

Hemosiderosis and Clinical Findings Consistent with Black Rhino Syndromes in Greater One Horned Rhinoceros (*Rhinoceros unicornis*)

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Introduction:

Hemosiderosis and hemochromatosis, manifestations of iron storage disease, are significant causes of morbidity and mortality of many species in zoological collections. Frugivorous birds, lemurs, and browsing mammalian herbivores are a small group of animals noted to have serious health problems related to hemosiderosis. Both browsing species of rhinoceros, black rhinoceros (*Diceros bicornis*) and Sumatran rhinoceros (*Dicerorhinus sumatrensis*), have documented hemosiderosis and hemochromatosis but no reports this condition in the grazing rhinos, white rhinoceros (*Ceratotherium simun*) and Greater One horned rhinoceros (*Rhinoceros unicornis*) exist. Explanation of the differences have focused on the absence of natural chelators in grass based preparations that would likely increase the bioavailability of iron and allow it to accumulate progressively in animals sustained largely on captive rations. (Dennis Paglia AAZV 1999). In the case of black rhinoceros many other inflammatory conditions exist concurrently with iron storage disease including ulcerative skin lesions and hepatopathies. The most common problem of captive black rhinoceros actually is diarrhea (Dennis Thesis). It is our thinking that iron storage disease is initiated by chronic gastrointestinal inflammation in many specialized feeders with black rhinoceros being an example. Two cases have recently been evaluated to support this ideal and demonstrate that even grazers such as the Greater One horned rhinoceros are susceptible to iron storage disease and that inflammatory states of the gastrointestinal tract may be an underlying source of this problem.

Case 1. A 13 yr-old male Greater one horned rhinoceros (*Rhinoceros unicornis*) was evaluated for chronic weight loss of over 2 years with progressively worsening malaise and extended periods of recumbency. The diet consistent of approximately 18kgs of various grains and concentrates offered twice daily for several years but this was increased to over 25kgs for one month prior to the initial diagnostic workup. Initial blood sampling demonstrated azotemia (creatinine 3.7 mg/dl), hypercalcemia (16.0mg/dl), hypophosphatemia (0.9mg/dl), and anemia (26%), Leptospirosis titers to the seven most common serovars in this area were all negative. Renal failure was diagnosed and severe hypophosphatemia was thought to be responsible for the malaise and recumbency. Daily phosphate enemas were prescribed and the rhinoceros showed some improvement in his condition. Follow-up diagnostic work-up was conducted with a combination of 10mg detomidine intramuscularly in a chute for blood collection, rectal exam with ultrasound, and upper GI endoscopy. An additional 50mg butorphanol and 25 mg midazolam was given via intravenous butterfly catheter in the left medial radial vein to allow rectal palpation and upper GI endoscopy. The rhinoceros was reversed with 30mg atipamezole IM and 250mg naltrexone IV and walked out of the chute normally within 5 minutes. Findings included anemia (23%), hypercalcemia (16.8mg/dl), hypophosphatemia (1.4mg/dl), and

azotemia (4.8mg/dl). Renal fibrosis was suspected due to the ultrasound exam and endoscopic biopsy of the lower esophagus revealed active inflammation and fibrosis in a very superficial sampling of the mucosa. Urine was collected and the fractional excretion of phosphorus was 1%. A normal reference value for horses is 0.16% and this is consistent with values obtained from young healthy black rhinoceros (Ball unpublished data). Serum was submitted to Kansas State University for iron metabolites revealed iron 58 ug/dl, total iron binding capacity (TIBC) 187 ug/dl, ferritin 369ng/ml, ceruloplasmin 62 mg/dl, and haptoglobin 175 mg/100ml. These values were considered normal by the in house levels established by the laboratory but there were no specific values for greater one horned rhinoceros. The rhinoceros declined in condition and one month later was humanely euthanized. Gross necropsy findings included generalized muscle wasting, pale kidneys, serous fat atrophy, bronzing of the gastro-intestinal viscera, and a firm swollen liver. Histological diagnosis revealed a marked glomerulonephropathy with chronic fibrosing interstitial nephritis, hemosiderosis in the spleen, pigment laden peribronchiolar macrophages, and marked sinusoidal pigment laden Kupffer cells of the liver. The liver was stained specifically for iron and an extensive accumulation of iron was found throughout the sample.

