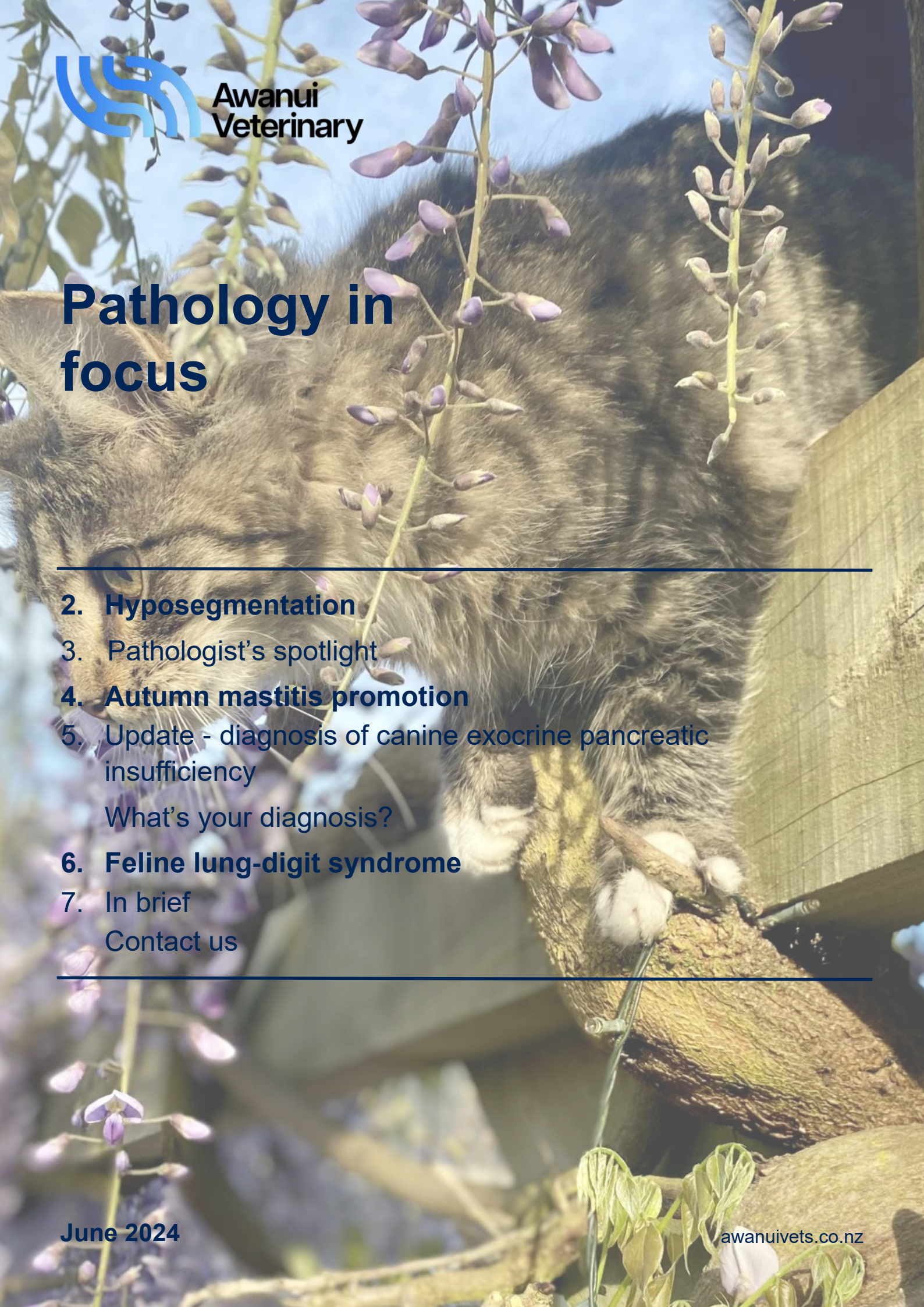

Awanui Veterinary

Pathology in focus

June 2024

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Hyposegmentation

Arefeh Ravanbakhsh

Pelger-Huët anomaly (PHA) is a genetic condition reported in numerous species characterised by nuclei hyposegmentation of granulocytes (neutrophils, eosinophils, and basophils).

