

CHAPTER

25

ONCOLOGY

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Neoplasia is an abnormal, uncontrolled, progressive proliferation of cells in any tissue or organ. Classification of neoplasms is based upon general tissue origin (epithelial vs. mesenchymal), specific cell lineage and whether the neoplasm is benign (-oma) or malignant (sarcoma or carcinoma). Classification of some neoplasms as benign or malignant may require knowledge of the biological behavior of the neoplasm.

The majority of the veterinary medical literature has reported the incidence, gross appearance and microscopic characteristics of neoplasms of domesticated birds, especially poultry.^{20,22,23,101,109} Furthermore, the study of retroviral-induced neoplasia in poultry has advanced medical knowledge of retroviral molecular biology, as well as that of neoplasm development, growth and metastasis.^{91,101} Similar information concerning neoplasms of captive and free-ranging birds is almost nonexistent. One ultrastructural survey of various budgerigar neoplasms failed to disclose retroviral particles, but sampling errors are a known complication of such studies.⁵² More recently, papillomaviruses have been demonstrated as the etiologic agents of cutaneous papillomas in African Grey Parrots, Chaffinches and Bramblings.^{73,87,94,96}

Reports of neoplasia are extant for captive as opposed to free-ranging birds,^{5,6,7,12,15,49,51,83,102,108} especially budgerigars, where the overall incidence of neoplasia ranges from 16.8% to 24.2%.^{12,15,51} In a veterinary diagnostic laboratory with a diverse avian caseload, budgerigars accounted for 69.7% of all psittacine neoplasms and 41% of all avian neoplasms recorded. The overall incidence of neoplasia approximated 3.8% in all avian submissions.¹⁰⁸

Compared to free-ranging birds, neoplasia is reported more frequently in companion and aviary birds because such birds are observed closely for abnormalities, have a longer life span and may have a genetic predisposition to neoplasia through inbreeding. Little is known, however, concerning the etiology, predisposing factors, development, biological behavior or treatment of neoplasms in companion and aviary birds. As more cases of avian neoplasia are studied and reported, our clinicopathologic knowledge will increase and treatment regimens will improve.

This chapter is written to provide a systems approach to avian neoplasia, with an emphasis on neoplasms of companion, aviary and free-ranging birds. Information is presented to assist the clinician in understanding the complexities and treatment of avian neoplasms (see Table 25.1). Lesions that mimic neoplasia also are discussed briefly. Lastly, the cytologic and histologic features of various neoplasms are presented to assist veterinary pathologists in the diagnosis of these neoplasms (see Table 25.2).

Integumentary System

Neoplasms of the integumentary system are common and account for 12% to 70% of all avian neoplasms.^{6,12,15,108} Of the various neoplasms reported, lipomas and fibrosarcomas are observed most frequently.

Adipose Neoplasms and Masses

Neoplasms associated with fatty tissue and lipid deposition in companion birds include lipoma, myelolipoma, liposarcoma and hibernoma. Lesions that mimic these neoplasms include xanthomas and lipogranulomas. Definitive diagnosis of each of these neoplasms or masses requires histopathologic examination of surgical biopsy specimens (Figure 25.1).

- **Lipoma:** Lipomas are benign proliferations of well differentiated adipocytes (lipocytes) that may exhibit slow-to-rapid, progressive growth over time. Lipomas are the most frequently observed neoplasm of companion birds, with a reported incidence of 10% to 40% in budgerigars.¹⁴³ Besides budgerigars, lipomas may be observed frequently in Rose-breasted Cockatoos (galahs) and Amazon parrots.^{98,143} Obesity, advancing age, species of bird and high-energy diets appear to be predisposing factors for tumor development. Based upon clinical observations, a genetic predisposition to lipoma development may exist in budgerigars.

Lipomas usually arise in the subcutis of the sternal or abdominal skin, but may also be observed on the wings, back, neck, legs or near the uropygial gland.^{6,12,15,30,49,51,69,72,86,102,108,127} In addition, lipomas may occur in the thoracoabdominal cavity (arising from thoracic or mesenteric fat, ovary, ventriculus and liver) or in association with skeletal mus-



FIG 25.1 A 15-year-old Amazon parrot was referred for evaluation of a tumor. A previous veterinarian had advised euthanasia. A large, pendulated, ulcerative mass was present on physical examination. The bird was in overall good condition, and abnormal clinicopathologic findings were limited to a mild heterophilia (18,000/ μ l). Cytology of a fine-needle aspirate revealed an accumulation of necrotic debris and reactive macrophages. The mass was surgically incised, and a piece of wood was found penetrating the esophageal wall. The granuloma was surgically removed, the esophageal defect was repaired and the surgical site was managed as an open wound. A mass should be considered of neoplastic origin only with the cytologic or histologic identification of suggestive cells.

cle.^{12,40,102,108,127} Tumor size typically ranges from 0.3 to 4.0 cm in diameter (Color 25.2).

Lipomas occur as single or multiple masses. Affected birds may be presented for diagnosis of a visible skin or subcutaneous mass or abdominal distention. Large tumors may interfere with leg movement, perching or flight. On palpation, lipomas are usually well defined and soft; the overlying skin is freely mobile.¹⁴³

Grossly, excised lipomas appear soft, round-to-multilobulated and pale yellow. On cut surface, they are thinly encapsulated and fatty. Histologically, lipomas appear as thinly encapsulated masses composed of lobules of well differentiated adipocytes. Scattered

blood vessels are also present. Central necrosis may be present in larger masses, especially those neoplasms that grow rapidly or are subjected to trauma.

Dietary changes and increased exercise are frequently curative in early cases and should be implemented prior to surgery to reduce the size of the mass. Because lipomas are often accompanied by body fat that may interfere with caudal air sac volume, exercise programs should be initiated with care, especially in tachypneic patients. Surgical excision is necessary if the tumor is causing clinical problems that are not resolved with diet change and increased exercise.^{25,30} Lipomas may be vascular; therefore, attention to hemostasis through the use of bipolar radiosurgery is important. Feeding formulated diets should prevent goiter and may also reduce the likelihood of a bird developing lipomas. Non-specific use of thyroxine should be avoided, and treatment of lipomas in the absence of hypothyroidism is not an indication for thyroxine administration.^{66,113}

- **Myelolipoma:** Myelolipomas are composed of adipose and hematopoietic tissues that may arise in the subcutis of the trunk, wings and legs. Occasionally they may occur in the liver or spleen. The outward appearance is similar to a lipoma.
- **Liposarcoma:** Liposarcomas are malignant, fatty neoplasms composed of lipoblasts and immature adipocytes. These neoplasms are firm on palpation, poorly encapsulated, highly vascularized and usually arise in the subcutis of the sternum or uropygial gland area.¹⁰² Infrequently, liposarcomas may present as poorly demarcated nodules in the thoracoabdominal cavity, liver or skeletal muscles.^{47,108} Liposarcomas are locally invasive, have the potential to metastasize and may arise in a multicentric pattern. Multicentric origin or widespread metastasis is typical.⁴⁷

Histologically, neoplastic cells appear spindle-like, stellate, round or polyhedral. Cell nuclei are round to oval and contain multiple nucleoli. The cytoplasm stains lightly eosinophilic or contains variably sized vacuoles. Larger vacuoles may cause peripheral nuclear displacement. Mitotic figures may be present but are not numerous. The presence of lipid within the cytoplasmic vacuoles may be demonstrated by fat-soluble stains, such as oil red O or Sudan IV, applied to frozen tissue sections. Alternatively, osmicated tissue specimens may be processed routinely and stained with hematoxylin and eosin. In these latter tissue sections, osmicated lipid will appear brown-black.

- **Hibernoma:** A hibernoma is a rare benign tumor of brown fat origin. A subconjunctival hibernoma was successfully excised from a two-year-old male white goose. The neoplasm involved the ventrolateral aspect of the right sclera and protruded through the palpebral fissure, interfering with eyelid closure.⁸⁹

Histologically, neoplastic cells stained faintly eosinophilic, appeared foamy, had central-to-paracentral nuclei and had a voluminous cytoplasm containing numerous, fine vacuoles and birefringent eosinophilic material. The neoplasm was well vascularized and contained a delicate stromal framework. Lipid was demonstrated within the cytoplasmic vacuoles by oil red O staining.⁸⁹

- **Xanthoma/Xanthomatosis:** The term xanthoma means “yellow mass.” An xanthoma is not a true neoplasm, but an inflammatory intumescence resulting from the accumulation of lipid-laden macrophages, giant cells, free cholesterol and variable degrees of fibrosis. Xanthomas occur frequently in gallinaceous and psittacine birds, appearing as yellow, single-to-multiple, discrete subcutaneous nodules or diffuse thickenings of skin that may be featherless, ulcerated or hemorrhagic (Color 25.15).^{25,143} These masses may occur anywhere on the skin or overlie other neoplasms, especially lipomas (Color 25.2).¹⁴³ Infrequently, xanthomas may have a periarticular arrangement or involve the oral cavity.^{60,111}

Although the precise etiology of xanthoma formation is unknown, various theories have been proposed including high-lipid diets or ingestion of toxic fat-soluble substances (such as aromatic chlorinated hydrocarbons) that might incite inflammation and trauma.^{25,98,117,143} Cellular infiltrates, lipid accumulation and fibroplasia give rise to the nodular or tumorous appearance of these lesions. Unresectable or multiple skin xanthomas may respond to irradiation (low-energy X-rays; 20 to 30 Gy) or hyperthermia.¹⁴³ Dietary restriction of oily seeds may be beneficial in the medical management of xanthomatosis.³⁴

Connective Tissue Neoplasms and Masses

Connective tissue neoplasms (fibrosarcoma, fibroma, myxosarcoma and myxoma) arise from the proliferation of fibroblasts or undifferentiated mesenchymal cells, which frequently assume a spindle-like appearance. These neoplasms contain a collagenous or mucinous stroma. Cellular morphology, mitotic index

and biological behavior are used to classify these neoplasms as benign or malignant.

In chickens, connective tissue neoplasms can arise following infection with specific strains of avian leukosis or sarcoma virus.¹⁰¹ The etiology of similar neoplasms in aviary and free-ranging birds is unknown.

- **Fibrosarcoma:** Fibrosarcoma is a malignant neoplasm of fibroblast or mesenchymal cells, which possess the ability to produce collagen fibers. Fibrosarcomas occur commonly in budgerigars, cockatiels, macaws and parrots.^{7, 25,49,108,110,143} Fibrosarcomas may constitute 3 to 14% of all neoplasms in budgerigars.¹⁴³

Clinically, fibrosarcomas are firm, single-to-multiple, broad-based, relatively immobile nodules or masses. Superficial fibrosarcomas may be covered by an intact-to-ulcerated epidermis accompanied by hemorrhage and secondary bacterial infections. Fibrosarcomas commonly arise from the soft tissues of the wing, leg, head, beak, cere and trunk (Color 25.1, 25.5, 24.19).^{6,11,12,15,72,75,102,108,110} They also may arise in the viscera and deep tissues including thoracoabdominal cavity, spleen, liver, mouth, tongue, syrinx, lung, small intestine, proventricular wall, testes and ovary (Figure 25.2).^{12,27,102,108} These neoplasms are locally invasive and may eventually metastasize, especially to the abdominal cavity, lungs, liver, kidney, heart base and bone (Figure 25.3).^{12,102,108,110,143} Intra-abdominal neoplasms also have been observed enveloping bowel loops and adhering to the pancreas.^{82,127} These neoplasms have been reported as neurofibrosarcomas based upon cellular arrangement or pattern, but a neural origin has not been demonstrated.

- **Fibroma:** A fibroma is an uncommon benign neoplasm composed of well differentiated fibroblasts distributed within a collagenous matrix. Fibromas are firm on palpation and may arise almost anywhere, but usually

involve a firm mass in the skin and subcutaneous tissues of the wing, leg, face, beak, neck or sternum.^{12,32,69,72,143}

- **Myxoma and Myxosarcoma:** These neoplasms are of fibroblast or mesenchymal cell origin, but possess abundant mucinous stroma. These rare neoplasms may arise wherever connective tissue exists including the foot pad, cranium, leg, kidney, commissure of the beak and within the thoracic cavity.^{15,108} Clinically, these masses may appear soft on palpation and gelatinous on cut surface. In myxosarcomas, neoplas-



FIG 25.2 A ten-year-old Amazon parrot was presented with a one-year history of a progressive swelling of the head and face (see Color 25.1). Physical examination revealed numerous masses throughout the body that were confirmed by radiographs. Histopathology indicated an invasive fibrosarcoma involving the soft tissues and bones of the head (courtesy of Jane Turrel).



FIG 25.3 An adult female dove was presented with a soft tissue swelling involving the right scapulohumeral region. Radiographically, a large, uniform, soft tissue mass with osteolysis involving the humeral head and diaphysis was noted. The increased medullary bone density was considered normal for a laying hen. Cytology of a fine-needle aspirate confirmed fibrosarcoma (courtesy of Marjorie McMillan).

tic cells appear to be more numerous and contain plump nuclei. Metastasis may occur, but is infrequent to rare.

- **Reactive Fibroplasia:** Granulation tissue exemplifies healing by second intention. Granulation tissue may be highly vascular and proliferative with variable degrees of inflammation. Grossly, granulation tissue may have a proliferative or neoplastic-like appearance. Cytologic specimens often contain a pleomorphic population of immature fibroblasts that mimic neoplasia. Inflammatory cells may be admixed with blood. Histologically, tissue architecture is a differentiating feature of the lesion wherein blood vessels are oriented at right angles to the surface of the lesion, while fibroblasts are oriented parallel to the surface of the lesion. Marked, proliferative fibroplasia with granuloma formation also may be observed in the ceca of gallinaceous birds, especially pheasants, infected with *Heterakis isolonche* (see Color 14). In such instances, nematode-induced reactive fibroplasia may be difficult to distinguish from neoplasia.^{57,62}

Epithelial Neoplasms and Cysts

- **Papillomas and Papilloma-like Lesions:** Cutaneous papillomas are observed occasionally in domestic, captive and free ranging birds.^{4,6,11,15,46,73,98} Multiple papillomas most frequently originate from the skin of the eyelids, at the junction of the beak and face, and on the feet and legs. The anatomic location of these benign neoplasms may interfere with vision, prehension of food or perching if the lesions are severe (Color 25.17). Histologically, these lesions consist of folds of hyperplastic stratified squamous epithelium over a fibrovascular stroma. Cutaneous papillomas are viral-induced, at least in African Grey Parrots, Chaffinches and Bramblings (Color 25.10) (see Chapter 32).^{73,87,96}
- **Squamous Cell Carcinoma:** Squamous cell carcinoma is observed most frequently in chickens but has also been described in captive and free-ranging birds in the skin of the head, eyelids, neck, chest, wings or around the beak (Color 25.9).^{6,7,15,29,49,59,108,135,142} Grossly, these neoplasms appear as multiple, raised masses with central craters or ulceration (Color 25.7). Multiple neoplasms usually are present, involving both feathered and unfeathered areas of the skin. An interesting recent study indicates that these neoplasms originate as elevated keratin-filled cysts that subsequently ulcerate and flatten. Some lesions may subsequently resolve as dermal scars.⁵⁹

Histologically, these dermal squamous cell carcinomas are characterized by epidermal ulceration and infiltration of the subjacent dermis by squamous cells. These cells are scattered singly or arranged in nests and cords. Infiltration of underlying skeletal muscle is rare. Laminated keratin pearls may be observed within epithelial cell cords in companion and free-ranging birds.¹⁰⁸ The etiology of multifocal, dermal squamous cell carcinoma of chickens has not been determined.

