

Feline UPDATE

The Feline Centre

Pfizer Animal Health

Spring 2011



The Feline Centre Langford and Pfizer Animal Health working together for the benefit of cats

Cytology: Common Feline Tumours

by *Kostas Papasouliotis DVM PhD DipRCPATH DipECVCP MRCVS.*

In this Feline Update, focus is on **Oncology**, both on the clinical and microscopic levels.

Articles Include:

- Cytology: Common Feline Tumours
- Treatment of Lymphoma
- What's your Diagnosis?
- The Fine Needle Aspirate
- The Problem with Polyps

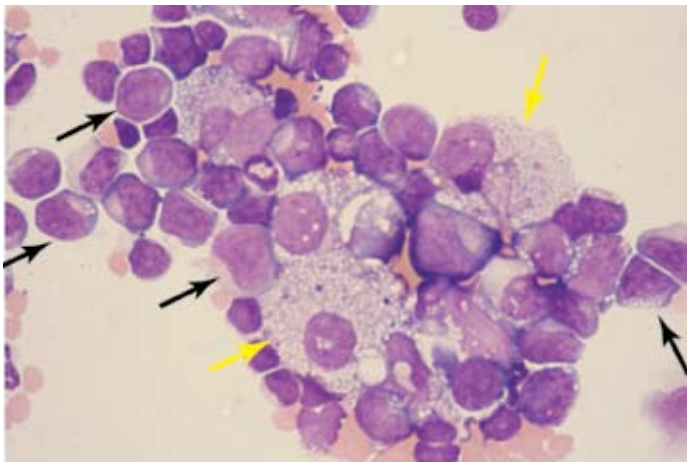


Figure 1a: Mediastinal lymphoma (pleural effusion).

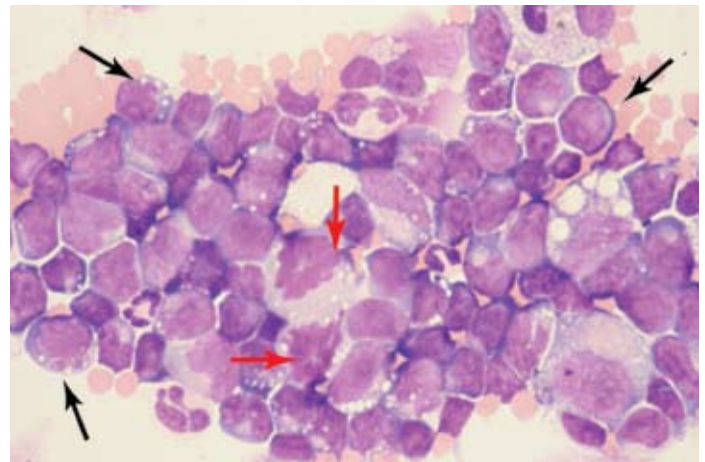


Figure 1b: Mediastinal lymphoma (pleural effusion).

Making sense of a fine needle aspirate in practice can be a daunting task.

In this issue of Feline Update, Kostas Papasouliotis, Head of the Langford Diagnostic Laboratory, provides an overview and "cheat sheet" for identifying common tumours of the cat.

Cancer is a common disease in cats. The overall incidence increases with age with a peak at approximately 10 to 12 years. Lymphoid tissue (lymphoma being the most common neoplasia) and skin are the most commonly affected sites. Skin tumours are more likely to be malignant than benign with fibrosarcoma (malignant mesenchymal tumour) and squamous cell carcinoma (malignant epithelial tumour) being the ones most frequently seen.

A subgroup of fibrosarcoma which is often referred to as "injection site sarcoma" is often seen within the intrascapular area and is considered more aggressive than other sarcomas. In young cats up to 1 year old, the most common neoplasms are lymphoma, sarcoma, mast cell tumour and squamous cell carcinoma. In young cats, the most commonly diagnosed benign skin neoplasm is lipoma.

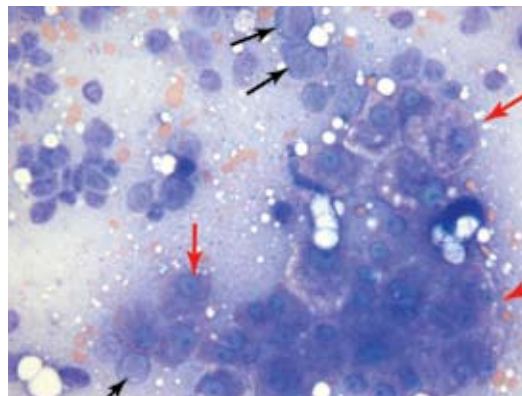


Figure 2a: Hepatic lymphoma (Liver aspirate) A.

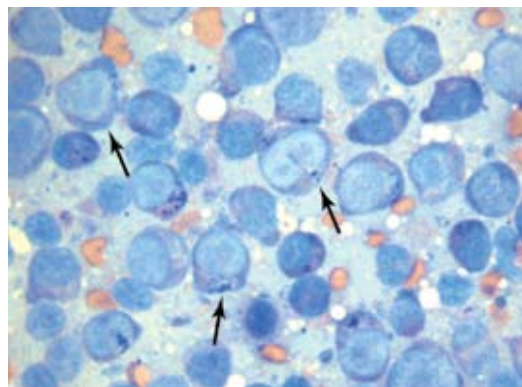


Figure 2b: Hepatic lymphoma (Liver aspirate)

Cytological examination of body cavity fluids and fine needle aspirates from masses can be very useful in the diagnosis of cancer. This article is a pictorial review of common tumour types that might arise in the feline patient.

Lymphoma (Figs. 1a & 1b): Pleural effusion from a 2 y.o. male DSH with pyrexia and dyspnoea. Presence of large lymphoid cells (≥ 3 red blood cells in diameter), with indented nucleus, prominent nucleolus and basophilic microvacuolated cytoplasm (*black arrows*). Notice the macrophages (*yellow arrows*) and the lymphoid mitotic figures (*red arrows*).

Lymphoma (Figs. 2a & 2b): Aspirates from a 12 y.o DLH, male cat with marked hepatomegaly. Presence of hepatocytes in a clump (*red arrows*). Large lymphoid cells with prominent nucleoli and basophilic microvacuolated cytoplasm are seen in association with the hepatocytes (*Fig 2a*) and in the remaining of the smear (*Fig 2b*).

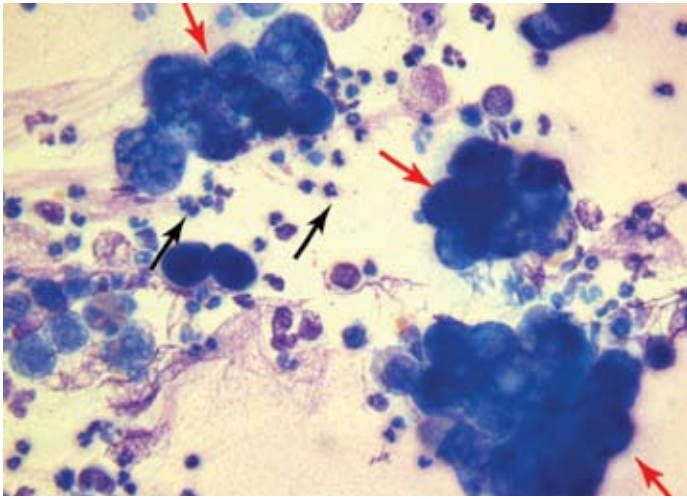


Figure 3a: Lung carcinoma
(pleural effusion; 14 y.o. FN, DSH cat).

Carcinoma (Fig 3a & 3b): Pleural effusions from two dyspnoeic cats. Presence of characteristic cohesive clumps of basophilic epithelial cells (*red arrows*) which are always

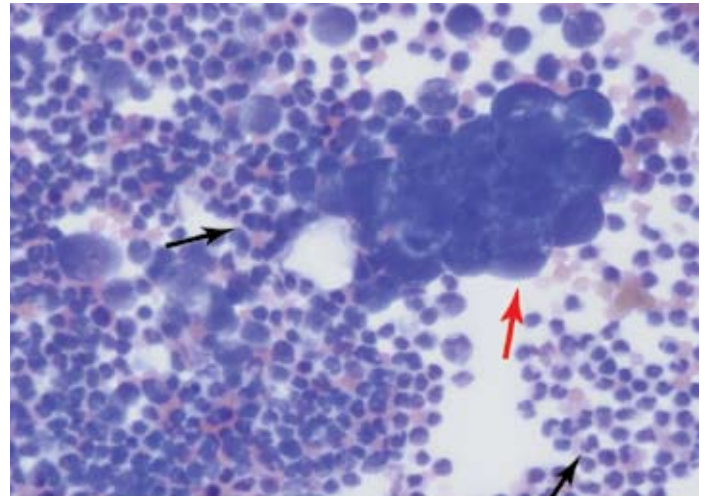


Figure 3b: Lung carcinoma
(Lung, pleural effusion; 13 .y.o. MN, DLH cat).

suspicious for the presence of an intracavitary neoplasia. Notice the neutrophils which are indicating inflammation.