Nuclei of granulocytes can appear oval, kidney-shaped, bean-shaped, band-shaped or bilobed.[1] This anomaly has been described in dogs, cats, horses, rabbits, and humans.[1] It is thought that a defect occurs at the stem cell level as bone marrow megakaryocytes can also be affected.[2] In humans. Pelger-Huët anomaly has been attributed to a mutation in lamin-B receptor gene which codes an integral nuclear envelope protein.[2] In most cases, this is an autosomal dominant hereditary anomaly, with no clinical consequences in heterozygous individuals; however, it can be lethal in homozygous individuals.[2,3]

Although uncommon, it is important to be aware of this anomaly to avoid misinterpretation of acute inflammation when examining blood smears.

Assessment of a blood smear as part of a routine CBC (such as a presurgical screen) in an otherwise healthy patient can be a fantastic way to pick up on this anomaly. In patients with PHA almost all of the neutrophils are hyposegmented. At first glance it may appear that the patient has a severe left shift, suggesting an overwhelming inflammatory response. However closer scrutiny of the neutrophils and other granulocytes reveals several clues to differentiate PHA from acute inflammation.

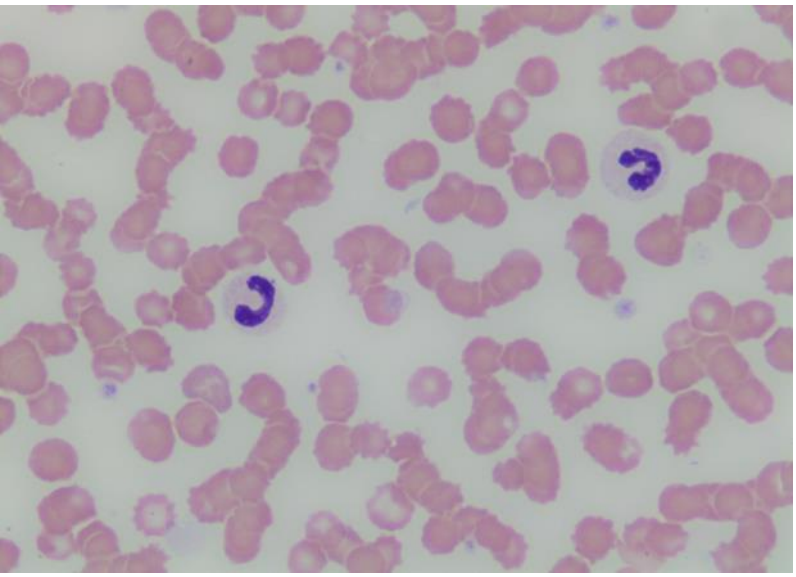

Figure 1: Blood smear from a canine patient with Pelger-Huet anomaly, 100x oil.

Figure 1 shows a blood smear from a patient with PHA while Figure 2 is from a diabetic patient with evidence of acute inflammation.

What differences can be appreciated and how can band neutrophils be distinguished from segmented neutrophils?

A band versus segmented neutrophil can be differentiated by closely examining the width of most narrow portion of the nucleus and comparing that to the widest part of the nucleus. Segmented neutrophils have a tight constriction between nuclear lobes. The narrowest part of the constriction should be <1/3 the width of the thickest part of the nucleus. If the width of a constricted part of the nucleus is >1/3 the width of the thickest part of the nucleus, the cell is a band. In both Figure 1 and Figure 2 neutrophils with a band-shaped nuclei are present (arrows). Further assessment of their cytoplasmic features and chromatin pattern can aid to determine if the band neutrophils are due to release of immature neutrophils secondary to a strong inflammatory stimulus vs a genetic anomaly.