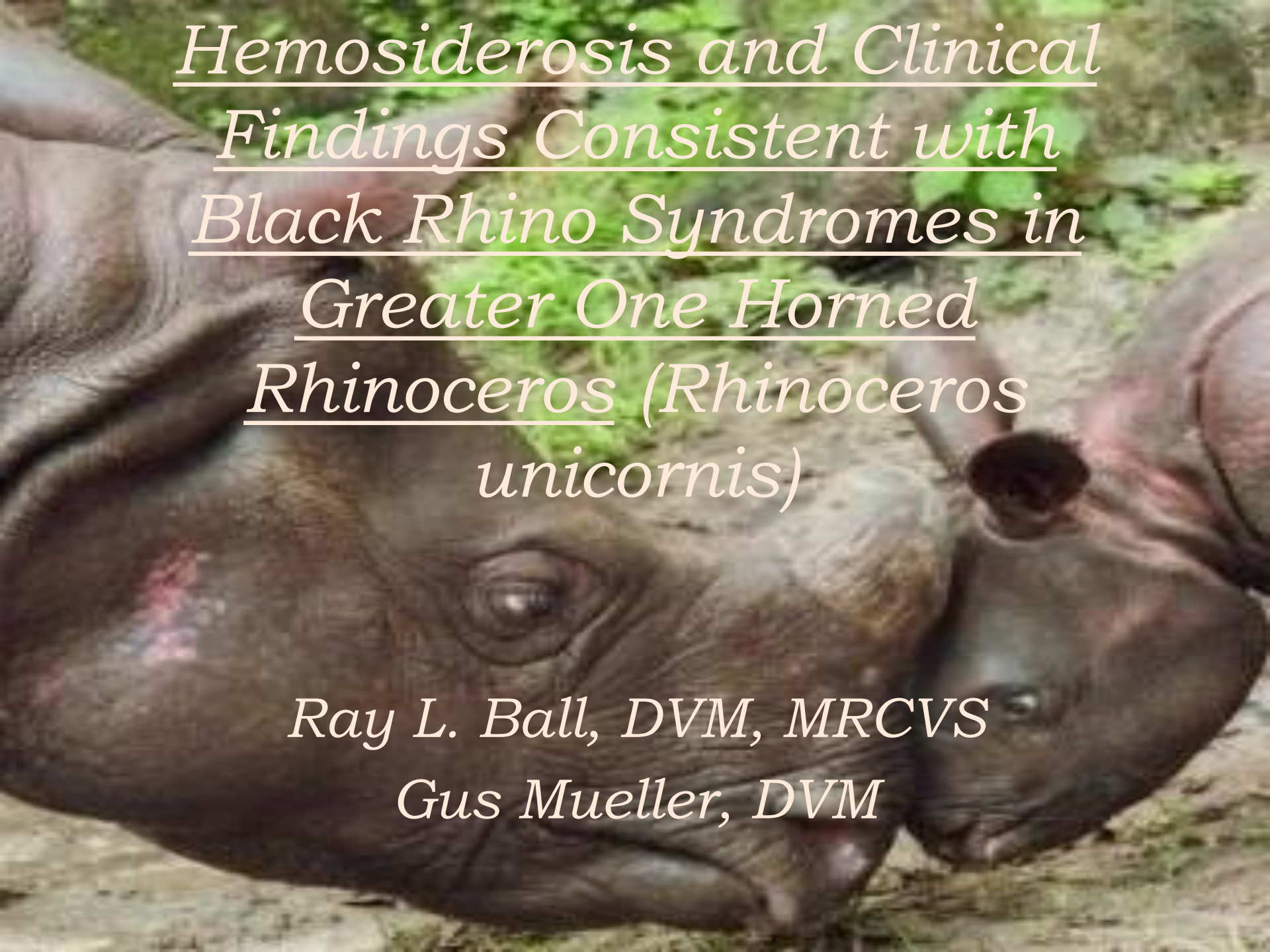
Case 2. A 10 yr-old female Greater one horned rhinoceros (*Rhinoceros unicornis*) had a history of recurring ulcerative, bulla cutaneous lesions, intermittent diarrhea with associated Hemacult positive fecal, and episodes of colic. The skin lesions were typically fluid filled bullae early and then had a cobblestone appearance. The mandible area was frequently involved but other areas in the folds of the dermal armor and the elbows were also affected. Touch prep of these skin lesions revealed an equal amount of eosinophil and neutrophil accumulation. Empiric therapy with diphenhydramine Hydrochloride (Benadryl™) at 1mg/kg PO SID to BID resulted in some relief of the lesions but only rarely complete resolution and recurrence was common after therapy ceased. Blood sampling has been opportunistic in this rhinoceros