- **Uropygial Gland Adenoma and Adenocarcinoma:** Uropygial gland neoplasms occur sporadically in captive birds, especially budgerigars and canaries.^{6,102,108} On physical examination, the uropygial gland may appear enlarged, ulcerated and hemorrhagic (Color 25.11). Neoplasia must be distinguished from adenitis, which usually requires histologic examination. Partial or complete removal of the affected gland is recommended (Figure 25.4).
- **Feather Folliculoma:** Feather folliculomas occur primarily in canaries and budgerigars.^{18,108,149} These neoplasms may appear as discrete, mobile, single or multiple dermal nodules that may ulcerate or hemorrhage (see Color 14). Microscopically, these lesions appear multilobulated and are lined with irregular, hyperplastic, basaloid cells that exhibit feather formation. Basal cells are arranged in barb ridges and undergo abrupt squamous differentiation in the center of the mass, forming laminations of free keratin.^{108,149}
- **Miscellaneous Basal Cell Tumors and Cutaneous Cysts:** All of these neoplasms present as discrete skin nodules. Basal cell tumors are composed of sheets, nests or cords of basaloid epithelial cells. This cell population does not exhibit terminal cellular or structural differentiation.^{5,25,108}

Intradermal cystic lesions occasionally are observed in captive and free-ranging birds. Histologically, these lesions often appear cystic as a result of glandular differentiation or keratin production. Those benign neoplasms that exhibit glandular differentiation are cystadenomas.⁶⁷ Cystic lesions with keratin production are classified on the basis of gradual or abrupt keratinization. Gradual keratinization is observed with epidermal inclusion cysts, follicular cysts and intracutaneous cornifying epitheliomas.^{88,108,130} Those cystic lesions with abrupt keratinization include trichoepithelioma and pilomatrixoma.^{88,108}

Miscellaneous Neoplasms

- **Cutaneous Lymphosarcoma:** Cutaneous lymphosarcoma is observed in chickens as a manifestation of

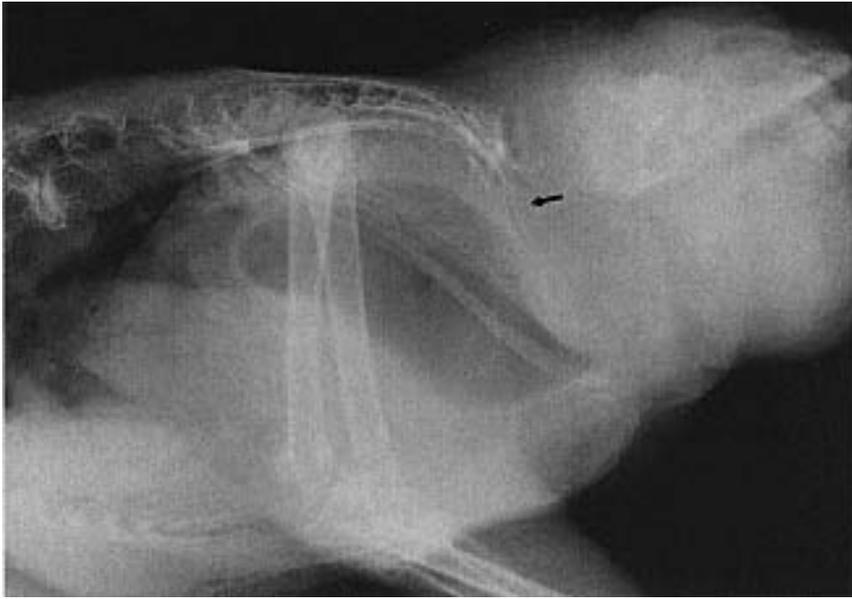


FIG 25.4 A 36-year-old macaw was presented for evaluation of a progressive mass over the dorsal spine and straining to defecate. On physical examination, a large mass was noted in the area of the uropygial gland and dried excrement had accumulated around the vent. Tenesmus was noted during the physical examination. Radiographs indicated a large mass that had invaded the synsacrum and was displacing the cloaca ventrally. The histopathologic diagnosis was adenocarcinoma of the uropygial gland (courtesy of Jane Turrel).

Marek's disease and may occasionally occur in captive and free-ranging birds.^{9,100,105} Neoplastic lymphocytes may exhibit multifocal to diffuse follicular and perifollicular infiltration, producing numerous skin nodules that may ulcerate along feather tracts.^{20,98} In psittacine birds, cutaneous neoplasms may develop under the skin of the face or neck, often in association with generalized or systemic lymphosarcoma.⁹

- **Mast Cell Tumor:** Mast cell tumors have been reported in three owls and a chicken.^{99,124,139} In owls, mast cell neoplasms usually are associated with the skin of the eyelid or auditory meatus, but may also be observed in the mouth.^{124,139} Generally, animal species with a higher circulating basophil count have fewer tissue mast cells, which may explain the rarity of mast cell tumors in avian species. Mast cell tumors appear grossly as raised-to-spherical, pink-to-red, dermal or submucosal masses. In some instances, neoplastic margins may be indistinct or the neoplasm will demonstrate marked local tissue invasion.^{124,139} Attempted surgical excision of a mast cell tumor was unsuccessful in one owl.¹²⁴

Respiratory System

The avian lung serves as a metastatic site for many neoplasms including fibrosarcoma, adenocarcinoma, hemangiosarcoma, malignant melanoma, mesothelioma and osteosarcoma (Figure 25.5).^{12,78,81,102,108,127} In contrast, primary neoplasms of the avian respiratory system are rare in species other than chickens.

- **Lymphosarcoma and Hemangiosarcoma:** Chickens with Marek's disease (Marek's lymphoma) often have herpesvirus-induced pulmonary lymphoid tumors.¹⁰⁹ Multicentric hemangiosarcomas of chickens also may originate in the pulmonary parenchyma.^{74,129} Hemangiosarcomas occur in fowl infected with retrovirus and are discussed under the circulatory system.
- **Papilloma:** Laryngeal papillomas are observed occasionally in psittacine birds, especially Amazon parrots and macaws.^{36,55,102} Papillomas also may occur within the nares and choanal area.^{36,55} Clinically, laryngeal papillomas may cause dyspnea. These lesions may be surgically excised, but will recur if excision is incomplete.¹⁰²
- **Bronchiolar Adenoma and Adenocarcinoma:** A bronchiolar adenoma has been reported in a parrot.¹⁰⁸ The neoplasm appeared as a large, lobulated, adenomatous nodule within a major bronchus. A bronchiogenic adenocarcinoma has been reported in a quail, but histologic features of the neoplasm were not described.⁴⁹
- **Fibrosarcoma:** A solitary pulmonary fibrosarcoma has been described in a cockatiel. Due to the absence of other neoplastic nodules, primary pulmonary origin was suggested.²⁷
- **Ectopic Pulmonary Ossification:** Ectopic pulmonary ossification may be confused radiographically with pulmonary metastasis. This subject is discussed below (bone proliferation resembling neoplasia; musculoskeletal system).

- **Ultimobranchial Cyst:** Ultimobranchial cysts develop from branchial pouch remnants following embryogenesis. A large ultimobranchial cyst has been observed in the lower neck of a lorikeet. The thyroid gland was displaced by this mass. Histologically, the neoplasm was lined by squamous epithelium and contained laminated keratin material and desquamated cells within the cyst lumen.¹⁰⁸

Circulatory System

Vasoformative neoplasms originate from endothelial cell proliferation with subsequent formation of irregular vascular channels and spaces filled with blood (or rarely with lymph). These neoplasms may form wherever endothelium exists; however, preferred sites of origin are apparent. Vasoformative neoplasms are classified as benign (hemangioma, lymphangioma) or malignant (hemangiosarcoma, lymphangiosarcoma).

Vasoformative neoplasms must be distinguished from non-neoplastic conditions such as vascular malformations (arteriovenous fistulas and aneurysms), hematomas, excessively vascularized granulation tissue or other neoplasms with a rich blood supply.^{84,88} Definitive diagnosis requires histopathology.

In chickens, vasoformative neoplasms may arise as a sequela to avian leukosis virus, subgroup F infection. These virus-induced neoplasms may progress from benign growths to fibrosarcoma-like neoplasms, analogous to Kaposi's sarcoma in human beings.⁴² In contrast, reports of vasoformative neoplasms in captive and free-ranging birds are sporadic and of undetermined etiology.^{14,72,85, 102,108,127,143}

On gross inspection, hemangiomas and hemangiosarcomas may appear as single-to-multiple; variably-sized; pink, red or blue-black nodules (blood blisters), swellings or multiloculated masses within the skin or abdominal viscera.^{22,74} Internal neo-

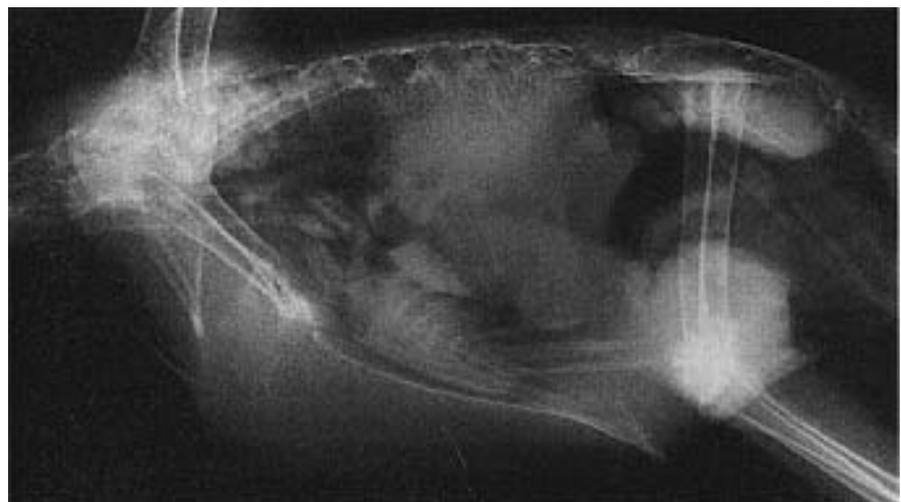
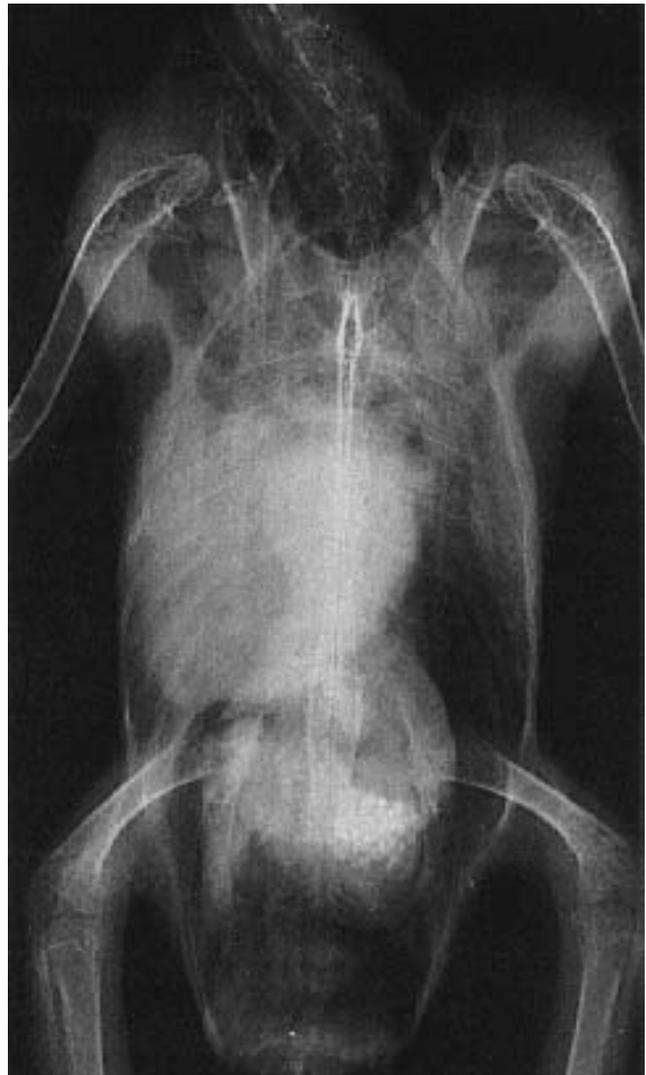


FIG 25.5 Radiographs of a four-year-old female African Grey Parrot indicated a large, soft tissue mass in the right thoracic area. Histopathology revealed a renal tubular adenocarcinoma with metastasis to the lung, liver and myocardium (see Color 25.13).

plasmas may present as primary abdominal distention from tumor mass or secondary abdominal distention from hemorrhage (hemoperitoneum). Vasoformative neoplasms may hemorrhage spontaneously or following minor trauma (palpation) resulting in anemia or exsanguination.^{19,25,98}

- **Hemangioma:** Cutaneous hemangiomas often arise within subcutaneous tissues of the dorsum of the neck, wing or legs.^{15,25,102} Feather follicles also may be involved.²⁵ Abdominal hemangiomas may arise in the spleen, liver, kidney or testicular capsule. These latter neoplasms may cause abdominal distention by tumor mass or hemorrhage (hemoperitoneum).^{22,49,102} External hemangiomas, particularly on the wing tips, are subject to trauma and may bleed profusely.

Cytologic aspirates of hemangiomas are of limited diagnostic value and generally consist of blood. Endothelial cells are rarely observed. Erythrophagocytosis, hemosiderin-laden macrophages and hematoidin crystals may be observed if concomitant hemorrhage is present. Hemosiderin is an iron pigment derived from erythrocyte catabolism. This pigment appears globular and blue, golden-brown or greenish-black in Romanowsky-stained cytology preparations. Hematoidin, a hemoglobin breakdown product, appears as small, bright-yellow, parallelogram-shaped crystals that are observed most frequently within the cytoplasm of macrophages. Hematoma, hemangioma and hemangiosarcoma may be difficult or impossible to distinguish cytologically.

Histologically, hemangiomas are composed of variably-sized vascular spaces and channels that are lined by flattened endothelium. Occasional solid areas of plump endothelial cells also may be observed. Vascular spaces typically contain blood, plasma or fibrin thrombi. On rare occasions, immature hematopoietic precursor cells may be adherent to the endothelium.

- **Hemangiosarcoma:** Hemangiosarcomas may arise singly or in a multicentric pattern. These neoplasms often arise in the skin, liver, lungs, spleen, muscle, mesentery, kidney, heart, oviduct, bone or synovium.^{19,49,74,102,108,127,128,129,143} Hemangiosarcomas that develop in the distal diaphysis of long bones may exhibit aggressive osteolysis and surface hemorrhage (Figure 25.6).¹⁴³ Hemangiosarcomas may metastasize to distant tissues including lung, liver or myocardium.^{102,143}

Cytologic aspirates are similar to those described for hemangiomas; however, widely scattered pleomor-

phic endothelial cells may be present. These endothelial cells usually appear polyhedral-to-spindle-shaped with round-to-oval nuclei and dark-blue, occasionally finely vacuolated, cytoplasm. Aspiration sites may hemorrhage profusely.

