

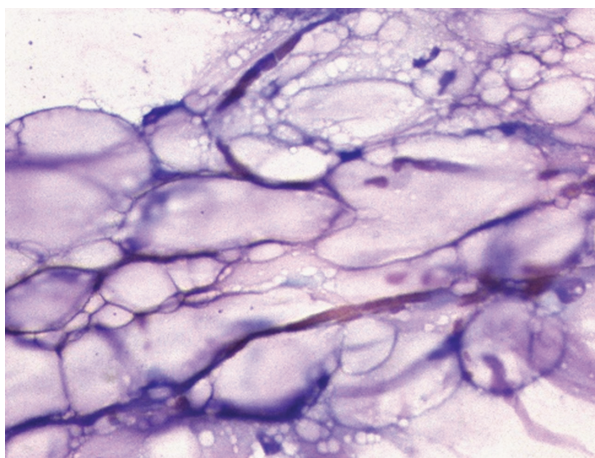
CYTOLOGICAL TUMOR DIAGNOSIS

A brief cytological overview of the most common tumors found in the School of Veterinary Medicine at University College Dublin by Dr. O'Brien and Dr. Balan.

From O'Brien PJ and Balan M. Practical diagnostic cytology for practitioners. *Vet. Focus* 2024;34.2:13-17.

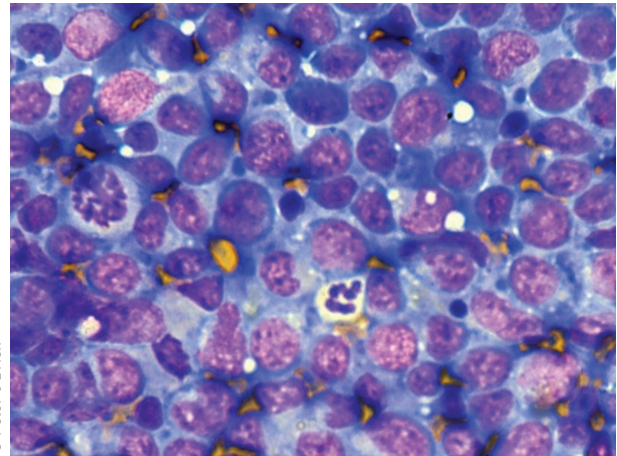
1 Lipoma

Lipoma was the most common benign, cutaneous or subcutaneous mesenchymal tumor, and had the highest overall prevalence of all canine tumors at 23%, but was uncommon in cats. It was twice as common amongst submissions from external practitioners than from the university referral practice. Macroscopically, slides had glistening, non-drying, poorly staining streaks and droplets of oily material on their surface, corresponding microscopically to variably sized lipid droplets. Commonly, there was low cellularity. Adipocytes were found in clumps or occur singly; these are large, three-dimensional cells with a peripherally displaced, oval-to-flattened, small to medium-sized, mostly single nuclei and abundant, non-staining cytoplasm, usually occupied by a single, large lipid droplet and delimited by a thin, dark membrane. The N/C (nucleus:cytoplasm) ratio was low (~1: 50-100) and cell clusters were often accompanied by fibrovascular stromal tissue with long, winding capillaries which had flattened, oval nuclei and trapped, elongated red blood cells (RBCs).



© Peter O'Brien

(~ 700x)

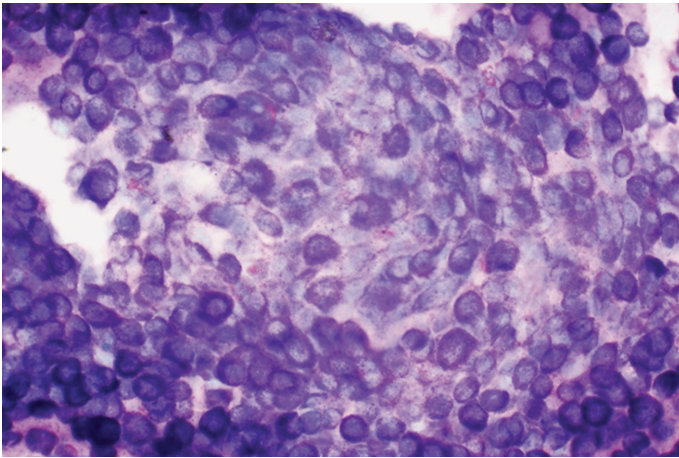


© Peter O'Brien

(~1100x)

