AMERICAN COLLEGE OF
ACVD
VETERINARY DERMATOLOGY

Credential Committee Guidelines
Updated January 2012
Sample case reports with comments and revisions

Dear Credentials Candidate,

Following are two sample case reports. Choosing a sample report is always a challenge for the committee because every report is going to have aspects that could be improved or decisions that may not have been acknowledged by all the reviewers as the best. In order to make this a more valuable example, the committee has decided to add the reviewers' comments as the residents received them when the reports were graded.

Additionally, the committee is adding a second report THAT DID NOT pass on the first grading, but the resident did a good job rewriting and addressing the reviewers concerns. In this case, both the original report and the revised reports are included, as well as the original comments and the resident's rebuttal. While the case reports and comments are anonymous, the rebuttal is not always completely anonymous and if there is any area where that occurs, those comments will be removed. Also, these reports were 20 pages long and paginated as directed by the guidelines. However, in creating this sample, changes to the formatting may have occurred and the reports may erroneously seem longer than allowed. Remember, any report longer than 20 pages will not be accepted.

We hope this is helpful! If you have any concerns please feel free to contact the committee chair with any questions!

Good Luck!

Colleen Mendelsohn, DVM Diplomate ACVD
Chair – ACVD Credentials Committee

THE FOLLOWING IS A REPORT THAT PASSED AFTER FIRST SUBMISSION – THE COMMENTS THE RESIDENT RECEIVED ARE FOUND AT THE END OF THIS REPORT.

Atypical Mycobacterial Infection in a Rhodesian Ridgeback

Signalment: 6 year old, male, castrated Rhodesian Ridgeback, weight = 39.5 kg

History: The patient presented for evaluation of a traumatically induced non-healing wound. Approximately 3 months prior (Day -96) the patient was wounded while playing in the owner's yard with his housemate (a spayed female Rhodesian Ridgeback). The patient ran into a tree branch resulting in a full-skin thickness laceration along his right dorso-lateral shoulder. He was immediately presented to an emergency clinic where the wound was cleaned and sutured with a penrose drain placed. Cefazolin 1,000 mg (25 mg/kg) was administered subcutaneously (SQ) and the patient was discharged with cephalexin 1,000mg (25 mg/kg) orally (PO) q8hr and tramadol 100mg (2.5 mg/kg) PO q8hr for 7 days. The drain was removed by the referring veterinarian (rDVM) 4 days later with healing noted.

Initially, wound healing progressed uneventfully. The patient represented to the rDVM on Day -85 due to development of swelling and thickening of the wound area. A small amount of fluid was drained and was considered to represent a seroma. On Day -70 the patient represented to the rDVM for lack of improvement. Medications dispensed included Deramaxx ® (deracoxib; Novartis) 75mg (1.9mg/kg) PO q24h and cephalexin 1000mg (25mg/kg) PO q12h, both for 7 days with instructions to then recheck. On Day -42 the patient presented to another DVM while on a trip out of town. The notes from this veterinarian indicated the wound, again, began to improve on the most recent course of medication, but in the past few days had opened up and began to drain. A sample (source not described) was submitted for aerobic bacterial culture and sensitivity (C&S) testing (Appendix 1). Pending the C&S results, the patient was placed on Clavamox® (amoxicillin/clavulanic acid; Pfizer) 500mg (12.6 mg/kg) PO q12hr. The culture grew light growth of *Staphylococcus pseudintermedius* with sensitivity to all antibiotics on the panel. The patient was continued on the Clavamox® for a total of 2 weeks. On Day -25 the

patient represented to the rDVM for continued failure of the wound to heal. At this point several open draining tracts with swelling were noted. Simplicef® (cefpodoxime; Pfizer) 200mg (5mg/kg) PO q24hr was dispensed. The patient was seen a final time on Day -8 for continued wound drainage and swelling. Blood work was performed on this date and revealed no significant abnormalities (Appendix 2). A dermatology referral was advised.

At presentation the patient was still receiving 5mg/kg/day cefpodoxime PO. He was also receiving Interceptor® (23mg milbemycin oxime; Novartis) monthly for heartworm prevention and Advantix® (Over 55 lbs imidacloprid/permethrin; Bayer) monthly for flea/tick control. He was current on routine vaccinations and de-worming and was fed Nature's Variety® Prairie Chicken Meal and Brown Rice supplemented occasionally with frozen raw beef. Aside from the non-healing wound the patient was not pruritic or exhibiting other dermatologic abnormalities and was otherwise healthy with no changes in activity level, appetite, water consumption, bathroom habits or general behavior noted. The housemate continued to exhibit no abnormalities and was also current on vaccines, and flea and heartworm prevention.

Day 0 – Physical/Dermatologic Exam: The patient was bright, alert, responsive and hydrated (BARH). He was in good body condition with a score of 3-3.5/5. His temperature was normal (101.2°F). Heart rate and respiratory rates were within normal limits. Mucous membranes were pink and moist with a capillary refill time of <2 seconds. Thoracic auscultation and abdominal palpation revealed no appreciable abnormalities. The oral exam was within normal limits and peripheral lymph nodes palpated benignly. Dermatologic exam revealed a 12.5cm horizontal scar representing the site of original primary closure of the wound on the lateral trunk just dorsal to the right scapula. Associated with it were several open tracts draining small amounts of serosanguinous to purulent material some of which had dried into crusts. Dorsal to the scar was

a 7.5cm diameter area of non-painful SQ swelling with normal appearing overlying skin. Eleven point two cm's ventral to the mid-portion of the scar was another open fistulous tract. This represented the site of exit from when the penrose drain was placed and a chord of thickened SQ tissue could be palpated along the path the drain had traveled from this opening to the wound site. The remainder of the dermatologic exam was within normal limits.

Day 0 – Problem Assessment: The problem list included Problem #1: Chronic non-healing traumatic wound over the right dorso-lateral shoulder region. Differential diagnoses for this problem included: 1) Infection: Given the lack of resolution with antibiotic therapy based off aerobic C&S testing and the traumatic nature of the wound high consideration was given to uncommon bacterial infections[1,2,3,4,5] (such as atypical mycobacteria, nocardia, L-form bacteria, actinomyces, and bacterial pseudomycetoma), as well as fungal infections[6,1,7] (sporotorichosis, pythiosis, lagenidiosis, zygomycosis, phaeohyphomycosis, eumycotic mycetoma, protothecosis, dermatophytosis (kerion), blastomycosis, histoplasmosis, cryptococcosis, and coccidiodomycosis). Additionally, some consideration was still given to more commonly encountered aerobic and facultative anaerobic Gram negative and positive bacteria, as well as anaerobic bacteria. 2) Foreign body reaction[8,9]: Either to material introduced into the tissue at the time of the initial wound or to any remaining suture material from previous surgical intervention. And 3) Trauma-induced panniculitis from fat necrosis.[10,11] Given the known history of trauma at the affected site other potential differential diagnoses such as idiopathic and immune-mediated conditions (sterile nodular panniculitis, sterile (pyo)granulomas, reactive histiocytosis and so forth) and neoplasia seemed much less likely but would still be considered if biopsies were supportive and further cultures negative. Problem #2: Feeding of raw meat. Although this was unlikely to be directly related to the skin disease it could negatively affect the

patient's overall health as a potential source of infectious disease. Also, if the patient's work-up resulted in a diagnosis requiring immunomodulation, feeding raw meat would be further contraindicated.

Day 0 – Diagnostic Plan: Multiple cytology samples were collected and evaluated to determine the cellular characteristics of the exudate and area of SQ swelling and to determine if any infectious agents could be identified (bacteria and/or fungal hyphae or spores). Glass slides were pressed firmly against the moist exudate or were used to lift up the edges of the crusted material and then firmly pressed against the skin collecting the underlying exudate. Fine needle aspirates of the area of SQ swelling were also collected. The slides were briefly heat-fixed and stained with a commercial modified Wright's stain (DipQuick®; Jorgensen Laboratories) and evaluated microscopically at 10x and 100x/oil immersion powers (Appendix 3). A Wood's lamp evaluation was performed of lesional areas to assess for green fluorescence of hair shafts that would suggest dermatophytosis, most specifically *Microsporum canis*.(Appendix 4) A DTM for further evaluation of dermatophytosis was not performed this day but was a consideration as one of the differential diagnoses was dermatophytic kerion. However, the diagnostic plan at this juncture was to pursue biopsy collection for histopathology and fungal culture which were thought to be adequate, if not superior, substitutes for assessment of dermatophytic kerions.[12,13,14] A skin scrape and/or trichogram to assess for Demodex mites were not evaluated this day given demodicosis seemed a highly unlikely cause for the lesions. However, on further reflection the author does realize these diagnostics are simple and inexpensive to perform, and for argument's sake could have been useful to pursue that day. Blood work was not assessed given it had very recently been performed by the rDVM, was normal, and the patient's general status had not changed appreciably in the interim.

Day 0 – Interpretation of Test Results: Cytologic examination revealed predominately pyogranulomatous inflammation with a lack of identifiable infectious agents. The identification of infectious agents could have provided a quick diagnosis for the cause of the patient's lesions, but unfortunately their absence did not rule-out an infectious etiology. The pyogranulomatous inflammation was not surprising given the chronic nature of the lesion and that it is a common finding with many of the listed potential etiologies.[1,15]

Day 0 – Revised Diagnostic Plan: To better characterize the nature of the lesions and to further assess for infectious agents the collection of samples for histopathology and tissue cultures were indicated. Because the patient was currently on systemic antimicrobial therapy there was concern that culture results could be negatively impacted if samples were collected on this day. Fortunately, the owner could readily bring the patient later in the week for sample collection after a 48 hour withdrawal from the antibiotic.

Day 0 – Treatment: The owner was instructed to discontinue the oral cefpodoxime. They would return following a 48 hour wash-out for biopsies for aerobic, anaerobic, fungal and mycobacterial tissue cultures and histopathology. The owner was also advised of the risks of infection from feeding uncooked meat and instructed to discontinue feeding the raw beef.

Day 2 – History: The patient presented for sedated biopsy collection for histopathology and tissue cultures. He had been off all systemic therapies since the initial visit. There were no changes in his skin lesions nor general status.

Day 2 – Physical/Dermatologic Exam: No appreciable changes were noted regarding the patient's skin lesions. His weight remained at 39.5kg and he was BARH. Heart rate was within normal limits at 102 beats/minute and respiratory rate was 24 breaths/minute with normal effort

and pattern. No abnormalities were appreciated on thoracic auscultation. Mucous membranes were pink and moist and had a capillary refill time of <2 seconds.

Day 2 - Problem Assessment: Problem #1: Unchanged from initial exam. Problem #2: Resolved- Owner was very receptive to no longer feeding raw meat and had discontinued it.

Day 2 – Diagnostic Plan: In preparation for biopsies the patient was sedated using xylazine. As per the practice's established protocol the patient was premedicated with 2mls atropine 0.54mg/ml (0.027 mg/kg) SQ. This was allowed to be absorbed over approximately 15 minutes. The patient was then sedated with 0.9mls xylazine 20mg/ml (0.45 mg/kg) intravenously. Respiratory rate, heart rate and pulse quality were monitored during the period of sedation. Five sites were selected from which to collect punch biopsy samples – 2 from the area of SQ swelling and 3 from intact skin just adjacent to the draining tracts. Local anesthesia was provided by infusing all biopsy sites locally with 2% lidocaine (1:8 sodium bicarbonate: lidocaine mixture). The 3 sites to be sampled for the aerobic and anaerobic bacterial, mycobacterial and fungal cultures were surface sterilized by swabbing with 70% alcohol and allowed to dry. Using 8mm punch biopsies (Acu-Punch®, Acuderm Inc.) the samples were collected by placing the instrument over each site and applying constant pressure in a clock-wise direction until it passed fully through the skin and into the SQ tissue. All punches were deep to ensure inclusion of adequate SQ fat. Each site was closed with 2 cruciate sutures (Fluorofil 3-0, Schering-Plough Animal Health). The 2 samples for histopathology (1 from the area of SQ swelling and 1 from near a draining tract) were placed in a jar containing 10% neutral buffered formalin (SARL Scientific). The remaining three samples were submitted for the cultures. Two were placed in a sterile glass vial containing a piece of saline moistened gauze. For the anaerobic sample, the

remaining specimen was fully submerged in 0.9% NaCl as instructed per the microbiology lab director[16]. Post-biopsy care instructions were provided (Appendix 5).

Day 2 – Treatment Plan: The history of trauma with the appearance of the lesions made atypical mycobacterial infection a strong possibility. To address this the patient was placed on marbofloxacin (Zeniquin®; Pfizer) at 200mg (5.1mg/kg) PO q24hr pending the histopathology and culture results. Marbofloxacin was selected as fluoroquinolone antibiotics are often found effective in treating atypical mycobacterial infections[2,3,17] and many of the previous mycobacterial cultures performed at the clinician's practice reported sensitivity to it. The owner would be updated as test results were received with recheck recommendations made at that time.

Day 9 – Phone Update: Spoke with owner regarding the histopathology (Appendix 6) and aerobic and anaerobic bacterial cultures (Appendix 7). The histopathology confirmed pyogranulomatous panniculitis, although no infectious agents were seen. A consideration expressed by the pathologist was the lesion could represent a trauma-induced panniculitis. However, any steroidal anti-inflammatory therapy would be postponed until the results of the mycobacterial and fungal cultures were received. There was no growth on the anaerobic culture but a few colonies of methicillin resistant *Staphylococcus pseudintermedius* (MRSP) grew on the aerobic. The owner was informed this was unlikely the primary source of the patient's skin disease and only a small amount was grown, but given the methicillin resistance it would be prudent to address it. The owner was educated about the salient features regarding MRSP infections in dogs[18,19](Appendix 8). The patient was scheduled to return in a couple of days for suture removal, at which time they would start the antibiotic.

Day 12 - History: Patient returned for suture removal, re-assessment and to make adjustments to therapy. The owner relayed there seemed to be mild improvement in the lesion's appearance. The dog was continuing to receive the marbofloxacin as previously directed.

Day 12 – Physical Exam/Lesion Description: The patient was BAHR with no change in weight. The lesion over the right shoulder was similar in appearance as at the previous visit. The area of SQ swelling had flattened but was still the same diameter and all of the initially noted draining tracts remained with the chord of thickened SQ tissue along the path of the penrose drain still palpable. The remainder of the physical exam was unremarkable.

Day 12 – Assessment: Problem #1: Panniculitis – possible mild improvement. Final etiologic diagnosis still pending the results of the mycobacterial and fungal cultures. Problem #3: MRSP – few colonies grown. As already mentioned, given the methicillin resistance it would seem prudent to address this with antimicrobial therapy.

Day 12 – Diagnostic Plan: No additional diagnostics were performed on this date.

Day 12 – Treatment Plan: Of the oral antibiotics reported as sensitive on the C&S profile the trimethoprim/sulfa and chloramphenicol were considered for therapy. The trimethoprim/sulfa was deemed preferable to the chloramphenicol as it required twice, instead of 3 times, daily dosing (so improved chances for compliance), did not pose the potential owner health risks associated with chloramphenicol[20] and it had been generally well-tolerated by other patients in which it was used to treat MRSP infections. The patient was placed on Trimethoprim/Sulfamethoxazole at 960mg (24.3mg/kg) PO q12hr. The owner was informed of possible side effects and advised to monitor closely for skin rashes/bruising, lethargy, lameness, eye inflammation or discharge, and gastrointestinal upset.[21,22] If any of these were seen the owner was instructed to discontinue the medication and call immediately. The marbofloxacin

was continued at 200mg PO q24hr for potential mycobacteria. The owner would be called with updates as the cultures were received and recheck was tentatively scheduled for 3 weeks.

Day 21 – Phone Consult: The owner called to relay the patient was not eating and lethargic which started about 2 days previously. No vomiting had been noted, but 1 bowel movement was a bit loose which had subsequently resolved. Because of these abnormalities the oral medications had been discontinued and he had been taken to his rDVM for further evaluation. No specific abnormalities were found on physical exam, but bloodwork was performed which was to be faxed over for review and recommendations.

Day 22 – rDVM Bloodwork Results and Interpretation: Elevations were noted in the liver enzymes and a hepatic insult was thought likely to be the source of the patient's clinical signs (Appendix 9). Given the known hepatic toxicity that can uncommonly occur with trimethoprim/sulfa antibiotics[21,22,23,24], specifically reversible cholestatic hepatitis and hepatic necrosis with failure, this was thought most likely to be the source of the elevations. Additional considerations also included other causes of hepatocyte damage and cholestasis[25] (such as other toxic insults, hypoxia, and inflammation –both infectious and non-infectious forms). Although the liver enzymes were elevated the other chemistry values that reflect the physiologic functioning ability of the liver (glucose, albumin, bilirubin, cholesterol and BUN) were still within normal limits. In addition to discontinuing the antibiotic and monitoring the patient's clinical response and serial blood panels, additional consideration was given to starting a liver support supplement (Denamarin®; Nutramax) and pursuing abdominal ultrasound and bile acids testing. The case was discussed with one of the internal medicine specialists at the practice[26] who concurred the liver damage could be antibiotic associated but if the patient clinically was remaining stable with adequate food and water intake, it would be fair to start the Denamarin®

(425mg SAMe/35mg silybin at 2 tablets PO q24hr on an empty stomach) and monitor the patient and bloodwork (BW) for improvement. If any worsening was noted then ultrasound and bile acids testing would be pursued with appropriate supportive care.

Day 22 – Phone Update: The owner was informed of the recommendations discussed with the internal medicine specialist. He would pick up the Denamarin® from his rDVM. The owner reported the patient was feeling better (more perky) with some appetite returning. Recheck was advised with bloodwork in 1 week as long the as the patient continued to exhibit progressive improvement. The owner was instructed to call with update if patient appetite and/or water consumption remained poor (<50% normal), if yellowing of mucous membranes were seen, if vomiting or diarrhea developed, or if the patient exhibited lethargy/pain/or other abnormalities.

Day 28 – History: Owner reported the patient was improved. He was still a bit lethargic but he ate all of his morning meal and most of the evening meal the night prior. Owner estimated was eating about 2/3's of normal amount. No vomiting, diarrhea or other abnormalities had been noted. There had been no significant worsening or improvement appreciated in the lesion over the right shoulder. The patient had not received any additional marbofloxacin from when it had been discontinued but was receiving the Denamarin® as previously directed.

Day 28 – Physical/Dermatologic Exam: Quiet(AHR). Weight 38.2kg. No pain or abnormalities noted on abdominal palpation. Mucous membranes were moist and pink with a CRT <2 sec. There were no signs of jaundice. The eyes were clear. Temperature was normal at 101.5 F. The remainder of the physical exam was unremarkable. Regarding the right shoulder lesion – the draining tract at the site of previous penrose drain exit was almost completely closed and the chord of thickened tissue was less obvious on palpation. The area of SQ swelling dorsal to the

wound was also flatter but thickening of the underlying tissue could still be palpated. The draining tracts along the scar remained and still exhibited similar amounts of exudation.

