Iron Storage Disease in Lemurs

A Report to the Prosimian Taxon Advisory Group
From the Advisor's Group* Meeting
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Background

A syndrome of excessive iron accumulation (hemosiderosis) was first recognized in lemurs as early as the 1960's but descriptive reports of the condition were not published until the 1980's.[1,4,11] The most well-known of these is a publication by Spelman et al. (1989) who reported 100% incidence of hemosiderosis in captive lemurs from the institution in her study.[11] As a result, many now consider iron accumulation to be a serious and persistent health threat to captive lemurs. This has prompted a number of individuals to recommend drastic changes in captive husbandry and diet practices in order to control the problem. In response to recent concerns regarding this issue, the PTAG advisors met in March 2003 to examine the extent of current knowledge about iron overload in lemurs and to develop recommendations for diet, husbandry, and future areas of research directed at gaining a more thorough understanding of iron storage disease in lemurs.

Munson and Lowenstine (1999) recently published a thorough review of iron overload in exotic species.[8] They note it is important to distinguish non-pathologic accumulation of iron pigment in tissues (hemosiderosis) from conditions in which there is functional or morphologic evidence of iron toxicity (hemochromatosis). In the published descriptions of iron storage disease in lemurs it is not possible to determine whether the amounts of iron noted on post-mortem exams represented a pathologic level of accumulation.[1,4,11] Despite this, authors suggested that health and longevity were compromised. Unpublished data from Duke University suggests that the incidence of hemosiderosis in captive lemurs may not be as high as previously suspected and that there may be species and institutional differences in the tendency to develop hemosiderosis as well.

Iron Physiology and Nutrition

Iron is an essential nutrient for all living organisms, however the metabolism and dietary requirements are undefined for most species. The National Research Council estimates the adequate dietary iron concentration (dry matter basis) for nonhuman primates to be 100 mg/kg.[9] A safe upper limit for dietary iron has not been established for nonhuman primates.

The bioavailability and absorption of iron from various food sources has been studied mainly in chickens, rats, and humans. Factors affecting bioavailability and absorption are numerous and include the animal's iron status (i.e. iron deficient or replete), the animal's age and sex, the

chemical form of iron in the diet, and levels of other dietary components including vitamins, minerals, fiber, and secondary plant compounds (polyphenols, tannins, phytates, etc.).[3,6,7,9] The impact on iron bioavailability and absorption by these factors, alone or in combination, may be highly variable depending on the species studied. Therefore, extrapolation of results of these studies to nonhuman primates such as lemurs may not be applicable.

Plant polyphenols have been shown to decrease iron absorption by binding dietary iron, making it unavailable for uptake.[3,6,7] It has been suggested that captive lemur diets are lacking in natural tannins compared to wild lemur diets. Complicating this issue, the term tannin is used to describe a variety of chemicals with marked variability in chemistry, toxicity, and binding specificity.[5] Further, tannins do not affect only iron availability – they can lower the digestibility and nutrient availability of other diet components as well. This said, the addition of tannins to the captive diet may result in deficiencies in other micronutrients and may not have the desired impact on iron absorption.

Spelman et al. proposed that high levels of vitamin C in the diets of captive lemurs contributed to the development of hemosiderosis by enhancing the absorption of iron.[11] Subsequently, some have suggested that foods high in vitamin C should be excluded from lemur diets. The extent of vitamin C's enhancement on iron absorption, however, depends on a number of factors including dietary levels of fiber, phosphates, and phytates. Additionally, it has been shown that in humans, vitamin C in the diet does not increase iron absorption in individuals with sufficient tissue stores of the mineral.[10] At this time there is not sufficient information to determine whether dietary levels of vitamin C contribute to the development of hemosiderosis in lemurs.

Diagnosis

The definitive diagnosis of iron storage disease can only be made by hepatic biopsy. Other diagnostic tests, including a complete blood count (CBC), serum biochemical profile, bile acid levels, and serum iron analyte panel (total serum iron, total iron binding capacity, ferritin, percent transferrin saturation) are supportive of liver disease, but not specific for iron storage disease. Although serum iron tests can be used to diagnose iron metabolism disorders in other species the value of these measurements in lemurs has not been determined. Reference ranges have been reported for wild ring-tailed lemurs, but are unavailable for most species. Unpublished preliminary data from Duke University indicates there may be significant interspecies and inter-individual variation.