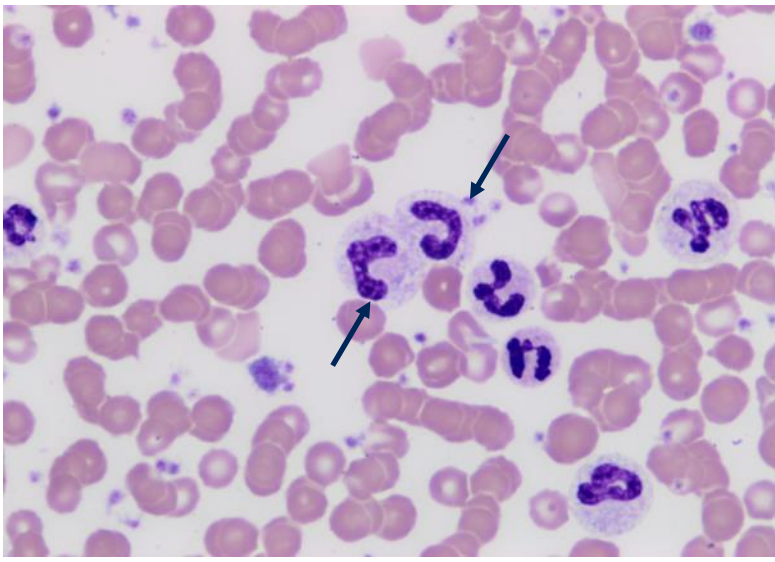

Figure 2: Blood smear from a canine patient with acute inflammation. Arrows indicating band-shaped nuclei. 100x oil.

The cytoplasm of the band neutrophils in Figure 2 display cytoplasmic basophilia and some contain Döhle bodies. Cytoplasmic basophilia, Döhle bodies as well as cytoplasmic vacuolation and toxic granulation are all signs of toxic change which indicates accelerated maturation through the bone marrow supporting an inflammatory response. The banded neutrophils in Figure 1 do not display toxic change and have cytoplasmic features of normal mature segmented neutrophils.

The second clue is the chromatin pattern. The banded cells in Figure 1 have densely clumped chromatin pattern while the banded cells in Figure 2 have more loosely clumped chromatin pattern.

Furthermore, patients with the inflammatory response have a mixture of bands and segmented neutrophils. Patients with PHA have uniformly hyposegmented neutrophils.