Histologically, vascular spaces in hemangiosarcomas are lined by plump endothelial cells with hyperchromatic nuclei. Mitoses may be observed. Neoplastic cells often dissect surrounding structures and exhibit vascular invasion. Secondary hemorrhage is common.

- **Lymphangioma:** Birds possess lymphatic channels but they appear less well developed than corresponding structures in mammals. Lymphangiomas are benign neoplasms wherein endothelial cells form lymphatic channels. These neoplasms are extremely rare in all species, especially birds. Lymphangioma has been reported in the mesentery and spleen of a rhea and budgerigar, respectively.^{72,102} However, the budgerigar neoplasm closely resembled an hemangioma.¹⁰²

Histologically, these neoplasms consist of vascular channels lined by flattened epithelium and filled with lymph. Lymph appears as a homogeneous, light-pink substance.



Musculoskeletal System

Neoplasms of Smooth and Striated Muscle

Neoplasms originating from striated or smooth muscle that are benign or malignant are observed occasionally in captive and free-ranging birds. Muscle neoplasms presumably arise from embryonic remnants of myotomes, from pluripotential cells of embryologic structures or from neoplastic transformation of myoblasts during degeneration or repair processes.⁸⁸ Generally, smooth muscle neoplasms are reported about twice as frequently as striated muscle tumors. Furthermore, malignant neoplasms are reported twice as frequently as their benign counterparts.

- **Leiomyoma:** Leiomyomas are benign neoplasms that generally are nodular and may arise from smooth muscle of the gastrointestinal or female reproductive tract, especially the oviduct. Other sites of origin include smooth muscle trabeculae within the spleen or smooth muscle associated with vessels or



FIG 25.6 A dove was presented with lameness and a large swelling of the metatarsal area. Radiographically, the mass involved proliferation of soft tissues and osteolysis resulting in a pathologic fracture. The histologic diagnosis was hemangiosarcoma (courtesy of Jane Turrel).

ducts in the pancreas.^{15,102,108} Leiomyomas usually exhibit slow growth and may be associated with abdominal distention, gastrointestinal or reproductive tract obstruction, or organ displacement.

Cytologic aspirates and imprints are sparsely cellular, containing only scattered free nuclei or a few spindle cells with elongate nuclei. Histopathology reveals a uniform population of elongate cells arranged in broad, interlacing bands. These cells have cigar-shaped nuclei and eosinophilic cytoplasm. Mitoses are observed infrequently.

- **Leiomyosarcoma:** Leiomyosarcomas are the most common muscle neoplasm reported in captive and free-ranging birds.^{15,102} They may arise from smooth muscle in any location, but usually arise from splenic smooth muscle trabeculae.^{12,15,102} Other sites of origin include crop, intestinal tract, trachea, pancreas, oviduct, ventral ligament of the oviduct, vas deferens and testicular capsule.^{12,15,25,102,133} Leiomyosarcomas may be locally invasive. Metastasis is a late and infrequent event, but has been documented to involve the liver, spleen, thoracic cavity and bone marrow.^{15,119}

Cytologic imprints of leiomyosarcomas may contain free nuclei and a pleomorphic but sparse population of spindle cells. Distinguishing leiomyosarcomas from fibrosarcomas may be difficult cytologically. Grossly, excised neoplasms appear firm, pink, poorly delineated and unencapsulated. Microscopically, leiomyosarcomas are hypercellular with spindle cells arranged in sheets, interlacing bundles or whorls. Neoplastic myocytes have plump often pleomorphic nuclei, occasional nucleoli and variable amounts of eosinophilic cytoplasm.

- **Rhabdomyoma:** Rhabdomyomas are benign neoplasms of striated muscle and are the rarest muscle neoplasm reported in captive birds. Reported sites of origin include the wing, tongue and eyelid.^{12,15,108} These neoplasms may be solitary or multinodular, blending with surrounding skeletal muscle.

Cytologic aspirates are unrewarding except for possible fragments of striated muscle cells. Histologically, rhabdomyomas are composed of cells ranging from a fibroblast appearance to multinucleated cells. Most cells have distinct fibrillar cross striations. Some cells may appear vacuolated and have high glycogen content demonstrated by diastase-labile, periodic acid Schiff (PAS)-positive granules.⁸⁸

- **Rhabdomyosarcoma:** Rhabdomyosarcomas are of skeletal muscle origin and frequently present as irregular, elevated, lobulated, relatively firm subcutaneous swellings of the wing or shoulder that limit the use of the wing.^{12,15,51,102} Because these neoplasms blend with surrounding skeletal muscle, they are immobile or firmly attached on palpation. Less frequently, neoplasms will arise from other sites such as the dorsal lumbar musculature.¹⁰⁷ Metastasis to the abdominal cavity and liver was reported in one bird.¹⁰⁷

Cytologic studies of rhabdomyosarcomas have not been reported. Microscopically, the neoplasms are composed of a pleomorphic population of fusiform-to-elongated cells. Anisokaryosis may be prominent with plump oval-to-elongated nuclei. Some elongated or “strap cells” will retain cross striations typical of skeletal muscle cells. Phosphotungstic acid hematoxylin (PTAH) staining may facilitate identification of these cross striations.

Neoplasms of Cartilage and Bone

Neoplasms arising from cartilage and bone are observed occasionally. Osseous neoplasms usually arise from the long bones, while cartilaginous neoplasms often arise on the foot. Cytology may suggest the

presence of mesenchymal neoplasia by demonstrating a pleomorphic population of spindle-to-polyhedral cells and possible matrix material; however, histopathology is required to determine whether the neoplasm originates from cartilage or bone and to determine whether the neoplasm is benign or malignant.

- **Chondroma:** Chondromas are reported occasionally in captive and free-ranging birds, especially of the order Anseriformes.¹⁰⁸ Grossly, these neoplasms may be single or multiple. They often arise on the plantar surface of the foot pad where they may be subjected to trauma with subsequent hemorrhage and ulceration of the overlying epidermis.¹⁰⁸ Other sites of origin of chondromas include the cranium (especially in canaries) and proximal humerus (Figure 25.7).¹⁰⁸

Histologically, these neoplasms consist of nodular, encapsulated foci of developing chondrocytes separated by connective tissue septa. Variable amounts of sulfated mucopolysaccharide matrix and lacunae may be observed.

- **Chondrosarcoma:** Chondrosarcomas are very rare in comparison to chondromas. A chondrosarcoma has been reported involving the metatarsal-phalangeal joint of a ruffed grouse; however, the histologic appearance of the lesion is similar to a multilobular chondroma.^{25,127}



FIG 25.7 A mature cockatiel from an aviary flight was presented with a mass that had been progressing in size for a year. The mass was fluid-filled (serosanguinous), and cytologic evaluation of the fluid was nondiagnostic. The mass was excised and the cranium formed the base of the mass. The bird recovered uneventfully. Histopathology indicated a bone cyst. Trauma was considered the most likely cause (courtesy of Tom Tully).

- **Osteoma:** Osteomas are observed infrequently in birds compared to osteosarcomas. Osteomas may originate from the cranium, scapula, tarsometatarsus, plantar foot pad and elbow joint.^{6,12,49,51,108} Histologically, osteomas are small, well encapsulated nodules composed of disorganized bony trabeculae and are attached to adjacent bone.¹⁰⁸ Surgical excision is the treatment of choice.

- **Osteosarcoma:** Osteosarcomas occur 3.5 times more frequently than osteomas and usually originate from the proximal or distal portion of long bones including the radius, humerus, femur, tibiotarsus and tarsometatarsus (Figure 25.8).^{5,6,12,51,72,81,102,108} Less frequent sites of origin include the ribs, phalanges, cranium, orbit and coccyx.^{6,102,108} Osteosarcomas may metastasize widely to such sites as the lungs, liver, kidney, ovary, mesentery and other bones (Color 25.16).⁸¹

Histologically, osteosarcomas are composed of polyhedral-to-spindle mesenchymal cells that produce osteoid. Bony trabeculae may be present but disorganized. Scattered islands of cartilage, fibrous connective tissue, and myxomatous matrix also may be present.¹⁰⁸ Scattered mitotic figures may be observed.

Bone Proliferation Resembling Neoplasia

Radiographically, skeletal hyperostosis is recognized by increased medullary bone density, increased bone thickness and deformities involving one or multiple long bones. The differential diagnosis for increased medullary opacity of long bones includes osteopetrosis, polyostotic hyperostosis, metastatic neoplasia, hypertrophic osteopathy and metabolic bone disease.

- **Osteopetrosis:** Osteopetrosis is defined as marked subperiosteal proliferation of bone resulting in loss of medullary space, increased bone thickness and deformity. Osteopetrosis in chickens occurs sporadically and is caused by leukosis/sarcoma virus infection. Depending upon the strain of virus, osteopetrosis may be experimentally induced within one to three months of virus inoculation with a disease frequency of 60-100%.^{125,126}

Histologically, decalcified sections of bone demonstrate marked proliferation of porous subperiosteal bone. Osteoclast numbers are normal, but a marked increase in osteoblastic activity exists.^{109,125,126}

▪ **Ovarian and Oviductal Neoplasms and Cysts:**

Cystic ovaries, oviductal carcinoma and ovarian neoplasms may induce generalized or localized bone formation in companion birds.^{5,12,132} Increased medullary bone density is apparent on survey radiographs. Histologically, the increased medullary density is the result of formation of bone spicules throughout the marrow cavity.

- **Ectopic Pulmonary Cartilage and Bone:** Ectopic pulmonary cartilage and bone formation may be observed in the lung parenchyma of chickens, especially broilers.^{16,109,150} The incidence varies with the strain of bird, suggesting a genetic predisposition to this condition. This condition probably represents abnormal embryonic induction of mesenchyme or germ cells displaced from adjacent bronchi during development.¹⁵⁰ Alternatively, osseous or cartilaginous metaplasia also may explain the development of this condition. Histologically, nodules of cartilage or bone are present within the pulmonary parenchyma.^{109,150}

Ectopic pulmonary ossification has been observed in an Orange-winged Amazon Parrot and a Senegal Parrot. Survey radiographs in both birds detected multifocal opacities throughout the lung fields, suggesting deep mycosis or metastatic neoplasia. Lung biopsy specimens, however, contained only small foci of osseous tissue within the parenchyma.

Urogenital System

Neoplasms of the urogenital system are reported frequently, especially in budgerigars. In a recent survey, urogenital tumors accounted for 12.5% (7.3% renal and 5.2% genital) of all neoplasms in a diverse avian population.¹⁰⁸ Surveys in budgerigars indicate an 11.2 to 66.0% incidence of urogenital neoplasia.^{7,12,15,92} Testicular neoplasms of captive and free-ranging birds are approximately three times as common as ovarian and oviductal neoplasms. This observation may be explained partially by the presence of bilateral testes in the male but only one functional ovary and oviduct in the normal hen.

Larger neoplasms may cause abdominal distention or respiratory embarrassment. Some renal, testicular, ovarian and oviductal neoplasms may cause unilateral or bilateral leg paresis or paralysis with difficulty or inability to perch.^{12,51,92} This occurs because the nerves of the sacral plexus pass through the mid portion of the kidney where they are subject to compression or infiltration by neoplastic cells. Lastly, gonadal neoplasms may be associated with various paraneoplastic syndromes such as feminization or



FIG 25.8 A nine-year-old Sulphur-crested Cockatoo was presented with a left limb lameness. An initial radiograph (left) indicated osteolysis of the distal femur that was diagnosed as osteomyelitis. A second radiograph (middle) taken seven weeks later indicated increased soft tissue swelling and osteolysis. A biopsy was non-diagnostic. A third radiograph (right) taken three months after initial presentation indicated a pathologic fracture with marked osteolysis. The histologic diagnosis was anaplastic sarcoma.

masculinization and localized or polyostotic hyperostosis (Figure 25.9).^{5,6,12,92,102,132} Feminization or masculinization is most apparent in budgerigars where the male's cere may change from blue to brown, or the female's cere may turn from brown to blue (see Color 24).^{6,12,102}

Renal Neoplasms

Renal neoplasms are observed occasionally in free-ranging and captive birds, especially budgerigars. Renal neoplasms usually occur unilaterally, but may occur bilaterally, and presenting complaints generally include an inability to perch or ambulate.^{12,51,102,108} Abdominal enlargement and articular gout also may occur.¹²

The etiology of renal neoplasms is obscure, but they may originate from embryonal nests in the avian kidney. In poultry, renal neoplasia is usually a sequela to avian leukosis virus infection.¹⁰¹

Renal neoplasms are difficult to manage surgically. Renal carcinomas may aggressively invade adjacent muscle and bone. Because the kidneys are located in the renal fossae, neoplasms are difficult to isolate and excise (Figure 25.10). The sacral plexus passes through the mid portion of the kidney and is subject to trauma. Finally, the kidneys are highly vascular and marked hemorrhage is expected. Treatment of renal neoplasms using radioisotope implants appears promising, but will require further evaluation.¹⁴³

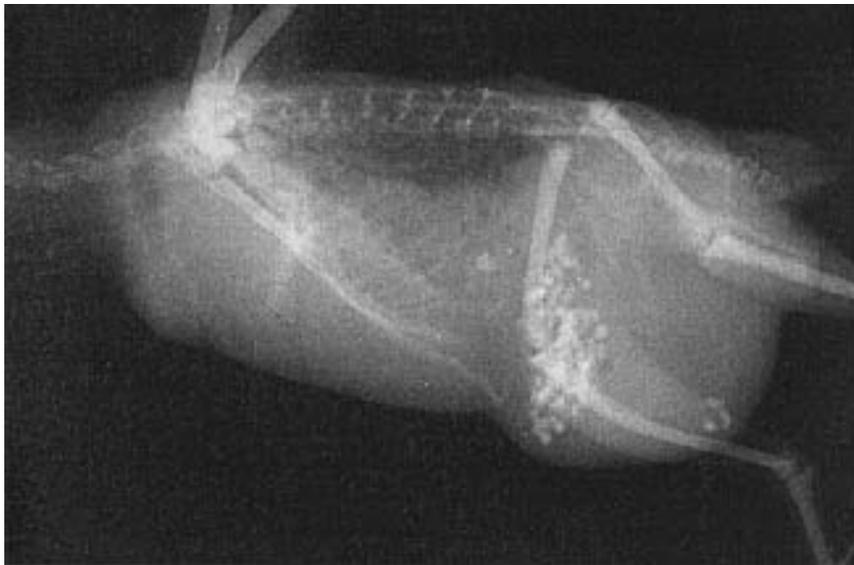


FIG 25.9 A five-year-old male budgerigar was presented because of a change in cere color (from blue to pink), abdominal distention and unilateral leg paresis. Radiographs indicated a large soft-tissue opacity in the abdomen and polyostotic endosteal hyperostosis of the long bones. The clinical and radiographic findings were highly suggestive of a gonadal tumor. Histopathology confirmed a sertoli cell tumor, which was probably secreting low levels of estrogen (courtesy of Jane Turrel).

