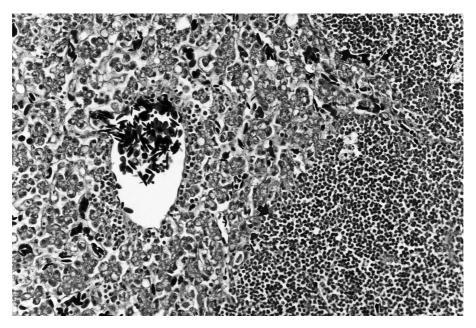


Fig. 2. Photomicrograph of the liver of the gaboon viper (Fig. 1) with multicentric lymphosarcoma. The hepatic parenchyma is effaced by infiltrates of monomorphic cells. HE. ×240.

at the Smithsonian Institution (Machotka and Whitney, 1980) and at the Sacramento Zoo (Ramsay *et al.*, 1996) were more often of epithelial than mesenchymal origin. It should be noted, however, that all cases of ophidian

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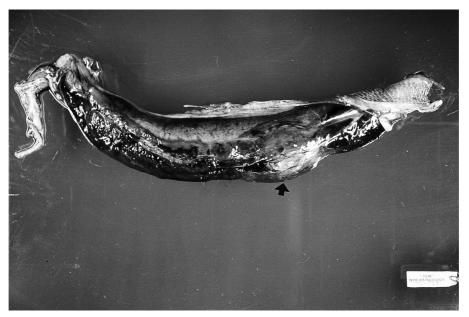


Fig. 3. Liver of an Asian cobra with hepatocellular carcinoma. A large oval-shaped mass (arrow) is located in the right side of the liver and has multiple blood clots adhering to its surface.

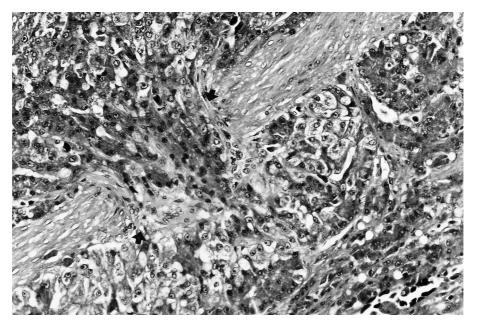


Fig. 4. Photomicrograph of the hepatocellular carcinoma shown in Fig. 3. The neoplasm is composed of cords and sheets of anaplastic cells. Focally, there is rupture of the surrounding fibrous tissue capsule with invasion of adjacent hepatic parenchyma by neoplastic cells (arrows). HE. × 240.

neoplasia reported at the San Antonio Zoo during a 10-year period were malignant and derived from mesenchymal tissue (Hubbard *et al.*, 1983).

Neoplasms arising from the lymphoid and haematopoietic tissues were the most common types in the present study, accounting for 30.8% of all tumours. This is consistent with previous reports from other institutions (Effron *et al.*, 1977; Machotka and Witney, 1980; Hruban *et al.*, 1992); it should be pointed out, however, that no tumours of this type were seen by Ramsay *et al.* (1996). The relatively high incidence of tumours of lymphoid and haematopoietic tissues suggests infection (Frye, 1991) with an agent such as a retrovirus or herpesvirus. The occurrence of virus-like intranuclear inclusions in a California kingsnake (*Lampropeltis getulus californiae*) lymphosarcoma was reported by Jacobson *et al.* (1980), but the presence of viral particles within these inclusions could not be confirmed by transmission electron microscopy.

The possible role played by oncogenic viruses in neoplastic disorders in reptiles has been discussed by others. Jacobson (1993) described papillomas associated with infection by a papovavirus in side-neck turtles (*Platemys platycephala*) and herpesvirus infection in European emerald lizards (*Lacerta viridis*). The presence of "C" type retrovirus in cultured spleen cells from a Russell's viper (*Vipera russellii*) with a splenic myxofibroma was reported by Ziegel and Clark (1969), and a similar virus was identified in an embryonal rhab-domyosarcoma in a cornsnake by Lunger *et al.* (1974).