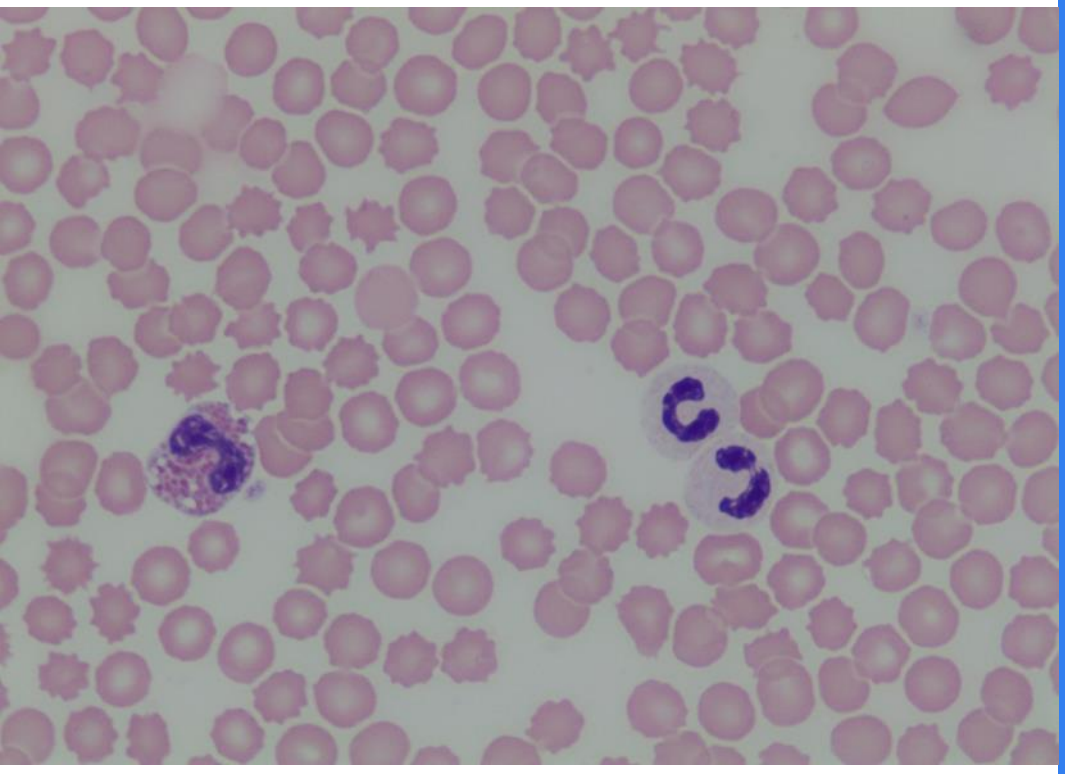

Figure 3: Blood smear from a canine patient with Pelger-Huet anomaly, 100x oil.

Another helpful hint would be to assess the nuclear morphology of other granulocytes. Figure 3 is from the same patient with PHA. Note that the eosinophil nuclei is also hyposegmented.

Pelger-Huët anomaly should also be differentiated from pseudo-Pelger-Huët anomaly where granulocyte hyposegmentation occurs not due to a genetic condition but rather secondary to other underlying pathology such as myelodysplastic syndrome, chronic infection, or administration of some drugs. In pseudo Pelger-Huët, only a minority of granulocytes display hyposegmentation.[2]

References:

1. Harvey JW. *Veterinary Haematology, A Diagnostic Guide and Color Atlas.* Elsevier St. Louis Missouri, USA, 2012.
2. Valenciano AC, Cowell RL. *Cowell and Tyler's Diagnostic cytology and Hematology of the Dog and Cat.* 5th Edtn. Elsevier St. Louis Missouri, USA, 2019
3. Vale A.M et al. Pelger-Huët anomaly in two related mixed-breed dogs. *J Vet Diagn Invest.* 4:863-5, 2011
4. Deshuillers. P, Raskin Rm Messick J. Pelger-Huët anomaly in a cat. *Vet Clin Pathol.* 3:337-41, 2014.

Pathologist spotlight

Arefeh Ravanbakhsh has been part of our team since 2020.

Feh completed a BSc. in 2012 and Doctor of Veterinary Medicine in 2016 (in Canada) and after graduating she entered mixed animal practice. Feh always enjoyed the "art" of clinical pathology and so decided to complete a combined Master's degree and residency in clinical pathology at the Western College of Veterinary Medicine.

Feh enjoys all aspects of clinical pathology, however, she has a particularly keen interest in the area of haematology and endocrinology. The most rewarding aspect of becoming a veterinary clinical pathologist for her has been helping veterinarians identify and diagnose disease processes in order to ultimately lead to best patient care and treatment.

Outside of work Arefeh enjoys long-distance running, hiking, playing soccer and volleyball, and spending quality time with family and friends.

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Image by Freddy from Pixabay

Update: Canine exocrine pancreatic insufficiency

Karen Bailey

In our February newsletter we advised you of a recent update to the interpretation guidelines for canine serum Trypsin-Like Immunoreactivity (TLI) test results. These changes were provisional pending further studies to refine the clinical cut-off limits for diagnosis of canine exocrine pancreatic insufficiency (EPI).

More information has recently become available confirming the original findings, whilst further defining the cut-offs. We will consequently be amending the guidelines as detailed below.

Current interpretive guidelines for canine TLI

- < 2.5 ng/mL diagnostic for EPI.
- 2.6 - 7.5 ng/mL subnormal cTLI concentration, highly suggestive of EPI. Assess response to pancreatic enzyme replacement therapy to confirm diagnosis.
- 7.6 - 10.0 ng/mL subnormal cTLI concentration, EPI cannot be excluded. If signs are consistent with EPI, consider assessing response to pancreatic enzyme replacement therapy to confirm diagnosis.
- 10.1 - 50.0 ng/mL result is within the reference interval.
- > 50 ng/mL The clinical significance of a cTLI concentration >50.0 ng/mL is uncertain. If you have also run a cPLI and this is within the reference interval, pancreatitis is unlikely.

From Monday 17 June 2024 the following amended interpretive guidelines will come into effect on reports. Of particular note is the change to the diagnostic cut-off level indicated in bold.