▪ **Renal Carcinoma:** Renal carcinoma is the most frequently observed renal neoplasm in captive and free-ranging birds.^{7,12,41,49,69,71,85,102,108,144} Renal adenocarcinomas may infiltrate adjacent muscle and bone with extension into the spinal canal. Distant metastasis to the liver and oviduct may occur, but is unusual (Color 25.13).^{69,71}

Affected kidneys contain large, pale, multilobulated masses. Histologically, these neoplasms are composed of vesicular epithelial cells arranged in sheets, nests, cords or tubules. Epithelial cells may be cuboidal to columnar, especially those cells involved in tubular formation. Fibrovascular stroma may be prominent. A few multinucleated cells and scattered mitoses may be observed within the neoplasm.^{102,108}

▪ **Renal Adenoma:** Renal adenomas are benign neoplasms that are observed infrequently compared to renal adenocarcinomas.^{7,49,85} Although gross enlargement of a portion of the kidney is apparent, the microscopic appearance of the tissue may be unremarkable-to-subtle in comparison to the normal kidney. Epithelial cell cytoplasm may be slightly more basophilic. Compression of adjacent normal parenchyma occurs as the neoplasm slowly enlarges.

▪ **Embryonal Nephroma:** Embryonal nephroma (nephroblastoma, Wilms's tumor) has been observed most commonly in chickens infected with leukosis (sarcoma) virus. In chickens, these neoplasms usually are unilateral but may arise bilaterally.^{23,101,109} In captive and free-ranging birds, these neoplasms are observed occasionally, especially in budgerigars.^{12,15,102} The literature suggests they are more frequent than adenomas but less common than adenocarcinomas. These neoplasms are believed to arise from the metanephric blastema.⁸⁸

On gross inspection, embryonal nephromas cannot be distinguished from renal adenocarcinomas. Histologically, epithelial cells are arranged in solid masses of variably-sized tubules or cords. Characteristic features include the formation of tubules and glomerulus-like structures. Variable quantities of mesenchymal stroma may be present, which further undercores the embryonal nature of the neoplasm.^{88,102} Rare metastasis to the liver and

spleen may occur, but is poorly documented.¹⁵

Testicular Neoplasms

Testicular neoplasms are usually unilateral, but may occur bilaterally. With unilateral neoplasms, atrophy of the contralateral testis may be observed. In rare instances, a collision tumor may be observed in which two or more cell lines are involved in the neoplastic process.¹² Cytologic studies have not been performed on avian testicular neoplasms. Definitive diagnosis of the following neoplasms is dependent upon histopathologic examination. Orchiectomy is the treatment of choice but must be initiated early for a successful outcome.

- **Sertoli Cell Tumor:** Sertoli cell tumor is one of the most frequent testicular neoplasms encountered in captive and free-ranging birds.^{5,12,49,51,53,102,108} These cells constitute a portion of the intratubular gonadal stroma, secreting testicular fluid and nourishing developing spermatids. If neoplastic Sertoli cells are synthesizing estrogen, feminization may be present. This phenomenon is most noticeable in male budgerigars in which the cere color changes from blue to brown (Figure 25.11).¹²

Neoplastic testes appear as enlarged, pale, firm, nodular masses. Neoplasms may have a pink tinge secondary to central necrosis and hemorrhage. Variably sized, fluid-filled cystic spaces also may be present.^{53,108} Serosal metastases are unusual but may occur.¹⁰⁸

Histologically, Sertoli cell tumors are composed of sheets, lobules and islands of cells. Cells within seminiferous tubule remnants may palisade. Individual neoplastic cells are elongate with round-to-oval basal nuclei. Cytoplasm is abundant, eosinophilic, and occasionally vacuolated. The mitotic rate is variable. A delicate-to-dense fibrovascular stroma is present.^{53,108}

- **Seminoma:** Seminomas are neoplasms of germ cell origin. These tumors also occur frequently in captive and free-ranging birds.^{5,12,44,49,51,54,85,102,108,141} The most common clinical signs include dyspnea, lethargy, anorexia, ascites and abdominal enlargement (occasionally with a palpable intra-abdominal mass).⁴⁴ Seminomas infrequently may be associated with signs of feminization in budgerigars.¹²

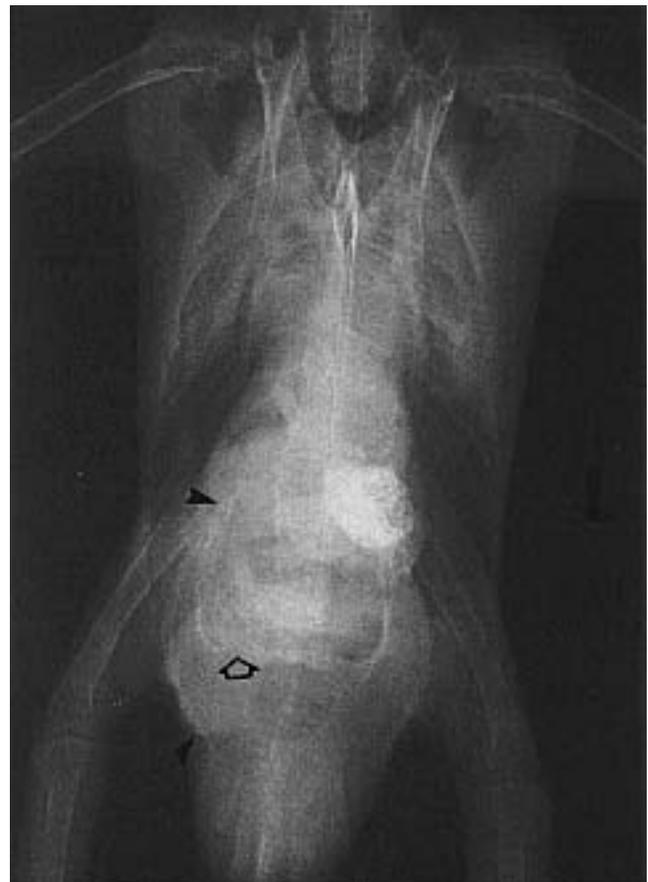
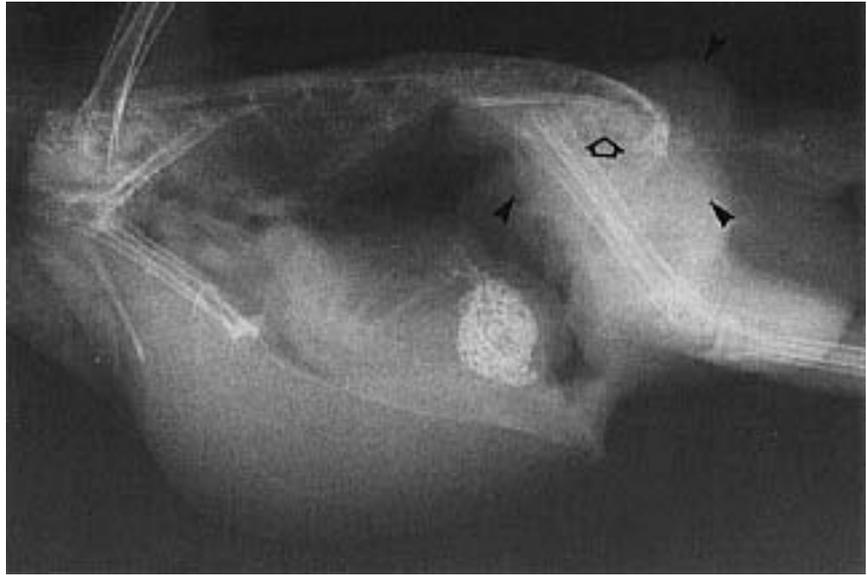


FIG 25.10 A Quaker Parakeet was presented for evaluation of a pericloacal and abdominal swelling. Radiographs indicated a renal mass that had invaded the synsacrum, causing osteolysis cranially and sclerosis caudally. The mass extended dorsally to the synsacrum and ventrally into the abdomen. The histopathologic diagnosis was renal carcinoma (courtesy of Jane Turrel).



FIG 25.11 A mature male budgerigar was presented with a progressive growth and discoloration of the cere. Brown hypertrophy of the cere is frequently encountered in older budgerigars with gonadal neoplasms. The hypertrophied tissue can be moistened with skin-softening creams and gently peeled away.

Neoplastic testes appear large, white-to-gray, firm and oval. Small cystic spaces also may be present. Occasionally, adherence to the kidneys, ureters and dorsal body wall may be observed.^{44,108} Seminomas are generally considered benign; however, metastasis to the liver may occur, presumably as a late event.^{5,49,54,102}

Histologically, seminomas are composed of pleomorphic germinal epithelial cells arranged in sheets, nests and irregularly shaped tubules. Seminiferous tubules may be filled, distended or disrupted by neoplastic cells. Nests and tubules of neoplastic germ cells are separated by thin bands of connective tissue. Individual cells are round-to-polygonal and exhibit anisocytosis. Nuclei are large and round with hyperchromatic, coarsely clumped chromatin and indistinct nucleoli. Multinucleated tumor cells and bizarre mitotic figures may be observed frequently.⁴⁴

- **Interstitial Cell Tumor:** Interstitial (Leydig) cell tumor is the least frequently reported gonadal stromal testicular neoplasm of birds.^{12,102,108} Neoplastic testes appear enlarged, fleshy, and occasionally cystic.^{12,108} The contralateral testis may be atrophied (Color 25.4).¹²

Microscopically, interstitial tumors have a dense fibrovascular stroma that divides the neoplasm into lobules. Individual neoplastic cells are large and polyhedral, containing eccentric nuclei and vacuolated eosinophilic cytoplasm.¹⁰⁸ The vacuolated cytoplasm is a reflection of steroid hormone (testosterone) production.

- **Miscellaneous Testicular Neoplasms:** Lymphosarcoma (Marek's disease, Marek's lymphoma) is the

most frequent testicular neoplasm of chickens. This neoplasm is herpesvirus-induced.^{20,109}

The testicular capsule or testis may be the site of origin for hemangioma, fibrosarcoma and leiomyosarcoma.^{102,108} Both carcinoma and leiomyosarcoma have been reported to arise from the epididymis and vas deferens, respectively.¹² Teratomas also may arise in the testis and are discussed under neoplasms of the nervous system.^{23,63,112}

Ovarian and Oviductal Neoplasms

Ovarian neoplasms are reported more frequently than neoplasms arising from the oviduct. Clinical signs may include abdominal distention, ascites, dyspnea, intra-abdominal mass and leg paresis or paralysis. Usually the left leg exhibits paresis or paralysis initially, but both limbs ultimately may be affected. Paraneoplastic syndromes that may be observed in conjunction with ovarian and oviductal neoplasms include localized exostosis or polyostotic hyperostosis.^{5,132}

Ovarian neoplasms are classified histologically according to cell lineage. Granulosa cell tumors are gonadal stromal neoplasms that originate from supportive tissues and are the most common type of ovarian neoplasm. Ovarian carcinomas are of epithelial cell origin and comprise the second most frequent classification of ovarian neoplasia. Dysgerminomas are germ cell tumors that are analogous to seminoma in males. This neoplasm is very rare and has been reported only in poultry and budgerigars.^{7,23} Oviductal neoplasms are also described, and most of these tumors are of epithelial cell origin. Ovariectomy or salpingectomy is the treatment of choice.

- **Granulosa Cell Tumor:** Granulosa cell tumors are the most frequently reported ovarian neoplasm in captive and free-ranging birds.^{12,28,49,51,102,108} These gonadal stromal neoplasms appear as large, pale, nodular masses. Central necrosis and hemorrhage may be present and impart a pink color to the neoplasm.

Histologically, these neoplasms are composed of islands of epithelial-like cells separated by fibrovascular stroma. Cells may form tubules or palisades around blood vessels. Individual neoplastic cells have cytoplasmic vacuoles. Plump, theca-like cells may be scattered throughout the neoplasm.¹⁰⁸

- **Ovarian Carcinoma:** Ovarian carcinomas or adenocarcinomas are the second most frequently reported neoplasm originating in the ovary.^{12,28,31,51,102,108,134,145} These neoplasms may appear

as large, firm, cystic, multilobulated-to-pedunculated masses.

Limited cytologic study of one ovarian cystadenocarcinoma in a budgerigar demonstrated putative neoplastic cells in abdominal effusion fluid.²⁸ A few large epithelial cells were observed that had oval nuclei, prominent nucleoli and abundant blue cytoplasm. Anisocytosis and occasional mitotic figures also were observed.²⁸ Histologically, ovarian carcinomas are composed of epithelial cells arranged in nests, cords, tubules and cysts. Foci of epithelial cell proliferation are separated by connective tissue septa. Papillary projections of epithelial cells may protrude into the cysts. Cystic spaces may contain a homogeneous eosinophilic secretory product. The mitotic rate is variable.

Ovarian carcinomas may metastasize to the mesentery, intestinal serosa, liver, lung, pancreas, muscle and bone.^{31,134,145}

▪ **Miscellaneous Ovarian/Oviductal Neoplasms:**

Stromal tissues of the ovary are infrequent sites of origin for lipomas and fibrosarcomas.^{12,108} Teratomas also may originate in the ovary and are discussed under neoplasms of the nervous system.²³

The oviduct and ventral ligament of the oviduct occasionally are the sites of origin of leiomyomas and leiomyosarcomas.^{102,108}

▪ **Oviductal Dysplasia, Adenomatous Hyperplasia,**

Adenoma and Adenocarcinoma: Studies of reproductive tracts from turkey hens suggest a progression of oviductal lesions in the development of neoplasia.¹³ Preneoplastic changes include epithelial dysplasia and adenomatous hyperplasia. With time, these lesions may progress to oviductal adenoma and adenocarcinoma.^{12,13,15,49,108,132} Oviduct adenocarcinomas may metastasize to abdominal serosal surfaces.¹⁵

Grossly, oviduct adenomas and adenocarcinomas may appear as firm nodular masses. Carcinomatosis, if present, will appear as multiple, small white nodules on serosal surfaces. Polyostotic hyperostosis is a rare paraneoplastic syndrome associated with oviductal adenocarcinoma.¹³²

Histologically, oviductal adenomas and adenocarcinomas are composed of sheets, nests, cords and tubules of cuboidal-to-elongate epithelial cells. Fibrovascular stroma is variable, but fibroplasia is more intense with adenocarcinomas.