Day 28 – Interpretation of Test Results: The results of the fungal (Appendix 10) and mycobacterial (Appendix 11) cultures had been received the previous day. The fungal culture had no growth supporting a lack of fungal involvement. There was growth on the mycobacterial culture, which was thought to be significant and the likely cause for the persistence of the wound.

Day 28 - Problem Assessment: Problem #1: Panniculitis due to atypical mycobacterial infection. To ensure appropriate antibiotic therapy species identification with sensitivity testing would be pursued. Culture guided antibiotic therapy would be continued for 4-6 weeks past complete resolution of the lesion or until clinical response plateaued. If plateau were to occur then surgical en-bloc resection of the area would be advised to attempt complete cure.[27] Problem #3: MRSP. The only other oral antibiotic options that showed sensitivity on the culture were rifampin and chloramphenicol, both of which are not advisable in patients with pre-existing hepatic dysfunction[20,28]. Since there had been only a small amount of growth on the culture and the alternative antibiotic choices were not good options, it was decided to postpone further therapy directed at the MRSP, unless repeat cytology and culture revealed continued presence of staphylococcal bacteria. Problem #4: Hepatic insult with elevated liver values (ALP, ALT, AST, GGT) and systemic signs - suspected to be due to toxicity from trimethoprim/sulfa antibiotic. The patient clinically appeared stable and improving. BW would be checked to monitor the liver values.

Day 28 – Diagnostic Plan: A cytology sample (Appendix 12) and swab for aerobic bacterial C&S were collected from beneath the crusted material of the draining tracts. Whole blood was

collected via venipuncture of the jugular vein for repeat CBC and chemistry panel to assess systemic status (Appendix 13). A schirmer tear test (STT) was performed by inserting a test strip into both eyes to determine the mm of tears produced per minute. This was to ensure keratoconjunctivitis sicca had not been induced by the trimethoprim/sulfa antibiotic (Appendix 14).

Day 28 – Interpretation of Results: Cytology did not support a staphylococcal component but repeat C&S was pending to determine if further treatment would be indicated. The liver enzymes were much improved, coupled with normal results on the remainder of the BW, suggesting the hepatic insult was resolving. Tear production appeared to be within normal limits.

Day 28 – Treatment Plan: The owner still had marbofloxacin remaining at home and since it seemed some mild response had been seen to it and the patient was feeling better the owner was directed to restart the antibiotic at 200mg q24hr. The prognosis and treatment objectives associated with atypical mycobacterial infections were discussed at length with the owner[3,27]. He was advised in general the prognosis for cure was guarded. Although there were cases in which affected dogs and cats have been cured, it generally required many months of antibiotic therapy, occasionally coupled with surgery, as medical treatment alone was not always adequate to fully clear the infection. The owner was advised owner compliance is a critical component in successfully treating these types of infections. Given the location of the patient's lesion, it would seem amendable to en-bloc surgical resection of any remaining infected tissue if it came to that, which did improve the prognosis for this patient. For continued liver support, the Denamarin® was also to be continued as previously directed. The owner was advised to continue monitoring patient status and call if patient lethargy and appetite didn't continue to improve. BW was to be

rechecked in 2 weeks. Dermatology recheck would be determined once the mycobacterial sensitivity results were received.

Day 31 – Phone Consult: Informed owner there was no growth on the aerobic bacterial C&S (Appendix 15). Thus further therapy directed at the MRSP would not be pursued.

Day 40 – Phone Consult: The owner was informed the mycobacterial sensitivity results had been received (Appendix 16). The owner relayed he had run out of the marbofloxacin the day previously. Although marbofloxacin was not directly tested on the panel, the organism was resistant to those fluoroquinolones that were assessed suggesting continuing the marbofloxacin would not be beneficial. Of the oral options reported as sensitive, the clarithromycin was considered a good choice for further anti-mycobacterial therapy.[17,27] A prescription was called into a commercial pharmacy for clarithromycin tablets (not extended release) 250mg at 1.5 tablet (9.8mg/kg) PO q12hr. The patient would be rechecked in 1 month to assess response. The owner was advised to not run out of the antibiotic before recheck as starting and stopping therapy would slow the patient's response and potentially contribute to resistance development. The owner relayed they were scheduled to have BW checked by the rDVM later that week and would have the results faxed over for review.

Day 44 – rDVM BW and Owner Phone Consult: The BW (Appendix 17) revealed continued improvement in the liver values with just a couple mild elevations remaining. The owner was informed of the results and advised to maintain the patient on the Denamarin® until all values had returned to normal limits.

Day 58 - Phone consult: Spoke with owner for update on patient. Owner reported the patient was tolerating the clarithromycin. Appetite was pretty much back to normal and he was playing

again with his housemate. He relayed the "oozing areas" on the patient seemed to be drying up and was optimistic.

Day 69 – History: The patient returned for a recheck. He continued to do well and was not exhibiting any persistent abnormalities related to hepatic insult. Albeit slow, the owner felt the patient's lesion was continuing to show steady improvement. The patient was still receiving daily Denamarin® and clarithromycin as previously directed.

Day 69 – Physical/Dermatologic Exam: BAHR, Weight 39.7kg. The physical exam was unremarkable. The draining tract openings along the scar were still present but were only minimally exudative with mild crusting. The tract at the site of the drain exit had closed completely. The SQ chord of thickened tissue was much less prominent on palpation. There remained a moderately raised area of SQ swelling just above the initial wound site which measured 4.3 x 5.6cm.

Day 69 - Problem Assessment: Problem #1: Panniculitis due to atypical mycobacterial infection that appeared to be responding to clarithromycin. Therapy would be continued as is for 4-6 weeks past complete clinical resolution or until a plateau in response occurred. Problem #3: MRSP - Resolved. Problem #4: Hepatic insult with elevated liver values (ALP, ALT, AST, GGT) and systemic signs –suspected trimethoprim/sulfa reaction: Previous BW showed liver values to be improving and the patient's associated clinical abnormalities (lethargy and anorexia) had resolved.

Day 69 – Diagnostic Plan: No diagnostics were performed this day, but BW would be repeated 1 month from the last evaluation.

Day 69 – Treatment Plan: The owner was instructed to continue the clarithromycin 250mg at 1.5 tablets PO q12hr and daily Denamarin® (425mg SAMe/35mg silybin) at 2 tablets PO q24hr.

Bloodwork was to be rechecked in the next 2 weeks (1 month from last evaluation) and the skin rechecked in 1 month.

Day 85 – rDVM BW and Owner Phone Consult: Owner had recheck BW performed by rDVM and results were faxed over for review (Appendix 18). The owner was informed all liver values were completely back to normal. Owner reported the patient was doing well and continuing to make steady improvement. Advised the owner they could stop the Denamarin®, but continue the clarithromycin as previously directed.

Day 97 – History: The patient was continuing to do well. His appetite and activity level were normal. The patient was continuing to receive the clarithromycin daily. The owner was diligent in ensuring the patient was receiving all doses. The owner was seeing progressive, improvement in the lesion, albeit it was slow.

Day 97 – Physical/Dermatologic Exam: BAHR, Weight 38.8kg. No abnormalities were noted on physical exam, the patient appeared to be in good general health. The previously noted open draining tracts along the scar were completely healed shut. Mild scale was present on the surface of these sites. The SQ chord of tissue was much less apparent - only minimally palpable at this point. The area of SQ swelling above the scar was still present but slightly smaller from last visit (3.9 x 4.8cm).

Day 97 - Problem Assessment: Problem #1: Panniculitis due to atypical mycobacterial infection. The infection was slowly but steadily responding to the clarithromycin. Problem #4: Hepatic insult with elevated liver values (ALP, ALT, AST, GGT) and systemic signs – Resolved.

Day 97 – Diagnostic Plan: No diagnostics were performed this day.

Day 97 – Treatment Plan: The owner was advised to continue the clarithromycin 250mg at 1.5 tablets PO q12hr. He was reminded to not stop before recheck, which was to be in 6 weeks as

long as the patient continued to show clinical improvement. The owner was advised to call if new draining tracts formed or if the areas of swelling became more notable.

Day 140 – History: The patient was still receiving the clarithromycin as previously directed. He was feeling well, with normal appetite and water consumption. Owner felt the lesion continued to show improvement.

Day 140 - Physical/Dermatologic Exam: BAHR, Weight 39.8kg. The area was much improved. There were no open tracts, the chord of SQ tissue was no longer palpable, and the area of SQ swelling dorsal to the scar was much less prominent, measuring 2.3 x 1.7cm. The tissue in this area still felt somewhat thickened on palpation. The remainder of the physical and dermatologic exam was unremarkable.

Day 140 - Problem Assessment: Problem #1: Panniculitis due to atypical mycobacterial infection –continued improvement.

Day 140 – Diagnostic Plan: As the patient continued to show progressive improvement in the lesion with no signs suggestive of systemic disease, no diagnostics were performed this day.

Day 140 – Treatment Plan: The clarithromycin was continued at 250mg - 1.5 tablets PO q12hr. The owner was reminded to not stop before recheck. Recheck was planned for 6 weeks as long as the patient continued to show clinical improvement. The owner was again advised to call if new draining tracts formed or if the areas of swelling became more notable.

Day 184 – History: The patient continued to improve and was still receiving clarithromycin. The owner felt the lesion appeared healed.

Day 184 - Physical/Dermatologic Exam: BAHR, Weight 40.1kg. The area of SQ swelling was almost completely resolved. The cranial portion was completely flush with the skin with no thickening of the SQ tissue. The caudal portion had very, very subtle SQ thickening felt.

Day 184 - Problem Assessment: Problem #1: Panniculitis due to atypical mycobacterial infection – resolved, or almost entirely resolved, with medical therapy alone. Very optimistic that surgical intervention would not be required in this patient.

Day 184 – Diagnostic Plan: A fine needle aspirate was collected from the remaining area of suspected SQ thickening to determine if any inflammatory cells could be observed to support remaining infection (Appendix 19).

Day 184 – Interpretation of Test Results: No inflammatory cells were seen on the cytology samples suggesting the area was not due to the infection, or if any infection remained it was minimal.

Day 184 – Treatment Plan: Given the good clinical response, the hope at this point was the patient's mycobacterial infection could be resolved with medical therapy alone. The infection/lesion on this day appeared almost, if not, completely healed. The patient would be kept on the clarithromycin for an additional 4 weeks and then the medication would be discontinued. The patient would be rechecked in 7-8 weeks (about 1 month after finishing the antibiotic.) The owner was advised to call immediately if any relapse was noted.

Day 216 – Phone Consult: Spoke with owner to see how the patient was doing. The owner reported the patient was off the oral antibiotic and seemed to be doing well. He could appreciate no abnormalities with the lesion. The owner had no questions or concerns and was planning to recheck as previously directed.

Day 243 – History: The patient had been off the clarithromycin for a little over 4 weeks with no evidence of relapse seen. The owner felt the affected area appeared completely healed.

Day 243 – Physical/Dermatologic Exam: QAHR, 39.5kg. Physical exam was within normal limits. Aside from the remaining scar, the site of the infection appeared normal on visual exam.

There were no open tracts or visibly raised areas present suggesting persisting infection. In addition, the area felt normal on palpation with even the mild area of SQ thickening felt at the last visit no longer appreciable.

Day 243 - Problem Assessment: Problem #1: Panniculitis due to atypical mycobacterial infection –Resolved. The infection was considered cured given there were no signs of infection returning despite the patient being off the antibiotic for over a month.

Day 243 – Diagnostic Plan: No diagnostics were performed this day.

Day 243 – Treatment Plan: The owner was advised to continue monitoring the area for any returning swelling, SQ thickening or drainage and to call if seen. Otherwise, the patient was considered cured, further rechecks would be on an as needed basis.

Day 301 – Phone Update: Spoke with the owner regarding an update on the patient. He reported the patient continued to do well. The area of the infection continued to appear unaffected and he had even noted that fur was regrowing over the site of the scar. The patient's general status (attitude, appetite, activity level) also continued to remain normal.

Summary

Mycobacteria are aerobic, non-spore-forming, non-motile bacteria with cell walls rich in lipids and waxes.[3,15] They are generally classified based on their culture characteristics with those that are easy and rapid-growing (RGM) associated with "atypical" or "opportunistic" mycobacterial skin infections.[3] The mycobacterial species in the RGM group have been further divided into the *Mycobacterium fortuitum* group, the *M. cheloneae/abscessus* group, and the *M. smegmatis* group. Although the laboratory was unable to identify the mycobacterial species affecting the patient in this report the *M. fortuitum* and *smegmatis* groups are most commonly isolated in the U.S.[17,27] Initially, infections caused by RGM were thought to be more common in tropical and

sub-tropical climates, but cases have now also been reported in temperate regions[30], highlighting the importance that all veterinary practitioners, irregardless of locale, should be well-educated in the recognition, diagnosis and therapy for this type of infection.

The RGM are recognized as causing panniculitis in cats and dogs. The bacteria are ubiquitous environmental saprophytes [27,29], and infection is thought to follow some form of traumatic introduction into the lipid-rich subcutaneous tissues[30]. The patient in this report had a history of known trauma (leading to a non-healing wound) which contributed to the initial suspicions this type of infection could be present.

The prognosis for RGM infection is guarded for several reasons. One, the bacteria are frequently resistant to numerous antibiotics, limiting therapeutic options[17,34,35]. Two, medical therapy typically must be maintained for an extended period which is heavily dependent upon owner compliance. The patient in this report was on the clarithromycin for approximately 23 wks (5.5-6 months) before his infection was considered resolved. Fortunately, his owner was conscientious about ensuring he received his medications as directed, which profoundly impacted the success of the patient's treatment. And three, not all infections will resolve with medical therapy alone, but also require surgical resection (en bloc) of any persistently infected tissue. This may not always be feasible depending on the location and extent of the infection.

Atypical mycobacterial infections have been reported relatively frequently in cats[29,30,31,32], but the number of documented canine cases are much fewer. [27,33,34,36] Although there are fewer reports in dogs, the general consensus is their infections tend to exhibit a more complete and rapid response than what is seen in cats.[17,33] This patient followed that trend in that his infection did respond readily and completely to oral antibiotic therapy.

Because atypical mycobacterial infections can closely resemble sterile forms of (pyo)granumolatous disease, it is imperative to give consideration to and adequately test for this type of infection when working up these cases. Generally, references will state diagnosis should be based upon history, physical exam, and diagnostics consisting of cytology, histopathology and tissue cultures (aerobic and anaerobic bacterial, mycobacterial and fungal).[1,15] However, even with this approach, newer studies assessing additional tests such as PCR and immunohistochemistry have shown there have been cases of infections associated with mycobacteria that have been misdiagnosed as "sterile" granulomatous disease when traditional diagnostics were used alone.[15] Thus, even with adequate suspicion, diagnosis of RGM infections can be difficult. Fortunately, with the patient in this report, traditional diagnostics were sufficient to identify the infection.

On a final note, because of the MRSP grown on culture, this patient was placed upon a sulfa-containing antibiotic which was very likely the source of his hepatopathy. TMS antibiotics are recognized for their potential to induce a number of idiosyncratic (aka hypersensitivity) reactions including hepatopathies consisting of hepatic necrosis and/or hepatitis with cholestasis.[23,24] These reactions, particularly those resulting in necrosis, can be fatal and close monitoring for early detection of abnormalities is critical when utilizing TMS antibiotics. Unfortunately, with the advent of MRSP infections, clinicians are sometimes left with few other preferable choices for therapy. Fortunately for this patient, the medication was quickly discontinued once signs were observed and he recovered uneventfully from the insult. Given the quick improvement in clinical signs and liver values it is suspected this patient experienced the reversible cholestatic hepatitis versus true hepatic necrosis.

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Appendices:

Appendix 1: Day -42 Culture and Sensitivity
Sample Source: Skin - wound
Organism(s): Light growth *Staphylococcus pseudintermedius*

Antibiotic	(µg/ml) MIC	Interpretation
Amoxi/Clav Acid	*	S
Amoxicillin	*	S
Ceftiofur	*	S
Chloramphenicol	*	S
Clindamycin	*	S
Enrofloxacin	*	S
Erythromycin	*	S
Gentamicin	*	S
Oxacillin	*	S
Penicillin	*	S
Tetracycline	*	S
Trimethoprim/Sulfa	*	S
Amikacin	*	S
Marbofloxacin	*	S
Cefpodoxime	*	S
Ampicillin	*	S

Note: "*" denotes no value reported by the lab.

Appendix 2: Day -8 Bloodwork

Chemistry	Results	Ref. Range	Units
ALP	56	23-212	IU/L
ALT	93	10-100	IU/L
Amylase	1012	500-1500	IU/L
Albumin	3.1	2.3-4.0	g/dL
Total Protein	7.2	5.2-8.2	g/dL
Globulin	4.1	2.5-4.5	g/dL
Total Bilirubin	0.5	0.0-0.9	mg/dL
BUN	12	7-27	mg/dL
Creatinine	1.6	0.5-1.8	mg/dL
Cholesterol	231	110-320	mg/dL
Glucose	124	74-143	mg/dL
Calcium	10.7	7.9-12.0	mg/dL
Phosphorus	3.8	2.5-6.8	mg/dL
Chloride	119	109-122	mEq/L
Potassium	4.6	3.5-5.8	mEq/L
Sodium	156	144-160	mEq/L

No significant hemolysis or lipemia reported.

CBC

WBC	9.13	5.5-16.9	$10^3/\mu L$
RBC	7.28	5.5-8.5	$10^6/\mu L$
HGB	18.0	12-18	g/dL
HCT	46.8	37-55	%
MCV	64.3	60-77	fL
MCH	24.9	18.5-30	pg
MCHC	37.0	30-37.5	g/dL
%Retic	0.3		%
Retic	23.9		$10^3/\mu L$
Neutrophil Seg	69.8	60-77	%
Lymphocytes	19.3	12-30	%
Monocytes	6.1	3-10	%
Eosinophils	4.5	2-10	%
Basophils	0.2	0-1	%
Platelets	200	175-500	$10^3/\mu L$
Absolute Neut Seg	6.38	2.0-12.0	$10^3/\mu L$
Absolute Lymphocyte	1.76	0.6-4.9	$10^3/\mu L$
Absolute Monocyte	0.56	0.3-2.0	$10^3/\mu L$
Absolute Eosinophil	0.42	0.1-1.49	$10^3/\mu L$
Absolute Basophil	0.02	0-0.10	$10^3/\mu L$

Appendix 3: Day 0 Cytology

All cytology samples revealed similar findings consisting of TNTC neutrophils and macrophages with lesser numbers of plasma cells and lymphocytes. No discrete infectious agents were observed.
(DipQuick® stain; 10x and oil immersion/100x)

Appendix 4: Day 0 Wood's Lamp

No fluorescence was observed.