2 Lymphoma

Lymphoma was the most prevalent tumor diagnosed in cats (52%) and the second most common tumor in dogs (18%). For both species, age varied from 2-16 years. Large-to-giant dog breeds were much more commonly affected than toy or small breeds. The most common clinical presentation in dogs was generalized lymph node enlargement and weight loss. Smears usually had a high cellularity and acceptable preservation of cells, however smudged cells (basket cells), and frequent variably sized, but smaller than a RBC, round, blue, extracellular cytoplasmic fragments (lymphoglandular bodies) were common. Typically, most lymphocytes had a diameter > 1.5 RBCs in dogs and > 2 RBCs in cats (larger than a neutrophil or 11 µm). Typically, tumoral lymphocytes tend to be found concentrated in small, multiple areas, rather than spread uniformly on the whole slide, except for obvious advanced cases. They had round, occasionally indented, rarely convoluted nuclei, with a lesser condensed chromatin pattern, lower N/C ratio, variably prominent, multiple nucleoli, and occasional cytoplasmic vacuolation. The cytoplasmic area was slightly-to-moderately increased, and staining intensity varied from pale-blue to dark basophilic, with a frequent 2-toned appearance – a lighter perinuclear area and a darker outer ring of the cytoplasm. So-called small-cell lymphomas were uncommon (< 5% of all lymphomas); these had increased numbers of small-to-medium-sized lymphocytes with small, unipolar cytoplasmic extensions (uropods) that resulted in an elongation of the cells giving the appearance reminiscent of a hand-mirror.



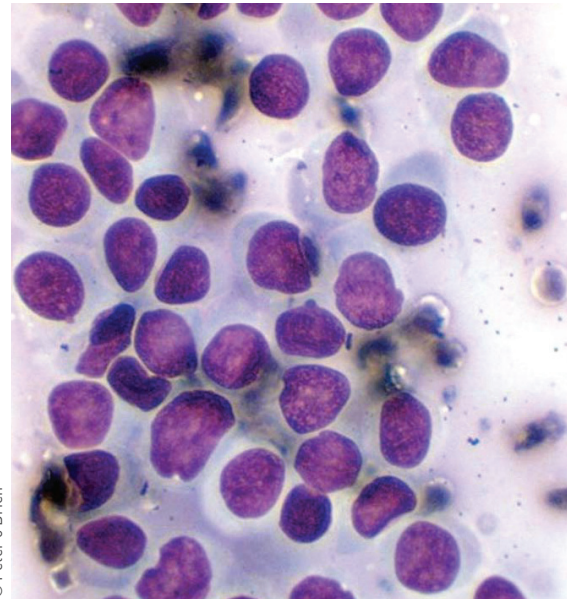
[-900x]

3 Mast cell tumor (MCT)

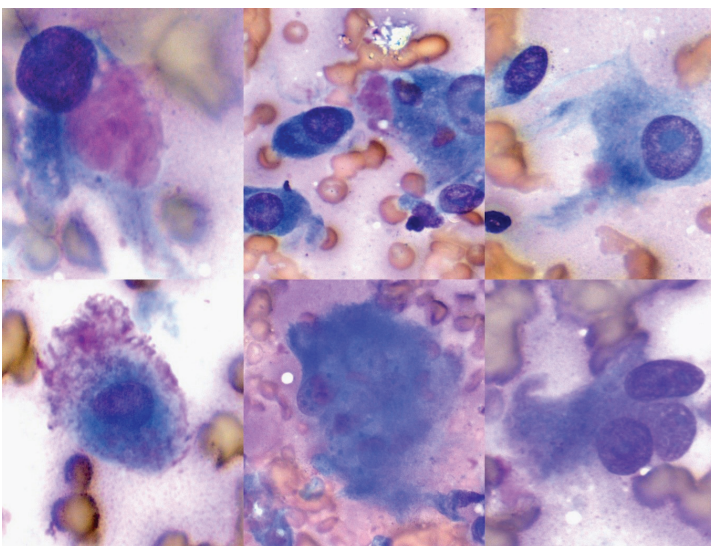
Mast cell tumor was the fifth most common tumor in dogs (8%, compared to 4% in cats). In most cases affected dogs were older than three years, with the trunk and legs commonly affected. Aspirates typically had high cellularity, with abundant dark-purple, uniform, small granules covering much of the typically clear background. Cells were medium-sized, round-oval with a central or paracentral nucleus and rarely eccentric with a plasmacytoid appearance; in these tumors the nucleus will frequently be pale-blue, poorly stained as an artefact in well-granulated cells. Cytoplasm was weakly eosinophilic and variably occupied by granules, with most of the tumors being well-granulated. Poorly differentiated MCT were uncommon; when found, evaluation of malignancy was done using the general criteria and evaluation of the granularity. Commonly accompanying these tumors were infiltrates of different severities (slight-to-marked) of: a) eosinophils; b) large, plump, spindloid cells with large, oval nucleus, prominent, small, round nucleoli and moderate amounts of blue, wispy cytoplasm, with occasional mild, fine, clear vacuolation, consistent with fibroblastic benign proliferation; c) bright-pink, homogenous fibers of different length and thickness, consistent with collagen as a result of collagenolysis. Mitoses were uncommon.