▪ **Carcinomatosis:** Carcinomatosis is the seeding of the thoracoabdominal cavity with neoplastic cells

that subsequently proliferate, forming variably sized white nodules. Carcinomatosis may be observed with ovarian and oviductal adenocarcinomas, intestinal adenocarcinoma, pancreatic adenocarcinoma, mesothelioma and undifferentiated adenocarcinoma (Figure 25.12).^{15,31,56,77,85,108,127,134} The pattern of metastasis may be governed partially by serosal membranes within the body cavity.⁷⁷ Both disseminated mycobacteriosis and egg-related peritonitis of hens may mimic neoplasia clinically and at necropsy. Both cytology and histopathology can confirm the presence of carcinomatosis.⁷⁷

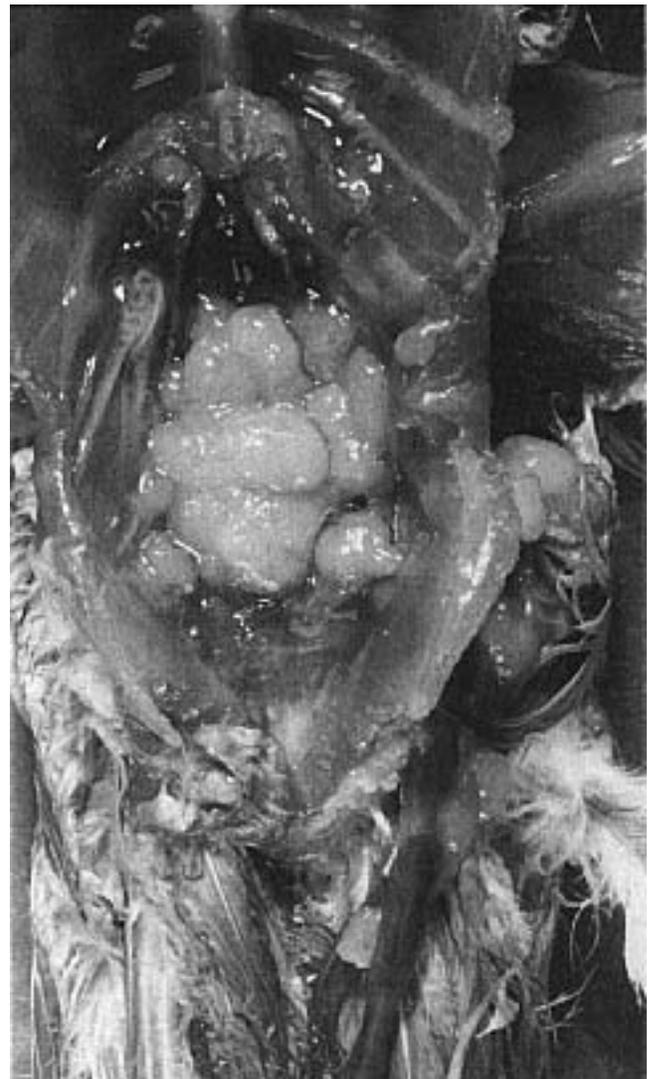


FIG 25.12 Carcinomatosis secondary to an anaplastic pancreatic carcinoma in a mature cockatiel (see Color 25.6) (courtesy Cheryl Greenacre).

Digestive System

Oral Cavity

- **Papilloma:** Papillomas are composed of proliferative squamous epithelium with a fibrovascular stroma. Oral papillomas are occasionally encountered, especially in psittacine birds, and may involve the oropharyngeal, choanal or laryngeal regions of the pharynx.^{24,36,55} Papillomas may undergo malignant transformation to squamous cell carcinoma.
- **Squamous Cell Carcinoma:** Squamous cell carcinomas are second to papillomas in frequency and may involve the oral cavity and tongue.^{3,33,72} These carcinomas appear as ulcerative-to-cauliflower-like, painful lesions or masses that are associated with inappetence, dysphagia, regurgitation, halitosis and frequent head shaking.^{3,33,143} The differential diagnosis for this lesion should include oral neoplasia, hypovitaminosis A, trauma, candidiasis or protozoal infection (trichomoniasis).

Cytologic examination may demonstrate a pleomorphic population of epithelial cells, but squamous cell hyperplasia and squamous cell carcinoma may be difficult or impossible to distinguish. Histologically, squamous cell carcinomas are composed of sheets, nests and cords of pleomorphic epithelial cells that infiltrate adjacent tissues. Anisocytosis, anisokaryosis, dyskeratosis and intercellular bridges usually are observed. Keratin pearl formation and adenoid patterns are observed less frequently. The mitotic rate is variable. Squamous cell carcinomas may be accompanied by inflammation and a scirrhous reaction. Local infiltration of surrounding tissues is common, but metastasis is rare.

- **Miscellaneous Neoplasms:** Miscellaneous oral neoplasms include a mast cell tumor in an owl and a fibrosarcoma in a budgerigar.^{102,124} These neoplasms are discussed in detail under the integumentary system. Mucinous adenocarcinoma of the tongue also has been described in an owl (Figure 25.13).⁴⁵

Esophagus and Crop

- **Squamous Plaque:** Squamous plaques are focal or multifocal thickening of stratified squamous epithelium that may be accompanied by dysplastic change. This lesion has been described as an “epithelioma” in the crop of a pigeon.¹⁰⁸ Squamous plaques are caused



FIG 25.13 Radiographs of the head of an Umbrella Cockatoo indicate the extent of a sublingual mass. Granulomatous response is considered a precursor to some oral tumors (see Color 25.20).

by chronic irritation and may undergo neoplastic transformation.

- **Papilloma:** Papillomas account for the vast majority of neoplasms observed on the mucosal surfaces of the esophagus and crop, especially in psittacine species.^{24,36,55,108} Papillomas may undergo malignant transformation.
- **Squamous Cell Carcinoma:** Squamous cell carcinoma of the crop has been observed in a budgerigar and an Amazon parrot.^{15,90} The most detailed description is given for the Amazon parrot.⁹⁰ Grossly, the esophageal wall was thickened (Figure 25.14). The neoplasm was circumferential with a dry, white, cauliflower-like surface (Color 25.8). Microscopically, the neoplasm was composed of aggregates of pleomorphic squamous epithelial cells that extended into the submucosa.
- **Leiomyosarcoma:** A multifocal leiomyosarcoma has been reported to originate in the crop wall of a budgerigar. The only clinical sign attributed to this neoplasm was difficulty in swallowing.¹⁰²

Proventriculus and Ventriculus

Neoplasms of the proventriculus are approximately twice as common compared to neoplasms of the ventriculus. Adenocarcinomas are most commonly ob-

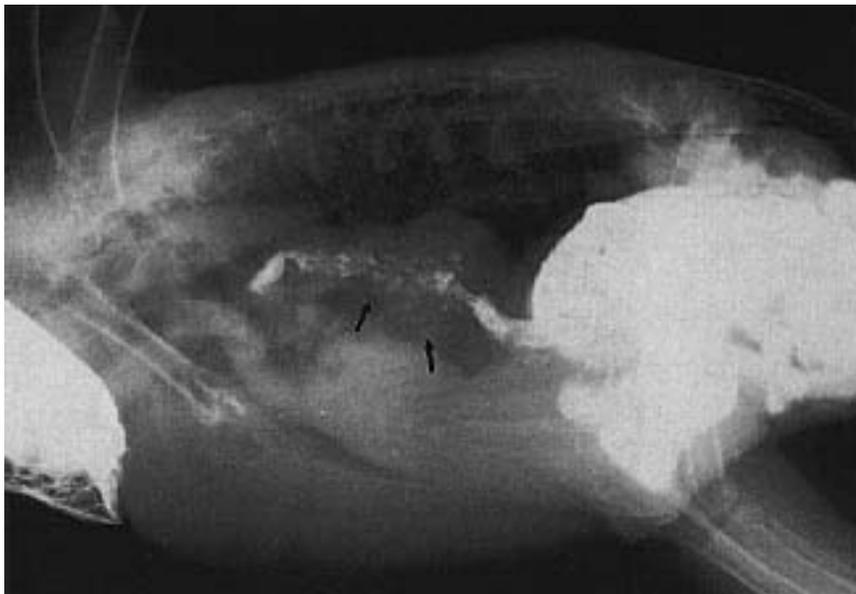


FIG 25.14 An esophagram of an adult Amazon parrot indicated an irregular mucosal filling pattern in the distal esophagus suggestive of a mass (see Color 25.8) (courtesy of Jane Turrel).

served and often arise from the junction of these two organs.

- **Proventricular Carcinoma:** Proventricular carcinoma is the most frequent neoplasm observed in this organ.^{79,80,104,108,123,143} These neoplasms are more common in psittacine species, especially Grey-cheeked Parakeets.^{79,104,123}

On gross inspection, proventricular carcinomas appear as ulcerated, thickened, raised or depressed lesions. Clinically, gastrointestinal bleeding, as determined by observation of melena, anemia or a positive fecal occult blood test, should alert the clinician to the possibility of gastrointestinal neoplasia. Severe bleeding, hypovolemic shock or exsanguination may occur.^{79,104} Proventricular carcinomas may exhibit rare transmural extension with serosal metastasis to the ventriculus, intestine and pancreas or hematologic metastasis to the spleen, liver, lungs and heart base.^{79,108}

Microscopically, these neoplasms are composed of columnar-to-cuboidal-to-squamous epithelial cells arranged in a tubuloacinar pattern. Individual cells have vesicular nuclei and eosinophilic-to-basophilic cytoplasm. Mitotic figures may be observed frequently. Many neoplasms are associated with a scirrhous reaction. The luminal surface of the neoplasm is often ulcerated, while deep margins of the neoplasm exhibit invasion of the muscularis.^{79,104,108} Pe-

riodic acid-Schiff (PAS) and alcian blue staining may help differentiate proventricular and ventricular carcinomas. Proventricular carcinoma cells and the secretory product are strongly PAS-positive and stain dark pink. In contrast, the koilin secretory product of ventricular epithelial cells is alcian blue-positive and appears bright blue.^{79,104}

- **Ventricular Carcinoma:**

Ventricular carcinomas are infrequent in comparison to proventricular carcinomas but the clinical signs are similar (Figure 25.15).^{79,104} These neoplasms have not been reported to metastasize. Microscopically, the appearance of ventricular carcinoma is similar to proventricular carcinoma except secretory cells are PAS-negative. The koilin secretory product is strongly alcian blue-positive. A single ventricular adenoma has been reported in a parrot but the neoplasm

was not characterized.⁴⁹

- **Papillomas:** Papillomas are reported to occur within the proventriculus and ventriculus.^{24,55} They are apparently more common in the ventriculus.⁵⁵

- **Proventricular Adenoma:** A proventricular adenoma has been observed in a teal. On gross examination, the proventriculus was spherical instead of fusiform. The luminal surface was covered by a hemorrhagic, fibrillated, plaque-like mass. Histologically, the mass was composed of tubuloacinar structures lined by one-to-four layers of short, columnar epithelial cells. Cellular nuclei were centrally located, vesicular and had a small nucleolus. Cellular cytoplasm was basophilic. Few mitotic figures were observed and fibrovascular stromal tissue was minimal. Hemorrhage and necrosis were present near the luminal surface.⁸

Intestine

Although rare, some neoplasms originating in the small intestine have been reported. Intestinal neoplasms can best be managed by surgical excision and intestinal anastomosis if the lesions are diagnosed early, if metastasis has not occurred and if the site can be adequately exposed.

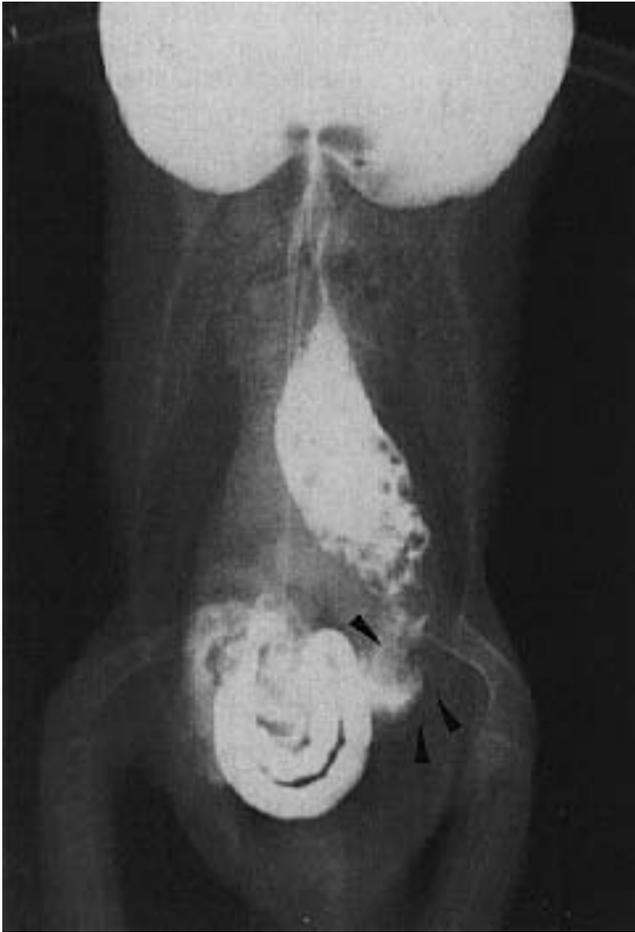


FIG 25.15 A six-year-old male budgerigar was presented with a history of regurgitation and weight loss. Radiographs taken 30 minutes after the administration of barium sulfate indicated filling defects in the proventriculus (consistent with ingesta) and an indistinct and irregular mucosal pattern in the lateral wall of the ventriculus (arrows) (consistent with neoplasm) (courtesy of Jane Turrel).

- **Leiomyosarcoma:** Primary intestinal leiomyosarcomas have been observed in budgerigars. Metastatic lesions were not observed.^{15,133}
- **Intestinal Carcinoma:** Intestinal carcinoma has been reported in a budgerigar, duck and gull.^{15,49,72} Metastatic foci were observed within the lung, liver and spleen.⁷²

Cloaca

Cloacal neoplasms and masses, including papillomas, adenocarcinomas, and adenomatous polyps and hyperplasia are observed most commonly in psittacine birds, especially Amazon parrots.^{35,37,49,51,55,65,102,136}

- **Cloacal Papilloma:** Cloacal papillomas are recognized frequently in psittacine birds.^{37,55,65,102,136} Cloa-

cal papillomas and bile duct carcinoma may show concurrent development, especially in Amazon parrots.^{55,65} Grossly, cloacal papillomas appear as broad-based, pink-to-red, proliferative-to-ulcerative masses. They may closely resemble granulation tissue (see Color 19). Major clinical signs associated with cloacal papillomas are straining, bleeding from the vent and cloacal prolapse. A viral etiology has been suggested for these neoplasms, but has yet to be confirmed.¹³⁶

Histologically, cloacal papillomas are composed of hyperplastic epithelium over a base of fibrovascular stroma. The epithelium may vary from 10- to 50-cell layers in thickness. Depending upon the biopsy site, epithelial cells may exhibit a transition from columnar to squamous morphology. Epithelial cells on the luminal surface may contain basophilic intracytoplasmic mucin granules that can be demonstrated by alcian blue and mucicarmine staining.¹³⁶

- **Cloacal Carcinoma:** Cloacal carcinomas are observed infrequently compared to papillomas.^{49,51,102,136} Histologically, these neoplasms contain a more pleomorphic epithelium, characterized by dysplasia and bizarre mitoses.¹³⁶ Transmural cellular invasion and penetration of the cloaca may be associated with sclerosing fibroplasia.^{51,102}
- **Cloacal Adenomatous Polyp or Hyperplasia:** Histologically, these lesions are characterized by epithelial cell hyperplasia resulting in a visible mass.^{35,102} It seems reasonable that a progression of cloacal lesions occurs, ranging from hyperplasia to neoplasia (usually benign papillomas). Furthermore, cloacal papillomas may rarely undergo malignant transformation to adenocarcinomas.

Hepatic Neoplasms

Both primary and metastatic neoplasia occur in the liver. The most frequent primary hepatic neoplasms are hepatocellular carcinoma and bile duct carcinoma. Conditions that must be differentiated from neoplasia include hepatic nodular hyperplasia, bile duct hyperplasia and biliary cysts (see Color 20).

- **Cholangiocarcinoma:** Cholangiocarcinoma (cholangiocellular carcinoma, bile duct carcinoma) originates from bile duct epithelium. This is the most frequent hepatic neoplasm reported in captive and free-ranging birds (lymphoid neoplasms are most common in gallinaceous birds).^{1,2,5,49,50,72,102,103,108,147,148} Specific clinical signs are infrequent, although emaciation, weakness, hepatomegaly, ataxia, trembling

and seizures have been observed.^{2,50,148} Some neurologic signs are suggestive of hepatoencephalopathy.