Appendix 5: Day 2 Post-Biopsy Care Instructions

The owner was instructed to refrain from bathing for 7 days to allow the sites to heal. The sites could be cleaned with hydrogen peroxide if any oozing or crusting was noted. The location of the sites made it unlikely the patient could reach them with his mouth, but if it at all appeared as though the patient was traumatizing the sites with his mouth he would need to wear an e-collar. The sutures could be removed in 10-14 days.

Appendix 6: Day 9 Histopathology Results

Source: 2 skin biopsies 1 cm- all tissue processed.

Microscopic description: There is epidermal acanthosis and hyperkeratosis. There is mild dermal fibroplasia and neovascularization with multifocal adnexal atrophy. In the deeper subcuticular elements there is rarefaction and cavitation surrounded by dense fibrous connective tissue peripherally. The focus of rarefaction is filled in with smudge eosinophilic material

interspersed with viable and degenerate inflammatory cells. There are large numbers of lymphocytes, plasma cells and macrophages with lesser numbers of neutrophils.

Microscopic Findings: Panniculitis, cavitating, necrotizing, neutrophilic, granulomatous with peripheral fibroplasia and neovascularization.

Comments: There is no evidence of neoplasia. No parasitic or fungal agents observed on routinely stained sections. A distinct foreign body is not visualized.

Special Stains: Acid fast and fungal stains are negative.

*There was a second opinion requested on this report to confirm the changes were consistent with panniculitis. (The original report was not read-out by one of the requested pathologists). This second pathologist suggested because of the eosinophilic necrotic and degenerative stroma, that trauma-induced panniculitis secondary to stromal necrosis would be a consideration.

Appendix 7: Day 9 Aerobic and Anaerobic Culture and Sensitivity

Sample Source: Skin (tissue)

Organisms: *Staphylococcus pseudintermedius* – very scant growth (4 colonies)
Isolate resistant to oxacillin and therefore is METHICILLIN RESISTANT
No obligate anaerobes isolated.

Organism #1: *Staphylococcus pseudintermedius* - methicillin resistant

Antibiotic	**(µg/ml) MIC**	**Interpretation**
Amoxi/Clav Acid	>=8	R
Azithromycin	>4	R
Ampicillin	>8	R
Cefazolin	16	R
Cefotaxime	>32	R
Cephalothin	<=8	R
Cefpodoxime	*	R
Chloramphenicol	<=8	S
Ciprofloxacin	>2	R
Clindamycin	>2	R
Erythromycin	>4	R
Enrofloxacin	*	R
Gatifloxacin	<=2	R
Gentamicin	>8	R
Imipenem	>8	R
Marbofloxacin	*	R
Moxifloxacin	*	I
Oxacillin	>2	R
Penicillin G	>8	R
Rifampin	<=1	S
Tetracycline	>4	R
Trimethoprim/Sulfa	<=2/38	S

Vancomycin	<2	S

Note: "*" denotes no value reported by the lab.

Appendix 8: Day 9 Methicillin Resistant Staphylococcus Risk Control Recommendations

The owner was advised that with this being the canine adapted strain of staphylococcus the risk of it causing infection in immunocompetent adults was low. However, the owner was advised to limit contact between the patient and higher-risk individuals (the very young, elderly and anyone else otherwise immune-compromised). Additionally, the owner was advised to avoid direct contact with the patient's wounds and to wear gloves and/or wash hands thoroughly with soap and water after each interaction.

Appendix 9: Day 22 Bloodwork

Chemistry	**Results**	**Ref. Range**	**Units**	
ALP	**513**	**10-150**	**IU/L**	**HIGH**
ALT	**1572**	**10-100**	**IU/L**	**HIGH**
AST	**110**	**5-55**	**IU/L**	**HIGH**
GGT	**70**	**0-14**	**IU/L**	**HIGH**
Amylase	1100	500-1500	IU/L	
Lipase	457	100-750	IU/L	
Albumin	3.0	2.3-4.0	g/dL	
Total Protein	7.3	5.2-8.2	g/dL	
Globulin	4.3	2.5-4.5	g/dL	
Total Bilirubin	0.2	0.0-0.9	mg/dL	
Direct Bilirubin	0.1	0.0-0.2	mg/dL	
BUN	15	7-27	mg/dL	
Creatinine	1.2	0.5-1.8	mg/dL	
Cholesterol	303	110-320	mg/dL	
CK	189	10-200	IU/L	
Glucose	102	74-143	mg/dL	
Calcium	9.4	7.9-12.0	mg/dL	
Phosphorus	5.4	2.5-6.8	mg/dL	
Chloride	107	109-122	mEq/L	
Potassium	4.6	3.5-5.8	mEq/L	
Sodium	144	144-160	mEq/L	

No significant hemolysis or lipemia reported.

CBC			
WBC	10.6	5.5-16.9	$10^3/\mu L$
RBC	8.19	5.5-8.5	$10^6/\mu L$
HGB	18.0	12-18	g/dL
HCT	53.6	37-55	%
MCV	65	60-77	fL
MCH	23.3	18.5-30	pg
MCHC	35.6	30-37.5	g/dL
Neutrophil Seg	76	60-77	%
Lymphocytes	17	12-30	%

Monocytes	3	3-10	%
Eosinophils	4	2-10	%
Basophils	0	0-1	%
Platelets	**93**	**175-500**	**10^3/µL**
Absolute Neut Seg	8268	3000-11500	10^3/µL
Absolute Lymphocyte	1696	1000-4800	10^3/µL
Absolute Monocyte	318	150-1350	10^3/µL
Absolute Eosinophil	424	100-1250	10^3/µL
Absolute Basophil	0	0-100	10^3/µL

Platelet comments: Scanning of the blood smear revealed adequate platelet numbers. Due to clumping and/or large platelets the automated platelet number cannot be accurately determined.

Appendix 10: Day 28 Fungal Culture Results
Sample Source: Skin (tissue)
Result: No growth.

Appendix 11: Day 28 Mycobacterial Culture Results
Sample Source: Skin (tissue)
Result: Growth of Atypical Mycobacterial Sp.

Appendix 12: Day 28 Cytology
Cytology revealed neutrophils and macrophages. No cocci bacteria were seen.
(DipQuick® stain; 10x and oil immersion/100x)

Appendix 13: Day 28 Bloodwork

Chemistry	**Results**	**Ref. Range**	**Units**	
ALP	**151**	**10-150**	**IU/L**	**HIGH**
ALT	**201**	**10-100**	**IU/L**	**HIGH**
AST	29	5-55	IU/L	
GGT	**28**	**0-14**	**IU/L**	**HIGH**
Amylase	1105	500-1500	IU/L	
Lipase	436	100-750	IU/L	
Albumin	3.2	2.3-4.0	g/dL	
Total Protein	7.0	5.2-8.2	g/dL	
Globulin	3.8	2.5-4.5	g/dL	
Total Bilirubin	0.0	0.0-0.9	mg/dL	
Direct Bilirubin	0.0	0.0-0.2	mg/dL	
BUN	14	7-27	mg/dL	
Creatinine	1.2	0.5-1.8	mg/dL	
Cholesterol	300	110-320	mg/dL	
CK	170	10-200	IU/L	
Glucose	100	74-143	mg/dL	
Calcium	9.2	7.9-12.0	mg/dL	
Phosphorus	5.5	2.5-6.8	mg/dL	
Chloride	104	109-122	mEq/L	
Potassium	4.5	3.5-5.8	mEq/L	

Sodium	154	144-160	mEq/L

No significant hemolysis or lipemia reported.

CBC

WBC	9.8	5.5-16.9	$10^3/\mu L$
RBC	8.13	5.5-8.5	$10^6/\mu L$
HGB	17.5	12-18	g/dL
HCT	52.1	37-55	%
MCV	65	60-77	fL
MCH	24.3	18.5-30	pg
MCHC	35.4	30-37.5	g/dL
Neutrophil Seg	72	60-77	%
Lymphocytes	19	12-30	%
Monocytes	5	3-10	%
Eosinophils	4	2-10	%
Basophils	0	0-1	%
Platelets	203	175-500	$10^3/\mu L$
Absolute Neut Seg	7056	3000-11500	$10^3/\mu L$
Absolute Lymphocyte	1862	1000-4800	$10^3/\mu L$
Absolute Monocyte	490	150-1350	$10^3/\mu L$
Absolute Eosinophil	392	100-1250	$10^3/\mu L$
Absolute Basophil	0	0-100	$10^3/\mu L$

Appendix 14: Day 28 SST results

OD: 16mm/min
OS: 18 mm/min

Appendix 15: Day 31 Aerobic Culture and Sensitivity

Sample Source: Skin (swab)
Results: No bacteria isolated.

Appendix 16: Day 40 Mycobacterial Identification and Sensitivity Panel

Specimen Source: skin
Medium Submitted: LJ Slant Culture
Identification: Mycobacterium sp Runyon group IV (unable to identify further without special testing)

Antibiotic	(µg/ml) MIC	Interpretation
Amikacin	16	S
Kanamycin	<=8	S
Tobramycin	>16	R
Gentamicin	16	R
Cefoxitin	<=16	S
Ceftriaxone	>64	R
Cefepime	>32	R
Cefotaxime	64	R
Imipenem	8	I

Ciprofloxacin	>8	R
Doxycycline	16	R
Minocycline	4	I
Moxifloxacin	>4	R
Tigecycline	<=0.25	S
Clarithromycin	<=0.25	S
Azithromycin	<=16	S
Augmentin	>32/16	R
Trimethoprim/Sulfa	>4/76	R
Linezolid	8	I
Doripenem	16	R

Appendix 17: Day 44 Bloodwork

Chemistry	**Results**	**Ref. Range**	**Units**	
ALP	62	10-150	IU/L	
ALT	**156**	**10-100**	**IU/L**	**HIGH**
AST	29	5-55	IU/L	
GGT	**17**	**0-14**	**IU/L**	**HIGH**
Amylase	1201	500-1500	IU/L	
Lipase	453	100-750	IU/L	
Albumin	3.3	2.3-4.0	g/dL	
Total Protein	6.6	5.2-8.2	g/dL	
Globulin	3.3	2.5-4.5	g/dL	
Total Bilirubin	0.0	0.0-0.9	mg/dL	
Direct Bilirubin	0.0	0.0-0.2	mg/dL	
BUN	13	7-27	mg/dL	
Creatinine	1.1	0.5-1.8	mg/dL	
Cholesterol	284	110-320	mg/dL	
CK	78	10-200	IU/L	
Glucose	82	74-143	mg/dL	
Calcium	8.9	7.9-12.0	mg/dL	
Phosphorus	5.3	2.5-6.8	mg/dL	
Chloride	102	109-122	mEq/L	
Potassium	4.6	3.5-5.8	mEq/L	
Sodium	153	144-160	mEq/L	

No significant hemolysis or lipemia reported.

CBC			
WBC	10.8	5.5-16.9	$10^3/\mu L$
RBC	6.8	5.5-8.5	$10^6/\mu L$
HGB	15.8	12-18	g/dL
HCT	45	37-55	%
MCV	66	60-77	fL
MCH	23.4	18.5-30	pg
MCHC	36	30-37.5	g/dL
Neutrophil Seg	66	60-77	%

Lymphocytes	26	12-30	%
Monocytes	4	3-10	%
Eosinophils	4	2-10	%
Basophils	0	0-1	%
Platelets	382	175-500	$10^3/\mu L$
Absolute Neut Seg	7128	3000-11500	$10^3/\mu L$
Absolute Lymphocyte	2808	1000-4800	$10^3/\mu L$
Absolute Monocyte	432	150-1350	$10^3/\mu L$
Absolute Eosinophil	432	100-1250	$10^3/\mu L$
Absolute Basophil	0	0-100	$10^3/\mu L$

Appendix 18: Day 85 Bloodwork

Chemistry	**Results**	**Ref. Range**	**Units**
ALP	41	10-150	IU/L
ALT	44	10-100	IU/L
AST	16	5-55	IU/L
GGT	4	0-14	IU/L
Amylase	1059	500-1500	IU/L
Lipase	352	100-750	IU/L
Albumin	3.1	2.3-4.0	g/dL
Total Protein	6.2	5.2-8.2	g/dL
Globulin	3.1	2.5-4.5	g/dL
Total Bilirubin	0.1	0.0-0.9	mg/dL
Direct Bilirubin	0.1	0.0-0.2	mg/dL
BUN	14	7-27	mg/dL
Creatinine	1.0	0.5-1.8	mg/dL
Cholesterol	229	110-320	mg/dL
CK	70	10-200	IU/L
Glucose	103	74-143	mg/dL
Calcium	9.2	7.9-12.0	mg/dL
Phosphorus	5.5	2.5-6.8	mg/dL
Chloride	105	109-122	mEq/L
Potassium	4.5	3.5-5.8	mEq/L
Sodium	150	144-160	mEq/L

No significant hemolysis or lipemia reported.

CBC			
WBC	10.6	5.5-16.9	$10^3/\mu L$
RBC	6.4	5.5-8.5	$10^6/\mu L$
HGB	15.4	12-18	g/dL
HCT	43	37-55	%
MCV	67	60-77	fL
MCH	23.9	18.5-30	pg
MCHC	36	30-37.5	g/dL
Neutrophil Seg	64	60-77	%
Lymphocytes	25	12-30	%

Monocytes	6	3-10	%
Eosinophils	5	2-10	%
Basophils	0	0-1	%
Platelets	215	175-500	$10^3/\mu L$
Absolute Neut Seg	6784	3000-11500	$10^3/\mu L$
Absolute Lymphocyte	2650	1000-4800	$10^3/\mu L$
Absolute Monocyte	636	150-1350	$10^3/\mu L$
Absolute Eosinophil	530	100-1250	$10^3/\mu L$
Absolute Basophil	0	0-100	$10^3/\mu L$

Appendix 19: Day 184 FNA - Cytology

The aspirated material consisted of lipid material and small numbers of lipocytes. No inflammatory cells or infectious organisms were seen.
(DipQuick® stain; 10x and oil immersion/100x)

Reviewers' comments:

The comments are separated into major points and detailed comments. Major points are those affecting the overall diagnosis and management of the case or the general presentation of the information. The detail comment focus on the details of the text, such as spelling and grammatical errors, appropriately marked abnormal lab values, etc. or specific decisions made on specific visit and don't always impact the grading of the case as a whole. These are included in order to provide a complete and thorough evaluation of the work submitted. The comments are in no particular order and represent a compilation of comments from all reviewers; therefore, at times there were will be multiple comments about the same issue, and those comments will not always agree.

Major points:

- Case was approached with thorough diagnostics and well managed. Not sure that it proved to be a therapeutic challenge to resident, but mycobacteiral infections are uncommon and likely the whole case was a challenge to resident and great learning opportunity.
- Overall a very simple, but well worked up case. Problems written up thoroughly and concisely
- Not much of a therapeutic challenge, but again thorough
- Would have liked to see discussion of significance of negative acid-fast staining
- In general a more simple case report in terms that this was not a serious diagnostic or therapeutic challenge, but it is a case not commonly encountered, and this was very well written and well thought through. Great job!

Detailed points:

- Avoid use of familiar language, ex "pretty much"
- Would like to have seen discussion of sensitivity to acid fast staining diagnosing mycobacterial infections as it was negative in this case
- When one reviewer uses TMS, they monitor STT, CBC, Chem every 2 weeks
- Colloquial language
- An important part of a dermatology history is to ask and note in the record whether owners had any skin lesions.
- May be good to mention to the reviewers and to the owners if there is or is not any zoonotic concern to them or any concern to the other dog in the house.
- Consider using dexdomitor instead of xylazine for sedation, as dexdomitor is more selective for receptors and has less cardiac depressive effects.
- Would like to see a little more discussion about the negative acid fast stain on histopathology.
- When TMS may be needed long-term, consider recommending to the owners to check cbc/chem q 2-4 weeks, also consider checking STT pre-treatment and during treatment.

THE FOLLOWING IS A REPORT THAT DID NOT PASS AFTER FIRST SUBMISSION – THE COMMENTS THE RESIDENT RECEIVED ARE FOUND AT THE END OF THIS REPORT. FOLLOWING THAT ARE THE RESIDENT'S REBUTTAL AND REVISED CASE REPORT (THIS IS A REPORT IN WHICH A LOT OF FORMATTING CHANGES OCCURRED WHEN THIS DOCUMENT WAS GENERATED)

FLEA ALLERGY DERMATITIS, SUPERFICIAL PYODERMA, BACTERIAL PODODERMATITIS, FURUNCULOSIS OF THE CHIN, CUTANEOUS ADVERSE FOOD REACTION, MALASSEZIA PODODERMATITIS AND ATOPIC DERMATITIS IN A FAWN GERMAN SHEPHARD, BELGIUM MALINOIS MIXED BREED DOG

Signalment: 19 month old, female spayed, fawn, German Shepherd/Belgian Malinois mixed breed dog, weighing 25.7kg.

Day O: History: The dog presented for evaluation of chronic pruritus of nine months duration. The dog was acquired from a local animal shelter at 10 months of age. There was no known history of skin disease prior to adoption. At the time of adoption the owners reported the dog had complete alopecia of the tail base and patchy alopecia of the caudal dorsum. The owners also reported that the alopecia resolved several months later. According to the owner, the pruritus was originally localized on the back end of the body, caudal thighs and tail base. At the time of presentation the dog was also observed to be "corn-cobbing" its forelimbs, rubbing its face on the carpet, and scratching under its axillae. The owners also reported that the dog continued to lick its inguinal region and caudal thighs, but much less than at the time of adoption. The owners gave the dog a score of 7.5 out of 10 on a pruritic scale. The owners were unable to determine any seasonality associated with the dog's pruritus.

According to available medical records, the dog had received Benadryl® (McNeil; diphenhydramine) at 0.5mg/kg two to three times a day for three weeks with no perceived benefit. The dog was then switched to Chlor-Trimeton® (Schering-Plough; chlorphenaramine) at 0.32mg/kg twice daily for three weeks, also without observed benefit. The dog was treated with Keflex® (Eli Lily; cephalexin) at 20mg/kg twice daily for two weeks for a superficial pyoderma with little improvement in the pruritus. The dog had been bathed with Chlorhexiderm® shampoo (DVM, 2% chlorhexidine) every 2 weeks with no reported decrease in pruritus. A diet trial using Hills® Prescription Diet d/d Canine Skin Support Potato and Duck had been attempted for 6 weeks, but the dog had continued to receive treats and flavored medications. The owners did not appreciate a decrease in pruritus during the diet trial.