New guidelines for canine serum TLI interpretation

< 5.5 ng/mL* diagnostic for EPI.

5.6 - 7.5 ng/mL subnormal cTLI concentration, EPI cannot be excluded. If signs are consistent with EPI, consider assessing response to pancreatic enzyme replacement therapy and/or retesting in 1-2 months using a fasting sample (enzyme therapy does not interfere with testing).

7.6 - 10.8 ng/mL subnormal cTLI concentration but EPI unlikely. Consider other differentials depending on clinical signs.

10.9 - 50.0 ng/mL result is within the reference interval.

> 50 ng/mL in dogs without clinical signs of pancreatitis or with a normal cPLI, results > 50 ng/mL are unlikely to be clinically important.

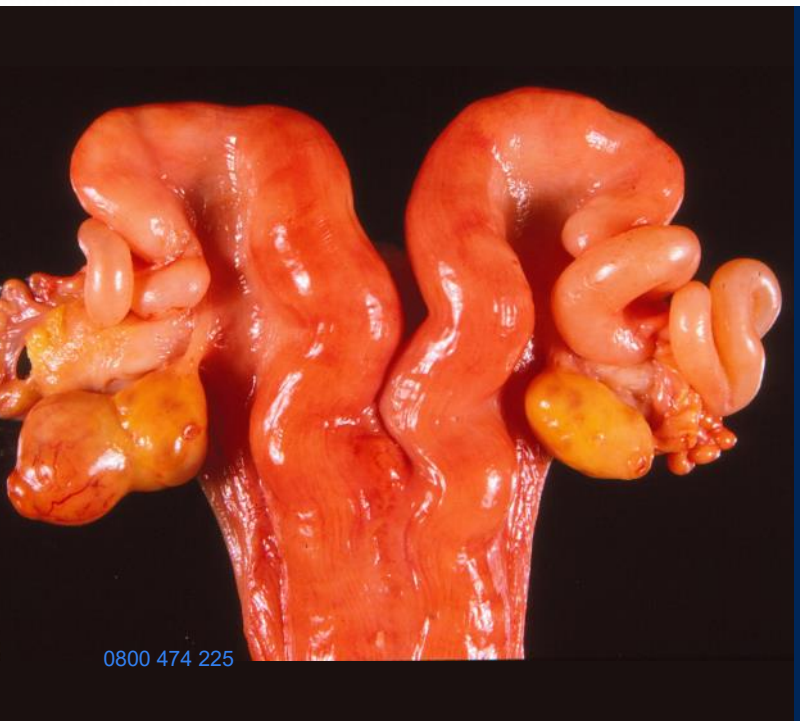
Comments

Elevations sometimes occur in postprandial samples. Food should be withdrawn for at least 12-15 hours before sampling. Concurrent active pancreatitis may also elevate TLI levels.

*Please be aware of this change when comparing current and historical results.

Reference

Texas A&M University Gastrointestinal Laboratory



What's your diagnosis?

A monthly spot quiz

Test your skills with this gross photo: A group of dairy heifers failed to get in calf and 8 of them went to the works and their uteruses were collected. Two of the heifers had this issue and one had a uterus unicornis.

What's your diagnosis? *(Answer can be found on last page).*

Feline lung-digit syndrome

Rebecca Allan

Clinical history

An otherwise well, 9-year-old male neutered domestic medium-hair cat, presented to the veterinarian after his owner discovered he had swollen crusted toes on one front foot and both back feet. Clinical examination revealed that affected toes were swollen, malodourous, with a necrotic appearance around the nail base (photos 1 and 2). The rest of the clinical examination was unremarkable.

Photos 1 & 2: Affected toes are swollen and crusted.

Aspirates of affected toes were submitted for cytology, swabs of the nail beds submitted for bacterial and fungal culture and a biopsy of nail bed from one affected toe, submitted for histopathology.

Cytology

Smear examination revealed a population of epithelial cells displaying moderate to marked atypia and criteria of malignancy, including a high N:C ratio, moderate variation in cell and nuclear size (photo 3), and occasional large mitotic figures (photo 4). Rarely, a fine eosinophilic fringe was noted on the free edge of some of the cells in the denser clusters (photo 5) and occasional cells with columnar morphology were identified (photo 6).

