Unintentional Intoxications of Nonhuman Primates

Subjects: Veterinary Sciences
Contributor: Jaco Bakker

Wild and captive nonhuman primates (NHP) are exposed and potentially vulnerable to many natural and man-made toxic threats. Nevertheless, wild NHP are capable of coping with these threats using strategies, namely avoidance, dilution, gastrointestinal degradation, or detoxification, which require genetic potential, learning from parents and conspecifics in their social group, or prior experience through random food sampling and experimentation. Captive NHP are also at high risk for intoxications when they are often housed in an outdoor enclosure in a vivarium or zoo that is in or close to a large urban and industrial city. These NHP are potentially exposed to urban-industrial air pollution due to industrial and vehicle exhausts, waste incineration, and the domestic and industrial use of petroleum-based products, cleaners, pesticides, and paints, amongst others.

Keywords: nonhuman primates ; poisoning ; intoxication ; chemical hazards

1. Lead

Lead is a naturally occurring metal that is found in small amounts in rocks and soils and is an abundant environmental contaminant. Until leaded motor vehicle fuels were phased out in the mid- to late-1990s, air emissions of lead from the transportation sector (vehicle exhausts) were the major contributors of atmospheric lead. Since lead is also used industrially in the production of ceramic products, paints, metal alloys, and batteries, lead emissions into the atmosphere nowadays are associated with these industrial operations. These air emissions can either be inhaled (dust inhalation) or the lead can be ingested after settling from the air; such ingestion is considered as the main route of exposure to lead. The amounts of lead in the environmental air, food, and water supply of captive NHP are small, do not cause lead poisoning, and are comparable to those that most humans in urban populations are exposed [1]. Notwithstanding, lead-based paints are still widely used in many low- and middle-income developing countries across Asia, Africa, Latin America, and Europe, and the production and trade of lead-based paints is still widespread globally [2].

The health risk associated with lead exposure and ingestion is well documented. After its adsorption, lead distributes throughout the body in the blood, where it adversely affects its oxygen-carrying capacity, and accumulates in the bones because it approximates calcium and other bone-seeking elements. Depending on the level and duration of exposure, lead can adversely affect the renal function, and the nervous, hematological, gastrointestinal, cardiovascular, musculoskeletal, immune, reproductive, and developmental systems [3][4][5][6][7][8][9][10]. In NHP, the clinical signs of a hematological and a central nervous system disorder should invoke suspicion of lead poisoning. It should be noted that some captive NHP may be predisposed to ingesting cage paint because of their foraging habits. It should also be noted that social stress and teething in immature captive NHP are associated with the gnawing of cage bars.

Although a diagnosis of lead poisoning in NHP can be based on history and clinical and laboratory findings, most diagnoses are usually made postmortem. The results of postmortem examinations on NHP from the taxa *Lemuroidea*, *Simioidea*, and *Catarhiniat* revealed that the NHP died from lead poisoning following ingestion of a lead-containing cage paint [3][4][5][6]. Prior to their death, the NHP usually exhibited non-specific signs of ill health, such as partial anorexia and lethargy. Although vomiting and diarrhea were seen in several NHP, others exhibited no clinical signs. Other reported clinical signs of lead poisoning include weakness, pallor of the mucous membranes, and jaundice. The reported neurological signs of lead poisoning in NHP for which histories were available include convulsions, which are typical of acute amaurotic epilepsy, transient paralysis, paresis, apparent blindness (vision loss), tremors, and ataxia. Laboratory testing of NHP with suspected lead poisoning revealed elevated blood lead levels and anemia with immature and stippled erythrocytes [7][8][9] and basophils [10]. The main postmortem findings are lesions of lead encephalopathy, acid-fast intranuclear inclusion bodies in renal epithelia or hepatocytes, excess lead in the liver, metaphyseal bone changes (lead lines in the bones of immature monkeys), and necrosis of striated muscle fibers [3][4][5][6].