At the time of presentation, the dog was receiving monthly heartworm prevention (Heartgard®, ivermectin, Merial) and monthly topical flea control (Frontline Plus®, fipronil, smethoprene;
Merial). The owners were bathing the dog every two weeks with Chlorhexiderm® shampoo and Resicort® Leave-On Conditioner (Virbac, 1% hydrocortisone). The dog had last received antibiotics four months prior to presentation. The dog's current diet consisted of Natural Balance® Duck and Potato Formula with occasional Milkbone® Dog Biscuits.
The owners reported that the dog was mostly indoors but did spend time in an outdoor dog run. The dog was reported to go to a dog park three times weekly and was walked within the neighborhood once daily. Other pets within the household included a guinea pig and a fish. The dog was reported to have minimal contact with the guinea pig. The guinea pig did not have any reported medical or dermatologic problems. The owners reported the dog did have regular contact with the neighbor's dog which was reported to be healthy and without any dermatologic disease. The owners reported having never seen fleas on the dog. The dog had no history of polyuria/polydipsia, coughing, sneezing, vomiting or diarrhea and was current on DHLPP and rabies vaccinations.
Day 0: Physical Exam: The examination revealed a bright, alert and responsive dog. The dog had a body condition score of 5/9. All vital signs were within normal limits. Thoracic auscultation was unremarkable, and pulses were strong and synchronous. Ophthalmologic examination was unremarkable. Examination of the oral cavity revealed pink, moist, mucus membranes with a normal capillary refill time and no dental calculi. Abdominal palpation was within normal limits. Palpation of superficial lymph nodes was unremarkable.
Dermatologic examination revealed numerous papules and moderate erythema extending

from the caudal dorsum to the tail base and involving the caudal thighs. There were multiple crusted papules and epidermal collarettes throughout the inguinal region. Axillae were moderately erythematous with evident excoriations. Mild erythema and salivary staining were noted in the interdigital webbing and on the palmar/plantar aspects of all four paws. Mild salivary staining was noted on the antebrachiae. Otoscopic examination was unremarkable. There was no erythema or swelling of the otic canals and both canals were pliable and nonpainful

when palpated externally. Tympanic membranes were visible and intact in both otic canals.

Day 0: Assessment: The problem list included: 1) pruritus, 2) papules and erythema of the caudal dorsum and tail base, 3) crusted papules and epidermal collarettes throughout the inguinal region and, 4) salivary staining and erythema of the thoracic limbs and interdigital webbing of all four paws.

The differential diagnoses considered for problem 1, pruritus, included allergic skin disease including atopic dermatitis (AD), cutaneous adverse food reaction (CAFR), and flea allergy dermatitis (FAD). Secondary bacterial or *Malassezia* infection were also considered as differential diagnoses that were possibly contributing to the development of pruritus. Ectoparasitism such as demodicosis, cheyletiellosis or sarcoptic acariasis was also considered.

The differential diagnoses for problem 2 included FAD with secondary bacterial or *Malassezia* dermatitis. AD and CAFR were considered less likely differentials due to the caudal distribution of the lesions. As in problem 1, ectoparasitism was also considered.

The differential diagnoses for problem 3 included a superficial pyoderma secondary to a primary pruritic process such as FAD, CAFR, or AD.

The differential diagnoses for problem 4 included self-trauma secondary to pruritus from either a primary hypersensitivity disease such as AD or CAFR and/or due to a *Malassezia* or bacterial dermatitis/pododermatitis[ii] [iii] Lastly, a contact reaction was considered as a possible differential, but deemed less likely.

Day 0: Diagnostic Plan: Acetate tape preparations were taken from the caudal dorsal trunk, inguinal region, interdigital spaces and palmar aspects of all four paws to evaluate for the presence of bacteria or *Malassezia* (Appendix 1). A flea comb was passed through the hair coat on the caudal dorsum near the tail base (Appendix 2). A deep skin scraping was performed to rule out demodicosis (Appendix 3). Multiple broad superficial skin scrapings were performed to rule out a *Sarcoptes* infestation (Appendix 4). An acetate tape preparation was performed to look for the presence of *Cheyletiella* (Appendix 5).

Day 0: Interpretation of Results: Skin cytology was consistent with a superficial pyoderma due to the presence of cocci-shaped bacteria and degenerate neutrophils. These two concurrent findings satisfy the cytologic definition of pyoderma in the canine patient[iv]. There were also cocci-shaped bacteria found in the interdigital webbing of all four paws making bacterial pododermatitis a contributing factor to the dog's overall pruritus.

Given the past history of severe caudal dorsal and tail base alopecia in conjunction with the current caudal dorsal distribution, a diagnosis of flea allergy dermatitis with secondary superficial pyoderma was made[v].

Because the paws, face, thoracic limbs, and axillae were also affected, AD and/or CAFR were also suspected to play a role in the development of the dog's pruritus and bacterial pododermatitis.

Day 0: Treatment Plan: As FAD was considered a likely diagnosis in this case, stringent flea

control using Capstar® (Novartis; nitenpyram) at 57 mg (0.45 mg/kg) PO once daily was prescribed to minimize exposure to flea salivary antigens. Daily Capstar® was the preferred treatment because it has been shown to have 99.1% efficacy within 3 hours against adult *Ctenocephalides felis* in canine patients[vi]. Capstar® has also been shown to diminish or eliminate exposure to allergenic proteins in the saliva of biting fleas as its speed of adulticidal activity is as rapid as thirty minutes[vii]. Oral flea control was also chosen due to the owner's desire to continue frequent bathing, which had the potential to make topical flea control administration less efficacious. The owners were instructed to discontinue the use of Frontline Plus®.

Cephalexin at 29.1mg/kg every 12 hours was prescribed to treat the superficial pyoderma. Cephalexin was chosen because it has broad antimicrobial activity and a good safety profile[viii]. The owners were also instructed to continue bathing with Chlorhexiderm® shampoo, but to increase the frequency to once weekly to reduce the bacterial numbers present on the skin surface.

An elimination diet trial was initiated, in order to evaluate the possibility that CAFR contributed to the dog's pedal, facial and axillary pruritus and the development of a superficial pyoderma. An extensive diet history was obtained from the owner prior to selecting the elimination diet. The dog had previously eaten duck, venison, chicken and beef based diets. The owners were instructed to transition the dog onto Iams® Response KO (kangaroo and oat) diet over a 3-4 day period. This diet was chosen based on a review of the dog's diet history, the need for a dry kibble diet, and because the owners were unwilling to perform a home-cooked diet trial. The owners were informed that the minimum length of time to utilize a strict limited antigen diet was 10-12 weeks[ix]. Day 1 of the 10 week diet trial would begin when the dog was eating solely

the new diet. The owners were instructed to feed only this diet and no other supplements, treats, or flavored medications. The owners were given written and verbal instructions that the only food to be fed during the diet trial was the prescription diet, and cooked plain oats mixed with water could be used as treats. They were also given a diary to record food offered, accidental ingestion of foodstuffs, and changes in activity, behavior or fecal output. Because the patient had been receiving Heartgard® (Merial) flavored heartworm tablets, Heartgard® unflavored tablets for monthly heartworm prevention were prescribed. The owners were instructed to give the cephalexin in the homemade oats.

The owners were instructed to make a follow-up appointment in 30 days in order to evaluate response to treatment.

Day 7: Telephone Update: The owners called to say they had successfully transitioned the dog onto the KO diet but they were having difficulty administering the cephalexin capsules in homemade oatmeal. The owners were given verbal instructions on how to administer the capsules directly into the back of their dog's mouth. If this continued to be a problem, the owners were instructed to call back and an alternative antibiotic would be attempted.

Day 37: Recheck: History: The dog was receiving all medications as directed and the owners did not report any adverse events related to the medications. The owners were able to administer the antibiotic directly into the dog's mouth without a problem and the dog had finished its full course of cephalexin 7 days prior to the recheck appointment. The owners reported that the dog's pruritus decreased from 7.5 out of 10 on a pruritic scale to a 5 out of 10. The owners noted that the dog was licking its inguinal area less frequently and was no longer biting at its tail base. They felt the "corn cobbing" of its forelimbs and licking of its paws was relatively unchanged. The owners reported being consistent with the food trial, and the dog had received no other food

items.

Day 37: Physical Exam: The general physical exam was relatively unchanged from day 0. All vital signs were within normal limits. The dog weighed 26.0 kg. Dermatologic examination revealed mild erythema from the caudal dorsum to the tail base and also involving the caudal thighs. There were 4 circular areas of hyperpigmentation on the ventrum. There were two nodules and moderate erythema noted on the ventral chin. Axillae were moderately erythematous but no excoriations were present. The mild erythema and salivary staining in the interdigital webbing and on the palmar/plantar aspects of all four paws was unchanged from the previous exam. Mild salivary staining on the medial aspect of the thoracic limbs was also unchanged from the previous exam. Otoscopic examination was unremarkable. There was no erythema or swelling of the otic canals and both canals were pliable and non-painful when palpated externally. Tympanic membranes were intact in both ear canals.

Day 37: Assessment: The pruritus, papules, and epidermal collarettes involving the caudal dorsum and inguinal region (problems 1, 2, and 3) had improved suggesting a response to initiation of strict flea control and antibiotic therapy. The four areas of hyperpigmentation were attributed to post-inflammatory hyperpigmentation secondary to the resolution of the epidermal collarettes. Problem 4, however, remained unchanged. This was attributed to insufficient time for the bacterial pododermatitis to resolve, the possible development of *Malassezia* dermatitis/pododermatitis or pruritus associated with underlying allergic dermatitis (CAFR or AD) that had not yet been fully addressed. A new problem of nodules on the ventral chin was added to the problem list (problem 5). Differentials for problem 5 included a bacterial folliculitis/furunculosis, demodicosis, or dermatophytosis. If these lesions were bacterial in nature, Problem 5 was considered likely to be secondary to an underlying allergic dermatitis

(CAFR or AD) causing pruritus, with secondary self-trauma likely leading to folliculitis/furunculosis.

Day 37: Diagnostic Plan: Acetate tape preparations were taken from the caudal dorsal trunk, inguinal region, interdigital spaces and palmar/plantar aspect of all four paws to evaluate the presence of bacteria or *Malassezia* (Appendix 6). A flea comb was passed through the hair coat on the caudal dorsum near the tail base (Appendix 7). An acetate tape preparation, hair plucks, and deep skin scrapings were taken from the ventral chin to evaluate for the presence of bacteria, *Malassezia*, dermatophytes and/or demodicosis (Appendix 8).

Day 37: Interpretation of results: Skin cytology showed a dramatic improvement from the previous month as there was no cytologic evidence of the superficial pyoderma or bacterial pododermatitis. There was however, small numbers of bacteria present from samples taken in the area of the nodules of the ventral chin, despite a 30-day course of cephalexin. This was most likely due to continued self-trauma secondary to pruritus which was considered to result from an underlying allergic trigger (CAFR or AD). However, a methicillin resistant *Staphylococcal* infection could have also been a contributing factor.

Day 37: Treatment Plan: As there was no evidence of the superficial pyoderma or bacterial pododermatitis the owners were instructed to discontinue antimicrobial therapy with cephalexin. They were also instructed to decrease bathing with Chlorhexiderm® shampoo to once monthly. In order to address the two presumed furuncles found on the ventral chin a fungal culture was recommended to rule out dermatophytosis, however the owners declined this test. Mupirocin ointment, USP (2% mupirocin) was prescribed. The owners were instructed to apply a thin film to the affected area on the ventral chin twice daily. The owners were informed that if there was no response to mupirocin ointment, then a bacterial culture to rule out an antibiotic resistant

infection would need to be performed. In addition to the mupirocin ointment, a tapering dose of Temaril-P® (Pfizer; trimeprazine tartrate, 5mg and prednisolone, 2mg) was also prescribed to help decrease pruritus and inflammation[x]. The owners were instructed to give 4 tablets (20mg of trimeprazine tartrate, 0.76mg/kg and 8mg prednisolone, 0.3mg/kg) once daily for seven days, then to decrease to 2 tablets (10mg of trimeprazine tartrate, 0.38mg/kg and 4mg prednisolone, 0.15mg/kg) once daily for seven days and finally to 2 tablets every other day for seven days. The owners were instructed to continue the Iams® Response KO diet. They were reminded to feed only this diet with no other supplements, treats or flavored medications. The owners were asked to schedule a recheck appointment in 30 days.

Day 67: Recheck: History: The owners reported giving oral medications as previously directed. The owners had stopped applying mupirocin ointment as they felt the two lesions on the ventral chin had resolved. The owners reported that the dog's pruritus decreased from a 5 out of 10 on a pruritic scale to a 2 out of 10 while receiving the Temaril-P® at 4 tablets (20mg of trimeprazine tartrate, 0.76mg/kg and 8mg prednisolone, 0.3mg/kg) once daily and then increased only slightly at 2 tablets (10mg of trimeprazine tartrate, 0.38mg/kg and 4mg prednisolone, 0.15mg/kg) once daily. The owners gave the dog a score of 3 out of 10 on the pruritic scale while receiving 2 tablets every other day. The dog had completed the prescribed course of Temaril-P® approximately 7 days prior to the recheck and the owners continued to rate the dog's pruritus at a 3-4 out of 10 on the pruritus scale. The owners felt the "corn cobbing" of the dog's forelimbs and licking of its paws were the dog's only areas of pruritus at the time of this recheck. The owners reported being consistent with the food trial however, they did report that the dog found some type of bone on the sidewalk and the owners were unable to retrieve it before it was eaten. The owners were unsure if they noted a subsequent increase in pruritus because it coincided with

a decrease in the Temaril-P.

Day 67: Physical Exam: The general physical exam was relatively unchanged from day 0. All vital signs were within normal limits. The dog weighed 25.9 kg. Dermatologic examination was unremarkable with the exception of mild erythema and salivary staining in the interdigital webbing and on the palmar/plantar aspects of all four paws which was slightly improved from the previous exam. Mild salivary staining was noted on medial aspect of the thoracic limbs and was also unchanged from the previous exam. The two presumed furuncles on the ventral chin noted on the previous exam were no longer present. Otoscopic examination continued to be unremarkable.

Day 67: Assessment: Problems 2, 3 and 5 were resolved. This was likely due to continued use of strict flea control and appropriate treatment for the superficial pyoderma and the presumed muzzle folliculitis/furunculosis. Problem 1 was improved but not resolved. The improvement in pruritus was likely due several factors including, resolution of the superficial pyoderma, strict flea control using Capstar®, and the tapering course of Temaril-P®. There may have also been improvement in the pruritus due to the ongoing novel protein diet but a dietary provocation would need to be performed before a diagnosis of CAFR could be confirmed. Problem 4 remained largely unchanged suggesting the underlying allergic hypersensitivity had yet to be fully defined and managed.

Day 67: Diagnostic Tests: Acetate tape preparations were taken from the interdigital spaces and palmar/plantar aspect of all four paws and from the ventral chin to evaluate the presence of bacteria or *Malassezia* (Appendix 9).

Day 67: Interpretation of Results: Cytology of the paws and ventral chin was unremarkable, leading to the conclusion that the remaining pruritus and erythema were likely due to underlying

allergic dermatitis caused by either CAFR and/or AD. Resolution of the folliculitis/furunculosis of the ventral chin was most likely due to a decrease in self-trauma associated with a decrease in pruritus as well as the use of topical mupirocin ointment. Persistent pruritus localized to the paws and face despite stringent flea control and the absence of secondary infections made CAFR and/or AD highly probable.

Day 67: Treatment Plan: Capstar® (Novartis; nitenpyram) at 57 mg (0.45 mg/kg) PO once daily was continued as the flea control because FAD had been confirmed as a contributing factor for pruritus in this dog. The owners were instructed to continue bathing with Chlorhexiderm® shampoo once monthly. The owners were also instructed to begin dietary provocation using the dog's original diet (Natural Balance® Duck and Potato Formula), treats and any human food the dog had previously consumed. The provocation phase would last for 2 weeks. If increased pruritus was noted, the owners were instructed to return to feeding the Iams® Response KO diet exclusively and to call with an update. The owners were asked to make a recheck appointment in 30 days.

Day 77: Telephone Update: Owners reported an increase in pruritus within 4 days of dietary provocation. They rated the dog a 7 out of 10 on the pruritic scale. They discontinued the Natural Balance® Duck and Potato Formula diet and re-instituted the Iams® Response KO diet. The owners expressed concern over continuing to feed only this diet. A sequential rechallenge of individual protein and carbohydrate sources to attempt to determine the exact cause of pruritus associated with CAFR was discussed. The owner was asked to continue to feed the dog Iams® Response KO diet and add beef, chicken, dairy, eggs, soy, and rice one item at a time for one week in addition to the KO diet. If increased pruritus was noted, the owner was instructed to continue feeding only the KO until the pruritus returned to the pre-rechallenge level. These

ingredients were chosen as they are known sources of allergens in the veterinary literature and had been part of the dogs diet history[xi]. The owners reported that the dog continued to be a 3-4 out of 10 on the pruritus scale despite management of the confirmed CAFR with the strict elimination diet. This persistent pruritus was consistent with a likely diagnosis of atopic dermatitis since FAD and CAFR were being well controlled. Options for diagnosis and treatment of atopic dermatitis including intradermal testing or serum allergy testing with subsequent allergen specific immunotherapy (ASIT), medical management with cyclosporine, and/or corticosteroids were all discussed in great detail with the owner[xii]. Given the young age of this dog, allergy testing and ASIT were strongly recommended.

Day 89: Recheck: History: The owners were continuing to administer Capstar® once daily as previously directed. They were continuing to feed the Iams® Response KO diet as directed on the day 77 telephone consultation. They were bathing the dog once monthly with Chlorhexiderm® shampoo. They continued to rate the dog's current level of pruritus at 3-4 out of 10 on the pruritic scale since resuming the KO diet alone. The owners had not yet begun to introduce individual proteins or carbohydrates into the KO diet.

Day 89: Physical Exam: The general physical exam was relatively unchanged from day 0. All vital signs were within normal limits. The dog weighed 26.0 kg. Dermatologic examination revealed mild erythema and salivary staining in the interdigital webbing and on the palmar aspects of all four paws which remained unchanged from the previous visit. Mild salivary staining was noted on medial aspect of the thoracic limbs and was also unchanged from previous visits.

Day 89: Assessment: Problems 2, 3 and 5 remained resolved. Problems 1 and 4 were unchanged from the previous visit. AD, a diagnosis made by exclusion of other causes of

pruritus, was thought to be causing the remaining pruritus in this dog, as evidenced by the interdigital erythema and salivary staining noted before the dietary provocation.

Day 89: Diagnostic Tests: Acetate tape preparations were taken from the interdigital spaces and palmar/plantar aspect of all four paws to evaluate for the presence of bacteria or *Malassezia* (Appendix 10). A serum sample was taken and submitted to Greer Laboratories for serum allergy testing (Appendix 11).