Diagnosis

A cytological diagnosis of epithelial neoplasia was made, suspicious of feline lung-digit syndrome due to the involvement of three digits on three different limbs and presence of cells with respiratory epithelial morphology. In light of this, thoracic imaging was recommended.

Additional testing

Subsequent histopathology of the nail bed biopsy revealed an infiltrative epithelial neoplasm, with marked nuclear and cellular atypia, numerous and bizarre mitotic figures and with rare cells displaying a fine ciliated border (photo 7 - next page). Results reflected cytology findings and confirmed a diagnosis of carcinoma, most likely metastatic pulmonary adenocarcinoma. Based on this news, the decision was made to euthanise the cat.

Discussion

Feline lung-digit syndrome refers to a clinical entity where primary lung tumours (often bronchogenic adenocarcinoma), which may themselves be clinically silent, as in this case, present because of metastatic lesions in one or more digits.[1] Affected digits involve the most distal phalanx. Tumour emboli can also lodge in other locations causing metastatic lesions in bone, skeletal muscle, skin, eyes, and distal aorta, leading to atypical or cryptic presentations.[1]

Differentials to consider include bacterial paronychia (e.g. *Nocardia* sp. or *Mycobacterium* sp.), fungal infection, and immune-mediated disease.[2]

Primary lung tumours are not common in the cat but tend to be malignant and carry a poor prognosis. Patients with feline lung-digit syndrome, have short median survival times of only a few weeks following diagnosis. Unfortunately, digital amputation has not been shown to be palliative as further metastases rapidly develop.[2]

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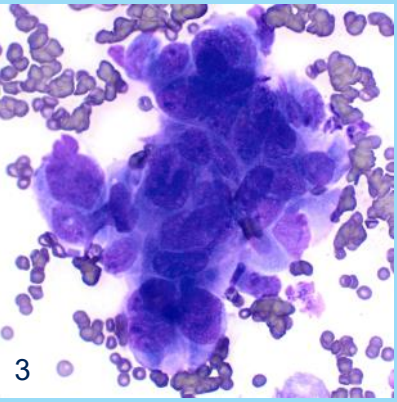

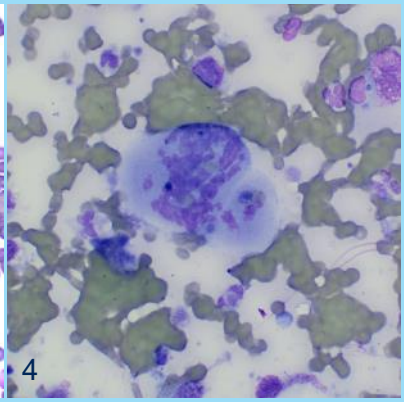

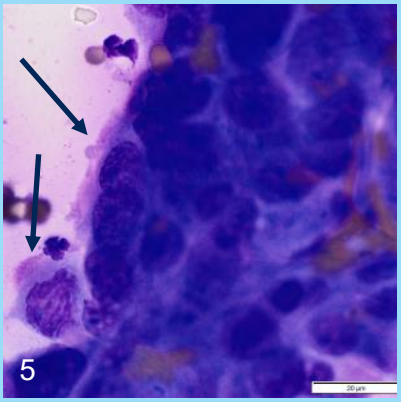

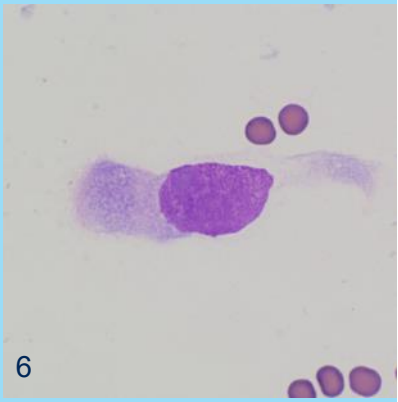

Photo 3: Atypical epithelial population, 50x oil. Photo 4: Large mitotic figure, 50x oil. Photo 5: Fine eosinophilic fringe noted along free edge of cell clusters (arrows). Photo 6: Individual cell with respiratory columnar epithelial morphology, 100x oil.