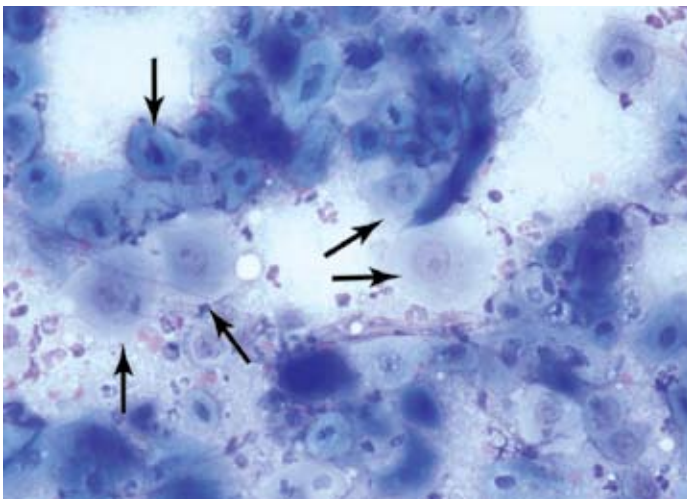


Figure 4: Squamous cell carcinoma (mass on the eyelid).

Squamous cell carcinoma (Fig 4): Aspirate from a 7 y.o. DSH cat. Presence of squamous epithelial cells exhibiting cytological characteristics of malignancy (anisocytosis, anisokaryosis

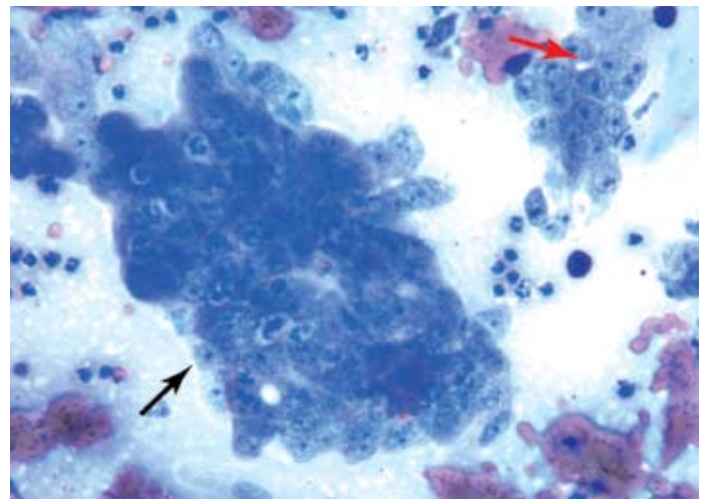


Figure 5a: Squamous cell carcinoma (laryngeal mass).

prominent nucleoli of different sizes and shapes, asynchronous keratinisation). Notice the light green/turquoise non-granular cytoplasm which indicates asynchronous keratinisation.

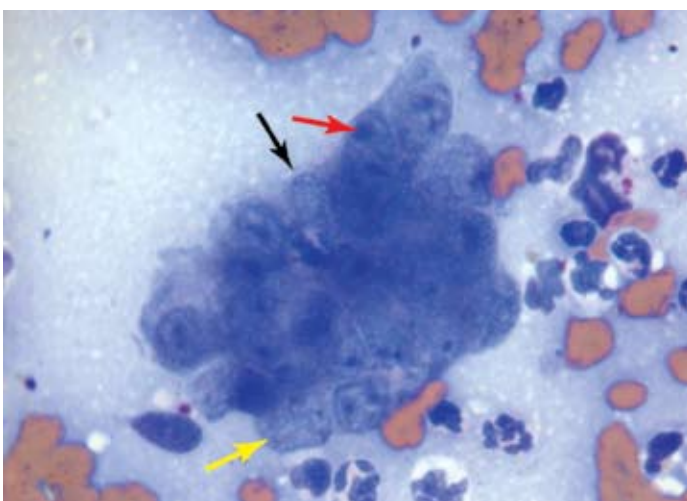


Figure 5b: Squamous cell carcinoma (laryngeal mass).

Squamous cell carcinoma (Fig 5a & 5b): Aspirate from a 11 y.o. MN DSH cat which was presented with dysphagia and dysphonia. Presence of malignant epithelial cells in clumps (*black arrow*). Notice the indistinct nuclear outline with prominent dark nucleoli of different shapes (*red arrow*) and asynchronous keratinisation. In these cells, the keratinisation is reflected by a diffuse, non-coloured microvacuolation/bubbling of the cytoplasm

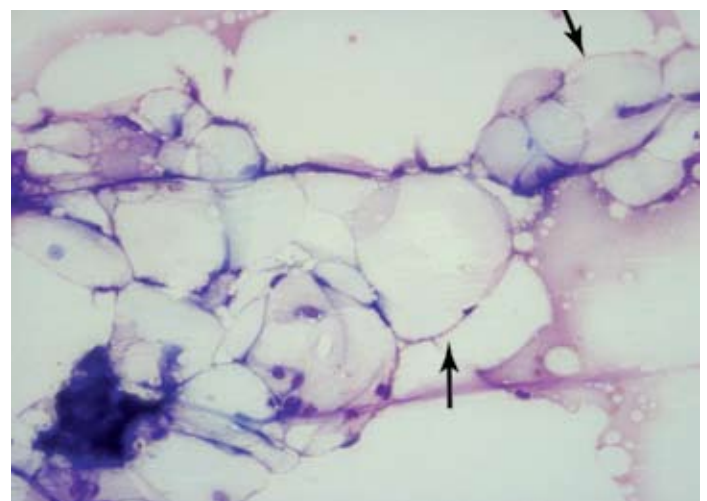


Figure 6: Lipoma (subcutaneous mass on the left side of the chest wall).

(*yellow arrow*). Also notice the presence of neutrophils (*Fig 9*) indicative of inflammation due to the presence of invading neoplastic cells and released keratin.

Lipoma (Fig 6): Aspirate from a 9 y.o. MN DSH cat. Presence of morphologically normal adipocytes (small round eccentric nucleus and clear, ballooned cytoplasm).

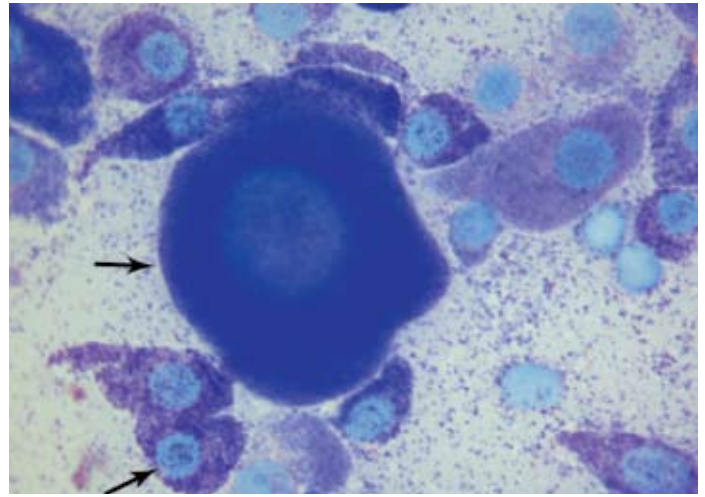
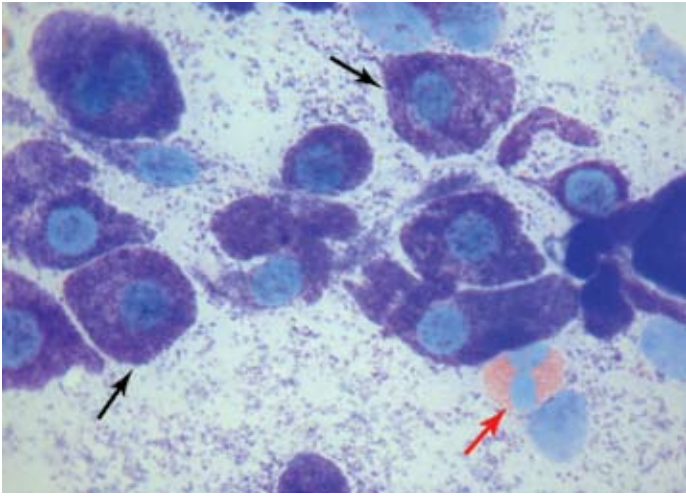


Figure 11: Mast cell tumour (skin mass on the right hind leg).
Mast cell tumour (Fig 11 & 12): Aspirate from a 10y.o. MN, Maine Coon cat. Numerous mast cells of different shapes and sizes, with distinct pale blue nucleus and cytoplasm exhibiting

Figure 12 : Mast cell tumour (skin mass on the right hind leg).
 different degrees of granulation. Notice the numerous free purple granules in the background and the eosinophil (red arrow).