On gross inspection, the hepatic parenchyma contains numerous, variably sized, firm, white-to-tan nodules. Histologically, these neoplasms consist of columnar-to-cuboidal epithelial cells arranged in ribbons, cords, tubules or ducts. Infiltration of the hepatic parenchyma is apparent. A few mitotic figures may be observed. In some neoplasms, a scirrhous reaction may be present.^{1,2,50,148}

Cholangiocarcinomas may exhibit vascular invasion with subsequent widespread metastasis to the lungs, brain, kidney, pleura and serosa of the ventriculus.^{1,43,72,102,147,148} There is no available treatment for cholangiocarcinoma.

- **Cholangioma:** Cholangiomas are of bile duct epithelial origin and are rare in comparison to cholangiocarcinoma.^{49,108} Cholangiomas may occur as single or multiple, firm nodules. Histologically, they appear as epithelial-lined tubular structures with a dense fibrous stroma.¹⁰⁸
- **Bile Duct Hyperplasia:** Bile duct hyperplasia is observed with some frequency in psittacine birds with liver disease. Bile duct hyperplasia is often seen concurrently with hepatic fibrosis and hepatocellular lipidosis. The gross and microscopic appearance of some livers may mimic cholangiocarcinoma. The etiology of bile duct hyperplasia is often undetermined; however, ingestion of mycotoxin-contaminated feed should be considered in the differential diagnosis (see Chapter 20).
- **Biliary Cyst:** Biliary cysts are reported infrequently in birds.⁹⁵ Such cysts are generally congenital and may be intra- or extra-hepatic. Biliary cysts may be observed in conjunction with polycystic kidneys.
- **Hepatocellular Carcinoma:** In captive and free-ranging birds, the incidence of hepatocellular carcinoma is superseded only by cholangiocarcinoma.^{12,43,51,108} Birds with hepatocellular carcinoma frequently present in a debilitated state with enlargement of one liver lobe. Abdominal enlargement may be apparent on physical examination.

Antemortem liver lobe enlargement may be confirmed by radiography, ultrasound, endoscopy or laparotomy. Postmortem confirmation of liver lobe enlargement is made by visual inspection at necropsy. Neoplasms may vary in size and color, ranging from light tan to a more normal red-brown. Microscopi-

cally, these neoplasms are composed of cords of hepatocyte-like cells with effacement of normal tissue architecture. Bizarre-to-multinucleated hepatocytes may be observed. Variable numbers of mitotic figures are present.^{43,108}

Metastases are rare, but when they occur the lungs are usually involved.^{43,147} Partial or full hepatic lobectomy may be attempted to excise these neoplasms.

- **Hepatocellular Adenoma:** Hepatocellular adenoma (hepatoma) is poorly documented in birds, having been reported in a cissa, guineafowl, hornbill and mynah bird.^{49,72,131,147} The multiple nodules within the hepatic parenchyma of the mynah bird were associated with osseous metaplasia and extramedullary hematopoiesis. These nodules probably represented hepatic nodular hyperplasia.¹³¹
- **Nodular Hyperplasia:** Nodular hyperplasia of the liver may be viewed as attempted parenchymal regeneration following injury. Nodular hyperplasia is usually an incidental finding at necropsy in birds with evidence of chronic liver disease.⁶⁴ The gross appearance of these pale nodules may be mistaken for hepatocellular adenoma or adenocarcinoma. The most common associations with nodular hyperplasia are mycotoxin exposure and iron-accumulating hepatopathy.
- **Miscellaneous Hepatic Neoplasms:** Miscellaneous neoplasms described in the liver include malignant lymphoma, fibrosarcoma, hemangioma, hemangiosarcoma and lipoma.^{12,64,102,108,109} Myelolipomas also may arise within the hepatic parenchyma. Furthermore, the liver may be involved in hematologic neoplasia, which can be difficult to distinguish from extramedullary hematopoiesis.

Pancreatic Neoplasms

Most pancreatic neoplasms reported in birds arise from the exocrine pancreas, especially ductular structures. These neoplasms may be single or multiple. Neoplasms arising from the endocrine pancreas are rare.

- **Pancreatic Adenoma:** Pancreatic adenomas occur in psittacine birds, especially Amazon parrots, macaws and budgerigars.^{15,49,56} In Amazon parrots, pancreatic adenomas may be associated with internal papillomas or may be observed as incidental findings at necropsy.⁵⁶

On gross inspection, multifocal pancreatic adenomas usually are observed associated with ductular struc-

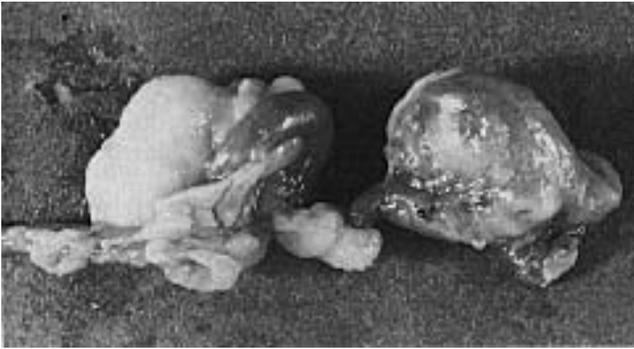


FIG 25.16 Pancreatic carcinoma with involvement of the serosal surface of the intestines in a cockatiel (see Color 25.6) (courtesy of Cheryl Greenacre).

tures. Intraductal neoplasms may cause local distention of affected ducts with concurrent compression atrophy of the adjacent pancreatic parenchyma.⁵⁶

Histologically, these neoplasms are composed of proliferating columnar epithelial cells arranged in cords or papillary projections. Epithelial cell proliferation may be accompanied by fibroplasia.⁵⁶

- **Pancreatic Adenocarcinoma:** Pancreatic adenocarcinoma may be observed in various species of birds including psittacines, doves, Anseriformes and ratites.^{49,56,72,108,137} These neoplasms occasionally may be quite large, envelop bowel loops and result in abdominal effusion.¹³⁷ They are not amenable to treatment (Figure 25.16).

Histologically, adenocarcinomas are composed of a pleomorphic population of epithelial cells that infiltrate or dissect local tissues. Metastasis may occur, usually by serosal seeding.⁵⁶ Pancreatic adenocarcinoma should be a diagnostic consideration when carcinomatosis is observed (Color 25.6).



Endocrine System

The endocrine system is composed of widely distributed tissues, glands and organs. The endocrine system, in conjunction with the nervous system, maintains homeostasis by the ability to synthesize, store and release various hormones. These hormones are distributed via the blood to effector cells, tissues or organs where their biological effect is mediated. Neoplasms usually affect only one endocrine cell type.

Rarely, neoplasia will involve two or more different endocrine cell lines, a condition called multiple endocrine neoplasia. Evidence suggests that multiple endocrine neoplasia occurs in birds as well as in mammals.⁴⁹

Pituitary Gland

Pituitary neoplasms are the most frequently reported endocrine neoplasm in birds and there is no effective treatment for them.^{10,12,102,121}

- **Pituitary Adenoma:** Pituitary adenoma is the most frequently reported endocrine neoplasm of birds, especially budgerigars.^{10,12,15,39,49,102,108,121} These neoplasms often originate from proliferation of chromophobe cells in the anterior lobe. Because of the anatomic location of the pituitary gland, expansive neoplasms follow the path of least resistance, compressing the hypothalamus and optic chiasm. Neurologic signs resulting from compression include incoordination, poor perching or posture, somnolence, seizures and convulsions, and visual impairment including blindness associated with dilated, fixed pupils.^{10,12,39,102,108,121} Unilateral or bilateral exophthalmos may result from neoplastic cell infiltration along the optic nerve(s).¹²¹

Pituitary adenomas also may be associated with polydypsia and polyuria.^{10,12,39,102} The mechanisms of polydypsia and polyuria have not been investigated in birds, but may be caused by decreased antidiuretic hormone (ADH) concentrations or by over-production of adrenocorticotrophic hormone (ACTH). Compression of the posterior lobe of the pituitary decreases ADH transport and storage with subsequent diuresis. Excessive production of ACTH might cause adrenal cortical hyperplasia with excess corticosterone secretion and steroid-induced diuresis.

Pigment changes such as alterations in feather coloration pattern and cere color have been reported in a cockatiel and budgerigar; however, hormonal changes were not investigated.^{10,39}

Necropsy usually reveals a mass in the location of the pituitary that compresses the overlying hypothalamus. Microscopically, these neoplasms are composed of round-to-cuboidal cells arranged in sheets or sinusoidal patterns containing a delicate fibrovascular stroma. Cells have round nuclei, stippled chromatin and variable quantities of cytoplasm. In chromophobe adenomas, the cytoplasm stains poorly. Mitoses are infrequent and a remnant of the pars distalis may be apparent.⁸⁸

- **Pituitary Carcinoma:** Pituitary carcinomas are rare neoplasms in birds, but have been reported and characterized in two budgerigars.¹²¹ Neoplastic cell invasion of the brain and formation of retrobulbar masses have been observed, along with distant metastasis to the liver and kidney. Histologically, these neoplasms are highly cellular and may contain foci of necrosis and hemorrhage. Confirmation of metastasis supports the presumptive diagnosis.

Pineal Gland

Neoplasms of the pineal gland are rare. These expansive neoplasms may displace or compress adjacent neural tissue resulting in neurologic deficits. Because of their anatomic location, surgical excision of pineal gland neoplasms is virtually impossible.

- **Pineoblastoma:** A pineoblastoma has been described in a cockatiel.¹⁵¹ Clinical signs included polydipsia, depression, right-sided head tilt and inability to grasp objects with the right foot.

Necropsy examination disclosed a grey suprachiasmatic mass extending into the right ventricle and compressing the right occipital lobe and thalamus. Microscopically, the mass consisted of sheets, cords and fewer palisades of round cells with round-to-oval nuclei, stippled chromatin and lightly basophilic cytoplasm. A delicate fibrovascular stroma was present. Occasional mitotic figures were observed throughout the mass.

- **Pinealoma:** Pinealoma has been reported in two chickens and a dove.^{22,108,138} The neoplasm apparently was an incidental finding in one chicken from a flock exhibiting increased mortality and trembling.¹³⁸ The neoplasm in the dove was a serendipitous discovery during postmortem assessment of cranial trauma.¹⁰⁸

On microscopic examination, the mass was encapsulated, cellular and displaced cerebellar folia and extended deeply between them. The mass had a lobular architecture, with some lobules containing single layers of ciliated columnar-to-pseudostratified-columnar epithelium. Neoplastic cells contained round-to-oval nuclei exhibiting mild anisokaryosis. Mitotic figures were observed occasionally.

Thyroid Gland

Enlargement of the thyroid glands may be observed with hyperplasia or neoplasia. Signs of thyroid gland enlargement may include dyspnea and a distinctive squawk on vocalization.^{6,12,118} Their anatomic location near the thoracic inlet precludes palpation of masses unless glandular enlargements are extreme.⁶ Thy-

roid hyperplasia can be managed medically. Theoretically, thyroid neoplasia can be managed surgically, but diagnosis and extirpation of intrathoracic lesions are difficult.

- **Thyroid Hyperplasia:** Thyroid hyperplasia (goiter) may be associated with iodine-deficient diets, ingestion of goitrogenic plants such as *Brassica* species, exposure to iodine-containing disinfectants or excessive dietary iodine.^{88,115} Thyroid hyperplasia is manifested by bilateral glandular enlargement. Colloid-distended follicles may result in glandular enlargements reaching 20 mm in diameter.¹² Because of improved diets for companion birds, thyroid hyperplasia is reported less frequently than three decades ago.^{6,12,15,118}

On gross necropsy examination, the thyroid glands are bilaterally enlarged and may appear cystic. Histologic sections of thyroid gland contain large, irregular follicles that are lined by columnar epithelium and distended with light-pink colloid. Papillary projections of epithelium may protrude into the lumen of some follicles (see Chapter 23).

- **Thyroid Adenoma:** Thyroid adenomas are usually unilateral but may occasionally cause bilateral glandular enlargement. These neoplasms usually represent incidental necropsy findings in birds.^{12,15,49,108}

Histologically, thyroid adenomas are poorly characterized in birds. Most thyroid adenomas appear as nodules of encapsulated glandular tissue.

- **Thyroid Carcinoma:** Thyroid carcinomas are rare and poorly characterized in birds.^{12,49,102} Thyroid gland enlargement may be unilateral or bilateral. Dyspnea may be a presenting complaint.¹⁰² Histologically, thyroid carcinomas may appear nodular, poorly encapsulated and invasive. These neoplasms are highly vascular.

Adrenal Gland

In contrast to mammals, avian adrenal glands have no distinct cortex or medulla. Both interrenal (cortical) and enterochromaffin (medullary) cells are intermingled throughout the gland.¹⁰⁹ Adrenal neoplasms are rare in captive and free-ranging birds and have not been studied in detail. When enlargement of the adrenal glands is observed at necropsy, a primary consideration is adrenal gland hyperplasia.

- **Adrenal Adenoma:** Adrenal adenomas arise from interrenal (cortical) cells and have rarely been re-

ported in birds and generally are not associated with clinical signs of disease.^{15,49,108}

Histologically, affected adrenal glands are replaced by a lobulated mass of tubuloacinar tissue. Epithelial cells appear pale with foamy cytoplasm and centrally located nuclei. Mitotic figures are uncommon.¹⁰⁸

- **Adrenal Carcinoma:** Adrenal carcinoma was described in a Mountain Duck that was depressed and had leg paralysis.⁴³

The adrenal gland neoplasm was unilateral and composed of a pleomorphic population of polyhedral-to-elongated cells arranged in a frond-like pattern. Marked anisocytosis and anisokaryosis was apparent, including the presence of tumor giant cells. Mitoses were observed infrequently. Neoplastic cells infiltrated adjacent nerves.⁴³

- **Pheochromocytoma:** A single pheochromocytoma has been reported in a Mouflon, but clinical, necropsy and histologic findings were not discussed.⁴⁹

Endocrine Pancreas

- **Islet Cell Carcinoma:** The islets of Langerhans constitute the endocrine portion of the pancreas. These scattered islets are composed of a diverse aggregation of alpha, beta and delta cells that secrete glucagon, insulin and gastrin, respectively. Islet cell neoplasms may be secretory or non-secretory. Secretory islet cell neoplasms may have diverse clinical presentations.

An islet cell carcinoma has been reported in a budgerigar with hyperglycemia.¹¹⁶ The neoplasm was presumed to be of alpha cell origin and associated with glucagon hypersecretion and diabetes mellitus, but this assumption was not proven. It must be noted that in health, birds have higher glucose values than mammals. In stressful situations, avian blood glucose values may temporarily approach or exceed 700 to 800 mg/dl. Therefore, persistent and dramatic hyperglycemia must be present to confirm a diagnosis of avian diabetes mellitus.