4 Histiocytoma

Histiocytoma is an almost-exclusively canine tumor, and had a prevalence of 2.4%, with reported sites being the nose/muzzle area, chest/axillary region and the forelimbs. Cells were monomorphic, singly occurring, round-to-oval, and medium-sized with round, central or rarely eccentric nuclei (~1.5-2 RBCs in diameter or over 11 µm), with a bland, homogeneous chromatin pattern and indistinct nucleoli. Light grey-blue cytoplasm was found in moderate amounts, with distinct borders and no significant vacuolation or granulation. N/C ratio was ~1:1-2. There were occasional mitotic figures. Infiltrates of small, well-differentiated plasma cells and lymphocytes admixed with the neoplastic cells were common as a result of tumoral regression.



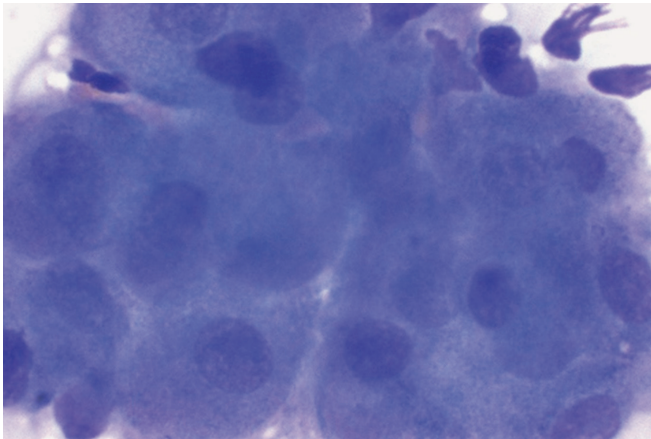
[-1100x]



[-700 to 900x]

5 Osteosarcoma

Osteosarcoma had a prevalence of ~2% of all tumors; this was the second most common malignant mesenchymal tumor, predominantly diagnosed in lytic bone lesions of the forelimbs (the humerus and radius). It was predominantly observed in middle-aged dogs, 4-8 years of age. A characteristic, extracellular eosinophilic osteoid matrix was commonly found in variable amounts and admixed with the neoplastic cells. The predominant cell type was the osteoblast: these had large, oval, eccentric nuclei (~2 RBCs in diameter) with unipolar/bipolar extensions of moderately blue, occasionally hyperchromatic cytoplasm with poorly defined borders and infrequently observed small, round, pink cytoplasmic granules. Osteoclasts had multiple, monomorphic nuclei and abundant, blue cytoplasm.



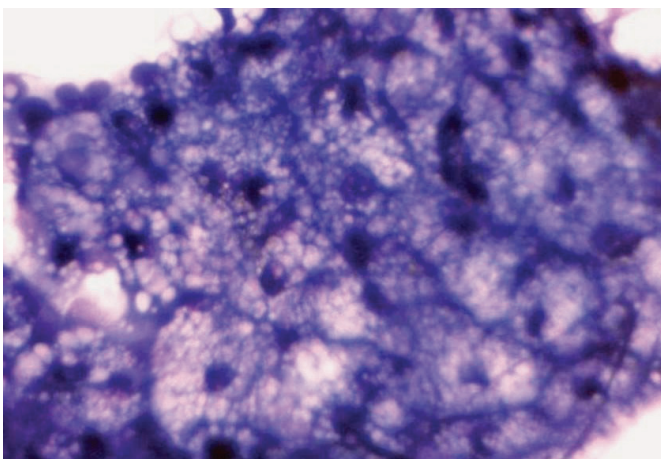
[~ 3700x]