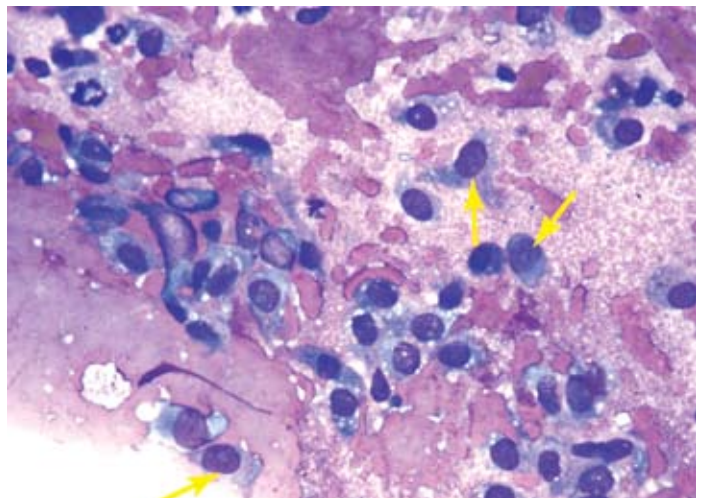
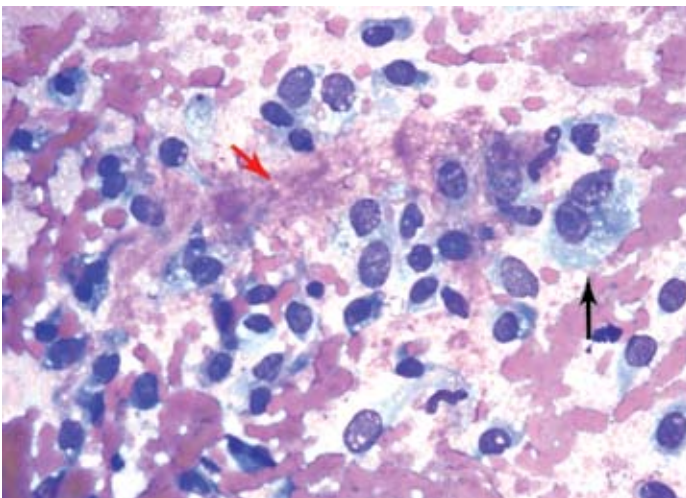


Figure 7a: Osteosarcoma (hard swelling on the caudal aspect of the left hind leg).

Figure 7b: Osteosarcoma (hard swelling on the caudal aspect of the left hind leg).

Osteosarcoma (Fig 7a & 7b): Aspirate from a 10y.o. MN DSH cat. Presence of pleomorphic spindle/oval/plump malignant cells exhibiting marked anisocytosis, anisokaryosis, bi-nucleation (black arrow), prominent nucleolus (yellow arrow) and basophilic (blue) occasionally microvacuolated cytoplasm. Notice the pink matrix of amorphous thick material amongst

the malignant cells and in the background (red arrows). This material is secreted by the cells (e.g. osteoid, collagen, cartilage). In this case the material was osteoid. malignant cells and in the background (red arrows). This material is secreted by the cells (e.g. osteoid, collagen, cartilage). In this case the material was osteoid.

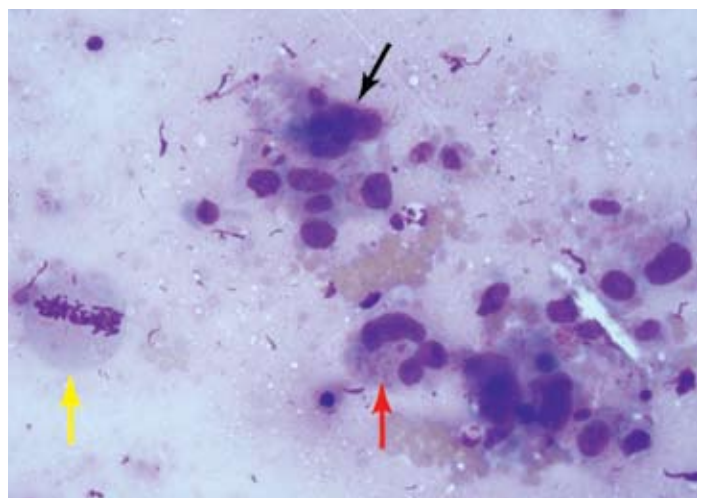
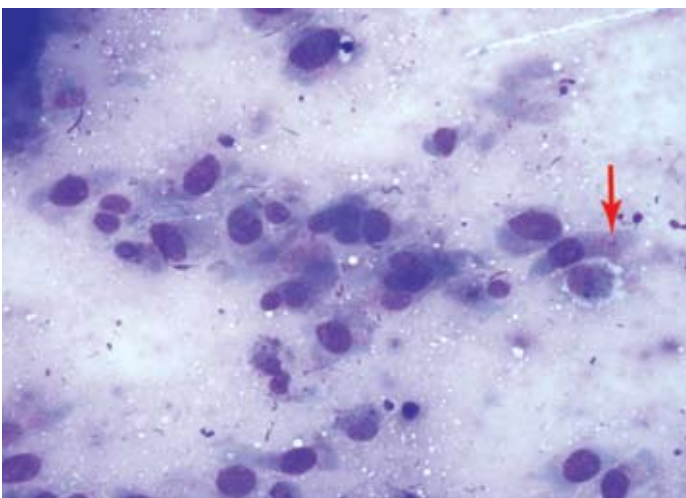


Figure 8a: Fibrosarcoma (firm cutaneous mass between the shoulder blades).

Figure 8b: Fibrosarcoma (firm cutaneous mass between the shoulder blades).

Fibrosarcoma (Fig 8a & 8b): Aspirate from a 19 yo M DSH. Presence of pleomorphic spindle/oval/plump malignant cells exhibiting marked anisocytosis, anisokaryosis, multinucleation

(black arrow) and basophilic cytoplasm which occasionally contains small amounts of amorphous pink material (red arrows). Notice the large cell in mitosis (yellow arrow).



THE TREATMENT OF FELINE LYMPHOMA IN A NUTSHELL

Lara Boland BVSc MACVSc MRCVS.

More and more vets in practice are being asked to treat and provide care for animals with cancer.

In this article, Lara Boland reviews management of the most common neoplasm seen in our feline patients, lymphoma.

Lymphoma continues to dominate feline oncology and comprises approximately one third of all feline neoplasia. It can manifest in a number of forms, which can vary in their prognoses, with survival times ranging from weeks to years with treatment.

What is lymphoma and how is it classified?

Lymphoma is a lymphoid malignancy that arises from solid organs, for example lymph nodes, spleen or liver. It is one of the most common feline malignancies. Treatment of feline lymphoma is a complex topic but the aim of this article is to give a clinically useful summary for veterinarians in general practice.

What classification systems are used for feline lymphoma?

Several anatomic forms of lymphoma are recognised in cats and include:

- **Alimentary:** solitary, multifocal or diffuse gastrointestinal tract infiltration with or without intra-abdominal lymphadenopathy
- **Mediastinal:** mediastinal lymphadenopathy with or without bone marrow involvement
- **Multicentric:** generalised lymphadenopathy with liver, spleen and/or bone marrow involvement
- **Extranodal:** involvement of any organ (e.g. nasopharyngeal, renal, cutaneous etc).

The alimentary and mediastinal forms are more common in cats.

Lymphoma may be further staged as follows:

- Stage I:** Single node or organ involved.
- Stage II:** Single extranodal tumour with regional lymph node involvement on the same side of the diaphragm.
- Stage III:** Two extranodal tumours and/or regional lymph node on opposite sides of the diaphragm.
- Stage IV:** Stage 1, 2 or 3 with spleen and/or liver involvement.
- Stage V:** Stage 1 to 4 with CNS and/or bone marrow involvement.

Substaging involves classification as substage A (absence of clinical signs of illness) or substage B (presence of clinical signs of illness). The value of clinical staging is discussed later.

Diagnosis

Lymphoma can cause a variety of clinical signs in cats dependent on the organs involved and may be challenging to diagnose in some patients. Lymphoma is diagnosed by cytology or histopathology of affected tissues. Histological grading classifies lymphomas based on the degree of anaplasia and other indices of malignancy, as well as immunophenotyping (B or T cell). Various diagnostic investigations may be required to reach a diagnosis depending on the organs involved. Paraneoplastic hypercalcaemia is rare in cats with lymphoma. Hypereosinophilia is occasionally seen as a paraneoplastic feature of disease. Immunophenotyping (classification as B-cell or T-cell) can provide some prognostic information and in some cases is required to reach a diagnosis (e.g. differentiation of severe inflammatory bowel disease from alimentary lymphoma).