Histologically, this islet cell carcinoma consisted of nests and lobules of pleomorphic, pale-staining cells with vesicular nuclei and a moderate mitotic index. The neoplasm was poorly circumscribed and contained a delicate fibrovascular stroma. Both compression and invasion of the adjacent exocrine pancreas were observed.¹¹⁶

Chemoreceptor Neoplasms

Chemoreceptors, in concert with the parasympathetic and sympathetic nervous systems, regulate blood pH, pCO₂ and pO₂. These neoplasms are very rare in birds. A carotid body tumor has been reported in a parakeet, but no details of the neoplasm were presented.¹⁵

Nervous System and Eye

Nervous system and ocular neoplasms apparently are infrequent in birds with the exception of pituitary adenomas in budgerigars and malignant lymphoma (leukosis) in chickens.^{48,49,121}

Central Nervous System

Neoplasms of the central nervous system may represent an interesting incidental finding at necropsy or may be related to profound neurologic deficits from compression and infiltration of neural tissue, obstruction of cerebrospinal flow, or secondary edema, hemorrhage or necrosis. These neoplasms have a poor prognosis, and effective treatment regimens have yet to be developed (Color 25.14). The discussion below is confined to those neoplasms recently reported in birds.

- **Astrocytoma:** An astrocytoma is a differentiated neoplasm of astrocytes that exhibits slow but progressive growth. These neoplasms usually arise in the cerebral hemispheres, thalamus, brainstem, cerebellum or spinal cord.⁸⁸ A single astrocytoma has been reported in a duck with neurologic signs (especially circling).¹⁰⁸ At necropsy, a lobulated mass was identified in the base of the cerebellum. Histologically, the neoplasm was lobulated and unencapsulated with large globular cells in a fibrillar network.¹⁰⁸ The tumor description suggests a gemistocytic astrocytoma.
- **Glioblastoma:** A glioblastoma is an undifferentiated neoplasm of astrocyte origin. These neoplasms grow rapidly, infiltrate surrounding neural tissue, and are very destructive. A glioblastoma has been described in a budgerigar with weakness, incoordination, inability to perch properly, tremors of the wings and rigidity of the legs.¹⁰⁶ Gross brain lesions were not observed at necropsy. Microscopically, a circumscribed mass occupied a large area of the diencephalon and mesencephalon. Neoplastic cells were pleo-

Oncology

Color 25.1

A ten-year-old Amazon parrot was presented with a one-year history of progressive swelling of the head and face. Numerous masses were palpable throughout the body, and their occurrence was confirmed by radiographs (see Figure 25.2). Histopathology indicated an invasive fibrosarcoma involving the soft tissues and bones of the head (courtesy of Jane Turrel).

Color 25.2

A six-year-old budgerigar was presented with a large, featherless mass involving the ventral abdomen. The mass interfered with the bird's ability to fly and perch. Cytology indicated a lipoma with xanthomatosis of the skin overlying the mass (note the yellowish, thickened skin). The tumor and associated xanthoma were surgically excised (courtesy of Jane Turrel).

Color 25.3

A four-year-old African Grey Parrot was presented with a history of anorexia, weight loss and depression. The bird did not respond to supportive care. Hepatomegaly and splenomegaly with raised white nodules in the liver were noted at necropsy. Histopathology revealed an accumulation of lymphoid cells in the nodules, consistent with a diagnosis of lymphosarcoma (courtesy of Jane Turrel).

Color 25.4

A five-year-old male budgerigar was presented for abdominal distention and left limb paresis. The bird did not respond to supportive care. Necropsy findings included seasonal testicular (t) hypertrophy (which should not be confused with neoplasm) and a renal mass (arrow). The renal mass was histologically identified as a renal carcinoma (courtesy of Jane Turrel).

Color 25.5

A five-year-old budgerigar was presented with a rapidly growing firm mass on the dorsal surface of the wing. Cytology indicated a pleomorphic population of spindle cells suggestive of fibrosarcoma. The mass was limited to the soft tissue of the wing and did not involve the underlying bones. The case was managed by amputating the affected wing (courtesy of Jane Turrel).

Color 25.6

An adult female cockatiel was presented for weight loss and a distended abdomen. On physical examination, the bird was bright,

alert and responsive, and weighed 91 g but was severely emaciated as detected by pectoral muscle atrophy. The abdomen was severely dilated and had a fluid consistency. Abdominocentesis was used to collect 10 mls of fluid that was used for cytologic evaluation. The fluid had the characteristics of a modified transudate and contained cells suggestive of neoplasm. The bird did not respond to supportive care. At necropsy, 20 mls of fluid were removed from the distended abdomen. A large mass was filling the space between the descending and ascending duodenum that is normally occupied by the pancreas. The histologic diagnosis was multicentric, anaplastic pancreatic carcinoma with carcinomatosis of the serosal surfaces of the abdomen and the tunica muscularis of the intestines (courtesy of Cheryl Greenacre).

Color 25.7

A captive Blue Jay was presented with a crusty, hemorrhagic, poorly defined mass on the wing. The lesion first appeared as a non-healing wound that progressively enlarged over a period of several months. Biopsy of the lesion revealed a squamous cell carcinoma (courtesy of Jane Turrel).

Color 25.8

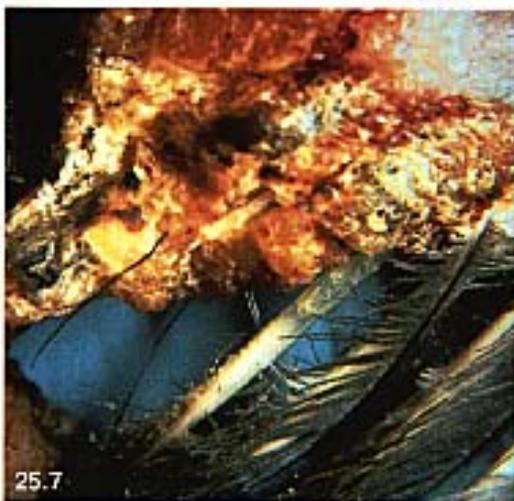
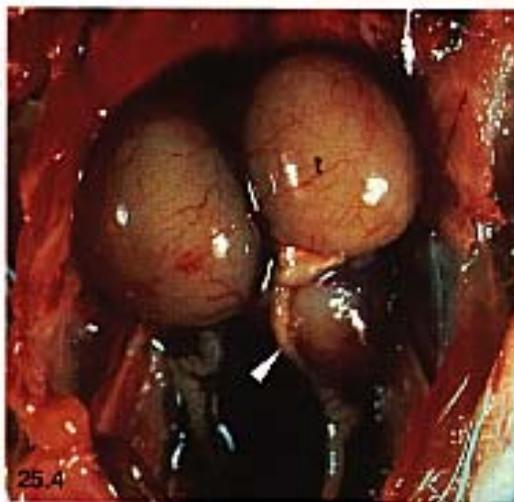
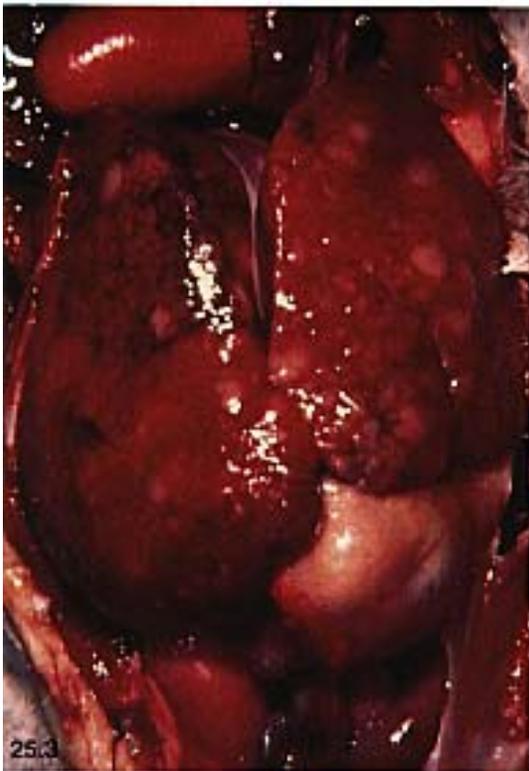
A 50-year-old Amazon parrot was presented with a history of dysphagia, regurgitation and weight loss of several months' duration. Histopathology of the mass confirmed a squamous cell carcinoma (see Figure 25.14) (courtesy of Jane Turrel).

Color 25.9

A two-year-old Umbrella Cockatoo was presented with epiphora and an ocular mass. The mass was debulked and the histologic diagnosis was squamous cell carcinoma. The tumor margin was irradiated with a strontium-90 ophthalmic probe (courtesy of Jane Turrel).

Color 25.10

A three-year-old cockatoo was presented with bilateral foot lesions characterized by depigmented, scaly, hard, thickened skin. The lesions were suggestive of a viral-induced papilloma. If not associated with any specific dysfunction, lesions such as these can remain untreated (courtesy of Jane Turrel).





Oncology

Color 25.11

A mature, male cockatiel was presented with a several-month history of poor generalized feather condition and feather loss around the uropygial gland. A raised, firm, uropygial gland mass was evident. Cytology of the mass revealed multiple mitotic figures. The mass was surgically removed and the histopathologic diagnosis was adenocarcinoma.

Color 25.12

A four-year-old female cockatiel on an all-seed diet was presented with a three-month history of a progressively enlarging abdominal mass. On presentation, the ventral surface of the mass was dragging on the ground and the bird was having trouble ambulating. The bird weighed 128 g. Note the rotund appearance of the pelvic musculature. This bird responded to a change in diet and increased exercise over a three-month period, followed by surgical excision of the mass that was half its original size at the time of surgery.

Color 25.13

A four-year-old female African Grey Parrot was presented for removal of a fibrosarcoma from the left dorsal humerus. Surgery was complete and uneventful. The bird was presented one year later with lethargy, anorexia, ataxia and severe dyspnea. Radiographs indicated a large, soft tissue mass in the cranial thorax. Cytology of a fine-needle aspirate indicated ovoid cells with large, eccentric nuclei suggestive of a neoplasm. The bird did not respond to supportive care. Histopathology revealed a renal tubular adenocarcinoma with metastasis to the lung, liver and myocardium. Interestingly, the bird's mate died from adenocarcinoma two years earlier.

Color 25.14

A four-year-old Blue-fronted Amazon Parrot was presented for an acute onset of depression and apparent blindness. The only abnormal physical examination finding was mild ataxia. Radiographs of the abdomen were unremarkable. Blood lead and zinc levels were normal. A mild heterophilia (19,000 cells/ μ l) was the only abnormal clinicopathologic finding. EEGs indicated diffuse cerebral inflammation. The bird would maintain weight and condition with supportive care but would deteriorate when the supportive care was stopped. After two months the bird was euthanatized. The ventral surface of the brain was nodular in appearance. The histopathologic diagnosis was meningioma.

Color 25.15

A two-year-old female cockatiel was presented for feather picking associated with

the right carpus. A diffuse, firm, yellow mass was noted in the carpal region on physical examination. The appearance of the lesion was suggestive of xanthoma, and the demonstration of vacuolated macrophages, lipids and cholesterol crystals in a fine-needle aspirate from the mass was confirmatory. The xanthoma was surgically excised.

Color 25.16

A mature Amazon parrot was presented with a non-weight-bearing lameness of one week's duration. Radiographs indicated a fracture of the mid-diaphyseal tibiotarsal bone. During surgery for placement of an IM pin, it was noted that the bone did not appear normal and a biopsy was performed. Surgical recovery was unremarkable. The biopsy report indicated osteosarcoma, and the client chose to have the bird euthanatized. Inset shows the dissected bone, which had healed from the pathologic fracture, with the pin in place.

Color 25.17

An adult Indian Ring-necked Parakeet was presented with a three-month history of a proliferating mass involving the cere and left periocular area. Note the defect in the rhamphotheca, indicating inflammation of the germinative layers of the beak. The masses were surgically removed. Histopathology was suggestive of a papilloma.

Color 25.18

A mature budgerigar was presented with progressive dysphagia, and a disfiguring oral lesion was noted on physical examination. Histologic lesions were consistent with adenocarcinoma.

Color 25.19

A four-year-old budgerigar was presented with a rapidly growing, necrotic mass of the upper beak. The mass was interfering with the bird's ability to eat, and the owners chose euthanasia. Histologic evaluation indicated the mass was a fibrosarcoma (courtesy of Jane Turrel).

Color 25.20

A ten-year-old Umbrella Cockatoo was presented for dysphagia, weight loss and poor feather formation. On physical examination, a large, pendulated, ulcerative sublingual mass was identified. The bird had dystrophic feathers and was positive for PBFV virus by DNA probe testing of whole blood. Cytology of a fine-needle aspirate of the oral mass was suggestive of a giant cell granuloma. Radiographs of the head indicated the extent of the sublingual mass (see Figure 25.13).

morphic and numerous multinucleated giant cells were observed.

- **Oligodendroglioma:** This neoplasm originates from oligodendroglial cells. These neoplasms usually arise in the cerebral hemispheres. Microscopically, they are composed of small cells with round, hyperchromatic nuclei arranged in a honeycomb pattern.⁸⁸ A single “glioma” has been reported in the left cerebral hemisphere of a budgerigar, but microscopic characteristics of the neoplasm were not reported.⁶
- **Choroid Plexus Papilloma:** These benign neoplasms originate from the choroid plexus epithelium, usually in the fourth ventricle at the cerebropontine angle.⁸⁸ A choroid plexus papilloma has been observed in a budgerigar with blindness, exophthalmos and seizures.¹⁰² A visible mass was not observed at necropsy; however, the tumor was apparent in tissue section. This neoplasm arose from the choroid plexus of the fourth ventricle. Rows of columnar cells were arranged in irregular papillary projections, small rosettes and contorted cysts. Neoplastic cells were columnar with round-to-oval, basal nuclei.
- **Neuroblastoma and Ganglioneuroma:** These neoplasms are derived from primitive neuroepithelial cells that differentiate toward neuroblasts (neuroblastoma) or neurons (ganglio-neuroma).⁸⁸ Ganglioneuromas have been reported in chickens where they may arise in the nervous system, gastrointestinal tract, ovary, muscle or heart.²³ These neoplasms are composed of ovoid, pyramidal or irregular neurons scattered among Schwann cells and fibrous stroma. Ganglioneuromas are usually benign, but may be malignant.
- **Vascular Neoplasms:** The most common vascular neoplasms observed in the central nervous system are hemangiosarcoma and hamartoma. A hamartoma is a benign tumor-like nodule composed of an overgrowth of mature cells. A hamartoma-like lesion has been reported in the brain of an 11-week-old budgerigar. Microscopically, the lesion was composed of blood-filled spaces within the neuropil that compressed adjacent tissue.¹² Vasoformative neoplasms are frequently observed in chickens; however, brain involvement has not been reported.^{74,129}
- **Teratoma:** Grossly, these primordial germ cell neoplasms, which may be large and cystic, have been observed in chickens and ducks.^{21,23,38,58,61,63,68,76,112} Teratomas have diverse sites of origin including the brain, pineal gland, testis, ovary, kidney, orbit, cranium, thoracoabdominal cavity and retroperitoneal

space. Teratomas arising within the cranial vault may cause neurologic deficits such as head tilt, circling and facial nerve paralysis.^{68,76}

The microscopic appearance of these neoplasms is quite striking, containing a mixture of tissue types derived from two or three germ cell layers. The differentiated tissues may include cartilage, bone, fat, keratin cysts, smooth muscle, epithelium, neural cells and melanocytes.