Discussion:

The clinical presentation, diagnostic findings and pathology findings in Case demonstrate what is believed to be the only documented incidence of iron storage disease in a Greater One horned rhinoceros. The high level of concentrates, with high levels of starches and potential antigenic items, fed to the rhinoceros in Case 1 suggest that chronic gastrointestinal inflammation may have been the source of the chronic active inflammation. Iron intake has been shown to not be directly related to the occurrence of hemosiderosis and hemochromatosis in rhinoceros but a nutritional feeding issue is still suspected. The chronic inflammation in this rhinoceros may have also lead directly to antigen complex deposition and resulted in the renal pathology. The serum assay for ferritin also does not appear to accurately reflect iron stores in Greater one horned rhinoceros and a more species specific assay may be needed. The clinical picture of Case 2 closely resembles the clinical findings seen in captive black rhinos. The possibility of a gastrointestinal hypersensitivity or an antigenic source of inflammation is suspected in black rhinos and in these Greater one horned rhinos based on the presence of gastrointestinal signs, consistency of eosinophil in the skin lesions and the temporary improvement with anti-histamines. The flare of this female rhinoceros skin lesion did occur in late pregnancy of consecutive gestations. In both occasions feed intake was higher as expected and the concentrate ration being increased in relation to the forage intake.

References

1. **Dennis, Patricia M.D., 2004.** Epidemiology of black rhinoceroses (*Diceros bicornis*) in captivity in the United States. Ohio State University, Thesis: pp. 1-138
2. **Paglia, D.E.; Dennis, P., 1999.** Role of chronic iron overload in multiple disorders of captive black rhinoceroses (*Diceros bicornis*). Proceedings of the American Association of Zoo Veterinarians 1999: 163-171



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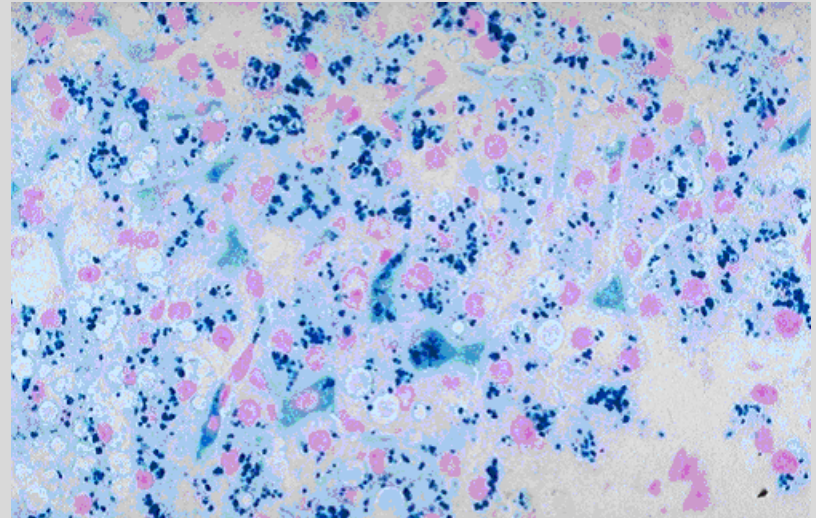
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Iron Storage Disease:

Hemosiderosis and Hemochromatosis

- Hemosiderosis: general increase in tissue iron stores
- Hemochromatosis: abnormal accumulation of iron in parenchymal organs, leading to organ dysfunction



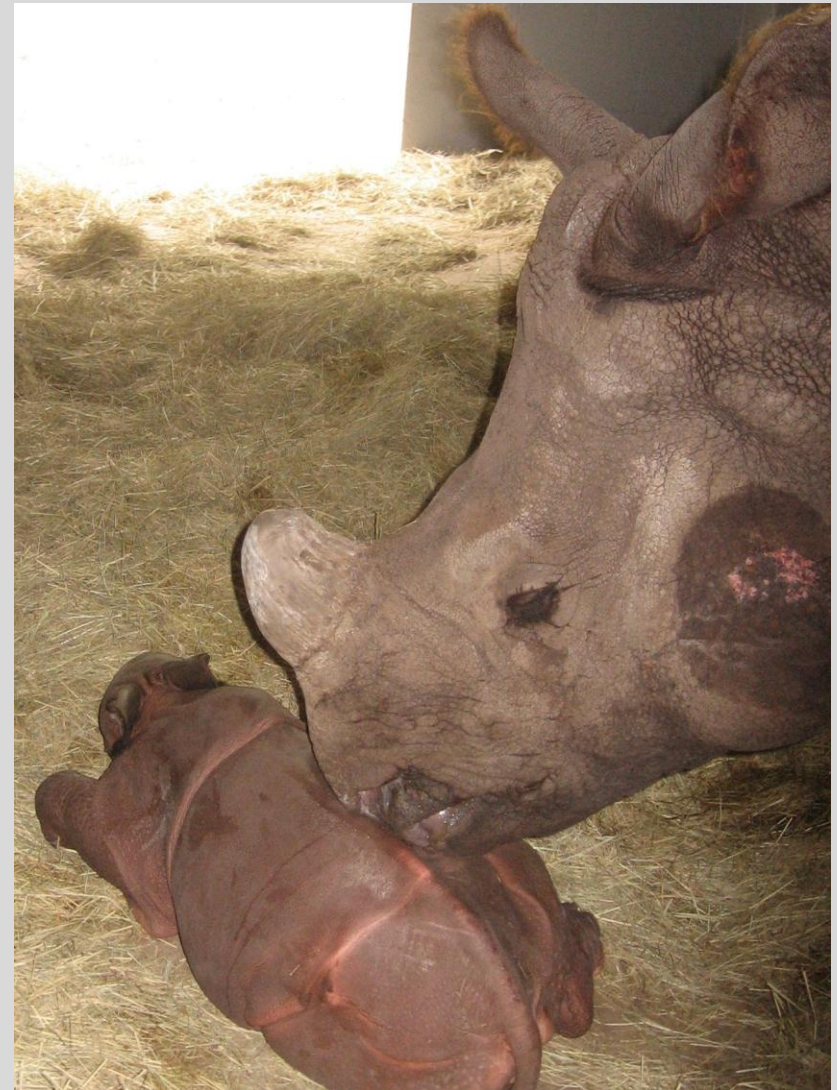
- Fruit Bats
- Soft bill birds
 - Toucans
 - Mynahs
- Lemurs
- Tapirs
- Many species





Dermatitis in GOH rhinoceros

- 10 year old female GOH
- Chronic intermittent GI signs
 - Colic
 - Diarrhea
 - Occult positive blood in fecals
- Bulla dermatitis
 - eosinophils





Dermatitis in GOH rhinoceros

- Skin disease with late term pregnancy
 - Increased concentrate intake??
- GI signs respond to removal of concentrates
- Skin lesions improve with oral diphenhydramine hydrochloride (Benadryl™)