Risk factors in cats

There is a bimodal age of presentation of cats with lymphoma. The two peaks occur at approximately two years of age and 10 years of age. Younger cats are more likely to be FeLV positive.

The prevalence of cats with lymphoma that are FeLV positive appears to be decreasing over time with effective vaccination programmes. Both FeLV and FIV infections increase the risk of lymphoma development in cats.

What pre-treatment screening should be performed?

Chemotherapy is the mainstay of lymphoma treatment. Essential pre-treatment screening includes haematology, biochemistry and urinalysis (and urine culture if indicated based on urinalysis findings). FIV/FeLV testing may provide prognostic information. Thoracic radiographs and abdominal ultrasound may be required during initial diagnostic investigations or to further assess possible comorbid disease which may alter treatment choices and prognosis, especially for older cats.

What are prognostic indicators in cats?

There is much debate about prognostic indicators in cats with lymphoma and reported study results vary.

Positive prognostic indicators in cats may include:

- **Initial response to treatment** –this is considered the most important prognostic indicator in cats.
- **Substage.** (i.e. substage A lymphoma cats may show to a longer duration of response to treatment).
- **Lymphoma stage and grade** (i.e. lower stage and grade lymphoma may be more likely to respond to treatment and more likely to have a longer duration of response).
- **Anatomic site** (i.e. cats with mediastinal and multicentric lymphoma may have a longer duration of response to treatment than cats with alimentary or renal forms)
- **Immunophenotype** (i.e. B cell forms may have a longer duration of response to treatment).

Negative prognostic indicators in cats may include:

- **Previous treatment with corticosteroids** may shorten survival times.

- **FelV positive cats** are likely to have shorter survival times.

What survival times can be expected?

Reported survival times vary according to site of disease and chemotherapy protocol. In general terms, remission rates of approximately 70% can be expected with median survival times of 6 to 9 months using multiple agent chemotherapy protocols. Untreated cats have survival times of weeks to 1-2 months.

What treatment options are available?

There are various multi agent chemotherapy protocols reported for treatment of feline lymphoma. Initial treatment involves a more intensive induction phase of 4-8 weeks which is used to induce remission. If complete remission does not occur then the induction phase may need to be continued for a longer period. At the end of the induction phase a less intensive maintenance phase of treatment is commenced.

One of the most commonly used and easily accessible protocols in general practice is the COP protocol (cyclophosphamide, vincristine and prednisolone); a high or low-dose protocol is detailed in the BSAVA formulary. For CNS lymphoma, cytosine may be added for the first two days of treatment (100mg/m² usually given as a divided dose e.g. 50mg/m² BID for 4 doses).

Another less intensive protocol involves the use of chlorambucil and prednisolone. This combination of treatment has been used most commonly for lymphocytic gastrointestinal lymphoma (low grade form), where median survival times of 15-25 months have been reported. Alternatively, the use of prednisolone alone may be a palliative treatment option for weeks to months before relapse occurs. Radiotherapy is another option which can be very effective for certain forms of lymphoma e.g. nasal lymphoma.

Prognosis: When to treat & with what?

Alimentary Lymphoma: As the face of feline lymphoma changed, with the decrease in FelV positive cases, there has been a shift in the types of lymphoma seen in the feline population. Alimentary lymphoma, which has always been a common type of lymphoma, has now become the most common form of feline lymphoma seen in practice. Two different forms of alimentary lymphoma are seen, each carrying very different prognoses:

- High grade (Large cell) alimentary lymphoma:** This form usually manifests as focal or multi-focal masses (often diffuse), and can involve the

lymph nodes, liver, spleen and kidneys. These cats tend to be clinically ill and the tumour can cause GI obstruction, perforation and sepsis. Treatment of these cases is based primarily on chemotherapy. Surgery is only considered in cases where obstruction or perforation has occurred.

Typically, an aggressive multi-agent chemotherapy protocols is employed for these cases (i.e. CHOP based, or University of Wisconsin, Madison). Success of treatment of these cats is determined by the individual's response to therapy, but only 50-60% of cats achieve a complete remission. Studies have found that response to treatment is the only predictor of outcome. Current reports suggest that the median survival time is between 6-8 months for these cases.

- Low grade (Small cell) alimentary lymphoma:** The low grade alimentary lymphoma is commonly associated with diffuse infiltration rather than discreet mass formation. Still it is not uncommon to see lymph node or liver involvement in this form as well. Treatment of this form is often based on long term low-dose chemotherapy with oral chemotherapeutic agents. A popular choice is prednisone and chlorambucil (Leukeran). These cases typically have a good response to this treatment and 95% achieve complete or partial remission. The median survival time for these cats has been reported to be as long as two years.

Mediastinal Lymphoma: Mediastinal lymphoma had been previously associated with the young FelV+ cat. In these cases, the tumour tends towards high grade and treatment is comprised of aggressive chemotherapy (i.e. CHOP based). In the case of the younger, FelV-negative cats, the prognosis has been more favourable and initial response to treatment can be a good predictor of long-term survival. In an Australian study, cats surviving the first 16 weeks of chemotherapy tended to have remission times of a year or more.

Nasal Lymphoma: Unlike other forms of lymphoma, nasal lymphoma often presents as a localized tumour. In these cases, radiation therapy can be used to focus treatment locally; though adjunct chemotherapy is often used due to lymphoma's systemic nature. These cases tend to have a longer survival time than some of the other forms of lymphoma with radiation AND chemotherapy. In one study in the US, it was found that these cats were surviving 2-3 years with treatment

CNS Lymphoma: A less common form is lymphoma of the central nervous system. More often this involves the

spinal cord rather than the brain. Historically, affected cats were young (< 3 years) and positive for FelV. More recently, it has been seen occasionally in older FelV negative cats. It is worth noting that approximately 50% of these cats will have other organ involvement, and this tumour has been known to spread to bone marrow or kidneys. Therefore, full staging is strongly recommended in these cases. Treatment for these cases is based on chemotherapy, and in some cases radiation is also recommended. Therapy usually is comprised of drugs that cross blood brain barrier (CCNU, cytosine arabinoside, steroids). In some cases, surgical decompression can be warranted for palliation. Survival time with this form is usually reduced and is typically 5 months or less.

What does the COP protocol involve?

COP protocol:

Induction Phase (maintain for 6-8 weeks):

Vincristine: 0.5-0.7 mg/m² IV once a week (via an intravenous catheter)

Cyclophosphamide: 150mg/m² once a week orally. The tablets cannot be split and so the frequency of dosing must be adjusted to provide the equivalent weekly dose.

Prednisolone: 40-50 mg/m² orally once a day

Maintenance Phase:

Vincristine: reduce to 0.5-0.7 mg/m² IV every 3 to 4 weeks

Cyclophosphamide: 150 mg/m² once a week orally. The tablets cannot be split and so the frequency of dosing must be adjusted to provide the equivalent weekly dose.

Prednisolone: gradually reduce to 20 mg/m² orally every second day

The length of treatment during the maintenance phase is controversial but it is often continued for 2-3 years.

What does the chlorambucil and prednisolone protocol involve?

Chlorambucil: 15 mg/m² orally once a day for 4 consecutive days every 3 weeks. The tablets cannot be split. x 3mg/kg orally once a day tapering to 1-2mg/kg orally every 24-48 hours once complete remission is achieved.

What side effects can occur with chemotherapy drug use?

The COP protocol is generally well tolerated in cats. Potential side effects of commonly used chemotherapeutic drugs include:

Vincristine: may cause myelosuppression. Perivascular necrosis if extravasation occurs during administration.

(continued on Page 9).

WHAT'S YOUR DIAGNOSIS?

Rachel Korman BVSc GPCertFelp MA CVSMRCVS.



CASE PRESENTATION

An 8 year old, male neutered Burmese was presented with intermittent vomiting, weight loss and inappetance for two months and diarrhoea for one month.

Faeces were loose with increased volume and frequency. Tenesmus, blood or mucus was not observed. The cat had outdoor access and ate a commercial diet. Vaccinations, anthelmintic and flea prevention were current. He was bright, alert and responsive. Body condition was reduced (BCS 1.5/5). Rectal temperature was 38.2°C, pulse and heart rate 180 bpm and respiratory rate 24 bpm.

Physical examination was otherwise unremarkable.

What differential diagnosis should be considered at this stage?