Day 89: Interpretation of Results: Skin cytology was unremarkable. There was no indication of secondary infections and the clinical improvement to this point was attributed to appropriate management of the superficial pyoderma, FAD and CAFR. By diagnosis of exclusion the remaining pruritus and erythema was likely resulting from AD.

Day 89: Treatment Plan: Capstar® (Novartis; nitenpyram) at 57 mg (0.45 mg/kg) PO once daily was continued as the flea control. The owners were told they no longer needed to continue bathing with Chlorhexiderm® shampoo as there was no longer any evidence of infection. There owners were told they would be called in two weeks with the results of the serum allergy test.

Day 106: Telephone Update: The results of the serum allergy test were discussed with the owner. It was recommended that the dog's bedding be washed frequently to limit exposure to house dust mite. In order to decrease exposure to storage mites it was also recommended to the owner to buy smaller bags of kibble and once opened to freeze the contents to avoid development of storage mites, keeping a few days worth of food in a sealed Tupperware container[xiii]. The owner agreed to start ASIT and the following allergens were included in the dog's ASIT: Kochia, Russian thistle, English plantain, Sage, Fescue, Timothy, Kentucky Blue, *Aspergillius niger, Penicillium notatum,* D. *farina,* D. *pteronyssinus,* and T. *putrescentiae*. These allergens were chosen because there were high levels of allergen specific IgE to these

allergens on the ELISA test and because they were known to be present in the dog's environment.

The owner also reported she had introduced ground beef into the dog's diet eight days earlier and had not seen an increase in pruritus.

Day 116: Recheck: History: The owners were continuing to administer Capstar® as previously directed. The owners had switched the dog to an over-the-counter oatmeal based shampoo and were continuing to bath once a month. The owners reported a significant increase in pruritus 2 days after introducing chicken into the diet. They had since discontinued the chicken and resumed feeding the KO diet alone and the dog's pruritus was at 4 out of 10 on the pruritic scale.

Day 116: Physical Exam: Both the physical exam and the dermatologic exam were unchanged from the previous visit. The dog weighed 26.4kg.

Day 116: Assessment: Assessment of all problems was considered to be the same as the Day 89 visit. The persistent pruritus in the absence of infection was considered likely due to unmanaged AD and the reintroduction of a chicken protein that caused a flare in the dog's clinical signs approximately 6 days earlier.

Day 116: Diagnostic Tests: Acetate tape preparations were taken from the interdigital spaces and palmar/plantar aspect of all four paws to evaluate for the presence of bacteria or *Malassezia* (Appendix 12).

Day 116: Interpretation of Results: There was no cytologic evidence of infection which continued to support a diagnosis of atopic dermatitis as the cause for the pedal erythema.

Day 116: Treatment Plan: The owner was shown how to administer a subcutaneous injection and advised on how to follow the protocol for ASIT subcutaneous injections (Appendix 13). Temaril-P ® (Pfizer; 5mg trimeprazine tartrate and 2mg prednisolone) was started to help control

the dog's pruritus during the induction phase of ASIT. The owners were asked to administer 2 tablets (10mg trimeprazine tartrate, 0.37mg/kg and 4mg prednisolone 0.15mg/kg) orally once daily for 7 days, then 1 tablet (5mg trimeprazine tartrate, 0.19mg/kg and 2mg prednisolone 0.08mg/kg) once daily for 7 days, and finally 1 tablet every other day until the next recheck. The owners were asked to continue administering Capstar® once daily.

Day 154: Telephone Update: The owner was contacted to assess the dog's progress. The owner reported the dog's pruritus decreased dramatically while receiving the Temaril-P® and was currently a 1 out of 10 on the pruritic scale. The owners had discontinued the Temaril-P® 2 days prior as they did not think the dog's level of pruritus warranted continuing the medication. The dog was continuing to receive ASIT and was currently receiving 1cc of the maintenance vial once weekly given by subcutaneous injections. The dog had not had any adverse reactions to ASIT.

Day 224: Recheck: History: The owners reported the dog had done extremely well until 2 weeks prior to this recheck when there was a significant increase in the amount of pedal pruritus as manifested by licking at the paws. The owners reported the dog's pruritus increased from a 1 out of 10 to 4 out of 10 on the pruritic scale. The owners were continuing to feed the KO diet alone and occasionally added cooked ground beef as a treat. They did not perceive an increase in pruritus following ingestion of beef. Two months earlier the owners ran out of the Heartgard® unflavored tablets and resumed using the Heartgard® flavored tablets. They did not perceive an increase in pruritus following reintroduction of the flavored tablets. The owners had not challenged the dog's diet with any other protein or carbohydrate sources. They were continuing to administer Capstar as previously directed.

Day 224: Physical Exam: The general physical exam was unchanged from day 0. All vital signs

were within normal limits. The dog weighed 26.5 kg. Dermatologic examination revealed mild to moderate erythema and salivary staining in the interdigital webbing and on the palmar/plantar aspects of all four paws. The salivary staining on the medial aspect of the thoracic limbs was no longer present.

Day 224: Assessment: Problems 2, 3, and 5 remained resolved. There had been significant improvement in problems 1 and 4 until two weeks prior to the recheck appointment. This was considered likely to either be a recurrence of secondary infection and/or an increased allergen load in the environment causing increased pruritus and paw licking.

Day 224: Diagnostic Tests: Acetate tape preparations were taken from the interdigital spaces and palmar/plantar aspect of all four paws to evaluate for the presence of bacteria or *Malassezia* (Appendix 14).

Day 224: Interpretation of Results: Cytology supported the presence of a *Malassezia* pododermatitis which was likely contributing to the increased pruritus seen in recent weeks. This new problem, problem 6, likely developed secondary to the atopic dermatitis as the dog's CAFR was well controlled with the KO diet.

Day 224: Treatment Plan: The owners were instructed to continue to administer Capstar® as previously prescribed, maintain the dog on the same diet and continue to administer the maintenance dose of ASIT injection on a weekly basis. Treatment for *Malassezia* pododermatitis was initiated and fluconazole (7.5mg/kg) PO once daily (one 200mg tablet) was prescribed to be given until recheck[xiv] [xv]. To decrease pruritus another tapering course of Temaril-P was prescribed. The owners were asked to administer 2 tablets (10mg trimeprazine tartrate, 0.37mg/kg and 4mg prednisolone 0.15mg/kg) orally once daily for 7 days, then 1 tablet (5mg trimeprazine tartrate, 0.19mg/kg and 2mg prednisolone 0.08mg/kg) once daily for 7 days,

and finally 1 tablet every other day until the next recheck.

Day 257: Recheck: History: The owners reported the dog's pruritus was currently very well controlled and the dog was observed to lick its feet only once or twice a day following breakfast and dinner. They scored the dog 's pruritus as a 1 out of 10 on a pruritic scale. The owners were continuing to feed the KO diet alone and continued to occasionally add cooked ground beef as a treat. They also began adding cheese into the dog's diet to administer pills. They did not perceive an increase in pruritus following ingestion of the cheese. The owners ran out of Temaril-P® three days prior to the recheck appointment and did not perceive an increase in the dog's pruritus since discontinuing the medication. The dog had been receiving 1 tablet of Temaril-P® (5mg trimeprazine tartrate, 0.19mg/kg and 2mg prednisolone 0.08mg/kg) every other day. The owners had also completed the prescribed course of fluconazole 3 days earlier. They were continuing to administer Capstar® as previously directed.

Day 257: Physical Exam: The general physical exam was unchanged from day 0. All vital signs were within normal limits. The dog weighed 26.5 kg. Dermatologic examination revealed mild salivary staining in the interdigital webbing and on the palmar aspects of all four paws.

Day 257: Assessment: Problems 2, 3, and 5 remained inactive/resolved. Problems 1 and 4 were significantly improved. The resolution of the pruritus, erythema and salivary staining was likely due to a combination of factors including, successful management of AD, CAFR, and FAD as well as treatment of *Malassezia* pododermatitis (problem 6). The dog had been receiving ASIT for almost 150 days and it was felt that this could also be contributing to successful management of pruritus.

Day 257: Diagnostic Tests: Acetate tape preparations were taken from the interdigital spaces and palmar/plantar aspect of all four paws (Appendix 15).

Day 257: Interpretation of Results: Cytology supported the clinical evidence that the *Malassezia* pododermatitis was resolved.

Day 257: Treatment Plan: The owners were instructed to continue administering ASIT on a weekly basis, to continue feeding the KO diet and to continue administering Capstar® as previously directed. They were instructed to make a recheck appointment in 12 weeks.

Day 351: Telephone Update: Owners called to report the dog was doing extremely well and had not had any other flare-ups of pruritus. The owner was unable to make her recheck appointment but wanted to reschedule and have the allergens refilled.

Day 397: Recheck: History: The dog presented for a recheck evaluation following 10 months of ASIT. The owners reported the dog had done extremely well and had not had an increase in pruritus since Day 224. The dog was currently receiving 1ml of the maintenance vial of ASIT subcutaneously once weekly, Capstar® once daily, and the owners were continuing to feed the KO diet with occasional beef and cheese. The dog had not required Temaril-P® for approximately 2 months.

Day 397: Physical Exam: The general physical exam was unchanged from day 0. All vital signs were within normal limits. The dog weighed 26.3 kg. Dermatologic examination revealed mild salivary staining in the interdigital webbing and on the palmar aspects of all four paws which was diminished from Day 257.

Day 397: Assessment: All problems remained resolved. Due to the successful management of FAD, CAFR, and AD as well as appropriate treatment of prior secondary infections

Day 397: Diagnostic Tests: None performed

Day 397: Interpretation of Results: N/A

Day 397: Treatment: The owner was instructed to continue all therapy previously prescribed and

to call if there was an increase in pruritus. A recheck was scheduled in 3 months.

Day 564: Recheck: History: The dog presented for a recheck evaluation following 12 months of ASIT. The owners reported the dog continued to do well. They gave the dog a 1 out of 10 on the pruritic scale. The dog was currently receiving 1ml of the maintenance vial of ASIT subcutaneously once weekly, Capstar® once daily, and the owners were continuing to feed the KO diet with occasional beef and cheese

Day 564: Physical Exam: The general physical exam was unchanged from day 0. Dermatologic examination was unremarkable with the exception of mild salivary staining on all 4 paws.

Day 564: Assessment: All problems remained resolved. This was due to the successful management of FAD, CAFR, and AD as well as appropriate treatment of secondary infections. ASIT had been administered for over 12 months and was considered to be a successful therapy for the management of AD in this dog.

Day 564: Diagnostic Tests: None performed

Day 564: Interpretation of Results: N/A

Day 564: Treatment: The owner was instructed to continue all therapy previously prescribed and to schedule a recheck appointment in 3 months.

Discussion: This case was selected because it represents the importance of the thorough work-up for a suspected allergic dog. This dog represented a case where FAD, CAFR and AD together with secondary infections were contributing to the dog's overall pruritus. Allergic patients need to be evaluated in a systematic fashion to determine all etiologies contributing to the overall pruritic threshold. If all etiologies for pruritus are not being managed simultaneously, the overall treatment protocol could be viewed as a failure. Additionally, secondary infections need to be identified and treated concurrently while attempting to manage the primary allergic dermatitis or,

again, the management of the allergic dermatitis could be viewed as a failure.

In this case a diagnosis of food allergy was not identified by the referring veterinarian .

The success of past attempted diet trials may have been compromised as the dog continued to receive treats, table food and flavored heartworm prevention all of which could have been potential food allergens for this dog. As a duck and potato diet was chosen as the trial diet and the dog was later confirmed to be allergic to chicken it is possible there was a cross reaction between the avian meats. Studies have shown that duck can cross-react with chicken protein[xvi].

Due to appropriate management of FAD and CAFR, AD was accurately diagnosed and treated in this dog. In this case the dog responded to ASIT within the first 6 months of therapy and continued to due well at 1 year. For this reason, ASIT can be continued to be used long term, which will minimize the need for corticosteroids.

This was an extremely rewarding case because this dog's FAD, CAFR and AD were able to be successfully diagnosed and managed early in its life which will hopefully improve the dog's quality of life as well as diminish the level of frustration that allergic skin disease can cause for the owner.

Appendices:

Cytology Abbreviations
TNTC Too numerous to count
4+ >20 organisms/oil immersion field (oif)
3+ 5-20 organisms/oif
2+ 2-5 organisms/oif
1+ 1-2 organisms/oif
0 None
NSF No significant findings

Miscellaneous abbreviations
AU Left and right ear
AD Right ear
AS Left ear
OD Right eye

Appendix 1: Day 0: "Diff Quik®" acetate tape skin cytology (100x objective)

- Ventral abdomen: 2+ degenerate neutrophils, 2+ cocci
- Dorsal trunk: 2+ cocci
- Interdigital/ palmar/plantar aspect of paws: 1+ cocci

Appendix 2: Day 0: Flea combing

- Negative for flea excrement; negative for fleas.

Appendix 3: Day 0: Deep skin scraping

- Negative for mites.

Appendix 4: Day 0: Superficial skin scraping

- Negative for mites.

Appendix 5: Day 0: *Cheyletiella* Preparation

- Negative for *Cheyletiella*

Appendix 6: Day 37: "Diff Quik®" acetate tape skin cytology (100x objective)

- Ventral abdomen: NSG
- Dorsal trunk: NSF
- Interdigital/ palmar aspect of paws: NSF

Appendix 7: Day 37: Flea combing

- Negative for flea excrement; negative for fleas.

Appendix 8: Day 37: "Diff Quik®" acetate tape skin cytology (100x objective), Trichogram, Skin scrape

- Ventral chin: 1+ cocci and 1+ degenerate neutrophils
- Tricogram: NSF

- Deep skin scrape: NSF

Appendix 9: Day 67: “Diff Quik®” acetate tape skin cytology (100x objective)

- Interdigital/ palmar/plantar aspect of paws: NSF
- Ventral chin: NSF

Appendix 10: Day 89: “Diff Quik®” acetate tape skin cytology (100x objective)

- Interdigital/ palmar/plantar aspect of paws: NSF

Appendix 11: Day 89: Serum Blood Allergy Test Results (Greer Laboratories)

Russian Thistle + 45
Scale mix Neg 35
Dock/sheep Sorrel Mix Neg 37
Lamb’s Quarter Neg 29
Sage Mix + 41
Dandelion Neg 5
Coclebur Neg 14
English Plantain + 43
Goldenrod Neg 11
Kochia + 51
Pigweed Mix Neg 13

Eucalyptus Neg 13
Cottonwood Neg 14
Oak Mix Neg 32
Ash Mix Neg 8
Orange Pollen Neg 0
Acacia Neg 0
Alder Neg 17
Cedar/juniper Neg 12
Maple/Box Elder Mix Neg 19
Mulberry Neg 37
Olive
Palm
Pine Mix
Walnut
Neg
Neg
Neg
Neg
0
22
22
0
25

Timothy + 48
Fescue + 51

Kentucky Blue/June + 42
Red Top Neg 28
Bermuda Neg 31
Quack + 40
Johnson Neg 27
Perennial Rye Neg 38

Penicillium + 50
Aspergillus +++ 60
Stemphylium Neg 25
Cladosporium Neg 27
Curvularia Neg 15
Pullularia Neg 35
Cephlasporium Neg 26
Alternaria Neg 29
Mucor Mix Neg 7

Mite – A. siro +++ 78
Mite- D. farina + 59
Mite- T. putrescentiae +++ 72
Mite- D. pteronyssinus + 53
Flea Neg 12

Interpretation:
MAU = Modified Absorbance Units which indicates the level of allergen specific IgE detected.
+ (40-59 MAU) = Scores in this range should be considered significant if the allergens are found in the pets environment and they relate to clinical history.
Appendix 12: Day 116: "Diff Quik" ® acetate tape skin cytology (100X objective)

- Interdigital/palmar aspect of paws: NSF

Appendix 13: Allergen Specific Immunotherapy Hyposensitization Protocol
The initial allergen treatment set contains 3 vials of varying concentrations which are to be kept refrigerated. Injections are administered subcutaneously every other day for the first 28 days, then weekly until further directed.
Vial #1: (200 PNU/cc) first 5 injections only then discard remainder of vial.
Vial #2: (2000 PNU/cc) second 5 injections only then discard remainder of vial.
Vial #3: (20,000 PNU/cc) all remaining injections (from day 20 onwards)

Vial #1 (200 PNU/cc)

Day	Day of treatment	Amount
0	116	0.1cc
2	118	0.2cc
4	120	0.4cc
6	122	0.8cc
8	124	1.0cc

Vial #2 (2000 PNU/cc)

Day	Day of treatment	Amount
10	126	0.1cc
12	128	0.2cc
14	130	0.4cc

16 132 0.8cc
18 134 1.0cc
Vial #3 (20,000 PNU/cc)
Day Day of treatment Amount
20 136 0.1cc
22 138 0.2cc
24 140 0.4cc
26 142 0.8cc
28 149 1.0cc
35 156 1.0cc
42 163 1.0cc
49 170 1.0cc
56 177 1.0cc
63 184 1.0cc
70 191 1.0cc
Appendix 14: Day 224: "Diff Quik" ® acetate tape skin cytology (100X objective)

- Interdigital/ palmar aspect of paws: 2+ *Malassezia*

Appendix 15: Day 257: "Diff Quik" ® acetate tape skin cytology (100X objective)

- Interdigital/ palmar aspect of paws: NSF

References:

[i] Medleau L, Hnilica K. Small Animal Dermatology: A Color Atlas and Therapeutic Guide. 2nd ed. St. Louis: Saunders Elsevier, 2006; Chapter 7: pp. 173-776.
[ii] Medleau L, Hnilica K. Small Animal Dermatology: A Color Atlas and Therapeutic Guide. 2nd ed. St. Louis: Saunders Elsevier, 2006; Chapter 7: pp. 186-187.
[iii] Scott D, Miller W, Griffin C. Muller & Kirk's: Small Animal Dermatology. 6th ed. Philadelphia: WB Saunders Co, 2001; Chapter 8: pp. 608-615.
[iv] Wildermuth BE, Griffin CE, Rosenkrantz WS. Feline pyoderma therapy. Clin Tech Small Anim Pract 21:150-156, 2006.
[v] Scott D, Miller W, Griffin C. Muller & Kirk's: Small Animal Dermatology. 6th ed. Philadelphia: WB Saunders Co, 2001; Chapter 8: pp. 627-629.
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[viii] Six et al. Efficacy and safety of cefovecin in treating bacterial folliculitis, abscesses, or infected wounds in dogs. JAVMA, Vol 233, issue 3, p433-9.
[ix] Medleau L, Hnilica K. Small Animal Dermatology: A Color Atlas and Therapeutic Guide. 2nd ed. St. Louis: Saunders Elsevier, 2006; Chapter 15: pp. 167-172.
[x] Plumb, D. Plumb's Veterinary Drug Handbook. (2008) p. 909-910.
[xi] Meyer, EK, et al. Responses of dogs with food allergies to single ingredient dietary provocation. JAVMA 1996; 209: 608-611.
[xii] Scott D, Miller W, Griffin C. Muller & Kirk's: Small Animal Dermatology. 6th ed. Philadelphia: WB Saunders Co, 2001; Chapter 8: pp. 581-601.
[xiii] Brazis P et al. Evaluation of storage mite contamination of commercial dry dog food.