Treating lead poisoning in NHP comprises removal of the lead source(s) and oral chelation therapy with either calcium disodium edetate (EDTA), 2,3-dimercapto-1-propanol (BAL), D-penicillamine, or 2,3-dimercaptosuccinic acid at the

manufacturer’s recommended dose for humans. Of these agents, 2,3-dimercaptosuccinic acid is often selected as the therapeutic agent because its adverse effects are minimal [11][12].

2. Zinc

Zinc is an essential trace element, ubiquitous in nature, and is biologically necessary for the function of many metalloenzymes and metalloproteins. It is dietary sourced from meats, eggs, dairy products, nuts, seeds, legumes, and cereals. After ingestion, the low pH of the stomach causes the release of free zinc. About 25–50% of ingested zinc is absorbed in the small intestine and this absorption is homeostatically controlled. Following its absorption, it accumulates in the liver, kidneys, pancreas, and spleen. Most absorbed zinc is excreted in the feces via biliary secretions. In cells, zinc participates directly in catalysis (metalloenzymes) and contributes to maintaining protein structure and stability (metalloproteins).

Galvanization is the process of applying a protective zinc coat to iron or steel in order to prevent corrosion and rusting. Zinc toxicosis mainly occurs in captive NHP and is usually the result of licking the galvanized metal of their cages or enclosures or the ingestion of galvanized nuts and bolts from their metal cages or enclosures [13][14][15]. Most of the toxic effects of zinc occur when free zinc is released and zinc salts such as zinc chloride are formed in the stomach’s acidic environment. These salts irritate and cause corrosion of the gastric and intestinal (duodenal) mucosa. Accordingly, the first clinical signs of zinc toxicosis, often vomiting, anorexia, and weight loss, are exhibited a few days after zinc ingestion. Prolonged zinc exposure has a deleterious effect on almost every organ system and zinc toxicosis can clinically manifest as a hematologic abnormality (cytopenias and coagulopathies), a gastrointestinal disorder, a cardiovascular disorder, a musculoskeletal disorder, a hepatic dysfunction, pancreatitis, renal failure, a reproductive or developmental disorder, and a neurotoxicity [13][14][15][16][17][18][19]. These manifestations are probably related to the duration of the zinc-containing object’s presence in the stomach’s acidic environment: the longer the object sits in the stomach, the more zinc is absorbed systemically. A prolonged and untreated exposure to zinc results in death.

Newborns obtain zinc from their mother’s milk during lactation. Accordingly, one of the consequences of zinc toxicosis in a lactating NHP is zinc toxicosis in her nursing infants. Overconsumption of dietary zinc is often associated with copper deficiency and results in a zinc–copper imbalance. This imbalance has been observed in both captive and wild nursing offspring and contributes to a clinical syndrome that is known as “white monkey syndrome” (WMS). WMS is characterized by alopecia, cachexia, dermatitis, diarrhea, dehydration, emaciation, and whitening of hair (blond color of the fur), skin, and mucous membranes [13][14][15].

The diagnosis of zinc toxicosis is based on clinical presentation, laboratory testing (serum zinc concentration), and abdominal imaging to detect the presence of a metal-dense foreign object in the gastrointestinal tract [19]. If a metal object is not detected in the gastrointestinal tract, zinc toxicosis is often attributed to another etiology because the clinical signs are not specific [14][16][17][18].

Treatment of zinc toxicosis comprises relocation, removal of the zinc source, and supportive care, which can include a proton pump inhibitor (omeprazole), a gastroprotectant (sucralfate), blood products, and fluids.