Current problems were **vomiting, diarrhoea, weight loss and poor appetite.**

Chronic vomiting may be caused by primary gastrointestinal disease or extra-intestinal disease e.g. hepatobiliary (e.g. cholangitis, lipidosis), renal, CNS or metabolic/endocrine diseases (e.g. hyperthyroidism). CNS disease was unlikely as neurological examination was normal.

Diarrhoea with increased volume and frequency and absence of mucous and/or blood with weight loss is consistent with small intestinal disease.

This type of diarrhoea may result from primary gastrointestinal disease e.g. inflammation, neoplasia, dietary intolerance/hypersensitivity, infection, foreign bodies and motility disorders.

Parameter	Results	Reference Interval
Urea	7.2	6.5-10.5 mmol/l
Creatinine	138	133-175 µmol/l
Total Protein	77	77-91.0 g/l
Albumin	34.6	24-35 g/l
Globulin	42.4	21-51.0 g/l
Albumin/globulin ratio	0.8	0.4-1.30
Glucose	5.3	3.9-8.3 mmol/l
ALT	40	15-45 IU/l
ALKP	24	15-60 IU/l
Total Bilirubin	5.5	0.0-10.0 µmol/l
GGT	1.9	0-2 IU/l
Potassium	4.98	4.0-5.0 mmol/l
Sodium	154.9	149-157.0 mmol/l
Chloride	119	115-130 mmol/l
Phosphate	1.05	0.9-1.55 mmol/l
Total Calcium	2.49	2.30-2.50 mmol/l
Fasting Bile Acid	5.7	0-15 µmol/l
Post Prandial Bile Acid	17	
Total Thyroxine	23	15-40 nmol/l

Figure 1: Serum Biochemistry Results.*

Parameter	Results	Reference Interval
Hb	9.79	8-15 g/dl
HCT	31.7	25-45 %
RBC	6.82	5.5-10 x10 ¹² /l
MCV	46.5	40 -55 fl
MCH	14.4	12.5 - 17.0 pg
MCHC	30.8	30-35 g/dl
Plt	267	200-700x10 ⁹ /l
WBC	26.4	4.9-19.0x10 ⁹ /l
Neutrophils	24.55	2.4-12.5x10 ⁹ /l
Lymphocytes	1.32	1.4-6.0x10 ⁹ /l
Monocytes	0.26	0.1-0.7x10 ⁹ /l
Eosinophils	0	0.1-1.60x10 ⁹ /l
Basophils	0.26	0-0.1x10 ⁹ /l

Figure 2: Haematology results.*

Parameter	Results
Source	Cystocentesis
Colour	Yellow
Appearance	Clear
Specific Gravity	1.044
pH	7.2
Blood	Trace
Protein	33.7 mg/dl
Creatinine	24.5 mmol/l
Protein: Creatinine ratio	0.12
Glucose	Negative
Ketones	Negative
Sediment	Unremarkable

Figure 3: Urinalysis results. *abnormal parameters in bold.

Extra-intestinal causes are also possible and include pancreatic (e.g. EPI), hepatobiliary and metabolic/endocrine diseases (e.g. hyperthyroidism).

Weight loss and inappetance are non-specific signs associated with neoplasia, infection or inflammation of any site or metabolic/endocrine (e.g. renal failure, apathetic hyperthyroidism or diabetes mellitus) disease.

Disease of the gastrointestinal tract, liver and pancreas may also result in inappetance and maldigestion or malabsorption could contribute to weight-loss.

What would you do next?

Serum biochemistry (including thyroxine and dynamic bile acids), haematology and urinalysis were performed to investigate metabolic and endocrine causes and/or complications of vomiting and diarrhoea (Figures 1, 2, 3).

The cat was hydrated and currently eating, therefore fluid therapy was not required.

How would you interpret these results?

Haematology revealed a mild mature neutrophilia, lymphopenia, eosinopenia and basophilia.

A mature neutrophilia may be due to many causes in cats. Stress is the most common however infection/inflammation or neoplasia are also possible. Lymphopenia and eosinopenia may be due to stress or acute infection/inflammation and basophilia may be due to allergic (e.g. hypersensitivity), parasitic or neoplastic disease.

In this case, the neutrophilia, lymphopenia and eosinopenia most likely reflected a stress leukogram. Normal serum T4, lack of azotaemia or hyperglycaemia excluded

renal failure and diabetes mellitus. Hepatobiliary disease was unlikely as liver enzymes and dynamic bile-acids were normal.

What would you do now?

Retrovirus testing (Figure 4) and faecal culture and parasitology (Figure 5) were performed to investigate infectious causes and/or secondary infections that could contribute to clinical signs. Cobalamin, folate, fPLI and TLI were measured to assess small intestinal function and identify pancreatic disorders (Figure 6).

Test	Results
FeLV antibody ELISA	Negative
FIV antigen ELISA	Negative

Figure 4: Retrovirus Testing.

Faecal Culture	Results
Salmonella	Negative
Clostridium difficile	Negative
Campylobacter	Negative
Faecal Parasitology	
Coccidia	Negative
Giardia	Negative
Worm eggs	Negative

Figure 5: Faecal Culture and Parasitology.

	Results	Reference Interval
Cobalamin	600	>150 ng/l
Folate	19.2	8.5-20.0 µg/l
fPLI	9.2	0.0-3.5 µg/l
Trypsin-like immunoreactivity	127	35-130 µg/l

Figure 6: Pancreatic and intestinal vitamins. (abnormal parameters in bold).

Results

Retrovirus screening was negative. Intestinal infection with pathogenic bacteria, parasites and protozoa were largely excluded, although some agents (e.g. Giardia spp) may be intermittently excreted and missed on single faecal samples.

The increase in fPLI was consistent with pancreatitis. Normal TLI concentration excluded EPI. Normal cobalamin and folate indicated supplementation was unnecessary. Although pancreatitis could explain weight loss, vomiting and diarrhoea in

Imaging	Results
Thoracic radiographs	Thoracic radiographs were unremarkable.
Abdominal radiographs	Abdominal radiographs were unremarkable.
Abdominal ultrasound	The pancreas and duodenal layering appeared normal. Some enlarged, heterogeneous lymph nodes were seen (9.1mm/7.8mm) close to an area of small intestinal wall with lack of layering and thickening. Examination was otherwise normal.

Figure 7: Radiograph and Ultrasound presentation.

cats with chronic pancreatitis is less common. Further investigations were pursued to establish if pancreatitis was present with concurrent disease e.g. triaditis, inflammatory bowel disease.

Now what would you do?

Abdominal radiographs (Figure 7) and ultrasound (Figure 7, Picture A, B, C) were performed to evaluate the pancreas and gastrointestinal tract for neoplasia (e.g. lymphoma), inflammation (e.g. IBD) or infection (e.g. abscessation) which could result in vomiting. Thoracic radiographs (Figure 7) were assessed for evidence of metastatic disease.

How would you interpret these findings?

Additional problems identified were **focal thickening** and **loss of small intestinal layering** and **mesenteric lymphadenomegaly**.

Thickening and loss of layering is associated with infiltrative diseases such as neoplasia (e.g. lymphoma, adenocarcinoma) or ischaemia. Thickening of the muscularis is also seen with inflammatory bowel disease (IBD) however architecture is normally maintained [2]. Ischaemia was unlikely as vomiting was chronic.

Mesenteric lymphadenomegaly could represent reactive change, metastatic disease or lymphoma. Both IBD and lymphoma can result in mesenteric lymphadenomegaly so this finding did not allow differentiation between the two diseases.

The imaging findings ruled out foreign bodies and motility disorders as causes for vomiting in this case. Although dietary intolerance/hypersensitivity could still contribute to the cat's signs, these diseases are unlikely to produce such marked layering changes on ultrasound. Neoplasia and/or IBD were now principle differentials. Both diseases are associated with pancreatitis and lymphadenomegaly.



Picture A: Ultrasound image demonstrating normal appearance to duodenal layering.



Picture B: Ultrasound image demonstrating jejunal wall thickening with loss of layering.



Picture C: Ultrasound image demonstrating enlarged heterogeneous lymph node (arrow) adjacent to area of thickened small intestine with loss of layering.

WHAT'S YOUR DIAGNOSIS?

Continued

Further investigations to assess the gastrointestinal tract and lymphadenomegaly were pursued.

How would you do this?

Ultrasound-guided fine needle aspirates can be useful in the diagnosis of lymphoma and were obtained from the liver and thickened intestinal wall, however this did not provide any further information due to limited cellularity. Lymph node cytology revealed a reactive lymphoid population suggesting localised or generalized infection/inflammation. Lymphoma/metastatic neoplasia wasn't excluded however due to the limited cellularity of the sample. Endoscopy (Figure 8) was performed to obtain biopsies for cytology (Figure 9) and histopathology (Figure 9). The oesophagus and stomach appeared unremarkable. The duodenum was friable with moderate hyperaemia, oedema and a cobblestoned appearance. Cytology from the stomach was unremarkable, however the duodenum demonstrated mixed, predominantly lymphocytic inflammation with a small population of atypical, large lymphoid cells.