Case 1

- 13 yr old male GOH rhinoceros
- Chronic weight loss
- Malaise & Recumbency
- Florida
 - Outdoors
- Grass hay
- ~15kgs twice daily concentrates and grains



Initial Diagnostic Workup

- CBC
 - PCV 26%
- Biochemistries
 - Creatinine 3.7mg/dl
 - Albumin 1.5mg/dl
 - BUN 52 mg/dl
 - Calcium 16.0 mg/dl
 - Phosphorus 1.0 mg/dl
- Anemia, regenerative
- Azotemia
- Hypercalcemia
- Hypophosphotemia
- Hypoalbuminemia

Dx: Renal failure

- Lepto serology negative

Follow up exam



- 20mg detomidine IM
 - 50mg butorphanol IV
 - 25mg midazolam IV
- Hematology
- Urine collection
- Upper GI endoscopy
- Rectal ultrasound
- Atipamezole
- Nalterexone

Laboratory Results

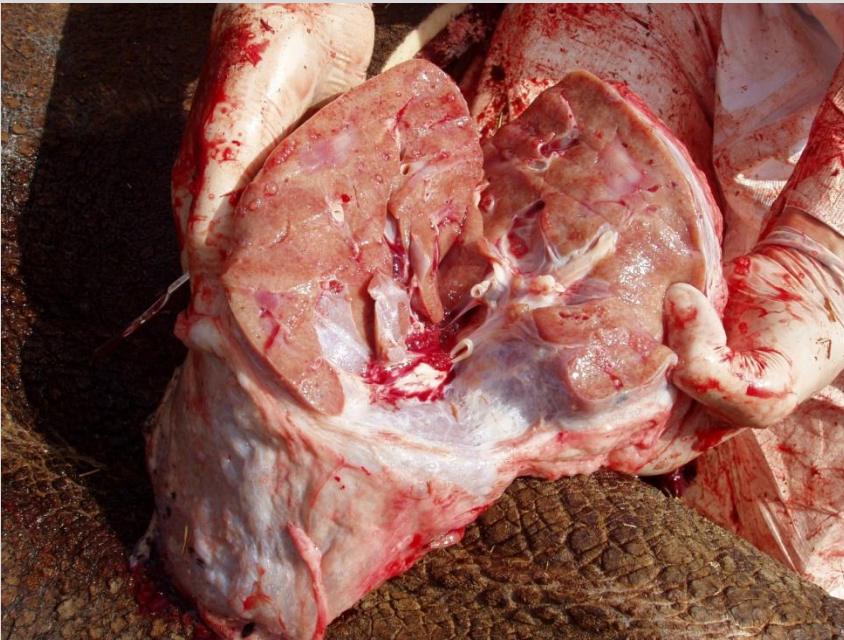
- Anemia
- Hypercalcemia
- Hypophosphatemia
- Azotemia
- Hypoalbuminemia
- Fractional excretion P
 - 1%
 - Horses & B rhinos 0.15%
- Endoscopic biopsy
 - Esophageal mucosa
 - Lymphocytic inflammation with fibrosis
- Rectal ultrasound
 - Renal Fibrosis

Iron Analysis Kansas State University

- Iron ug/dl 58
- TIBC ug/dl 187
- Ferritin ng/ml 369
- Cerulo mg/dl 82
- Haptomg/100ml 175
- Black rhino
 - Iron 214-1014
 - TIBC 365-1097
 - Haptoglobin 39-67
- White rhino
 - Iron 113-261
 - TIBC 310-1192
 - Haptoglobin 31-66

Necropsy

- muscle wasting
- pale kidneys
- serous fat atrophy
- bronzing of the gastrointestinal viscera
- firm swollen liver



Histopathology

- Glomerulonephropathy
 - chronic fibrosing interstitial nephritis
- Hemosiderosis in the spleen
- Pigment laden peribronchiolar macrophages
- Sinusoidal pigment laden Kupffer cells of the liver.
 - extensive accumulation of iron
 - Hemosiderosis