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[xv] Scott D, Miller W, Griffin C. Muller & Kirk's: Small Animal Dermatology. 6th ed. Philadelphia: WB Saunders Co, 2001; Chapter 5: pp. 373.
[xvi] Cahen, YD. et al. Food allergy with monovalent sensitivity to poultry meat. Clin Exp Allergy. 1998 Aug;28(8):1026-30.

Reviewers' comments:

The comments are separated into major points and detailed comments. Major points are those affecting the overall diagnosis and management of the case or the general presentation of the information. The detail comment focus on the details of the text, such as spelling and grammatical errors, appropriately marked abnormal lab values, etc. or specific decisions made on specific visit and don't necessarily impact the grading of the case as a whole. These are included in order to provide a complete and thorough evaluation of the work submitted. The comments are in no particular order and represent a compilation of comments from all reviewers; therefore, at times there were will be multiple comments about the same issue.

Major points:

- Overall this is a classic complex case presented to dermatologists.
- While it happens that clients do not want to rechallenge the diet – that makes the case less appropriate for a case report – however as this represents a real life, well managed case the reviewers would like to read the corrected report addressing the issues below.
- There is a concern for MRSP – but no discussion about a culture
- Diet rechallenge – Instructing to challenge with 6 ingredients added in one week? Please explain how the diagnosis of individual allergies could or could not be made.

Detail comments:

- No discussion of other topical therapies or why the use of mupirocin on the chin
- Dermatophytosis was not included as a ddx in pruritus
- Without a diet challenge cannot definitely diagnose CAFR – would like to see that in the actual report or discussed in the summary.
    - Summary is not the place to let the reader know about the diet rechallenge
- References belong at the end of the report rather than the index
- Weak references – mostly book references
- Why was Capstar used and not Comfortis?
- No discussion or mention of tick protection once off Frontline
- Unorganized, run on sentences leading to run on paragraphs.
- The title is too long. It can be reduced to "Flea allergy, adverse food reaction and atopy in a mixed breed dog" or even "Flea allergy, adverse food reaction and atopy with superficial and deep pyoderma and Malassezia dermatitis in a mixed breed dog.
- The report is difficult to read. Run on sentences. The entire report needs to be more concisely described.
- Day 0: Sentence 3 and 4 on the first page contradict each other. "There was no known history of skin disease prior to adoption" … BUT …"At the time of adoption the dog had complete alopecia of the tail base and etc…".
- Day 116: No visual pruritus score was reported when chicken was fed and the dog got itchy.
- One reviewer felt that the assessment on d0 was poorly organized and would have liked to see more differentials for all problems listed (esp. 2 – 4); list the problems without making sentences out of every statement. No ranking of ddx was done that could have lead to a statement regarding a tentative diagnosis.
- There was no discussion on IDST vs serum allergy testing…why the serum test was chosen…pros and cons.
- What was the dose in mg's of the cephalexin?
- Is the flavoring in Capstar a concern during a food trial?
- Could have started antihistamines alone as starting ASIT if owner only rating pruritus at a 4? Especially as still on a food trial and the itch is decreasing?
- On Day 564: Dog is doing very well but is still on a weekly ASIT injection of 1 ml. The reviewers would like discussion on possibility of changing the antigen interval?
- The reviewers liked that a food trial and a flea trial were all started on d0

- The references should have come before the appendices.
- The references are sloppy. Needs to be redone in proper format. Needs to use a format consistently throughout the list. Dates missing.
- Good job siting the poultry meat cross reactivity reference (Cahen, 1998).
- For the summary: The author calls this section “Discussion” and it should be called “Summary” as the instructions say to do.
- In the summary there is no discussion regarding the use of Capstar for what appears to be life-long flea control? Expense? Safety? No other management possibilities for fleas?
- In the summary there is no discussion on why weekly immunotherapy injections are being given since it has been greater than 1 year from the start of ASIT. No thought about increasing the interval of injections?

FOLLOWING IS THE AUTHOR'S REBUTTAL TO THE REVIEWER'S COMMENTS (AGAIN – THIS IS NOT HOW IT WAS FORMATTED FROM THE AUTHOR FORMATTED):

ACVD Credentials Committee

Dear Members of the ACVD Credentials Committee:
I have carefully reviewed all of the comments and suggestions regarding my case report entitled "*Flea Allergy Dermatitis, Superficial Pyoderma, Bacterial Pododermatitis, Funuculosis Of The Chin, Cutaneous Adverse Food Reaction, Malassezia Pododermatitis And Atopic Dermatitis In A Fawn German Shepherd, Belgium Malinois Mixed Breed Dog"*. I greatly appreciate the opportunity to make the requested changes in the revised version of my case report. Please find a detailed explanation addressing each **comment** made in your letter below.

Major points:

 While it happens that clients do not want to rechallenge the diet – that makes the case less appropriate for a case report – however as this represents a real life, well managed case the reviewers would like to read the corrected report addressing the issues below.

 Diet rechallenge – Instructing to challenge with 6 ingredients added in one week? How could you possible diagnose individual allergies?

Thank you for your comments. I did in fact rechallenge the diet trial but perhaps I was not clear about how the dietary rechallenge or provocation was performed. On day 67 the patient returned for a recheck examination. The only food the dog had received for the past 9 weeks was Iams® Response KO diet. The dog's pruritus had diminished substantially and the dog's secondary infections had resolved. Listed under day 67 treatment plan the owners were instructed on how to begin the dietary provocation. They were asked to return the dogs to its original diet (Natural Balance® Duck and Potato Formula) and to resume feeding any treats that dog had previously been given. The dietary provocation was to last for 2 weeks. During the period of the dietary challenge the owners were asked to keep all medications and bathing previously prescribed exactly the same so as not to confound the challenge results. If increased pruritus was noted within 2 weeks the owners were instructed to return to feeding Iams® Response KO diet and to

call with an update. On day 77 (listed under telephone update) the owners phoned to report an increase in pruritus within 4 days of initiating the dietary challenge. They had stopped the original diet and had restarted feeding only the Iams® Response KO diet. At this point a sequential rechallenge of individual protein and carbohydrate sources was discussed with the owner in order to determine the exact source of the cutaneous adverse food reaction. The owner was asked to continue feeding the Iams® Response KO diet. They were also asked to continue all medications and bathing as previously directed. The owners were then asked to add one individual ingredient (i.e. chicken) to the KO diet. This one single ingredient was to be fed with the KO for 2 weeks. If an increase in pruritus was noted after introducing chicken the owners were instructed to stop feeding the chicken, and resume feeding just the KO diet until the dog's level of pruritus returned to normal. Once the dog's pruritus had returned to the pre-challenge level the owners were instructed to start feeding a new ingredient (i.e. beef) for the next 2 weeks and so on until all of the most common allergens were tested. In the text from day 67 (telephone update) it states: *"The owner was asked to continue to feed the dog Iams® Response KO diet and add beef, chicken, dairy, eggs, soy, and rice one item at a time for one week in addition to the KO diet".* This may have been misinterpreted as if I was instructing them to feed all ingredients at the same time, but this was not the case and I have reworded the text to be more clear and concise.

On day 106, listed under telephone update, the owner reported introducing beef into the dog's diet eight days earlier and had not seen an increase in the pruritus. On day 116, listed under history, the owner's reported an increase in pruritus 2 days after introduction of chicken to the KO diet. I neglected to list the pruritus score given by the owner after the introduction of the chicken to the diet. I have updated the case report to reflect that score. Given that the introduction of chicken caused an increase in pruritus and withdrawal a decrease in pruritus, it is likely that chicken protein was at least one allergen causing an adverse food reaction in this dog. The owners discontinued the chicken and resumed feeding just the KO diet. On day 224, listed under history, the owners reported continuing to feed the KO diet and occasionally added cooked ground beef as a treat without any adverse reactions. They had also run out of unflavored Heartgard® tablets and had resumed using the Heartgard® flavored tablets without any adverse reactions. On day 257, listed under history, the owners reported adding cheese to the dog's diet. The owners did not add anything else to the dog's diet during the time

they added beef, chicken, or cheese (individually) to the dog's diet and all other medications remained the same. Therefore, it was concluded that chicken protein was the food allergen partially responsible (in addition to flea allergy and atopic dermatitis) for inducing pruritus in this dog.

In the summary I discussed why a food allergy may have been missed by the referring veterinarian in the past. The dog had continued to receive treats, flavored heartworm medication and had been placed on a diet trial of duck and potato. All of these, particularly the duck diet trial could have been contributing factors to the misdiagnosis. The cross-reactivity between duck and chicken protein most certainly may have played a role in this case (Cahen, 1998).

There is a concern for MRSP – but no discussion about a culture

The dog was diagnosed with a superficial pyoderma on day 0 and was treated with cephalexin at 29.1mg/kg (750mg) twice daily for 30 days. At the day 37 recheck examination there was substantial clinical improvement and cytologic resolution of the superficial pyoderma. The dog did develop bacterial furunculosis of the ventral chin and this was suspected to be secondary to self trauma due to persistent pruritus. A fungal culture and bacterial culture were discussed with the owner. The owner elected to treat the bacterial infection identified on cytology (Appendix 8) with topical therapy. Listed under day 37 treatment plan it states, "*The owners were informed that if there was no response to mupirocin ointment, then a bacterial culture to rule out an antibiotic resistant infection would need to be performed."* I did not feel a bacterial culture and sensitivity was absolutely necessary on day 37 as this dog had responded well to the previously prescribed course of antibiotics, the localized location of the lesions made topical therapy easy to administer, the young age of the dog, and the minimal use of antibiotics in this dog's history. Both older age and antibiotic pressure have been shown to increase the risk of the development of a methicillin-resistant *Staphylococcus* infection in dogs (Nienhoff, 2011). In this case mupirocin ointment was prescribed not only because of the ease of administration but also because resistance to mupirocin has been found to be relatively low (Fulham, 2011). It has also been shown to be effective in treating recurrent interdigital furunculosis, callus pyoderma and muzzle acne (Werner, 1999).

Detail Comments:

No discussion of other topical therapies or why the use of mupirocin on the chin

Please see explanation for use of mupirocin above.

Dermatophytosis was not included as a ddx in pruritus

Thank you for your comment. Dermatophytosis should have been considered as a differential diagnosis and was added under day 0 assessment.

Without a diet challenge cannot definitely diagnose CAFR – would like to see that in the actual report or discussed in the summary.

A dietary rechallenge was performed. Please see explanation above.

References would be better placed at the end of the report rather than the index

Thank you for your comment. I have moved the references to the end of the report.

Weak references – mostly book references

Thank you for your comment. Eight references were from peer reviewed journal articles and I have added an additional 6 as an addendum listed below. The remaining references were taken from books because much of the information referenced is related to basic dermatology (i.e. definition of pyoderma, differential diagnoses for pruritus etc.) which is primarily described in text books.

Why was Capstar used and not Comfortis?

Thank you for your question. Capstar was chosen as flea control because this dog was suspected to be flea allergic and as found under day 0 treatment plan it states: "*Daily Capstar® was the preferred treatment because it has been shown to have 99.1% efficacy within 3 hours against adult Ctenocephalides felis in canine patientsi. Capstar® has also been shown to diminish or eliminate exposure to allergenic proteins in the saliva of biting fleas as its speed of adulticidal activity is as rapid as thirty minutes"ii.* It was chosen over Comfortis because of the reasons stated above and also because Comfortis® is a beef flavored tablet and I did not want this to interfere with the food trial that was initiated on day 0.

No discussion or mention of tick protection once off Frontline

Thank you for your comment. Tick protection was discussed with the owner and I have updated the text to reflect this. The owner did not report having a problem with ticks, but was told she could continue to use Frontline Plus or another product such as Advantix, or a Preventic collar should ticks become a problem.

Unorganized, run on sentences leading to run on paragraphs.

Thank you for your comment. I have reviewed the report and corrected the run on sentences when appropriate.

The title is too long. It can be reduced to "Flea allergy, adverse food reaction and atopy in a mixed breed dog" or even "Flea allergy, adverse food reaction and atopy with superficial and deep pyoderma and Malassezia dermatitis in a mixed breed dog.

Thank you for your comment. I changed the title to make it more concise. I chose the original title because a comment on the last case report I submitted said my title was not detailed enough.

Day 0: Sentence 3 and 4 on the first page contradict each other. "There was no known history of skin disease prior to adoption" … BUT …"At the time of adoption the dog had complete alopecia of the tail base and etc…".

Thank you for your comment. I have deleted: *There was no known history of skin disease prior to adoption*" to make this clear. What I was trying to say was that the shelter did not have any prior history on the dog.

Day 116: No visual pruritus score was reported when chicken was fed and the dog got itchy.

Thank you for your comment. I neglected to include that and I have updated the text to reflect this.

One reviewer felt that the assessment on d0 was poorly organized and would have liked to see more differentials for all problems listed (esp. 2 – 4); list the problems without making sentences out of every statement. No ranking of ddx was done that could have lead to a statement regarding a tentative diagnosis.

Thank you for your comment. The differentials were listed from the most likely differential diagnoses to the least likely. For example, in problem 1 (pruritus), allergic dermatitis (flea, food and atopy) is listed first because this was considered the most likely differential diagnosis and ectoparasitism (*Cheyletiella*, *Demodex* and sarcoptic acariasis) was listed last as this was considered the least likely diagnosis. I have made some minor changes to this section, but feel that the problems and their most likely differentials are clearly organized.

There was no discussion on IDST vs serum allergy testing…why the serum test was chosen…pros and cons.

Thank you for your comment. Both intradermal skin testing and serum allergy testing were discussed and offered to the owner (day 77, telephone update). In this case serum allergy testing

was chosen by the owner because it was less invasive (no sedation or shaving). The owner was informed about the potential for negative test results and was willing to do an intradermal skin test in the future if necessary. Studies comparing both serum allergy tests and intradermal skin tests have found similarities and discrepancies between both making neither test better or worse than the other (Foster, 2003; DeBoer, 2001; Mueller, 1999). As a clinician it is important to recognize atopic dermatitis is a diagnosis of exclusion and cannot be confirmed by an allergy test (serum or intradermal) alone but requires extensive knowledge of history and clinical signs as well as exclusion of cutaneous adverse food reaction and flea allergy dermatitis as confounding factors in pruritus.

What was the dose in mg's of the cephalexin?

Thank you for pointing this out the dog was treated with 750mg. The text has been updated to reflect this.

Is the flavoring in Capstar a concern during a food trial?

Capstar® is not flavored which is one of the reasons it was chosen over Comfortis® which is flavored.

Could have started antihistmaines alone as starting ASIT if owner only rating pruritus at a 4? Especially as still on a food trial and the itch is decreasing?

Yes, an antihistamine trial could have been attempted at this point but the dog had already been treated with diphenhydramine and chlorphenaramine with no success and the dog was only receiving 0.15mg/kg of prednisolone in the Temaril-P. This is considered a very low dose of corticosteroids and the dog had previously responded very well to Temaril-P. It was considered safe to use on a short term basis which is why it was selected in this case.

The reviewers liked that a food trial and a flea trial were all started on d0

Thanks!

The references are sloppy. Needs to be redone in proper format. Needs to use a format consistently throughout the list. Dates missing.

Thank you for your comment. I have corrected the reference list.

Good job siting the poultry meat cross reactivity reference (Cahen, 1998).

Thanks!

For the summary: The author calls this section "Discussion" and it should be called "Summary" as the instructions say to do.

Thank you for pointing this out. I have changed the text to reflect this.

In the summary there is no discussion regarding the use of Capstar for what appears to be life-long flea control? Expense? Safety? No other management possibilities for fleas?

The cost of Capstar® is subsidized at the hospital where this dog was treated and the cost is far below what this product costs in private practice. Capstar® is actually less expensive to use on a daily basis than Comfortis® monthly. The active ingredient in Capstar®, nitenpyram, is a systemic flea adulticide has a wide margin of safety and can be used on a daily basis. Nitenpyram interferes with normal nerve transmission in the fleas and leads to the death of these parasites it does not interfere with the mammalian nervous system.

In the summary there is no discussion on why weekly immunotherapy injections are being given since it has been greater than 1 year from the start of ASIT. No thought about increasing the interval of injections?

Thank you for your comment. The geographic location where this dog lives is considered an area that remains relatively warm throughout the year and is known for having very high pollen counts. In the experience of the faculty clinicians the ability to increase the intervals between allergy injections has not proven to be as effective as weekly injections. The owner was pleased with the dog's progress and had not expressed concern over giving a weekly injection. At future visits this could certainly be considered if this dog continues to do well with ASIT.

New References:

Cahen YD, Fritsch R, and Wuthrich B. Food allergy with monovalent sensitivity to poultry meat. Clinical and Experimental Allergy 1998; 28: 1026-30.

Nienhoff U, Kadlec K, Chaberny IF, et al. Methicillin resistant Staphylococcus pseudintermedius among dogs admitted to a small animal hospital. Veterinary Microbioly. 2011 May 12;150(1-2):191-7.

Fulham KS, Lemarie SL, Hosgood G, Dick HL. In vitro susceptibility testing of of meticillin-resistant and meticillin-susceptible staphylococci to mupirocin and novobiocin. Veterinary Dermatology 2011: Feb (22) 88-94.

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FOLLOWING IS THE CORRECTED REPORT THAT THE RESIDENT SUBMITTED THAT DID PASS CREDENTIAL REVIEW

Flea allergy, adverse food reaction and atopic dermatitis in a mixed breed dog

Signalment: 19 month old, female spayed, fawn, German Shepherd/Belgian Malinois mixed breed dog, weighing 25.7kg.

Day O: History: The dog presented for evaluation of chronic pruritus of nine months duration. The dog was acquired from a local animal shelter at 10 months of age. At the time of adoption the owners reported the dog had complete alopecia of the tail base and patchy alopecia of the caudal dorsum. The owners also reported that the alopecia resolved several months later. According to the owner, the pruritus was originally localized on the back end of the body, caudal thighs and tail base. At the time of presentation the dog was also observed to be "corn-cobbing" its forelimbs, rubbing its face on the carpet, and scratching under its axillae. The dog also licked its inguinal region and caudal thighs, but much less than at the time of adoption. The owners gave the dog a score of 7.5 out of 10 on a **pruritus scale**. The owners were unable to determine any seasonality associated with the dog's pruritus.