While histopathology results were pending, anti-emetic therapy (maropitant 1 mg/kg subcutaneously q 24hrs) and supportive treatment for



Figure 8: Image demonstrating moderate irregularity and oedema of the duodenum with mild hyperaemia.

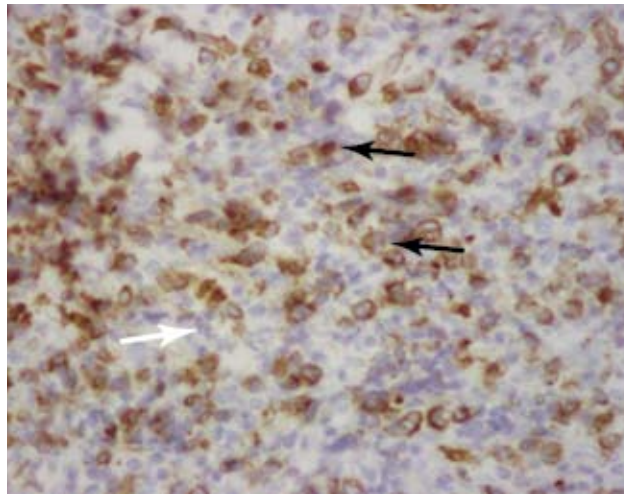


Figure 9: Duodenum: (Wright stain x 500 original magnification) Image demonstrating atypical intermediate to large lymphoid cells with large, round to convoluted nuclei, coarse to reticulated chromatin, no obvious nucleoli and pale basophilic cytoplasm with small clear vacuolations.

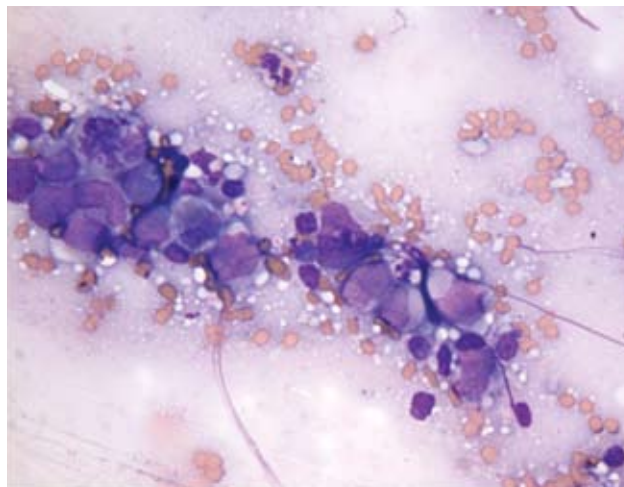


Figure 10: Duodenum; Image demonstrating large cells with cytoplasmic staining, but smaller lymphocytes without uptake of stain. The black arrow identifies the large intensely staining cell, whereas the white arrow demonstrates small lymphocytes without stain uptake. (Stained for CD79A x 40 original magnification).

pancreatitis (buprenorphine analgesia (0.01mg/kg sublingually q 8hrs) and fluid therapy) were administered. Diet modification with a hypoallergenic diet was initiated, as this can be helpful in management of inflammatory bowel disease. Histopathology revealed patchy, moderate lymphoplasmacytic gastritis and enteritis.

What do you think of these results and what would you do next?

The cobblestone appearance of the

duodenum on endoscopy may be seen with both IBD and lymphoma. Adenocarcinoma was unlikely now as focal, ulcerated, annular masses would be more common.

Duodenal cytology revealed large atypical lymphocytes suggestive of lymphoma.

These cells were not identified on histopathology, which suggested

lymphoplasmacytic (LP) enteritis.

Although LP enteritis could explain all the presenting signs, cytology had identified atypical cells and intestinal layering was lost on ultrasound, which was strongly suggestive of neoplasia. The endoscopic biopsies may not be completely representative and so, full-thickness biopsy samples were sought via exploratory laparotomy. Additionally, this approach is able to obtain more distal biopsies which increased the likelihood of diagnosing lymphoma as changes are frequently identified predominantly in the jejunum or ileum which is difficult to reach endoscopically. Pre-operative haematology was assessed and was unremarkable. The basophilia had now resolved.

Exploratory laparotomy revealed the liver, stomach, duodenum, jejunum, ileum, caecum and colon were grossly normal. The pancreas contained two small nodules. A single mesenteric lymph node was firm on palpation. Biopsies were obtained from all of these areas for histopathology. Post-operatively, analgesia (buprenorphine 0.01-0.02 mg/kg q 6-8 hours IV), intravenous fluid therapy and anti-emetic therapy

(maropitant 1 mg/kg subcutaneously q 24hrs) were continued for 2 days whereupon the cat was comfortable, eating and maintaining hydration. Post-operative recovery was uncomplicated.

Histopathology revealed neoplastic round cells within the villi, lamina propria and muscularis of the duodenum (Figure 10) and jejunum consistent with alimentary lymphoma. An identical population of cells were identified within the mesenteric lymph node. Immunohistochemical staining later identified these cells as neoplastic B-cells. Pancreatic histopathology confirmed nodular hyperplasia and mild islet amyloidosis of the pancreas consistent with pancreatitis.

DIAGNOSIS:
B-CELL ALIMENTARY LYMPHOMA (LYMPHOBLASTIC) AND PANCREATITIS.

How would you further manage this case?

Further WHO staging (e.g. bone marrow aspirate) was not performed as this is not predictive of outcome and was unlikely to provide additional information that would alter the cat's management. A low-dose COP chemotherapeutic induction protocol (Figure 11) was initiated 14 days after surgery. Cyclophosphamide was delayed to avoid complications such as dehiscence following surgery. Haematology was monitored for myelosuppression, fPLI for pancreatitis and cobalamin was regularly monitored as malabsorption secondary to alimentary lymphoma can result in deficiency.

At the time of writing, the cat remains in remission (12 months).

DISCUSSION

Weight-loss and small intestinal diarrhoea in this cat could have been due to either lymphoma or pancreatitis resulting in malabsorption and maldigestion. Vomiting and inappetence may have resulted from either pancreatitis or lymphoma.

Imaging indicated infiltrative intestinal disease (most likely neoplastic) causing vomiting. Mesenteric lymphadenomegaly could have been associated with either lymphoma and IBD and definitive diagnosis would require histopathology.

Lymphoma was not identified by endoscopic biopsies which were more suggestive of IBD.

The Treatment of Feline Lymphoma in a Nutshell

(continued from Page 5).

Cyclophosphamide: may cause myelosuppression which usually affects white cell lines but may affect red blood cell and platelet production. The neutropenia nadir usually occurs at 7 to 14 days post treatment. It may cause gastrointestinal side effects (e.g. vomiting, diarrhoea, inappetence). Cyclophosphamide induced cystitis is rare in cats. The drug is potentially hepatotoxic and nephrotoxic.

Chlorambucil: may cause myelosuppression with leucopenia, anaemia and thrombocytopenia. It may cause gastrointestinal side effects and rarely neurotoxicity. If unacceptable side effects occur then treatment may need to be postponed and drug doses should be reduced by 25%.

What monitoring should be performed during treatment?

Haematology should be monitored during treatment just prior to the administration of myelosuppressive drugs; be aware that some in house analysers do not provide accurate estimates of neutrophil and platelet numbers and samples are ideally analysed at a reference laboratory. If neutropenia is present ($<2.5 \times 10^9/l$) then treatment should be delayed for 2-3 days and haematology reassessed. Renal and hepatic parameters should be monitored in cats with suspected functional impairment identified prior to the commencement of chemotherapy; reduced doses of chemotherapeutics may be required in such cases. Additional monitoring of patients receiving drugs with the potential to be hepatotoxic or nephrotoxic (biochemistry) is warranted.

What rescue protocols can be used if a cat comes out of clinical remission?

Repeat remission may be difficult to achieve in cats after relapse of lymphoma. Various rescue protocols are reported. Repeating the original COP induction phase, if this was initially effective, is an option with or without the addition of L-asparaginase.

How long to treat?

There is no clear-cut answer to this question and this remains a controversial topic. Some sources advise continued therapy for the life of the cat, while others suggest stopping at periods varying from six months to three years if there is no evidence of recurrence.

Drug	Dosage
Vincristine	0.5mg/m ² IV q 7days for 6 doses then reducing to every 3 weeks for maintenance
Cyclophosphamide	50m/m ² on alternate days PO or IV every 10days
Prednisolone	40mg/m ² PO q 24hrs for 7days reducing to 20mg/m ² q 48 hours thereafter

Figure 11: Chemotherapy protocol, Low dose COP Protocol (BSAVA Small Animal Formulary protocol; adapted from reference 9).