The relatively high frequency of neoplastic diseases in snakes in the present report and in that of Ramsay *et al.* (1996) indicates the need for further research into the aetiology and pathophysiology of ophidian neoplasia. As improved husbandry conditions continue to increase the life span of captive snakes, it is likely that other institutions will experience an increasing incidence of ophidian neoplasia.

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References

- Done, L.B. (1996). Neoplasia. In: *Reptile Medicine and Surgery*, D.R. Mader, Ed., W.B. Saunders, Philadelphia, pp. 125–141.
- Effron, M., Griner, L. and Bernirschke, K. (1977). Nature and rate of neoplasia found in captive wild mammals, birds and reptiles at necropsy. *Journal of the National Cancer Institute*, **59**, 185–198.
- Frye, F.L. (1991). Common pathologic lesions and disease processes: neoplasia. In: *Reptile Care. An Atlas of Diseases and Treatments*, F.L Frye, Ed., T.H.F. Publications Inc., Neptune City, New Jersey, pp. 576–619.
- Griner, L.A. (1983). Pathology of Zoo Animals. Zoological Society of San Diego, San Diego, California, pp. 60-64.
- Harshbarger, J.C. and Ippen, R. (1991). Reptile neoplasms from the Berlin Animal Park and Dresden Zoological Park in the Registry of Tumours in Lower Animals.

In: Proceedings of the 4th International Colloquium on Pathology of Reptiles and Amphibians. Giessen, Germany, pp. 181-190.

Hruban, Z., Vardiman, J., Meehan, T., Frye, F. and Carter W.E. (1992). Haematopoietic malignancies in zoo animals. Journal of Comparative Pathology, 106, 15-24.

Hubbard, G.B., Schmidt, R.E. and Fletcher, K.C. (1983). Neoplasia in zoo animals.

Journal of Zoo Animal Medicine, 14, 33-40. Jacobson, E.R. (1981). Neoplastic diseases. In: Diseases of Reptilia, J.E. Cooper and

O.F. Jackson, Eds, Academic Press, London, pp. 429–468. Jacobson, E.R. (1993). Viral diseases of reptiles. In: Zoo and Wild Animal Medicine. Current Therapy 3, M.E. Fowler, Ed., W.B. Saunders, Philadelphia, pp.153-159.

- Jacobson, E.R., Seely, J.C. and Novilla, M.N. (1980). Lymphosarcoma associated with virus-like intranuclear inclusions in a California king snake (Colubridae: Lampropeltis). Journal of the National Cancer Institute, 65, 577–579.
- Lucké, B. and Schlumberger, H.G. (1949). Neoplasia in cold-blooded vertebrates. Physiological Review, 29, 91–126.
- Lunger, P.D., Hardy, W. Jr and Clark, H. (1974). "C"-type particles in a reptilian tumour. *Journal of the National Cancer Institute*, 52, 1231–1235.
 Machotka, S.V. and Whitney, G.D. (1980). Neoplasms in snakes: report of a probable
- mesothelioma in a rattlesnake and thorough tabulation of earlier cases. In: Comparative Pathology of Zoo Animals, R.J. Montali and G. Migaki, Eds, Smithsonian Institution Press, Washington, D.C., pp. 593–602. Montali, R.J. (1980). An overview of tumours in zoo animals. In: Comparative
- Pathology of Zoo Animals, R.J. Montali and G. Migaki, Eds, Smithsonian Institution Press, Washington, D.C., pp. 531-542.
- Moulton, J.E. (1990). Tumours in Domestic Animals, 3rd Edit. University of California Press, Berkeley, California.
- Ramsay, E.C. and Fowler, M. (1992). Reptile neoplasms at the Sacramento Zoo, 1981-1991. In: Proceedings of the Joint Conference of the American Association of Zoo Veterinarians and the American Association of Wildlife Veterinarians, Oakland, California, pp. 153–155.
- Ramsay, E.C., Munson, L., Lowenstine, L. and Fowler, M.E. (1996). A retrospective study of neoplasia in a collection of snakes. Journal of Zoo and Wildlife Medicine, **27,** 28–34.
- Zeigel, R.F. and Clark, H. (1969). Electron microscopic observations on a "C"-type virus in cell cultures derived from a tumour-bearing viper. Journal of the National Cancer Institute, 43, 1097–1102.

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