Black Rhino Syndromes

- IVHS
- Anemia
- Superficial necrotizing dermatitis (SND) and blister disease
- Infectious diseases
- Encephalomalacia
- Chronic weight loss
- Shifting leg lameness
- Diarrhea
- Iron Storage Disease



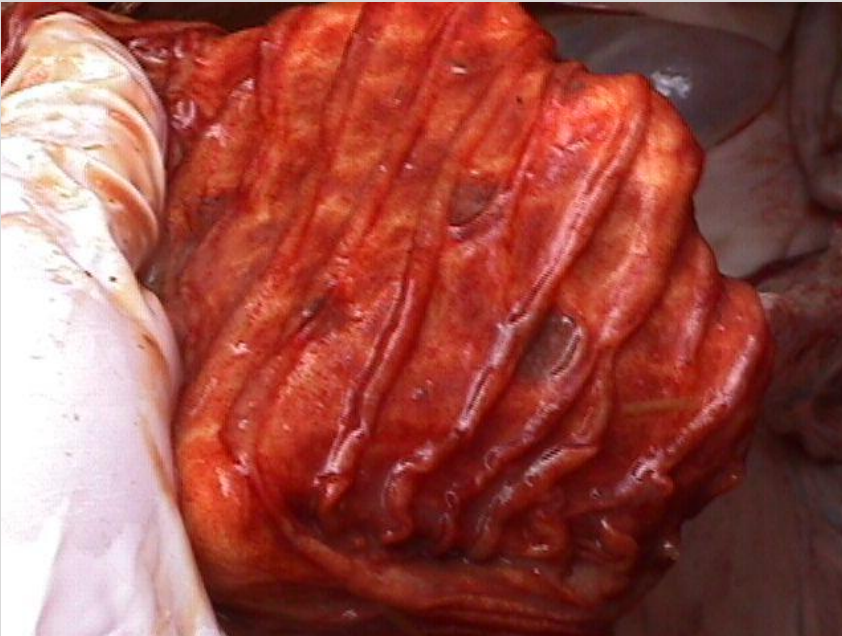


Gastrointestinal issues

- Diarrhea
 - Most common problem listed in North America
 - P Dennis 2005
 - Fecal hemacult
 - Often positive in managed care
 - Discounted in equid medicine
 - 11/11 negative in wild caught
 - September 2005
 - Hluhuwe-Imfolozi Wildlife Park
- Overlooked in GOH???

Inflammation in Black rhinos

- Ferritin
- Anti-phospholipids (APhL)
- More inflammation in captive black rhinos
- GI issues very common
- Evidence that length in captivity increases inflammation
 - Diet transition wild to captive
 - Weaning to captive foods



Is nutrition an aetiological factor for inflammatory bowel disease?

Kevin D. Cashman^{a,b} and F. Shanahan^b

Inflammatory bowel disease (IBD) is a chronic inflammatory process, the aetiology of which is complex and probably multi-factorial. Nutrition has been proposed to be an important aetiological factor for IBD. The present review critically examines the relationship between components of the diet (such as sugar, fat, fibre, fruit and vegetables, and protein) and IBD, including ulcerative colitis and Crohn's disease. In addition, it investigates the possible role of infant feeding practices in the development of IBD. *Eur J Gastroenterol Hepatol* 15:607–613 © 2003 Lippincott Williams & Wilkins