6 Perianal gland adenoma

Perianal gland adenoma was found in 1.5% of all tumors. Cytology samples were highly cellular, with occasionally 3-dimensional clusters of large, round-to-polygonal epithelial cells with distinct borders, resembling hepatocytes. Nuclei were round-to-oval with small, conspicuous nucleoli (up to three) and abundant, finely granular, basophilic cytoplasm. There was up to 2-fold anisokaryosis and no atypical features. At the periphery of clusters were small numbers of small, cuboidal cells, with oval, dense nuclei, consistent with basal epithelium ("reserve cells").

8 Sebaceous gland adenoma

Sebaceous gland adenoma had a prevalence of < 1% and was diagnosed in dogs only. Aspirates had large, well-organized 3-dimensional clusters of round-to-polygonal cells. Cytoplasm was abundant, moderately basophilic and highly vacuolated with heterogeneous, small, clear vacuoles, occupying entirely the cytoplasmic area and often pushing the round nuclei peripherally. N/C ratio was low, with ~6x more cytoplasmic than nuclear area and with distinct cell borders. Occasionally, small numbers of epithelial reserve cells were seen.

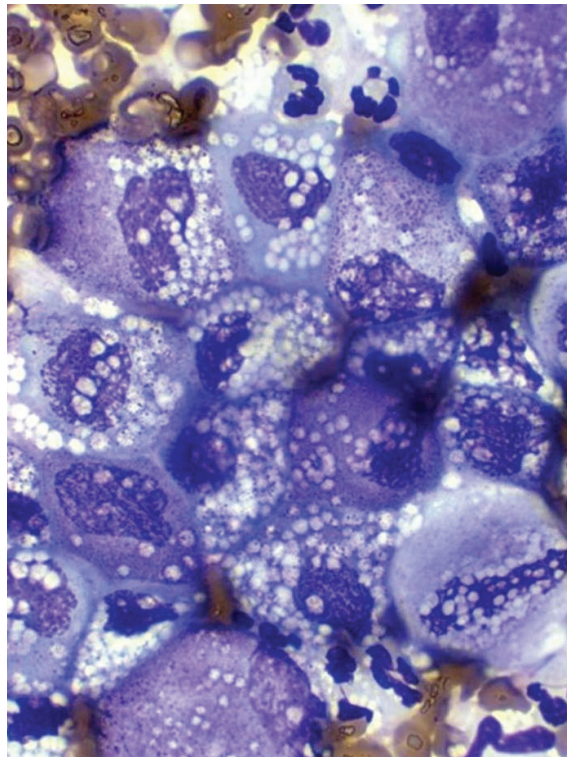


[~ 1100x]

7 Squamous cell carcinoma

Squamous cell carcinoma was found twice as commonly in dogs than in cats, with an overall prevalence of ~1%. It was frequently diagnosed from mandibular (rarely maxillary) masses. Aspirates were moderately cellular and almost always accompanied by marked, mostly non-septic, neutrophilic inflammation and abundant, superficial, blue, keratinized debris. Cells occurred singly or in sheets with round-to-polyhedral shape, round-to-oval nuclei (1-3 RBCs in diameter), and usually prominent, large nucleoli. Cytoplasm was typically sky-blue, with variation from light-to-deep blue, the latter consistent with keratinization. The nuclei were non-pyknotic despite keratinization, thus nuclear-cytoplasmic asynchrony was commonly observed. Perinuclear vacuolation with discrete, tiny-to-small, cytoplasmic vacuoles, typically around the nucleus, was a constant feature. Criteria of malignancy included frequent binucleation and multinucleation (up to 6 nuclei), prominent cell pleomorphism, marked variation in N/C ratio (1:1 to 1:25), frequent, large nucleoli (2/3 and up to one RBC in size) and with elongated-to-angular shapes, frequent micronuclei and rare mitotic figures.