Then what happened?

Clinical remission of alimentary lymphoma was demonstrated by weight gain and resolution of vomiting, diarrhoea and inappetence. Relapse of pancreatitis was suspected after two months as inappetence and diarrhoea recurred, however ultrasound and fPLI concentration were unremarkable. Gastrointestinal toxicity associated with vincristine administration was considered more likely and a 25% reduction of the dose was implemented.

The cat remained in remission on maintenance chemotherapy for 5 months until vomiting, inappetence, weight-loss and diarrhoea returned. fPLI assessment excluded pancreatitis as the cause. Abdominal ultrasound demonstrated recurrence of loss of small intestinal layering indicating lymphoma relapse.

The owners were reluctant to continue with intravenous chemotherapy agents. An alternative protocol utilising chlorambucil and prednisolone was prescribed suggestive of IBD. (Figure 12).

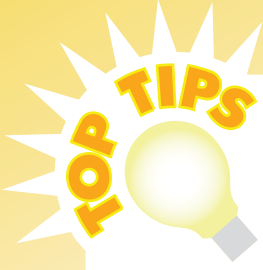
This could have been due to overlapping histopathological characteristics between IBD and lymphoma, inadequate tissue specimens, inadequate biopsy depth and/or concurrent LP-IBD. Also, malignant lymphocytes may be unevenly distributed within villi and LP-IBD can progress to lymphoma further complicating diagnosis. Endoscopy is also not able to fully evaluate the jejunum and ileum, where many lymphoma lesions are located. Full-thickness specimens are often required to achieve definitive diagnosis, as in this case.

While not a common feature of gastrointestinal lymphoma, pancreatitis was seen in this case. In this instance, it complicated ongoing monitoring, as weight loss and inappetence can be a feature secondary to either lymphoma or pancreatitis.

Drug	Dosage
Prednisolone	10 mg/cat q 24 hours PO
Chlorambucil	2 mg/cat every other day PO

Figure 12: Chemotherapy protocol.

On occasion, reference may be made to drugs which are not licensed for use in animals. The Editor does not take any responsibility for the safety and efficacy of such products. Any persons using these products do so entirely at their own risk.



The Fine Needle Aspirate

Anna Brunetti BSc BVMS MRCVS.

How many times a day does a patient walk into your office because their owner has found a lump? You have a poke, a prod, or a squeeze and your suspicions are raised – but does it need surgery, or is this a case for benign neglect? Before considering either option there is one way to quickly assess the situation.

Fine needle aspiration (FNA) may not always give the definitive answer, but it can help to decide on the next step. With the help of a nurse and a few special tools, you can go from 'no clue' to 'in the know' in record time.

Having the right approach to sampling can decrease the number of those disappointing 'non diagnostic' reports from your cytologist and the need to recall the cat and owner for another go...

Here are some top tips for obtaining the perfect F.N.A.

- There is no hard and fast rule about which needle size to use when aspirating a mass. So, try a variety. Smaller needles can help decrease the degree of blood contamination, though might also lead to a smaller cell harvest. Larger gauge needles can be useful for some harder, non exfoliating masses to grab enough cellular sample for evaluation. It is always worth trying the passive needle-only technique, redirecting the needle in multiple directions through the mass. If this results in a poor sample yield, then employing some active aspiration using a 5ml syringe may give a more representative sample. Active aspiration is often required to gain adequate samples from low cellularity, firm masses such as fibromas, but be careful: in well-vascularised tumours this can lead to significant blood contamination. Spinal needles can be the perfect tools for reaching deeper or intracavitary masses. Finally, do not forget if aspirating to make sure the negative pressure is fully released from the syringe before the needle is withdrawn, or the cells you have harvested will end up in the syringe and not on your slide.
- Cats have very mobile skin (and some breeds have lots of skin folds) so make sure to keep the mass firmly held and

stable when performing your fine needle aspiration to avoid tracking cells through neighbouring tissue. While tumour seeding via fine needle aspirate is extremely low risk, it is good practice to aspirate through skin you would resect if removing the mass.

- For ultrasound guided aspirates, care should be taken not to contaminate your samples with ultrasound gel. The key to avoiding accidental gel aspiration from the skin surface is to wipe any excess gel from the area you will be aspirating through and making sure you completely release the negative pressure on the syringe before withdrawing the needle. The problem with gel contamination of samples is two-fold. Firstly, the gel has a high affinity for the standard stains. If too much gel is present, even perfectly aspirated and stained cells may be physically obscured.
- Once you have the material, the next challenge is preparing the perfect smear. Avoid using a forceful spraying action to spread the cells over the slide. Use of too much force will lead to the sample coalescing into droplets on the slide which may be too thick for your clinical pathologist to evaluate. Instead you should aim to spread the material into a thin layer, so cells will flatten out without much lysis. To achieve this, squirt the sample out on to one end of the slide using a syringe, and spread it using a second slide placed at 90 degrees. Allow the top slide to glide along the bottom slide creating a thin, even layer. Knowing how much pressure to apply comes with experience, which you can attain by checking your own slides under the microscope. If you use too little pressure, your samples will be too thick, and too much pressure will lyse the cells. Remember that your clinical pathologist can only interpret undamaged cells, so the goal is to have many intact cells as possible.
- Before you can stain or post your slides make sure you give them time to dry. Always let your smears air dry first (it may help to use a hair dryer). Patience will pay off, as this will preserve the cell morphology and avoids slow drying artefacts. This is especially important for proteinaceous fluids (i.e. joint fluid). Wet samples take much longer to dry

once you seal them up into slide holders and this can reduce cell quality by the time it arrives at the lab.

- Finally, the clinical pathologists remind us to always submit all the smears you have taken the time to make. Often the slide used to spread the samples is not included with submitted samples, but it could be the one holding the perfect cells and the key to diagnosis. Most clinical pathology laboratories charge by the number of sites aspirated rather than the number of smears – and the more representative cells there are, the greater the chance that the diagnosis will be correct!

Introducing Anna Brunetti *The Pfizer Feline Scholar*



Originally from California, Anna crossed the Atlantic to obtain her veterinary degree at the University of Glasgow in 2008. After graduation she applied her passion for cats and infectious disease as the Locum Virology Registrar at the University of Glasgow's Companion Animal Diagnostics. She then worked in a small animal general practice in Lincolnshire; but missed being part of a dedicated feline medicine and infectious disease environment. In October 2010, Anna was appointed the new Pfizer Feline Scholar at the Feline Centre, University of Bristol, Langford; where she dedicates her time to seeing feline medicine cases and undertaking feline-focused research.

The Problem with Polyps

**Karen Crawford BVMS MRCVS,
Anna Brunetti BSc BVMS MRCVS.**

While nasopharyngeal polyps are not particularly a concern from an oncology stand point, not all polyps behave as "benignly" as their histology might suggest. While they may not show malignant tendencies, nasopharyngeal polyps can still be problematic. This article outlines how to approach these cases & reviews a case seen at Langford of a polyp which was not straightforward.

THE CLINICAL PICTURE

The underlying cause of the nasopharyngeal polyp is not completely understood. They may arise from the mucosal lining of the tympanic bulla, the pharyngeal mucosa, or the auditory tube. It is suspected that they may develop as a congenital entity or as a consequence of inflammation. Nasopharyngeal polyps are typically found in young cats, on average approximately 1.5 years old. Nevertheless, polyp development isn't restricted to these ages, and even older cats can be affected. No studies have identified a sex or breed predisposition.

The presentation of patients with nasopharyngeal polyps can be quite varied. The most common presenting sign is upper respiratory obstruction. These cases can be presented with nasal discharge, stertor, sneezing, coughing and/or dysphagia. Some cats will be presented in your consult room without that noisy snuffling and may just have aural irritation and otitis. Others may just present with vestibular signs. While facial nerve paralysis can occur as a side effect of nasopharyngeal polyps, it has not been reported in affected cats as a presenting sign.

DIAGNOSIS

The easiest way to achieve a diagnosis is by identifying a soft tissue mass above the soft palate, in the nasopharynx, or in the external ear canal. Successful visualization of the polyp usually requires a careful examination of the nasopharynx; which may necessitate a general anaesthetic. When examining the oro-pharynx, the caudal edge of the soft palate can be brought forward with a blunt hook to allow inspection of the mass. Evaluation of the area of the soft palate can be aided by the use of a dental mirror placed

within the caudal aspect of the pharynx. Grossly, polyps usually appear as glistening, pedunculated, red, pink or grey masses.