- **Lymphosarcoma:** Lymphosarcoma of the central nervous system may be classified as a primary or secondary disease. Primary lymphosarcoma originates in the CNS, while secondary lymphosarcoma represents a metastatic event. Evidence exists for both of these presentations of lymphoid neoplasia in birds, although metastatic neoplasia is more common.^{9,49} Most instances of CNS lymphosarcoma occur in poultry and are viral-induced.^{20,101} Lymphosarcoma is discussed in detail under the hemolymphatic system.
- **Meningioma:** Meningiomas originate from neural crest cells or mesenchymal cells in contact with neural crest cells. Microscopically, meningiomas are often characterized by whorls of crescent-shaped cells.⁸⁸ Meningiomas have been reported in chickens, but have not been characterized in detail.²³

Peripheral Nervous System

Peripheral nervous system neoplasms arise in nervous tissues other than the brain and spinal cord. Localized neoplasms may be amenable to surgical excision based upon their location, size and proximity to vital structures.

- **Schwannoma:** These neoplasms previously have been reported as neurolemmomas or neurofibroma, the latter term being a misnomer.⁸⁸ Schwannomas may arise from Schwann cells or perineural cells of the peripheral nerve sheaths in any location including unspecified peripheral nerves, cranial nerves, sciatic plexus, gastrointestinal tract, testis, pineal gland, kidney, skin, muscle and spleen.^{17,23,85,108}
- Grossly, these neoplasms appear as single-to-multiple nodular masses or varicose thickenings of the nerve sheath. Histologically, fusiform cells are arranged in interwoven bundles, whorls or palisade arrangements. Specific diagnosis relies upon observation of the associated nerve of origin.^{17,88}
- **Malignant Schwannoma:** Malignant schwannomas (neurofibrosarcoma is a misnomer) also originate

from Schwann cells or perineural cells. These neoplasms have greater cellularity, marked anaplasia, an increased mitotic rate and may metastasize. Malignant schwannomas have been reported to occur in Canada Geese, but histologic studies have failed to demonstrate a neural origin.^{82,127} Therefore, those neoplasms should be classified as fibrosarcomas instead of malignant schwannomas.

- **Lymphoid Neoplasia (Lymphosarcoma):** Marek's disease in chickens is often associated with leg paralysis secondary to ischiatic nerve infiltration by neoplastic lymphocytes. Affected nerves appear thickened. Microscopically, the lymphoid infiltrates may vary from small lymphocytes and plasma cells to lymphoblasts.²⁰ The former infiltrates appear inflammatory, while the latter infiltrates clearly are neoplastic.

Ocular Neoplasms

The following discussion is concerned with primary and metastatic intraocular neoplasms of birds. Neoplasms involving the eyelids, conjunctiva and orbit are discussed under appropriate organ systems and will not be considered here (Figure 25.17).

Intraocular neoplasms in birds may be associated with blindness, hyphema or aqueous flare. Some neoplasms, such as malignant lymphoma, may be visualized occasionally by ophthalmoscopy. Because the avian eye is reinforced by scleral ossicles, buphthalmos is not expected. In contrast, exophthalmos occurs with some frequency and usually indicates a retrobulbar space-occupying lesion or extension of malignant ocular neoplasia into the retrobulbar area. In birds, exophthalmos has been associated with various retrobulbar neoplasms including malignant lymphoma, pituitary adenoma and adenocarcinoma, malignant intraocular medulloepithelioma, intraocular rhabdomyosarcoma, undifferentiated carcinoma, teratoma, and glioma.^{15,23,48,51,100,105,121,122}

- **Lymphosarcoma:** Lymphosarcoma (malignant lymphoma) involving the iris, ciliary body and choroid is observed most frequently in chickens with Marek's disease.⁴⁸ When visualized, these neoplasms may appear as yellow-to-white proliferative masses. Most occurrences of ocular lymphoid neoplasia represent metastatic lesions.
- **Rhabdomyosarcoma:** Intraocular rhabdomyosarcomas have been reported in two chickens.⁴⁸ These neoplasms may have arisen from the ciliary muscles, which are striated in birds. One neoplasm extended



FIG 25.17 A mature African Grey Parrot was presented with a space-occupying mass involving the right periorbital area and globe. The mass was surgically removed in conjunction with enucleation. The mass reappeared two years later and the bird was euthanatized.

into the retrobulbar space. The other neoplasm replaced the iris, ciliary body and choroid.

- **Malignant Medulloepithelioma:** Intraocular medulloepitheliomas are primitive neoplasms that originate from the optic cup epithelium⁸⁸ and have been described in two cockatiels.¹²² The neoplasms were composed of tall columnar neuroepithelial cells with well defined limiting membranes. These cells were arranged in nests, sheets and rosettes. Foci of necrosis also were observed. Neoplastic cells extended into the retrobulbar spaces, infiltrating the optic nerve and adjacent skeletal muscle.
- **Malignant Melanoma:** Metastatic ocular malignant melanoma has been reported in a Pintail Duck in association with multiple neoplasms involving adrenal gland, skin, liver, skeletal muscle, heart, lung, kidney, brain and bone.⁷²



Hemolymphatic System

The hemolymphatic system encompasses those tissues and organs that are involved in leukocyte, erythrocyte and thrombocyte production. The bone marrow produces thrombocytes, erythrocytes and most of

the leukocytes with the exception of lymphocytes. Lymphocyte production occurs within lymphoid tissues, which can be divided into primary and secondary lymphoid tissues. The thymus and bursa of Fabricius are the primary lymphoid tissues. The secondary lymphoid tissues are more diverse and, depending upon the species of bird, include the spleen; conjunctival, nasal and bronchial-associated lymphoid tissues; cecal tonsils, Peyer's patches, Meckel's diverticulum and other gut-associated lymphoid tissues; lymph nodes and lymphoid aggregates distributed throughout the body.¹⁰⁹ The majority of the lymphocytes are produced in the secondary lymphoid tissues.

Clinical signs related to hemolymphatic neoplasia are variable and vague including lethargy, anorexia, weight loss, lameness, swellings, dyspnea, loose droppings and petechial-to-ecchymotic hemorrhages. Death often occurs from organ dysfunction secondary to infiltrative disease.

Lymphoid Neoplasia

Lymphoid neoplasia is the most common form of hemolymphatic neoplasia occurring in domestic, captive, and free-ranging birds.^{9,20,49,70,72,97,108,146} This form of neoplasia may originate from the peripheral lymphoid tissues as lymphosarcoma (malignant lymphoma) or in the bone marrow as leukemia.

Lymphoid neoplasia of poultry has been studied extensively. In chickens, lymphoid neoplasms may be induced by herpesvirus or retrovirus infections. Herpesvirus infection causes Marek's disease. In this disease, early lymphoid infiltrates may appear inflammatory and consist of a mixture of small lymphocytes, plasma cells and lymphoblasts. Following neoplastic transformation, lymphoid neoplasms appear more progressive and are composed of lymphoblasts. In contrast, lymphoid leukosis is caused by retroviral-induced neoplastic transformation of B-lymphocytes. The presentations of Marek's disease and lymphoid leukosis may differ considerably.²⁰

Lymphoid neoplasia of free-ranging and captive birds has not been studied in detail. A recent pathologic survey subclassified avian lymphoid neoplasia as plasmacytoma or fibrifying, lymphoblastic, lymphocytic or mixed-cell lymphosarcoma.¹⁰⁸ However, the prognostic importance of these subclassifications has not been demonstrated and requires further clinicopathologic study.

Currently, there is no effective treatment for avian lymphoid neoplasia. Radiation therapy may be pal-

liative.¹⁰⁰ Combination chemotherapy with vincristine sulfate, prednisone and chlorambucil appears promising but requires more clinical research.⁹³

- **Lymphosarcoma:** Lymphosarcoma (malignant lymphoma) is defined as any lymphoid neoplasm that originates in the peripheral lymphoid tissues. This form of lymphoid neoplasia is commonly observed in birds and is characterized by the formation of white-to-yellow tissue discolorations or sarcomatous masses.

Lymphosarcoma usually presents as a disseminated multisystemic disease that can involve all tissues of the body, including bone marrow.^{9,20,97,108,146} The abdominal viscera often are involved (visceral leukosis), especially the liver, spleen and kidney (Color 25.3). Occasionally, lymphosarcoma may show tissue tropism with multiple neoplasms being observed in one tissue such as skin.⁹ The rarest presentation of lymphosarcoma is the presence of a single, localized neoplasm. This presentation was documented as a single neoplasm at the optic chiasm of a cockatiel.⁹

A presumptive diagnosis of neoplasia may be apparent after physical examination by observing swellings of the skin or retrobulbar masses.^{9,100,105} Abdominal enlargement and hepatomegaly also may be present. In addition, soft tissue masses, hepatomegaly or osteolysis may be detected or confirmed radiographically.^{100,105} A complete blood count may be beneficial in diagnosing lymphoid neoplasia by detecting lymphocytosis and demonstrating variable numbers of immature (neoplastic) lymphocytes in the blood film.⁹ The latter finding is termed a "leukemic blood picture" and indicates hematogenous dissemination of the neoplasm.

- **Lymphoid Leukemia:** Lymphoid leukemia originates in the bone marrow and disseminates to various body tissues. This presentation of lymphoid neoplasia is rare compared to lymphosarcoma.⁹³ Birds with lymphocytic leukemia may have anemia, thrombocytopenia and marked lymphocytosis. Lymphocytes in blood smears may be well differentiated or blastic. Bone marrow aspirates contain innumerable lymphocytes. Sarcomatous masses are not observed in tissues at necropsy; however, hepatosplenomegaly may be prominent. Infiltration of various tissues by neoplastic lymphocytes is observed microscopically.
- **Thymoma:** Thymoma is a localized form of lymphoid neoplasia that is confined to one or more thymic lobes. Histologically, thymomas may present as lymphocytic or epithelial masses.

Thymoma has been observed in two budgerigars.^{15,152} Only one neoplasm has been described in detail and presented as a palpable mass on the right side of the base of the neck.¹⁵² Histologically, the neoplasm was an epithelial-type thymoma, consisting of aggregates of small lymphocytes and epithelial cells encased in a dense fibrous stroma. The epithelial cells had a “clear cell” morphology.

Nonlymphoid Neoplasia

Nonlymphoid hematologic neoplasia is observed most frequently in chickens infected with certain strains of leukosis (sarcoma) retroviruses.¹⁰¹ Some strains of virus are associated with the development of granulocytic leukemia (myelocytomatosis) or erythremic myelosis (erythroblastosis).

- **Granulocytic Leukemia:** Granulocytic leukemia is the unregulated proliferation of granulocytes. In chickens, this disease (myeloblastosis) is caused by retrovirus infection; the etiology in captive and free-ranging birds has not been identified.¹⁰¹

Granulocytic leukemia in birds is sometimes associated with the formation of sarcomatous masses called myelocytomas. These lesions are analogous to chloromas in mammals. More commonly, tissue infiltration by neoplastic granulocytes results in hepatosplenomegaly. Microscopically, the neoplastic cells

appear either blastic (myeloblastosis) or exhibit heterophilic (myelocytic) differentiation.¹⁰⁸ Differentiation is appreciated more readily, however, in blood and bone marrow smears as opposed to histologic sections.

- **Erythremic Myelosis:** Erythremic myelosis is the unregulated production of erythrocyte precursors. This form of leukemia is caused by retrovirus infection in chickens and has been called erythroblastosis.¹⁰¹

An erythremic myelosis-like syndrome has been described in conures.¹¹⁴ Most of these birds appear weak and have a history of spontaneous hemorrhage. Histopathology has documented acute and chronic hemorrhages within various tissues in conjunction with erythrocyte proliferation in the bone marrow, hepatic sinusoids and splenic red pulp.¹¹⁴ Although the evidence occasionally appears supportive of erythremic myelosis, marked extramedullary erythropoiesis cannot be excluded. In comparison to mammalian erythrocytes, avian erythrocytes have a very short life span (20 to 25 days). Following acute and ongoing hemorrhage, intense extramedullary erythropoiesis could occur, especially with concurrent recycling of iron from internal hemorrhage. Therefore, the conure bleeding syndrome will require further hematologic characterization before it can be classified absolutely as erythremic myelosis.

TABLE 25.1 Specific Treatment Concerns of Neoplasms*

Lipomas	Frequently recur following excision
Liposarcomas	Locally invasive and metastatic
Xanthomas	Excise localized masses, amputate limb if deeper tissues involved, irradiation (see text)
Fibrosarcomas	Generally unrewarding, locally invasive, if in extremities amputate ASAP
Hemangioma	Highly vascularized and must be excised with great care
Hemangiosarcomas	Frequently recur after surgical excision, amputate affected limb
Leiomyosarcoma	Must excise before metastasis occurs
Rhabdomyomas	Radical excisions necessary, margins difficult to define
Rhabdomyosarcomas	Radical excision before metastasis, bleed extensively
Chondromas/sarcomas	Difficult to remove without extensive damage to surrounding tissues
Osteosarcomas	Remove affected bone or limb; endoscopy, radiology and biopsy to check for metastasis
Renal adenocarcinomas	Generally considered untreatable, radioisotopes hold some promise
Embryonal nephroma**	Non-reported, difficult to remove because of underlying sacral plexus

*Surgical excision is the treatment of choice for all tumors that are not listed.

**All renal tumors are difficult to excise because of potential damage to sacral plexus.

TABLE 25.2 Cytologic and Histologic Differentiation of Integumentary and Connective Tissue Neoplasms and Masses

Mass	Cytology	Histopathology
Lipoma	Abundant free lipid, some intact adipocytes	See text
Myelolipoma	Hematopoietic precursors, differentiated hematopoietic cells, free lipid and intact adipocytes	Hematopoiesis (particularly heterophils) mixed with mature adipose tissue
Liposarcoma	Free lipid, scattered polyhedral cells with cytoplasmic vacuoles similar to xanthomas	See text
Xanthoma	Vacuolated macrophages, multinucleated giant cells, lipids, cholesterol clefts (appear as parallelograms with notched corners), rarely fibroblasts	Lipid-laden macrophages, multinucleated giant cells, cholesterol clefts, varying fibroplasia ¹⁷
Fibrosarcoma	Pleomorphic spindle cells, multinucleated tumor giant cells, similar to reactive fibroplasia	Pleomorphic to spindle-shaped cells, plump nuclei, eosinophilic fibrillar cytoplasm, cells in bundles, sheets, whorls, mitotic figures may be numerous
Fibromas	Sparsely cellular, similar to fibrosarcomas, reactive fibroplasia	Compressed fibroblasts, dense collagenous stroma cells in sheets, swirls, or interlacing bundles
Myxoma/sarcoma	Viscous aspirate, free nuclei, spindle cells (singular or clusters)	Spindle cells in loose collagen matrix, alcian blue-positive mucinous ground substance, rare mitotic figures
Papilloma	See text	See text
Squamous cell carcinoma	See text	See text
Basal cell tumors	See text	See text
Cutaneous lymphosarcoma	See text	Neoplastic lymphocytes in the dermis or pulp cavity
Mast cell tumors	Round cell population with fine, purple cytoplasmic granules that may obscure nuclear detail (Romanowsky stain)	Uniform population of round cells, central round-to-oval nuclei and abundant eosinophilic cytoplasm, metachromatic granules (Giemsa stain)

Cytology based on fine-needle aspirates unless otherwise noted. The presence of lipid in cells and the background of the smears may be indirectly demonstrated by new methylene blue staining (fat- and aqueous-based stains do not mix). Histopathology is usually necessary to definitively diagnose the type of tumor.

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