According to available medical records, the dog had received Benadryl® (McNeil; diphenhydramine) at 0.5mg/kg two to three times a day for three weeks with no perceived benefit. The dog was then switched to Chlor-Trimeton® (Schering-Plough; chlorphenaramine) at 0.32mg/kg twice daily for three weeks, also without observed benefit. The dog was treated with Keflex® (Eli Lily; cephalexin) at 20mg/kg twice daily for two weeks for a superficial pyoderma with little improvement in the pruritus. The dog had been bathed with Chlorhexiderm® shampoo (DVM, 2% chlorhexidine) every 2 weeks with no reported decrease in pruritus. A diet trial using Hills® Prescription Diet d/d Canine Skin Support Potato and Duck had been attempted for 6 weeks, but the dog had continued to receive treats and flavored medications. The owners did not appreciate a decrease in pruritus during the diet trial.

At the time of presentation, the dog was receiving monthly heartworm prevention (Heartgard®, ivermectin, Merial) and monthly topical flea control (Frontline Plus®, fipronil, s-methoprene; Merial). The owners were bathing the dog every two weeks with Chlorhexiderm® shampoo and Resicort® Leave-On Conditioner (Virbac, 1% hydrocortisone). The dog had last received antibiotics four months prior to presentation. The dog's current diet consisted of Natural Balance® Duck and Potato Formula with occasional Milkbone® Dog Biscuits.

The owners reported that the dog was mostly indoors but did spend time in an outdoor dog run. The dog was reported to go to a dog park three times weekly and was walked within the neighborhood once daily. Other pets within the household included a guinea pig and a fish. The dog was reported to have minimal contact with the guinea pig. The guinea pig did not have any reported medical or dermatologic problems. The owners reported the dog did have regular contact with the neighbor's dog which was reported to be healthy and without any dermatologic disease. The owners reported having never seen fleas **or ticks** on the dog. The dog had no history of polyuria/polydipsia, coughing, sneezing, vomiting or diarrhea and was current on DHLPP and rabies vaccinations.

Day 0: Physical Exam: The examination revealed a bright, alert and responsive dog. The dog had a body condition score of 5/9. All vital signs were within normal limits. Thoracic auscultation was unremarkable, and pulses were strong and synchronous. Ophthalmologic examination was unremarkable. Examination of the oral cavity revealed pink, moist mucus membranes with a normal capillary refill time and no dental calculi. Abdominal palpation was within normal limits. Palpation of superficial lymph nodes was unremarkable.

Dermatologic examination revealed numerous papules and moderate erythema extending from the caudal dorsum to the tail base and involving the caudal thighs. There were multiple crusted papules and epidermal collarettes throughout the inguinal region. Axillae were moderately erythematous with evident excoriations. Mild erythema and salivary staining were noted in the interdigital webbing and on the palmar/plantar aspects of all four paws. Mild salivary staining was noted on the antebrachiae. Otoscopic examination was unremarkable. There was no erythema or swelling of the otic canals and both canals were pliable and non-painful when palpated externally. Tympanic membranes were visible and intact in both otic canals.

Day 0: Assessment: The problem list included: 1) pruritus, 2) papules and erythema of the caudal dorsum and tail base, 3) crusted papules and epidermal collarettes throughout the inguinal region and, 4) salivary staining and erythema of the thoracic limbs and interdigital webbing of all four paws.

The differential diagnoses considered for problem 1, pruritus, included allergic skin disease including atopic dermatitis (AD), cutaneous adverse food reaction (CAFR), and flea allergy dermatitis (FAD). **Infectious causes including** secondary bacterial or *Malassezia* infection **and dermatophytosis** were also considered as differential diagnoses. Ectoparasitism such as demodicosis, cheyletiellosis or sarcoptic acariasis was also considered.

The differential diagnoses for problem 2 included FAD with secondary bacterial or *Malassezia* dermatitis[i]. AD and CAFR were considered less likely differentials due to the caudal distribution of the lesions. As in problem 1, ectoparasitism was also considered.

The differential diagnoses for problem 3 included a superficial pyoderma secondary to a primary pruritic process such as FAD, CAFR, or AD.

The differential diagnoses for problem 4 included self-trauma secondary to pruritus from either a primary hypersensitivity disease such as AD or CAFR and/or due to a *Malassezia* or bacterial dermatitis/pododermatitis[ii] [iii] Lastly, a contact reaction was considered as a possible differential, but deemed less likely.

Day 0: Diagnostic Plan: Acetate tape preparations were taken from the caudal dorsal trunk, inguinal region, interdigital spaces and palmar aspects of all four paws to evaluate for the presence of bacteria or *Malassezia* (Appendix 1). A flea comb was passed through the hair coat on the caudal dorsum near the tail base (Appendix 2). A deep skin scraping was performed to rule out demodicosis (Appendix 3). Multiple broad superficial skin scrapings were performed **looking for** a *Sarcoptes* infestation (Appendix 4). An acetate tape preparation was performed to look for the presence of *Cheyletiella* (Appendix 5).

Day 0: Interpretation of Results: Skin cytology was consistent with a superficial pyoderma due to the presence of cocci-shaped bacteria and degenerate neutrophils. These two concurrent findings satisfy the cytologic definition of pyoderma in the canine patient[iv]. There were also cocci-shaped bacteria found in the interdigital webbing of all four paws making bacterial pododermatitis a contributing factor to the dog's overall pruritus.

Given the past history of severe caudal dorsal and tail base alopecia in conjunction with the current caudal dorsal distribution, a diagnosis of flea allergy dermatitis with secondary superficial pyoderma was made[v].

Because the paws, face, thoracic limbs, and axillae were also affected, AD and/or CAFR were also suspected to play a role in the development of the dog's pruritus and bacterial pododermatitis.

Day 0: Treatment Plan: As FAD was considered a likely diagnosis in this case stringent flea control using Capstar® (Novartis; nitenpyram) at 57 mg (0.45 mg/kg) PO once daily was prescribed. Daily Capstar® was the preferred treatment because it has been shown to have 99.1% efficacy within 3 hours against adult *Ctenocephalides felis* in canine patients[vi]. Capstar® has also been shown to diminish or eliminate exposure to allergenic proteins in the saliva of biting fleas as its speed of adulticidal activity is as rapid as thirty minutes[vii]. Oral flea control was also chosen due to the owner's desire to continue frequent bathing, which had the potential to make topical flea control administration less efficacious. The owners were instructed to discontinue the use of Frontline Plus® **unless it was required for tick protection**.

Cephalexin at 29.1mg/kg **(750mg)** every 12 hours was prescribed to treat the superficial pyoderma. Cephalexin was chosen because it has broad antimicrobial activity and a good safety profile[viii]. The owners were also instructed to continue bathing with Chlorhexiderm® shampoo, but to increase the frequency to once weekly to reduce the bacterial numbers present on the skin surface.

An elimination diet trial was initiated, in order to evaluate the possibility that CAFR contributed to the dog's pedal, facial and axillary pruritus and the development of a superficial pyoderma. An extensive diet history was obtained from the owner prior to selecting the elimination diet. The dog had previously eaten duck, venison, chicken and beef based diets. The owners were instructed to transition the dog onto Iams® Response KO (kangaroo and oat) diet

over a 3-4 day period. This diet was chosen based on a review of the dog's diet history, the need for a dry kibble diet, and because the owners were unwilling to perform a home-cooked diet trial. The owners were informed that the minimum length of time to utilize a strict limited antigen diet was 10-12 weeks[ix]. Day 1 of the 10 week diet trial would begin when the dog was eating solely the new diet. The owners were instructed to feed only this diet and no other supplements, treats, or flavored medications. The owners were given written and verbal instructions that the only food to be fed during the diet trial was the prescription diet, and cooked plain oats mixed with water could be used as treats. They were also given a diary to record food offered, accidental ingestion of foodstuffs, and changes in activity, behavior or fecal output. Because the patient had been receiving Heartgard® (Merial) flavored heartworm tablets, Heartgard® unflavored tablets for monthly heartworm prevention were prescribed. The owners were instructed to give the cephalexin in the homemade oats.

A follow-up appointment was made in 30 days in order to evaluate response to treatment.

Day 7: Telephone Update: The owners called to say they had successfully transitioned the dog onto the KO diet but they were having difficulty administering the cephalexin capsules in homemade oatmeal. The owners were given verbal instructions on how to administer the capsules directly into the back of their dog's mouth. If this continued to be a problem, the owners were instructed to call back and an alternative antibiotic would be attempted.

Day 37: Recheck: History: The dog was receiving all medications as directed and the owners did not report any adverse events related to the medications. The owners were able to administer the antibiotic directly into the dog's mouth without a problem and the dog had finished its full course of cephalexin 7 days prior to the recheck appointment. The owners reported that the dog's

pruritus decreased from 7.5 out of 10 on a **pruritus scale** to 5 out of 10. The owners noted that the dog was licking its inguinal area less frequently and was no longer biting at its tail base. They felt the "corn cobbing" of its forelimbs and licking of its paws was relatively unchanged. The owners reported being consistent with the food trial, and the dog had received no other food items.

Day 37: Physical Exam: The general physical exam was relatively unchanged from day 0. All vital signs were within normal limits. The dog weighed 26.0 kg. Dermatologic examination revealed mild erythema from the caudal dorsum to the tail base and also involving the caudal thighs. There were 4 circular areas of hyperpigmentation on the ventrum. There were two nodules and moderate erythema noted on the ventral chin. Axillae were moderately erythematous but no excoriations were present. The mild erythema and salivary staining in the interdigital webbing and on the palmar/plantar aspects of all four paws was unchanged from the previous exam. Mild salivary staining on the medial aspect of the thoracic limbs was also unchanged from the previous exam. Otoscopic examination was unremarkable. There was no erythema or swelling of the otic canals and both canals were pliable and non-painful when palpated externally. Tympanic membranes were intact in both ear canals.

Day 37: Assessment: The pruritus, papules, and epidermal collarettes involving the caudal dorsum and inguinal region (problems 1, 2, and 3) had improved suggesting a response to initiation of strict flea control and antibiotic therapy. The four areas of hyperpigmentation were attributed to post-inflammatory hyperpigmentation secondary to the resolution of the superficial pyoderma's epidermal collarettes. Problem 4, however, remained unchanged. This was attributed to insufficient time for the bacterial pododermatitis to resolve, the possible development of *Malassezia* dermatitis/pododermatitis or pruritus associated with underlying

allergic dermatitis (CAFR or AD) that had not yet been fully addressed. A new problem of nodules on the ventral chin was added to the problem list (problem 5). Differentials for problem 5 included a bacterial folliculitis/furunculosis, demodicosis, or dermatophytosis. If these lesions were bacterial in nature, Problem 5 was considered likely to be secondary to an underlying allergic dermatitis (CAFR or AD) causing pruritus, with secondary self-trauma likely leading to folliculitis/furunculosis.

Day 37: Diagnostic Plan: Acetate tape preparations were taken from the caudal dorsal trunk, inguinal region, interdigital spaces and palmar/plantar aspect of all four paws to evaluate the presence of bacteria or *Malassezia* (Appendix 6). A flea comb was passed through the hair coat on the caudal dorsum near the tail base (Appendix 7). An acetate tape preparation, hair plucks, and deep skin scrapings were taken from the ventral chin to evaluate for the presence of bacteria, *Malassezia*, dermatophytes and/or demodicosis (Appendix 8).

Day 37: Interpretation of results: Skin cytology showed a dramatic improvement from the previous month as there was no cytologic evidence of the superficial pyoderma or bacterial pododermatitis. There were however, small numbers of bacteria present from samples taken in the area of the nodules of the ventral chin, despite a 30-day course of cephalexin. This was most likely due to continued self-trauma secondary to pruritus which was considered to result from an underlying allergic trigger (CAFR or AD). However, a methicillin resistant *Staphylococcal* infection could have also been a contributing factor.

Day 37: Treatment Plan: As there was no evidence of the superficial pyoderma or bacterial pododermatitis the owners were instructed to discontinue antimicrobial therapy with cephalexin. They were also instructed to decrease bathing with Chlorhexiderm® shampoo to once monthly.

In order to address the two presumed furuncles found on the ventral chin a fungal **and bacterial** culture was recommended to rule out dermatophytosis and a resistant bacterial infection, however the owners declined these tests. Mupirocin ointment, USP (2% mupirocin) was prescribed. The owners were instructed to apply a thin film to the affected area on the ventral chin twice daily. The owners were informed that if there was no response to mupirocin ointment, then a bacterial culture to rule out an antibiotic resistant infection would need to be performed. In addition to the mupirocin ointment, a tapering dose of Temaril-P® (Pfizer; trimeprazine tartrate, 5mg and prednisolone, 2mg) was also prescribed to help decrease pruritus and inflammation[x]. The owners were instructed to give 4 tablets (20mg of trimeprazine tartrate, 0.76mg/kg and 8mg prednisolone, 0.3mg/kg) once daily for seven days, then to decrease to 2 tablets (10mg of trimeprazine tartrate, 0.38mg/kg and 4mg prednisolone, 0.15mg/kg) once daily for seven days and finally to 2 tablets every other day for seven days. The owners were instructed to continue the Iams® Response KO diet. They were reminded to feed only this diet with no other supplements, treats or flavored medications. The owners were asked to schedule a recheck appointment in 30 days.

Day 67: Recheck: History: The owners reported giving oral medications as previously directed. The owners had stopped applying mupirocin ointment as they felt the two lesions on the ventral chin had resolved. The owners reported that the dog's pruritus decreased from a 5 out of 10 on a pruritus scale to a 2 out of 10 while receiving the Temaril-P® at 4 tablets (20mg of trimeprazine tartrate, 0.76mg/kg and 8mg prednisolone, 0.3mg/kg) once daily. Pruritus increased only slightly at 2 tablets (10mg of trimeprazine tartrate, 0.38mg/kg and 4mg prednisolone, 0.15mg/kg) once daily. The owners gave the dog a score of 3 out of 10 on the pruritus scale while receiving 2 tablets every other day. The dog had completed the prescribed course of Temaril-P®

approximately 7 days prior to the recheck and the owners continued to rate the dog's pruritus at a 3-4 out of 10 on the pruritus scale. The owners felt the "corn cobbing" of the dog's forelimbs and licking of its paws were the dog's only areas of pruritus at the time of this recheck. The owners reported being consistent with the food trial however, they did report that the dog found some type of bone on the sidewalk and the owners were unable to retrieve it before it was eaten. The owners were unsure if they noted a subsequent increase in pruritus because it coincided with a decrease in the Temaril-P.

Day 67: Physical Exam: The general physical exam was relatively unchanged from day 0. All vital signs were within normal limits. The dog weighed 25.9 kg. Dermatologic examination was unremarkable with the exception of mild erythema and salivary staining in the interdigital webbing and on the palmar/plantar aspects of all four paws which was slightly improved from the previous exam. Mild salivary staining was noted on the medial aspect of the thoracic limbs and was also unchanged from the previous exam. The two presumed furuncles on the ventral chin noted on the previous exam were no longer present. Otoscopic examination continued to be unremarkable.

Day 67: Assessment: Problems 2, 3 and 5 were resolved. This was likely due to continued use of strict flea control and appropriate treatment for the superficial pyoderma and the presumed chin folliculitis/furunculosis. Problem 1 was improved but not resolved. The improvement in pruritus was likely due several factors including resolution of the superficial pyoderma, strict flea control using Capstar®, and the tapering course of Temaril-P®. There may have also been improvement in the pruritus due to the ongoing novel protein diet but a dietary provocation would need to be performed before a diagnosis of CAFR could be confirmed. Problem 4

remained largely unchanged suggesting the underlying allergic hypersensitivity had yet to be fully defined and managed.

Day 67: Diagnostic Tests: Acetate tape preparations were taken from the interdigital spaces and palmar/plantar aspect of all four paws and from the ventral chin to evaluate the presence of bacteria or *Malassezia* (Appendix 9).

Day 67: Interpretation of Results: Cytology of the paws and ventral chin was unremarkable, leading to the conclusion that the remaining pruritus and erythema were likely due to underlying allergic dermatitis caused by either CAFR and/or AD. Resolution of the folliculitis/furunculosis of the ventral chin was most likely due to a decrease in self-trauma associated with a decrease in pruritus as well as the use of topical mupirocin ointment. Persistent pruritus localized to the paws and face despite stringent flea control and the absence of secondary infections made CAFR and/or AD highly probable.

Day 67: Treatment Plan: Capstar® (Novartis; nitenpyram) at 57 mg (0.45 mg/kg) PO once daily was continued as the flea control because FAD had been confirmed as a contributing factor for pruritus in this dog. The owners were instructed to continue bathing with Chlorhexiderm® shampoo once monthly. The owners were also instructed to begin dietary provocation using the dog's original diet (Natural Balance® Duck and Potato Formula), treats and any human food the dog had previously consumed. The provocation phase would last for 2 weeks. If increased pruritus was noted, the owners were instructed to return to feeding the Iams® Response KO diet exclusively and to call with an update. The owners were asked to make a recheck appointment in 30 days.

Day 77: Telephone Update: Owners reported an increase in pruritus within 4 days of dietary provocation. They rated the dog a 7 out of 10 on the pruritus scale. They had discontinued the Natural Balance® Duck and Potato Formula diet and re-instituted the Iams® Response KO diet. The owners expressed concern over continuing to feed only this diet. A sequential rechallenge of individual protein and carbohydrate sources to attempt to determine the exact cause of pruritus associated with CAFR was discussed. The owner was asked to continue to feed the dog Iams® Response KO diet and add **one individual protein or carbohydrate source (i.e. beef) at a time for two weeks.** If increased pruritus was noted, the owner was instructed to **discontinue the newly introduced protein or carbohydrate source and resume** feeding only the KO until the pruritus returned to the pre-rechallenge level. **Once the dog's pruritus returned to the pre-challenge level the owners were instructed to add another single protein or carbohydrate source (i.e. chicken) to the KO diet. The protein and carbohydrate sources included** beef, chicken, dairy, eggs, soy, and rice. These ingredients were chosen as they are known sources of allergens in the veterinary literature and had been part of the dog's diet history[xi]. The owners reported that the dog continued to be a 3-4 out of 10 on the pruritus scale despite management of the confirmed CAFR with the strict elimination diet. This persistent pruritus was consistent with a likely diagnosis of atopic dermatitis since FAD and CAFR were being well controlled. Options for diagnosis and treatment of atopic dermatitis including intradermal testing or serum allergy testing with subsequent allergen specific immunotherapy (ASIT), medical management with cyclosporine, and/or corticosteroids were all discussed in great detail with the owner[xii]. Given the young age of this dog, allergy testing and ASIT were strongly recommended.

Day 89: Recheck: History: The owners were continuing to administer Capstar® once daily as previously directed. They were continuing to feed the Iams® Response KO diet as directed on

the day 77 telephone consultation. They were bathing the dog once monthly with Chlorhexiderm® shampoo. They continued to rate the dog's current level of pruritus at 3-4 out of 10 on the pruritus scale since resuming the KO diet alone. The owners had not yet begun to introduce individual proteins or carbohydrates into the KO diet.