European Journal of Gastroenterology & Hepatology 2003, 15:607–613

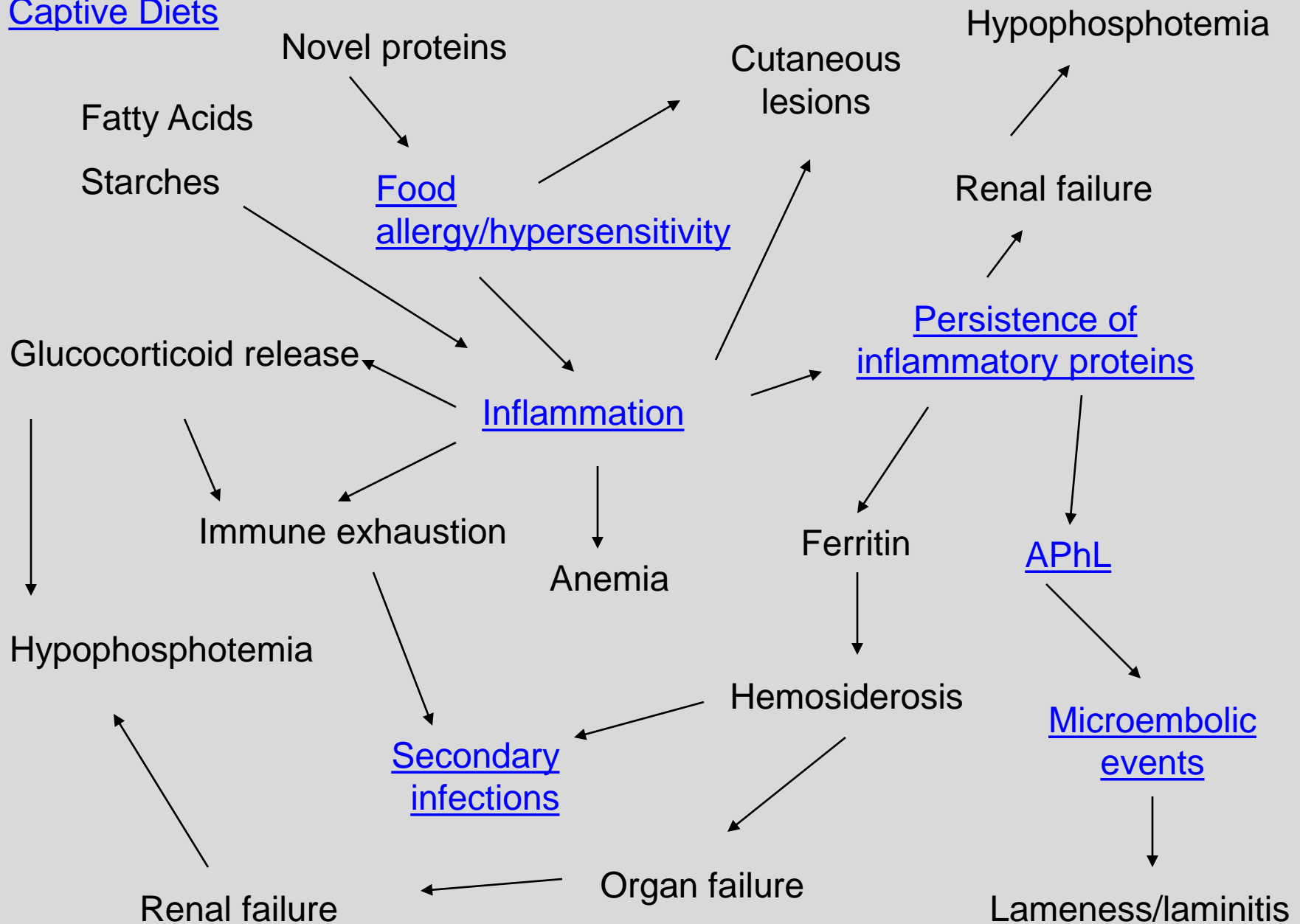
Keywords: inflammatory bowel disease, nutrition, aetiology

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Captive Diets



Conclusions

- Iron storage disease occurs in a wide variety of species
 - Can occur in novel species in extreme conditions
- Serum ferritin is not reflective of iron nor inflammation in GOH (Sumatran?) rhinos
 - Species specific development
- These GOH cases suggest an inflammatory role in the diet and feeding practices

Acknowledgements

A photograph of two hippos in a natural enclosure. One hippo is in the foreground, looking towards the camera, while another is partially visible behind it. The background shows green grass and a dirt ground.

- Animal Medical Center, Gulf Breeze Florida
- Asia Staff at Lowry Park Zoo