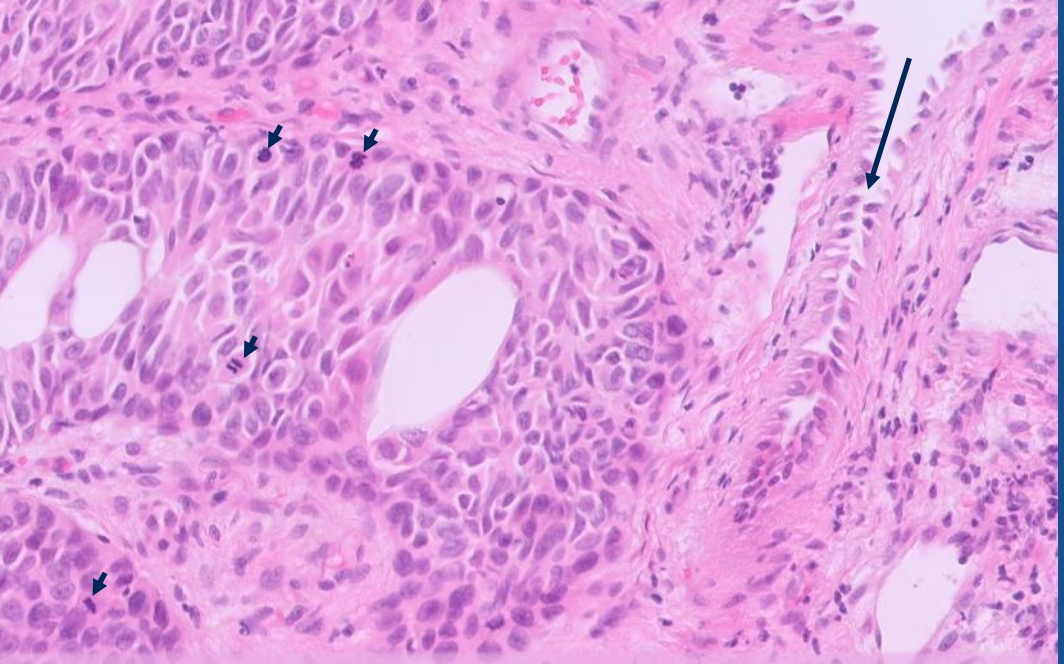

Photo 7: Nail bed biopsy, 20x. Atypical epithelial cell population demonstrating numerous mitotic figures (arrow heads) and cells with a fine ciliated border (arrow).

In brief

- All of our laboratories will be closed 28-30 June for **Matariki weekend**, reopening Monday 1 July.
- Promotional ACTH testing vouchers from Boehringer Ingelheim will entitle you to **one free test** on a horse not previously diagnosed with PPID and are valid until 31 July 2024.

Acknowledgements

Thanks to Vetlife Richmond for the interesting case and clinical photos.

References

1. Thrift E, Greenwell C, Turner AL, Harvey AM, Maher D, Malik R. Metastatic pulmonary carcinomas in cats ('feline lung-digit syndrome'): further variations on a theme. *JFMS Open Rep*. 3:2055116917691069, 2017.
2. Goldfinch N, Argyle DJ. Feline lung-digit syndrome: unusual metastatic patterns of primary lung tumours in cats. *J Feline Med Surg*. 14:202-208, 2012.

From page 3: What's your diagnosis? *There is bilateral cystic distension of the uterine tubes (hydrosalpinx). The uterine tubes (oviducts) are affected segmentally with parts unaffected. The one on the right is more severely affected. The lesions are presumably the result of inflammation in the uterus extending into the uterine tubes resulting in scarring and blockage of the ducts. What might cause this in heifers? We asked Rob Foster, a reproductive pathology expert, and he thought post breeding acquisition of infection with Ureaplasma, Campylobacter fetus subsp. venerealis, or Tritrichomonas foetus as the most likely causes.*

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- contacting Awanui Veterinary couldn't be easier.

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