While the cat is under anaesthesia, this is a good opportunity to perform a thorough otoscopic examination of the ear canals, as it may allow visualization of polyps based there. As well, this will give the opportunity to examine the tympanic membranes, as a number of cats with nasopharyngeal polyps have otitis media as well. It is also wise to evaluate the cat's tympanic bullae with radiography, as a means of assessing possible bony destruction of the bullae.

Visualization of the polyp is not always possible. Radiography, computed tomography or MRI may be helpful in these situations. Haematology and serum biochemistry values in cats with nasopharyngeal polyps are typically unremarkable.

TREATMENT

There are different approaches possible for the removal of a nasopharyngeal polyp. The treatment of choice is surgical resection of the polyp. Removal can usually be performed by using traction, and tends to be an uncomplicated procedure. In cases where the middle ear is involved or the base of the polyp is in the tympanic bulla, a bulla osteotomy may be required.

Whichever technique is utilized, incomplete removal of the polyp may lead to rapid regrowth and a recurrence of clinical signs. When removing a polyp, it is advisable to send the mass for histology to ensure a more serious underlying pathology is not present.

A NASOPHARYNGEAL POLYP AT THE FELINE CENTRE

Crystal, a six month old female entire Bengal, was presented to the Feline Centre at Langford with a chronic history of otitis externa that had started to turn into something more serious. Despite conventional treatment with oral and topical antibiotics, she had continued to

deteriorate and had shown signs of intermittent pyrexia, purulent discharge and pain associated with palpation of the base of the left ear, and vestibular signs; anisocoria, head tilt to the left, ataxia, horizontal and rotatory nystagmus.

INITIAL PRESENTATION

Crystal was quiet but responsive. She was small for her age and in poor body condition (1.5/5). Her external ear canals appeared clean bilaterally on examination but Crystal



Figure 1: Crystal on presentation.

resented palpation and examination of the left ear. She had a severe left sided head tilt and mild anisocoria. She was also severely ataxic and frequently turned to the left when walking around the consult room.

INITIAL DIAGNOSTICS

Bloods: Bloods were found to be fairly unremarkable. Given Crystal's small stature and poor body condition, bile acids were also measured to assess hepatic function and rule out the presence of a portal systemic shunt, but were within normal limits. Retrovirus serology (FIV Ab and FeLV Ag) was negative.

Imaging: Radiographs taken prior to referral were reviewed by the imaging

Applications are invited for the Pfizer Feline Fellowship based at the University of Bristol School of Veterinary Science

This post offers an opportunity for veterinary surgeons with a particular interest in feline medicine to gain specialist experience and expertise in this field. Funded by Pfizer Animal Health, it is based at the Bristol University Veterinary School at Langford.

The successful applicant will join a strong team working in the field of feline medicine involving both clinical and research activity. Current areas of particular interest are infectious diseases, feline immunology, endocrinology and gastroenterology. The major objectives of the Pfizer Fellowship are to provide a link between feline clinical and research work in the department, assist in the development of feline projects and to assist in supporting the busy specialist feline diagnostic service. The Pfizer Fellow works very closely with the Feline Advisory Bureau Residents who have responsibility for most of the feline referrals but there is some opportunity for clinical work and there is encouragement to develop a particular aspect of feline medicine. Previous Fellows have developed a particular interest in FIV, FIP, endocrine diseases (mainly diabetes mellitus) and allergic skin disease.

Newly qualified veterinary surgeons will be considered for this post but some experience is an advantage. The post is ideal for veterinary surgeons wishing to pursue an interest in feline medicine. It provides an insight into an academic/research career and is particularly suitable for the graduate who wishes to consider this without making a long term commitment. The Pfizer Feline Fellowship provides an excellent basis for a subsequent academic or research career and previous Fellows have subsequently undertaken PhD projects arising from their year. This position normally starts in October and is for one year although reappointment at the end of the first year may be considered.

Further details of the post are available from:

**Prof. T.J. Gruffydd-Jones, The Feline Centre
Department of Clinical Veterinary Science
University of Bristol Langford House, Langford,
BRISTOL BS40 5DU**

Tel: 0117 928 9558 or e-mail: lvs@langfordvets.co.uk
Prospective applicants are invited to visit Langford and to talk to the current Pfizer Feline Fellow.

department and confirmed an increased opacity in the left tympanic bulla and mild thickening of the bone in this region.

Video-otoscopy: Crystal was anaesthetized and underwent video-otoscopy. This confirmed that the tympanic membranes were intact bilaterally and the external ear canals were clean with no evidence of inflammation. Cytology of the left ear revealed a large population of Malassezia, but no bacteria were identified. At this point, it was decided that MRI would be the most appropriate course of action to further evaluate the changes in Crystal's middle and inner ear.

Management: Prior to MRI scanning, Crystal was treated with oral itraconazole (for the Malassezia) and buprenorphine and continued the course of marbofloxacin initiated by her referring vets. She initially showed some improvements in response to this treatment, but 48hrs later Crystal deteriorated and became withdrawn, depressed and pyrexia (40.1 C). Intravenous fluids therapy and antibiotics (cefuroxime and metronidazole) were incorporated into her treatment regime and she immediately underwent an emergency MRI scan.

FURTHER DIAGNOSTICS

MRI: The scan revealed heterogeneous material filling the left tympanic bulla. The proximal left external ear canal also appeared fluid filled. There was marked, heterogeneous enhancement of the contents of the tympanic bulla after administration of contrast (Gadolinium). Parts of the brainstem, and potentially the cerebellum, also appeared hyperechoic.

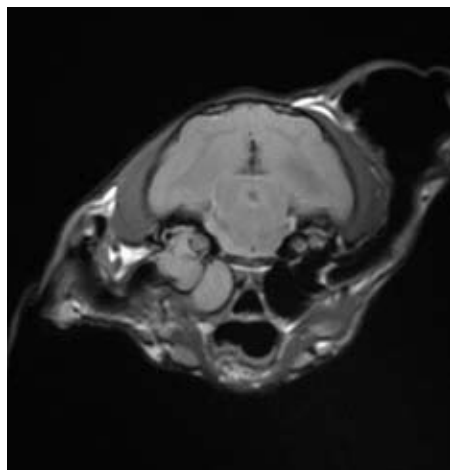


Figure 2: MRI: T2 weighted transverse image showing heterogeneous material/tissue filling the left tympanic bulla and fluid filling the proximal left ear canal.

These findings were consistent with severe otitis externa, otitis media, and otitis interna with involvement of the brain stem, cortex, and potentially the cerebellum on the left

side which was consistent with a polyp associated with inflammation or infection.

Surgery: Based on the MRI findings, a left sided ventral bulla-osteotomy was undertaken. During the procedure, they were able to visualize a large soft tissue mass in the bulla, which was removed and submitted for histopathological evaluation. Cultures of this tissue were negative at 48 hours, likely due to current antibiotic therapy. Aerobic culture results demonstrated a scant growth of a Gram negative bacillus. Histological evaluation was consistent with an inflammatory polyp.

Recovery: Post-operatively, Crystal made a marked improvement. She continued to demonstrate a mild head tilt to the left and did display Horner's syndrome, however her balance improved significantly.



Figure 3: Crystal, six months after her treatment at the Feline Centre.

Over time, her Horner's signs resolved completely though a slight head tilt has remained. Intravenous antibiotics were continued for 3 days post-operatively, and Crystal remained hospitalised for 2 days after the transition to oral antibiotics was made to ensure that she did not deteriorate. Crystal remained well, and was discharged from hospital with instructions to continue antibiotic treatment (cephalexin and metronidazole) for 6 weeks. The course of itraconazole (for treatment of Malassezia) was also continued, and Crystal's referring vet monitored her on a weekly basis throughout the treatment period. Crystal returned to the Feline Centre for re-evaluation at the end of her antibiotic course and was like a different cat! She had gained weight and was in good body condition. A subtle head tilt persisted but physical examination was otherwise unremarkable. She continues to do extremely well at home and her owners report that she is back to normal and bossing the other cats in the household around.

DISCUSSION

Crystal is an interesting example of a case where a nasopharyngeal polyp became more complicated than might typically be expected. Although the majority of polyps are relatively benign and can be dealt with fairly easily, in Crystal's case the complications were severe and potentially life threatening, and required the expertise and care of a multi-disciplinary team involving the staff of the Feline Centre, intensive care unit, and our soft tissue surgeons to enable her to make a full recovery.



Clearing the way to a
flea-free environment.



Only Stronghold treats fleas and eggs on the pet **and** existing eggs and larvae in the environment.

stronghold
For protection of pet and home

For further information please contact Pfizer Animal Health, Walton Oaks, Tadworth, Surrey KT20 7NS **POM-V**
Stronghold contains selamectin. Use medicines responsibly www.noah.co.uk/responsible

AH280/10