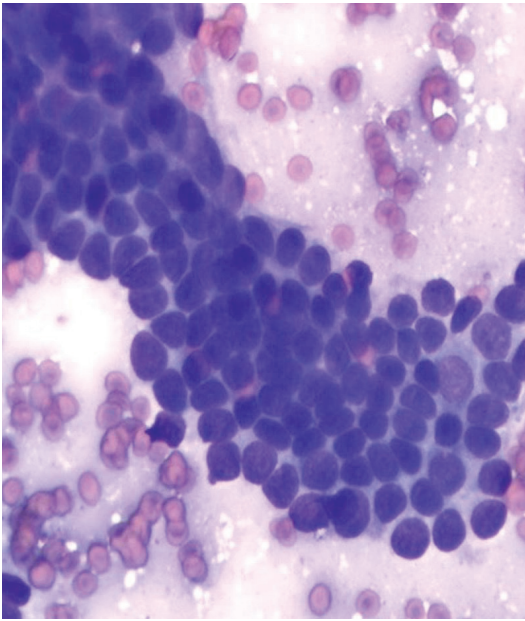
Occasionally, neutrophils were observed passing through the epithelial cells (a process called emperipolesis) and tadpole cells were seen rarely.



[~ 1100x]

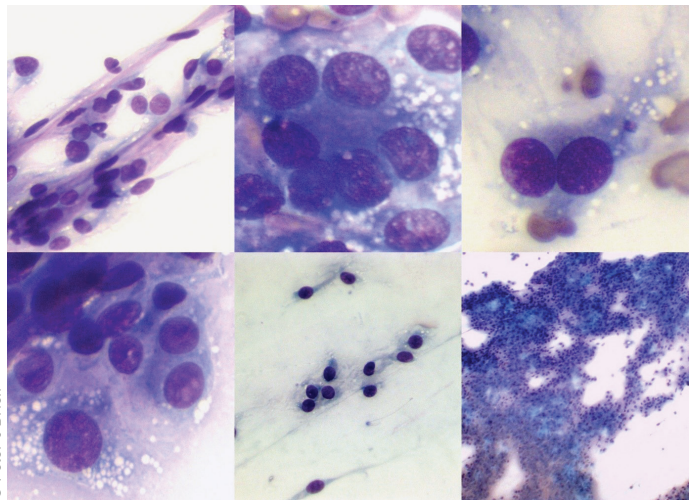
9 Basal cell tumor

Basal cell tumor was found in around 1% of canine tumor samples (mostly on the limbs) from dogs, but was rare in cats. Cells were arranged in small-to-large, cohesive sheets of regular epithelial cells, with 80-90% of the area comprised of round-to-oval, uniform nuclei (~1-1.5 RBCs in diameter) with finely stippled chromatin and indistinct nucleoli. There was scant basophilic cytoplasm with indistinct cell borders, typical nuclear molding and mild anisokaryosis.



© Peter O'Brien

(~ 900x)



© Peter O'Brien

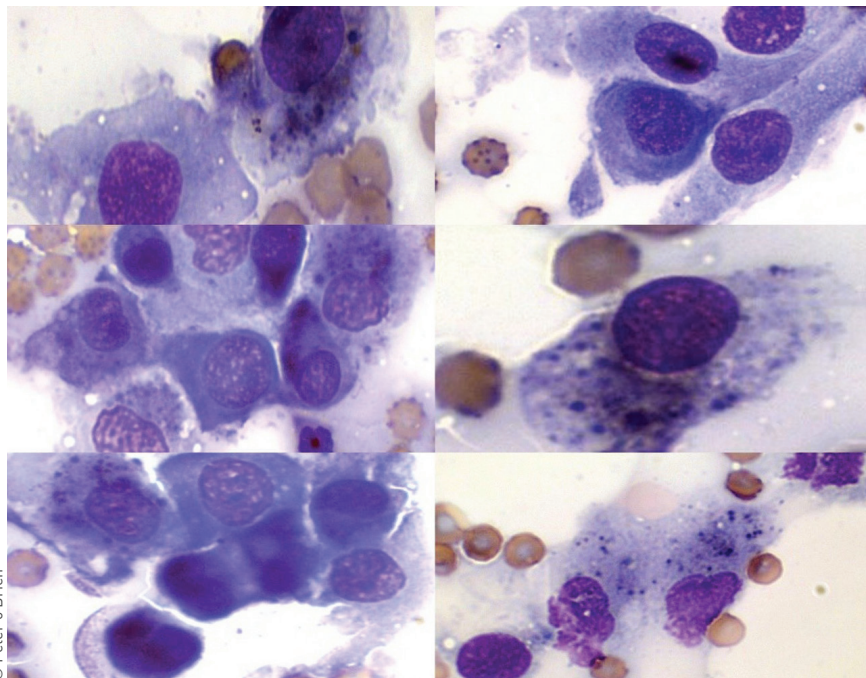
(~ 1200x for 3 largest; 100x for smallest, ~600 for others)