Recommendations

Lemurs suspected of having iron storage disease should have a complete medical evaluation, including a thorough physical examination, CBC, serum biochemical profile, serum iron analyte panel, and liver biopsy. Formalin-fixed liver biopsy tissue should be stained with Prussian blue for iron detection as well as with hematoxylin-eosin for evaluation of tissue morphology. A frozen serum sample (1/2 ml on ice) should be sent to Kansas State University (contact Sue Chavey, Comparative Hematology, 785-532-4424) to have the iron analyte panel run using

reagents specific for lemurs (cost is $30 / sample). If additional liver tissue can be obtained by biopsy frozen liver tissue (ideally 1 g) should be submitted to KSU for non-heme iron determination (contact the lab for submission details and cost).

Lemur diets should be balanced and nutritionally complete in concordance with the current standards for primates published by the National Research Council.[9] The inclusion of nutritionally complete, manufactured diets is essential to meet suggested adequate nutrient levels. Iron levels should meet, but not greatly exceed, recommendations. Dietary manipulations to change vitamin C and tannin levels do not appear warranted at this time and manipulations of tannin levels (i.e. adding tea) are potentially dangerous.

Lemurs should not be given vitamin or mineral supplements containing iron. Supplements are not needed if animals are fed a well balanced diet in proper proportions and amounts.

Areas for Future Research

Little is presently known about iron metabolism in lemurs. Normal reference ranges for serum iron, TIBC, and serum ferritin do not currently exist and the utility of these tests as predictors of total body iron stores in lemurs remains to be determined. It is possible that the relationships between specific iron tests and total body iron stores in lemurs may need to be determined separately for each species. Specific areas in need of research are listed below.

1) Determine the incidence and severity of iron overload in the captive lemur population over time and at multiple institutions. Evaluate whether the levels currently present are associated with morbidity and/or mortality and to what extent.
2) Establish a reliable and safe ante-mortem test for evaluating total body iron status in lemurs. A first step is to establish normal baseline values for serum iron measurements (iron analyte panel) in each species and determine what correlation, if any, serum tests have to total body iron stores.
3) Continue research to determine the iron status of free-ranging wild lemur populations for comparison to captive populations. Preliminary serum iron analyte values have recently been reported for wild ring-tailed lemurs but information is completely lacking for all other species.[2]
4) Until the extent and severity of iron overload is defined and techniques are developed to accurately assess total body iron status in lemurs, research into modifying dietary iron levels is premature.
5) The development of manufactured diets that are lower in iron content appears warranted since products currently available are 2 - 3 times higher than the NRC's recommendations for nonhuman primates.[9]

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* Meeting Attendees:

Ingrid Porton – Mammal Curator, St. Louis Zoo. Prosimian TAG Chair
Randy Junge, DVM, Dipl.ACZM – Staff veterinarian, St. Louis Zoo, Veterinary Advisor, Prosimian TAG and Black Lemur SSP.
Jan Dempsey – Nutritionist, St. Louis Zoo. Prosimian TAG Nutrition Advisor.
Mary Duncan, BVSc, PhD, Dipl.ACVP - Pathologist, St. Louis Zoo.
Cathy Williams, DVM - Staff Veterinarian, Duke University Primate Center, Veterinary Advisor, Sifaka, Bamboo Lemurs, Aye-aye:Mongoose Lemur SSP

Martha Weber, DVM – Staff Veterinarian, Disney's Animal Kingdom, Veterinary Advisor, Ruffed Lemur SSP.
Dorrance Haught, PhD - Technical Director, Lab/Zoo, Purina Mills, St. Louis MO.

Sue Chavey, MT(ASCP) - Department of Diagnostic Medicine/Pathobiology, Kansas State University
Gordon Andrews, DVM, PhD, DACVP - Department of Diagnostic Medicine/ Pathobiology, Kansas State University
Monty Kerley, PhD - Professor, Animal Nutrition, Animal Sciences Department, University of Missouri-Columbia.
Reviewed by Ilse Stalis, DVM, Dipl.ACVP, San Diego Zoo, Pathology Advisor, Prosimian Taxon Advisory Group.