Day 89: Physical Exam: The general physical exam was relatively unchanged from day 0. All vital signs were within normal limits. The dog weighed 26.0 kg. Dermatologic examination revealed mild erythema and salivary staining in the interdigital webbing and on the palmar aspects of all four paws which remained unchanged from the previous visit. Mild salivary staining was noted on medial aspect of the thoracic limbs and was also unchanged from previous visits.

Day 89: Assessment: Problems 2, 3 and 5 remained resolved. Problems 1 and 4 were unchanged from the previous visit. AD, a diagnosis made by exclusion of other causes of pruritus, was thought to be causing the remaining pruritus in this dog, as evidenced by the interdigital erythema and salivary staining noted before the dietary provocation.

Day 89: Diagnostic Tests: Acetate tape preparations were taken from the interdigital spaces and palmar/plantar aspect of all four paws to evaluate for the presence of bacteria or *Malassezia* (Appendix 10). A serum sample was taken and submitted to Greer Laboratories for serum allergy testing (Appendix 11).

Day 89: Interpretation of Results: Skin cytology was unremarkable. There was no indication of secondary infections and the clinical improvement to this point was attributed to appropriate management of the superficial pyoderma, FAD and CAFR. By diagnosis of exclusion the remaining pruritus and erythema was likely resulting from AD.

Day 89: Treatment Plan: Capstar® (Novartis; nitenpyram) at 57 mg (0.45 mg/kg) PO once daily was continued as the flea control. The owners were told they no longer needed to continue bathing with Chlorhexiderm® shampoo as there was no longer any evidence of infection. The owners were told they would be called in two weeks with the results of the serum allergy test.

Day 106: Telephone Update: The results of the serum allergy test were discussed with the owner. It was recommended that the dog's bedding be washed frequently to limit exposure to house dust mite. In order to decrease exposure to storage mites it was also recommended to the owner to buy smaller bags of kibble and once opened to freeze the contents to avoid development of storage mites, keeping a few days worth of food in a sealed Tupperware® container[xiii]. The owner agreed to start ASIT and the following allergens were included in the dog's ASIT: Kochia, Russian thistle, English plantain, Sage, Fescue, Timothy, Kentucky Blue, *Aspergillius niger, Penicillium notatum,* D. *farina,* D. *pteronyssinus,* and T. *putrescentiae*. These allergens were chosen because there were high levels of allergen specific IgE to these allergens on the ELISA test and because they were known to be present in the dog's environment.

The owner also reported she had introduced ground beef into the dog's diet eight days earlier and had not seen an increase in pruritus.

Day 116: Recheck: History: The owners were continuing to administer Capstar® as previously directed. The owners had switched the dog to an over-the-counter oatmeal based shampoo and were continuing to bathe the dog once a month. **The owners reported the dog's pruritus had increased from 4 out of 10 to a 9 out of 10 two** days after introducing chicken into the diet**.**

They had since discontinued the chicken and resumed feeding the KO diet alone and the dog's pruritus decreased to 4 out of 10 on the pruritus scale.

Day 116: Physical Exam: Both the physical exam and the dermatologic exam were unchanged from the previous visit. The dog weighed 26.4kg.

Day 116: Assessment: Assessment of all problems was considered to be the same as the Day 89 visit. The persistent pruritus in the absence of infection was considered likely due to unmanaged AD and the reintroduction of a chicken protein that caused a flare in the dog's clinical signs approximately 6 days earlier.

Day 116: Diagnostic Tests: Acetate tape preparations were taken from the interdigital spaces and palmar/plantar aspect of all four paws to evaluate for the presence of bacteria or *Malassezia* (Appendix 12).

Day 116: Interpretation of Results: There was no cytologic evidence of infection which continued to support a diagnosis of atopic dermatitis as the cause for the pedal erythema.

Day 116: Treatment Plan: The owner was shown how to administer a subcutaneous injection and advised on how to follow the protocol for ASIT subcutaneous injections (Appendix 13). Temaril-P ® (Pfizer; 5mg trimeprazine tartrate and 2mg prednisolone) was started to help control the dog's pruritus during the induction phase of ASIT. The owners were asked to administer 2 tablets (10mg trimeprazine tartrate, 0.37mg/kg and 4mg prednisolone 0.15mg/kg) orally once daily for 7 days, then 1 tablet (5mg trimeprazine tartrate, 0.19mg/kg and 2mg prednisolone 0.08mg/kg) once daily for 7 days, and finally 1 tablet every other day until the next recheck. The owners were asked to continue administering Capstar® once daily.

Day 154: Telephone Update: The owner was contacted to assess the dog's progress. The owner reported the dog's pruritus decreased dramatically while receiving the Temaril-P® and was currently a 1 out of 10 on the pruritus scale. The owners had discontinued the Temaril-P® 2 days prior as they did not think the dog's level of pruritus warranted continuing the medication. The dog was continuing to receive ASIT and was currently receiving 1cc of the maintenance vial once weekly given by subcutaneous injections. The dog had not had any adverse reactions to ASIT.

Day 224: Recheck: History: The owners reported the dog had done extremely well until 2 weeks prior to this recheck when there was a significant increase in the amount of pedal pruritus as manifested by licking at the paws. The owners reported the dog's pruritus increased from a 1 out of 10 to 4 out of 10 on the pruritus scale. The owners were continuing to feed the KO diet alone and occasionally added cooked ground beef as a treat. They did not perceive an increase in pruritus following ingestion of beef. Two months earlier the owners ran out of the Heartgard® unflavored tablets and resumed using the Heartgard® flavored tablets. They did not perceive an increase in pruritus following reintroduction of the flavored tablets. The owners had not challenged the dog's diet with any other protein or carbohydrate sources. They were continuing to administer Capstar as previously directed.

Day 224: Physical Exam: The general physical exam was unchanged from day 0. All vital signs were within normal limits. The dog weighed 26.5 kg. Dermatologic examination revealed mild to moderate erythema and salivary staining in the interdigital webbing and on the palmar/plantar aspects of all four paws. The salivary staining on the medial aspect of the thoracic limbs was no longer present.

Day 224: Assessment: Problems 2, 3, and 5 remained resolved. There had been significant improvement in problems 1 and 4 until two weeks prior to the recheck appointment. This was considered likely to either be a recurrence of secondary infection and/or an increased allergen load in the environment causing increased pruritus and paw licking.

Day 224: Diagnostic Tests: Acetate tape preparations were taken from the interdigital spaces and palmar/plantar aspect of all four paws to evaluate for the presence of bacteria or *Malassezia* (Appendix 14).

Day 224: Interpretation of Results: Cytology supported the presence of a *Malassezia* pododermatitis which was likely contributing to the increased pruritus seen in recent weeks. This new problem, problem 6, likely developed secondary to the atopic dermatitis as the dog's CAFR was well controlled with the KO diet.

Day 224: Treatment Plan: The owners were instructed to continue to administer Capstar® as previously prescribed, maintain the dog on the same diet and continue to administer the maintenance dose of ASIT injection on a weekly basis. Treatment for *Malassezia* pododermatitis was initiated and fluconazole (7.5mg/kg) PO once daily (one 200mg tablet) was prescribed to be given until recheck[xiv] [xv]. To decrease pruritus another tapering course of Temaril-P was prescribed. The owners were asked to administer 2 tablets (10mg trimeprazine tartrate, 0.37mg/kg and 4mg prednisolone 0.15mg/kg) orally once daily for 7 days, then 1 tablet (5mg trimeprazine tartrate, 0.19mg/kg and 2mg prednisolone 0.08mg/kg) once daily for 7 days, and finally 1 tablet every other day until the next recheck.

Day 257: Recheck: History: The owners reported the dog's pruritus was currently very well controlled and the dog was observed to lick its feet only once or twice a day following breakfast

and dinner. They scored the dog-'s pruritus as a 1 out of 10 on a pruritus scale. The owners were continuing to feed the KO diet alone and continued to occasionally add cooked ground beef as a treat. They also began adding cheese into the dog's diet to administer pills. They did not perceive an increase in pruritus following ingestion of the cheese. The owners ran out of Temaril-P® three days prior to the recheck appointment and did not perceive an increase in the dog's pruritus since discontinuing the medication. The dog had been receiving 1 tablet of Temaril-P® (5mg trimeprazine tartrate, 0.19mg/kg and 2mg prednisolone 0.08mg/kg) every other day. The owners had also completed the prescribed course of fluconazole 3 days earlier. They were continuing to administer Capstar® as previously directed.

Day 257: Physical Exam: The general physical exam was unchanged from day 0. All vital signs were within normal limits. The dog weighed 26.5 kg. Dermatologic examination revealed mild salivary staining in the interdigital webbing and on the palmar aspects of all four paws.

Day 257: Assessment: Problems 2, 3, and 5 remained inactive/resolved. Problems 1 and 4 were significantly improved. The resolution of the pruritus, erythema and salivary staining was likely due to a combination of factors including, successful management of AD, CAFR, and FAD as well as treatment of *Malassezia* pododermatitis (problem 6). The dog had been receiving ASIT for almost 150 days and it was felt that this could also -be contributing to successful management of pruritus.

Day 257: Diagnostic Tests: Acetate tape preparations were taken from the interdigital spaces and palmar/plantar aspect of all four paws (Appendix 15).

Day 257: Interpretation of Results: Cytology supported the clinical evidence that the *Malassezia* pododermatitis was resolved.

Day 257: Treatment Plan: The owners were instructed to continue administering ASIT on a weekly basis, to continue feeding the KO diet and to continue administering Capstar® as previously directed. They were instructed to make a recheck appointment in 12 weeks.

Day 351: Telephone Update: Owners called to report the dog was doing extremely well and had not had any other flare-ups of pruritus. The owner was unable to make her recheck appointment but wanted to reschedule and have the allergens refilled.

Day 397: Recheck: History: The dog presented for a recheck evaluation following 10 months of ASIT. The owners reported the dog had done extremely well and had not had an increase in pruritus since Day 224. The dog was currently receiving 1ml of the maintenance vial of ASIT subcutaneously once weekly, Capstar® once daily, and the owners were continuing to feed the KO diet with occasional beef and cheese. The dog had not required Temaril-P® for approximately 2 months.

Day 397: Physical Exam: The general physical exam was unchanged from day 0. All vital signs were within normal limits. The dog weighed 26.3 kg. Dermatologic examination revealed mild salivary staining in the interdigital webbing and on the palmar aspects of all four paws which was diminished from Day 257.

Day 397: Assessment: All problems remained resolved due to the successful management of FAD, CAFR, and AD as well as appropriate treatment of prior secondary infections

Day 397: Diagnostic Tests: None performed

Day 397: Interpretation of Results: N/A

Day 397: Treatment: The owner was instructed to continue all therapy previously prescribed and to call if there was an increase in pruritus. A recheck was scheduled in 3 months.

Day 564: Recheck: History: The dog presented for a recheck evaluation following 12 months of ASIT. The owners reported the dog continued to do well. They gave the dog a 1 out of 10 on the pruritus scale. The dog was currently receiving 1ml of the maintenance vial of ASIT subcutaneously once weekly, Capstar® once daily, and the owners were continuing to feed the KO diet with occasional beef and cheese

Day 564: Physical Exam: The general physical exam was unchanged from day 0. Dermatologic examination was unremarkable with the exception of mild salivary staining on all 4 paws.

Day 564: Assessment: All problems remained resolved. This was due to the successful management of FAD, CAFR, and AD as well as appropriate treatment of secondary infections. ASIT had been administered for over 12 months and was considered to be a successful therapy for the management of AD in this dog.

Day 564: Diagnostic Tests: None performed

Day 564: Interpretation of Results: N/A

Day 564: Treatment: The owner was instructed to continue all therapy previously prescribed and to schedule a recheck appointment in 3 months.

Summary: This case was selected because it represents the importance of the thorough work-up for a suspected allergic dog. This dog represented a case where FAD, CAFR and AD together with secondary infections were contributing to the dog's overall pruritus. Allergic patients need to be evaluated in a systematic fashion to determine all etiologies contributing to the overall

pruritic threshold. If all etiologies for pruritus are not being managed simultaneously, the overall treatment protocol could be viewed as a failure. Additionally, secondary infections need to be identified and treated concurrently while attempting to manage the primary allergic dermatitis or, again, the management of the allergic dermatitis could be viewed as a failure.

In this case a diagnosis of food allergy was not identified by the referring veterinarian. The success of past attempted diet trials may have been compromised as the dog continued to receive treats, table food and flavored heartworm prevention all of which could have been potential food allergens for this dog. As a duck and potato diet was chosen as the trial diet and the dog was later confirmed to be allergic to chicken it is possible there was a cross reaction between the avian meats. Studies have shown that duck can cross-react with chicken protein[xvi].

Due to appropriate management of FAD and CAFR, AD was accurately diagnosed and treated in this dog. In this case the dog responded to ASIT within the first 6 months of therapy and continued to due well at 1 year. For this reason, ASIT can be continued to be used long term, which will minimize the need for corticosteroids.

This was an extremely rewarding case because this dog's FAD, CAFR and AD were able to be successfully diagnosed and managed early in its life which will hopefully improve the dog's quality of life as well as diminish the level of frustration that allergic skin disease can cause for the owner.

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Appendices:

Cytology Abbreviations	
TNTC	Too numerous to count
4+	>20 organisms/oil immersion field (oif)
3+	5-20 organisms/oif
2+	2-5 organisms/oif
1+	1-2 organisms/oif
0	None
NSF	No significant findings

Miscellaneous abbreviations	
AU	Left and right ear
AD	Right ear
AS	Left ear

OD	Right eye

Appendix 1: Day 0: "Diff Quik®" acetate tape skin cytology (100x objective)

- Ventral abdomen: 2+ degenerate neutrophils, 2+ cocci
- Dorsal trunk: 2+ cocci
- Interdigital/ palmar/plantar aspect of paws: 1+ cocci

Appendix 2: Day 0: Flea combing

- Negative for flea excrement; negative for fleas.

Appendix 3: Day 0: Deep skin scraping

- Negative for mites.

Appendix 4: Day 0: Superficial skin scraping

- Negative for mites.

Appendix 5: Day 0: *Cheyletiella* Preparation

- Negative for *Cheyletiella*

Appendix 6: Day 37: "Diff Quik®" acetate tape skin cytology (100x objective)

- Ventral abdomen: NSG
- Dorsal trunk: NSF
- Interdigital/ palmar aspect of paws: NSF

Appendix 7: Day 37: Flea combing

- Negative for flea excrement; negative for fleas.

Appendix 8: Day 37: "Diff Quik®" acetate tape skin cytology (100x objective), Trichogram, Skin scrape

- Ventral chin: 1+ cocci and 1+ degenerate neutrophils
- Tricogram: NSF
- Deep skin scrape: NSF

Appendix 9: Day 67: "Diff Quik®" acetate tape skin cytology (100x objective)

- Interdigital/ palmar/plantar aspect of paws: NSF
- Ventral chin: NSF

Appendix 10: Day 89: "Diff Quik®" acetate tape skin cytology (100x objective)

- Interdigital/ palmar/plantar aspect of paws: NSF

Appendix 11: Day 89: Serum Blood Allergy Test Results (Greer Laboratories)

Weed	Interpretive Score	MAU	
Russian Thistle	+	45	
Scale mix	Neg	35	
Dock/sheep Sorrel Mix	Neg	37	
Lamb's Quarter	Neg	29	
Sage Mix	+	41	
Dandelion	Neg	5	
Coclebur	Neg	14	
English Plantain	+	43	

Goldenrod	Neg	11
Kochia	+	51
Pigweed Mix	Neg	13

Tree	Interpretive Score	MAU
Eucalyptus	Neg	13
Cottonwood	Neg	14
Oak Mix	Neg	32
Ash Mix	Neg	8
Orange Pollen	Neg	0
Acacia	Neg	0
Alder	Neg	17
Cedar/juniper	Neg	12
Maple/Box Elder Mix	Neg	19
Mulberry	Neg	37
Olive	Neg	0
Palm	Neg	22
Pine Mix	Neg	22
Walnut	Neg	0

Grass	Interpretive Score	MAU	
Timothy	+	48	
Fescue	+	51	
Kentucky Blue/June	+	42	
Red Top	Neg	28	
Bermuda	Neg	31	
Quack	+	40	
Johnson	Neg	27	
Perennial Rye	Neg	38	

Fungal	Interpretive Score	MAU	
Penicillium	+	50	
Aspergillus	+++	60	
Stemphylium	Neg	25	
Cladosporium	Neg	27	
Curvularia	Neg	15	

Pullularia	Neg	35
Cephlasporium	Neg	26
Alternaria	Neg	29
Mucor Mix	Neg	7

Environmental	Interpretive Score	MAU
Mite – A. siro	+++	78
Mite- D. farina	+	59
Mite- T. putrescentiae	+++	72
Mite- D. pteronyssinus	+	53
Flea	Neg	12

Interpretation:

MAU = Modified Absorbance Units which indicates the level of allergen specific IgE detected.

+ (40-59 MAU) = Scores in this range should be considered significant if the allergens are found in the pets environment and they relate to clinical history.

Appendix 12: Day 116: "Diff Quik" ® acetate tape skin cytology (100X objective)

- Interdigital/palmar aspect of paws: NSF

Appendix 13: Allergen Specific Immunotherapy Hyposensitization Protocol

The initial allergen treatment set contains 3 vials of varying concentrations which are to be kept refrigerated. Injections are administered subcutaneously every other day for the first 28 days, then weekly until further directed.

Vial #1: (200 PNU/cc) first 5 injections only then discard remainder of vial.

Vial #2: (2000 PNU/cc) second 5 injections only then discard remainder of vial.

Vial #3: (20,000 PNU/cc) all remaining injections (from day 20 onwards)

Vial #1 (200 PNU/cc)

Day	Day of treatment	Amount
0	116	0.1cc
2	118	0.2cc
4	120	0.4cc
6	122	0.8cc
8	124	1.0cc

Vial #2 (2000 PNU/cc)

Day	Day of treatment	Amount
10	126	0.1cc
12	128	0.2cc
14	130	0.4cc

16	132	0.8cc
18	134	1.0cc

Vial #3 (20,000 PNU/cc)

Day	Day of treatment	Amount
20	136	0.1cc
22	138	0.2cc
24	140	0.4cc
26	142	0.8cc
28	149	1.0cc
35	156	1.0cc
42	163	1.0cc
49	170	1.0cc
56	177	1.0cc
63	184	1.0cc
70	191	1.0cc

Appendix 14: Day 224: "Diff Quik" ® acetate tape skin cytology (100X objective)

- Interdigital/ palmar aspect of paws: 2+ *Malassezia*

Appendix 15: Day 257: "Diff Quik" ® acetate tape skin cytology (100X objective)

- Interdigital/ palmar aspect of paws: NSF