10 Hemangiopericytoma

Hemangiopericytoma was almost exclusively seen in dogs > 8 years, and predominantly from external practices. This tumor was typically found over joints, especially the carpus. Cytologically it is a tumor at the border between benign and malignancy, although only ~1% metastasize in dogs. Cellularity was high, with singly occurring cells and large, densely packed, cohesive clusters, occasionally associated with a pink matrix, frequently with long capillaries. Cells were plump-spindloid, with wispy, veil-like, light-blue cytoplasm and occasional sparse fine vacuolation. Binucleation, in the form of "insect-eye" cells (two opposing nuclei bulging the cytoplasm), and multinucleation (observed as "crown cells", with peripheralized, concentric placement of three or more nuclei), were consistent findings. Frequently micronuclei and occasional large nucleoli were seen.

11 Melanoma

Melanoma was most frequently diagnosed in older dogs, on and around the face and oral cavity, with a prevalence of < 1%. Melanocytes were observed most commonly as mesenchymal, spindloid cells, although they also presented as discrete solitary cells or having an epithelial morphology; however, they usually had no well-defined cellular limits. Cells occurred singly or were arranged in small clusters. They had medium-sized nuclei (~2 RBCs diameter or ~14 µm) and small to medium-sized nucleoli with moderate amounts of light-blue, occasionally wispy cytoplasm. In well-differentiated tumors, small, dark-green to black melanin granules were found in small numbers, or abundantly, covering both nuclear and cytoplasmic areas and obscuring cellular detail. Granules were also frequently observed extracellularly from ruptured cells. There was typically up to two-fold variation in the size of cells, and the malignant potential was assessed based on nuclear and nucleolar size, variation and atypia.

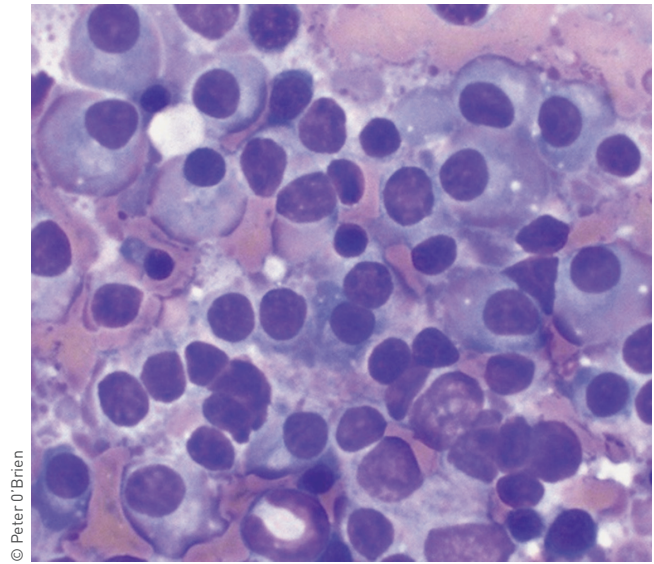


© Peter O'Brien

(~ 220x for largest, ~110 for rest)

