WHAT IS YOUR DIAGNOSIS?

An 8-year old, male neutered, Border collie presented as a routine referral with a three week history of lethargy, inappetance and nasal discharge. The discharge was initially serous, but subsequently progressed to mucopurulent in nature. The dog was fully vaccinated, fed a proprietary commercial dog diet and did not have a history of travel outwith the United Kingdom.

On examination, he was bright, alert and responsive. Mucous membranes were pink and moist, with a capillary refill time of less than two seconds. The submandibular lymph nodes were moderately enlarged, with the remaining peripheral lymph nodes within normal limits. He had a heart rate of 80 beats/minute, with good quality, synchronous pulses. Lung sounds were clear in all fields, with no additional effort on respiration. Abdominal palpation was unremarkable and he was normothermic at 38.4°C. He had a body condition score of 3/9, with a poor muscle score.

There was airflow bilaterally from both nares, and evidence of discomfort on palpation of the nasal bones.

1. **What is your problem list for this patient?**

2. **What are your differential diagnoses for this patient?**

3. **How would you investigate this case further?**
1. **Problem list:**

Lethargy
Inappetance
Nasal discharge - mucopurulent
Nasal discomfort/pain
Submandibular lymphadenopathy
Weight loss/cachexia

2. **Differential diagnosis:**

Chronic rhinitis
Nasal foreign body
Nasal neoplasia e.g. carcinoma, sarcoma, lymphoma, osteosarcoma
Aspergillus
Extension of dental disease e.g. oronasal fistula, dental abscess
Inflammatory polyp

3. **Further investigation:**

**Comprehensive haematology and biochemistry** should be performed to evaluate for underlying conditions as these signs could be attributable to a more systemic disease, such as lymphoma. It is also likely that this patient will require further investigations for which anaesthesia or sedation may be indicated, in which case information regarding organ function is important. This patient had a hypoalbuminaemia of 19.6 g/l. The platelet count was also within normal limits, and there was a mild, mature neutrophilia of $14.6 \times 10^9/l$ (ref. $4 – 12.0 \times 10^9/l$).

**What is the most likely reason for the hypoalbuminaemia in this patient?**

Albumin is a negative acute phase protein, meaning that in response to inflammation, the liver decreases albumin production in favour of inflammatory proteins such as fibrinogen and other acute phase proteins. This is not a specific response, and would be expected to resolve upon the underlying condition being addressed. Other causes, such as primary liver disease, protein-losing nephropathy and protein-losing enteropathy, were considered less likely given lack of clinical signs, normal bile acids and a normal urine protein:creatinine ratio.

Again, given that it is likely further investigations will be undertaken including nasal biopsy, **clotting times** were also performed in this case, evaluating the extrinsic (prothrombin time, PT) and intrinsic (activated partial thromboplastin time, APTT) components of secondary haemostasis. In this patient, both were within normal limits.

The referring veterinarian had already performed radiographs of the nasal cavity, seen below, which one can subjectively appreciate a mild increased lucency within the right nasal cavity, although radiographs have limited sensitivity in evaluating the nasal cavity.
Intraoral DV view of the nasal cavity

To appreciate the internal nasal structures in more detail, a head CT was performed.

What is your interpretation of the images below?
There is marked turbinate destruction within the right nasal cavity, alongside fluid which is obliterating the normal nasal turbinates. There is milder turbinate loss in the left nasal cavity. Within the frontal sinus, there is a marked soft tissue density lesion, with evidence of extension through the septum which is separating the frontal sinuses. Although not clearly evident on these images, there was also evidence of communication between the calvarium and frontal sinus, as well as loss of cribriform plate integrity.

Based on the findings thus far, what is the most likely cause for the signs?
The florid appearance of the lesion within the frontal sinus, alongside the marked destruction of the nasal turbinates is most consistent with *Aspergillus* infection.

Rhinoscopy was performed in this case. Prior to this, a buccal mucosal bleeding time was performed, with it taking 2 minutes 40 seconds for an adequate clot to form (ref. < 4 minutes), to evaluate platelet function. There was more space within the nasal cavity, secondary to the turbinate destruction affecting the right nasal cavity. The floor of the frontal sinus was completely occupied by a fluffy appearing, extensive fungal plaque, as shown in the images below. There was also areas of the septal bone which were necrotic and avascular. Biopsies were taken at the time and submitted for histopathology and fungal culture.
There is limited value in nasal swabs for culture and sensitivity testing. In any of the differential diagnoses above there will be inflammation of the nasal cavity, which will allow bacterial population changes and overgrowths. Primary bacterial rhinitis is extremely rare and therefore any cultured bacteria from swabs are most likely commensals. A pure positive culture from a biopsy is more suggestive of a deep seated infection and provided another cause cannot be identified, then treatment of this may be justified.

Given the extensive nature of the fungal plaque, and necrotic underlying bone, there is likely to be limited vascular delivery to this area, thus making the efficacy of systemic therapy in such advanced disease questionable. The most effective treatment in this case is local therapy.

This involves manual debridement of the fungal plaques, to remove as much of the disease burden as possible. As there was already demonstrated to be communication between the frontal sinus and calvarium, debridement was only performed cautiously to minimise the risk of iatrogenic introduction of infection or trauma to the brain.

Copious lavage is then performed with saline, to expel as much of the fungal plaque as possible.

Finally, using the Seldinger technique, a catheter is placed within the most affected area. Correct placement is confirmed endoscopically. Clotrimazole is then instilled to ensure the most severely affected areas are directly treated.
The clotrimazole cream is instilled within the frontal sinus.

The patient’s position is then rotated under anaesthetic to maximise coating of the nasal cavity.

Post procedure, one of the main concerns is aspiration of the clotrimazole cream. To minimise the risk of this, throat packs are utilised to pack the caudal pharynx preventing accumulation of the medication. The patient is extubated as late as possible to ensure that they are able to protect their own airway.

Another concern is that, secondary to the altered bone integrity, there could be direct contact of the clotrimazole with the meninges and brain, therefore the owners should be warned prior that neurological signs are possible and the patient monitored for these in the recovery period.

Summary
The culture and histopathology confirmed the clinical suspicion of *Aspergillus* infection. The patient required a further treatment, as detailed above. Biopsies taken on the third rhinoscopic evaluation, when no gross disease was evident, showed resolution of fungal infection and an additional treatment was performed at this time, pending biopsy results.

Aspergillus serology can be performed to help with diagnostic certainty, but as with all serology studies, a positive titre only demonstrates exposure and not necessarily active infection. Additionally,
patients which are seronegative may still be infected, either as a result of early infection or inadequate immune response.

As alluded to above, systemic treatment solely is rarely as effective as topical therapy, and with the additional risk of causing hepatotoxicity, it was avoided in this patient given the raised liver enzymes. The infection was cleared with local therapy alone, with the biochemical abnormalities resolving at re-evaluation.