References

1. Schillaci, M.A.; Lee, B.P.; Castellini, J.M.; Reid, M.J.; O’Hara, T.M. Lead levels in long-tailed macaque (Macaca fascicularis) hair from Singapore. Primates 2011, 52, 163–170.
2. O’Connor, D.; Hou, D.; Ye, J.; Zhang, Y.; Ok, Y.S.; Song, Y.; Coulon, F.; Peng, T.; Tian, L. Lead-based paint remains a major public health concern: A critical review of global production, trade, use, exposure, health risk, and implications. Environ. Int. 2018, 121, 85–101.
3. Zook, B.C.; Eisenberg, J.F.; McLanahan, E. Some Factors Affecting the Occurence of Lead Poisoning in Captive Primates. J. Med. Primatol. 1973, 2, 206–217.
4. Zook, B.C.; Sauer, R.M.; Bush, M.; Gray, C.W. Lead poisoning in zoo-dwelling primates. Am. J. Phys. Anthropol. 1973, 38, 415–423.
5. Zook, B.C.; Sauer, R.M.; Garner, F.M. Lead poisoning in captive wild animals. J. Wildl. Dis. 1972, 8, 264–272.
6. Zook, B.C.; Sauer, R.M.; Garner, F.M. Acute amaurotic epilepsy caused by lead poisoning in nonhuman primates. J. Am. Vet. Med. Assoc. 1972, 161, 683–686.

7. Lumeij, J.T.; Dorrestein, G.M. Icterus and amaurosis caused by lead poisoning in a cynomolgus monkey (Macaca fascicularis). Vet. Rec. 1986, 118, 70–72.
8. Mautino, M. Lead and zinc intoxication in zoological medicine: A review. J. Zoo Wildl. Med. 1997, 28, 28–35.
9. Young, L.A.; Lung, N.P.; Isaza, R.; Heard, D.J. Anemia Associated with Lead Intoxication and Uterine Leiomyoma in a Chimpanzee (Pan troglodytes). J. Zoo Wildl. Med. 1996, 27, 96–100.
10. Hopkins, A. Experimental lead poisoning in the baboon. Br. J. Ind. Med. 1970, 27, 130–140.
11. Chisolm, J.J., Jr. Treatment of acute lead intoxication--choice of chelating agents and supportive therapeutic measures. Clin. Toxicol. 1970, 3, 527–540.
12. Graziano, J.H.; Siris, E.S.; LoIacono, N.; Silverberg, S.J.; Turgeon, L. 2,3-Dimercaptosuccinic acid as an antidote for lead intoxication. Clin. Pharmacol. Ther. 1985, 37, 431–438.
13. Frost, P.A.; Hubbard, G.B.; Dammann, M.J.; Snider, C.L.; Moore, C.M.; Hodara, V.L.; Giavedoni, L.D.; Rohwer, R.; Mahaney, M.C.; Butler, T.M.; et al. White monkey syndrome in infant baboons (Papio species). J. Med. Primatol. 2004, 33, 197–213.
14. Markham, A.C.; Gesquiere, L.R.; Bellenger, J.P.; Alberts, S.C.; Altmann, J. White monkey syndrome and presumptive copper deficiency in wild savannah baboons. Am. J. Primatol. 2011, 73, 1160–1168.
15. Obeck, D.K. Galvanized caging as a potential factor in the development of the “fading infant” or “white monkey” syndrome. Lab. Anim. Sci. 1978, 28, 698–704.
16. Altmann, J.; Altmann, S.; Hausfater, G. Physical maturation and age estimates of yellow baboons, Papio cynocephalus, in Amboseli National Park, Kenya. Am. J. Primatol. 1981, 1, 389–399.
17. Altmann, J.; Schoeller, D.; Altmann, S.A.; Muruthi, P.; Sapolsky, R.M. Body size and fatness of free-living baboons reflect food availability and activity levels. Am. J. Primatol. 1993, 30, 149–161.
18. Dick, E.J., Jr.; Owston, M.A.; David, J.M.; Sharp, R.M.; Rouse, S.; Hubbard, G.B. Mortality in captive baboons (Papio spp.): A-23-year study. J. Med. Primatol. 2014, 43, 169–196.
19. Murray, S.; Tell, L.A.; Bush, M. Zinc toxicosis in a Celebes ape (Macaca nigra) following ingestion of pennies. J. Zoo Wildl. Med. 1997, 28, 101–104.