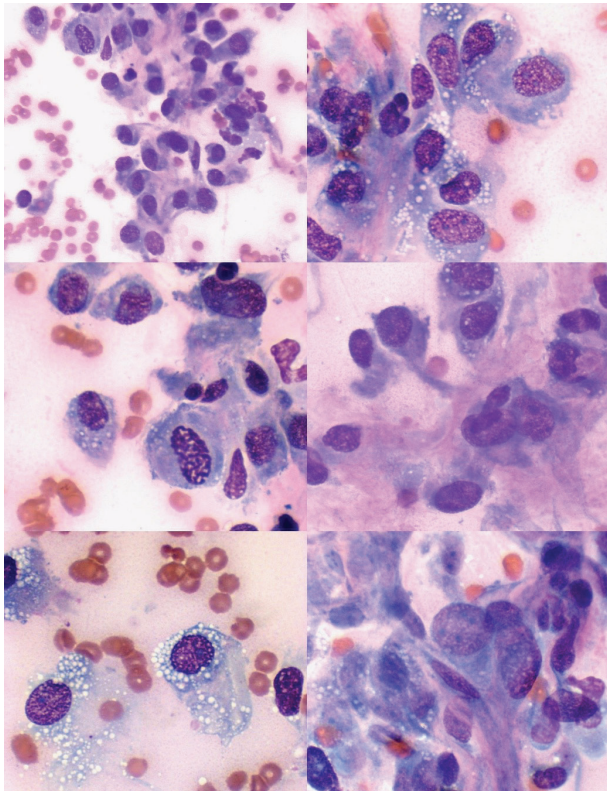
12 Plasma cell tumor/multiple myeloma

Extramedullary, non-cutaneous **plasma cell tumors** were diagnosed primarily from sinus, nose and nasopharyngeal masses in dogs. There were two canine and one feline reports of lymph node metastasis. Cells were oval, with eccentrically placed nuclei, coarsely stippled or clumped chromatin and indistinct nucleoli. Cytoplasm was moderate, basophilic, with distinct borders and characterized by a perinuclear, lightly stained Golgi zone. Observed in both reactive and neoplastic conditions, two variants of plasma cells were identified by their specific morphology: the Mott cell and the flame cell. Mott cells had prominent, round, pale-blue vacuoles (Russell bodies) covering usually the entire cytoplasmic area, while the flame cells were more darkly stained and larger than plasma cells and had a purple-pink, characteristic cytoplasmic rim. Atypical features included pleomorphism, bi- and tri-nucleation, marked (2-3 fold) anisocytosis and anisokaryosis with prominent anisonucleoliosis, increased N/C ratios and abnormal mitoses.



© Peter O'Brien

(~ 1400x)



© Peter O'Brien

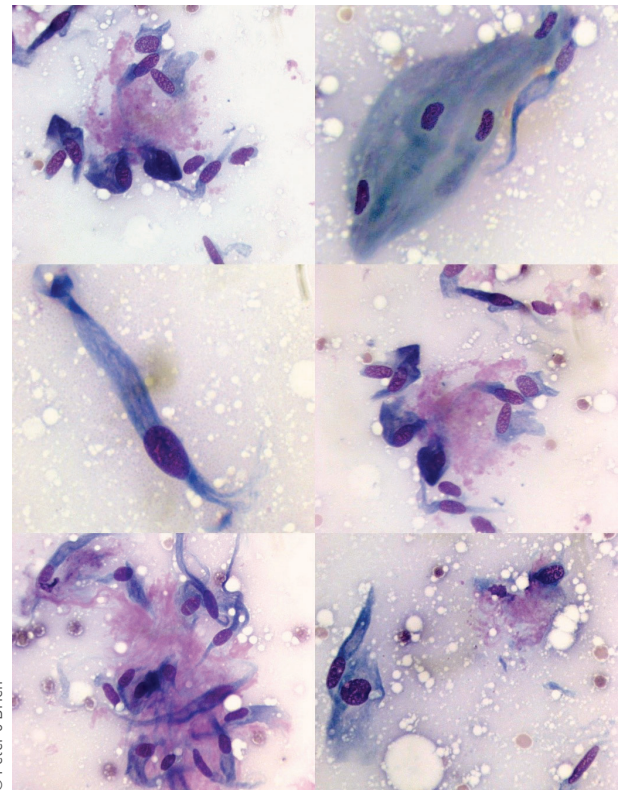
(~ 700x)

13 Fibrosarcoma

Fibrosarcoma accounted for 0.4% of all tumors. Cells were large and spindle-shaped, with bipolar extensions of the cytoplasm and occasionally intracytoplasmic, pink, tiny granules. Nuclei were oval, with moderate-to-marked anisokaryosis and had multiple prominent, occasionally bizarre, nucleoli.

14 Fibroma

Fibroma was rarely seen (0.3%), characterized by a poorly exfoliative population of spindle cells with oval, elongated nuclei, typically 2-10x longer than wide. Cytoplasm was found in moderate amounts, blue and with unipolar extensions. There was up to 2-fold anisokaryosis and moderate pleomorphism, with cells displaying round nuclei or highly elongated ones. The background usually displayed variable amounts of eosinophilic, proteinaceous material, consistent with collagen.



© Peter O'Brien

(~350x (top middle photo ~700x))